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# Cracking the code of crying babies: how adults learn to understand the baby's pain

Siloé Corvin

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**Cracking the code of crying babies:  
how adults learn to understand the  
baby's pain**

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*« ...quod eo in loco diuinitus uox edita erat,  
ita Vaticanus deus nominatus penes quem essent uocis humanae initia,  
quoniam pueri, simul atque parti sunt,  
eam primam uocem edunt quae prima in Vaticano syllabast idcircoque ‘uagire’ dicitur,  
exprimente uerbo sonum uocis recentis »*

« ... parce qu'en ce lieu s'était faite entendre une voix d'origine divine,  
de même le dieu qui préside aux balbutiements de la voix humaine est appelé *Vatican*,  
puisque les enfants, dès leur naissance,  
laissent entendre ce premier cri que l'on retrouve dans la première syllabe de *Vatican*,  
et c'est pourquoi "vagir" désigne, comme onomatopée, le son de la voix d'un nouveau-né »

Aulu-Gelle, IIe siècle

# Abstract

Babies crying is an essential signal to elicit care, conveying both information on the baby's identity and current physiological state (discomfort, hunger or pain). The aim of my thesis is to investigate how adults perceive information contained in babies cries, especially cries produced in a painful condition, and how being familiar with one given baby, or with babies in general, shape this perception.

First, I investigated how pain in cries interacts with information related to the baby's identity. My results show that the individual vocal signatures carried by discomfort cries converge in pain cries towards a common expression of pain by babies, at the cost of a loss of individuality. Knowing this shared expression of pain in cries, I then explore with psychoacoustic experiments how adults identify this information. Pain identification ability is gain through experience in babies care, either parental or professional, and does not seem to decline with listener's age. Acoustic chaos and vibrato characterize pain in cries and drive pain perception. Finally, I investigated in an fMRI study the neural correlates of both aspects (identity and pain recognition) in expert participants, professional caregivers and parents. Baby identification engages brain areas involved in voice recognition, while contexts identification is more difficult and involve high-level non-specific cognitive processing.

To sum up, this work shows that babies cries are a complex communicative signal, rich in information. Decoding this information is learned with experience and time spent caring for a baby, enabling everyone to find a legitimate place in baby care.

Key-words: baby cry, pain, psychoacoustic, fMRI, parenting

# Résumé

Les pleurs de bébé sont un signal essentiel pour susciter des soins, transmettant des informations sur l'identité du bébé et son état physiologique (inconfort, faim ou douleur). L'objectif de ma thèse est d'étudier comment les adultes perçoivent les informations portées par les pleurs, en particulier émis dans un contexte de douleur, et comment être familier avec un bébé donné ou avec les bébés en général module cette perception.

J'ai d'abord étudié comment la douleur interagit avec les informations liées à l'identité du bébé. Mes résultats montrent une perte de la signature vocale individuelle présente dans les pleurs d'inconfort, convergeant vers une expression commune de la douleur. J'ai ensuite conduit des expériences psychoacoustiques pour déterminer comment les adultes identifient la douleur dans les pleurs. Cette capacité d'identification vient avec l'expérience dans le soin aux nourrissons, qu'elle soit parentale ou professionnelle, et semble conservée quel que soit l'âge de l'auditeur. Le vibrato et chaos acoustiques caractérisent la douleur dans les pleurs et déterminent la perception de la douleur. Enfin, j'ai étudié les corrélats neuronaux des deux aspects (reconnaissance de l'identité et de la douleur) dans une étude en IRM fonctionnelle, chez des experts parents ou professionnels. Identifier un bébé donné engage des aires cérébrales impliquées dans la reconnaissance des voix, alors qu'identifier le contexte est plus difficile et mobilise des aires cognitives de haut-niveau.

Pour résumer, ces travaux montrent que les pleurs de bébé sont un signal complexe, riche en informations. Décoder ces informations s'apprend avec l'expérience et le temps passé à s'occuper d'un bébé.

Mots-clés : pleur de bébé, douleur, psychoacoustique, IRMf, parentalité

# Résumé substantiel

Les pleurs de bébé sont un signal essentiel pour susciter des soins, transmettant des informations à la fois sur l'identité du bébé et sur son état physiologique (inconfort, faim ou douleur). Des travaux précédents ont montré que l'identité vocale d'un bébé est portée par les propriétés de la fréquence fondamentale, permettant d'identifier les pleurs d'un bébé donné. Cette capacité a été mise en évidence pour des pleurs d'inconfort modéré, chez des parents et des non-parents, influencée par l'expérience dans le soin aux nourrissons. D'un autre côté, les pleurs de douleur, par exemple enregistrés lors des vaccinations de routine, sont caractérisés par une rugosité acoustique, c'est-à-dire moins harmoniques et contenant des phénomènes non linéaires. Les parents sont capables d'évaluer la douleur pour leur propre enfant. L'objectif de ma thèse est d'étudier comment les adultes perçoivent les informations sur l'identité et le contexte portées par les pleurs, particulièrement pour les pleurs de douleur, et comment ces informations interagissent entre elles. J'ai également investigué comment être familier avec un bébé donné, ou avec les bébés en général, module cette perception.

Tout d'abord, nous avons combiné des analyses acoustiques, du machine learning et une expérience en psychoacoustique pour étudier comment la douleur interagit avec les informations liées à l'identité du bébé. Les pleurs de douleur sont caractérisés par une fréquence fondamentale plus variable et plus de modulations de fréquence, ce qui conduit à une réduction des informations liées à l'identité du bébé. Néanmoins, les pleurs contiennent des informations sur l'identité, mais elles sont atténuées par rapport aux pleurs d'inconfort, ce qui fait qu'il est plus difficile d'identifier un bébé donné, aussi bien par des algorithmes de classification que par des humains parents ou non-parents. Cette perte des informations individuelles montre une convergence des pleurs de différents bébés vers une expression commune de la douleur.

J'ai ensuite conduit des expériences psychoacoustiques pour déterminer comment les adultes identifient la douleur dans les pleurs, et les facteurs qui modulent cette capacité. Dans un premier temps, j'ai montré que cette capacité d'identification est progressivement acquise grâce à l'expérience des soins aux bébés, qu'elle soit parentale ou professionnelle. Les adultes totalement inexpérimentés dans le soin aux nourrissons sont incapables d'identifier la douleur dans les pleurs. Malgré l'aspect commun de l'expression de la douleur, le fait d'être familier avec un bébé facilite l'identification de la douleur pour ce bébé donné pour les adultes ayant une expérience modérée. Les adultes plus expérimentés, c'est-à-dire les parents d'enfants de moins de deux ans, sont capables de reconnaître la douleur dans les pleurs, même pour un bébé

qui ne leur est pas du tout familier. L'expérience dans le soin aux nourrissons est donc un facteur essentiel pour réussir à identifier la douleur dans les pleurs, et cette capacité n'est pas restreinte aux seuls parents de l'enfant. En effet, d'autres adultes peuvent être impliqués dans le soin aux nourrissons, en particulier les grands-parents. Alors qu'on sait que la capacité générale à identifier les émotions diminue en vieillissant, j'ai étudié dans une deuxième étude si la capacité à reconnaître les pleurs diminue également avec l'âge, en testant des adultes âgés de 20 à 87 ans. Quel que soit l'âge, l'expérience antérieure avec les bébés et la familiarité avec un bébé donné permettent aux adultes de mieux distinguer la douleur de l'inconfort dans les pleurs d'un bébé. Cette capacité reste conservée même chez les participants très âgés, suggérant que l'accumulation de l'exposition et de l'expérience avec les bébés au cours d'une vie pourrait contrecarrer l'effet du vieillissement. Dans une troisième étude, je me suis intéressée aux propriétés acoustiques qui sous-tendent cette perception de la douleur, en particulier les phénomènes non-linéaires. Les pleurs de douleur contiennent plus de phénomènes non linéaires, les pleurs produits dans un contexte de douleur aigue au moment de l'injection étant caractérisés par des épisodes plus longs de chaos et de sous-harmoniques, alors que ceux correspondant à une douleur résiduelle, dans un deuxième temps après l'injection du vaccin, sont caractérisés par plus de vibrato. Les adultes s'appuient sur ces propriétés acoustiques pour évaluer la douleur, les pleurs contenant plus de chaos et de vibrato étant évalués comme exprimant plus de douleur.

Enfin, j'ai étudié les corrélats neuronaux de la perception des pleurs chez des adultes parents et non-parents. Dans une étude préliminaire en imagerie par résonance magnétique fonctionnelle (IRMf), il a été montré qu'être parent entraîne une spécialisation du connectome cérébral engagé par l'écoute des pleurs. Les parents montrent une connectivité plus importante que les non-parents, avec un passage d'une réaction aversive et émotionnelle chez les non-parents à un traitement plus cognitif chez les parents. J'ai ensuite mené une deuxième étude en IRMf pour investiguer les corrélats neuronaux de la reconnaissance des informations portées par les pleurs, en me focalisant sur des experts du soin aux nourrissons, parents et professionnelles travaillant en pédiatrie. Les participants ont réussi à reconnaître les pleurs d'un bébé donné en mobilisant des zones cérébrales impliquées dans la reconnaissance des voix (sulci pariétaux inférieurs bilatéraux, précuneus et gyrus frontal moyen gauche, associé à des diminutions d'activité dans les aires auditives), même si la douleur a perturbé cette capacité. L'identification des contextes à l'origine du pleur (douleur ou inconfort) est plus difficile et implique un traitement cognitif de haut niveau, mais non-spécifique de la douleur (gyrus frontal inférieur et structures sous-

corticales). Aucune différence dans la perception des informations ni dans les activations cérébrales induites par ces tâches d'identification n'a été observée, que ce soit entre pères et mères, ou selon le type d'expérience, entre mères et professionnelles travaillant en pédiatrie. Il est donc probable que les pleurs soient intégrés comme un signal de communication vocale complexe par ces experts dans le soin aux nourrissons, plutôt que comme une basique alerte aversive.

Pour résumer, ces différentes études montrent que les pleurs de bébé sont un signal vocal complexe, riche en informations. Décoder ces informations s'apprend avec l'expérience et le temps passé à s'occuper d'un bébé, permettant à chacun de trouver une place dans le soin apporté aux nourrissons.

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# Abbreviation list

ACC	Anterior Cingulate Cortex
f <sub>0</sub>	Fundamental frequency
fMRI	functional Magnetic Resonance Imaging
HG	Heschl's gyrus
IFG	Inferior Frontal Gyrus
IPL	Inferior Parietal Lobule
MCC	Medial Cingulate Cortex
MPOA	Medial Pre-Optic Area
MPS	Modulation Power Spectrum
MTG	Middle Temporal Gyrus
NAcc	Nucleus Accumbens
NLP	Nonlinear phenomena
mOFC	medial Orbito-Frontal Cortex
PAG	PeriAqueducal Grey matter
mPFC/dmPFC/vmPFC	medial/dorso-medial/ventro-medial Pre-Frontal Cortex
PCC	Posterior Cingulate Cortex
SMA	Supplementary Motor Area
SFG	Superior Frontal Gyrus
STG	Superior Temporal Gyrus
STS	Superior Temporal Sulcus
TPJ	Temporo-Parietal Junction

# Preface

Babies crying is an essential signal to elicit parental care. It is generally triggered by pain, discomfort, hunger or separation from parents or other caregivers (Lingle et al., 2012; Soltis, 2004). These cries contain both static information on the baby's identity (Gustafson et al., 1984; Gustafsson et al., 2013), stable over time, and dynamic one linked to contexts and/or baby's current physiological state (Koutseff et al., 2017; Porter et al., 1986). Among dynamic information, pain is particularly relevant to detect, in order to provide adapted care. These two kinds of information are encoded by specific acoustic parameters, and decoded with varying difficulty by adult caregivers.

Previous work has shown that individual vocal signature, specific to each baby, is linked to fundamental frequency parameters responsible of perceived pitch. This allows a reliable identification of one given baby based on cries emitted in situation of low-distress (hunger or mild-discomfort during bathing). This baby recognition is strong and reliable, acquired in the first days of the baby's life. Fathers perform as well as mothers when they spend time caring for their babies (Gustafsson et al., 2013), and even nonparents can quickly learn to recognize a given baby by listening to his/her cries (Bouchet et al., 2020). However, whether pain disturbs this vocal signature and the recognition of a familiar baby remains unknown. Pain is linked to dynamic information in cries such as the acoustic roughness, pain cries being less harmonic and containing some nonlinear phenomena (Koutseff et al., 2017). Parents are able to assess pain for their own baby, but there is no evidence whether being a parent is necessary, or whether pain can only be assessed for one's own child. Additionally, while brain regions involved in cry processing are well described (Feldman, 2015; Witteman et al., 2019), there is very few evidence on how static (baby identity) and dynamic (pain) information in cries can modulate their activities.

After a general introduction that will present the state of the literature in more detail, I will focus in the first chapter of my thesis on the encoding and decoding of information on baby's identity in pain cries. In the second chapter, I will explore the perception of pain in cries, along with the factors that modulate this perception: parenthood, familiarity with a given baby, age of listeners and acoustic properties underlying this identification. Finally, using functional magnetic resonance imaging, I will investigate the neural correlates of baby's identity and pain identification.

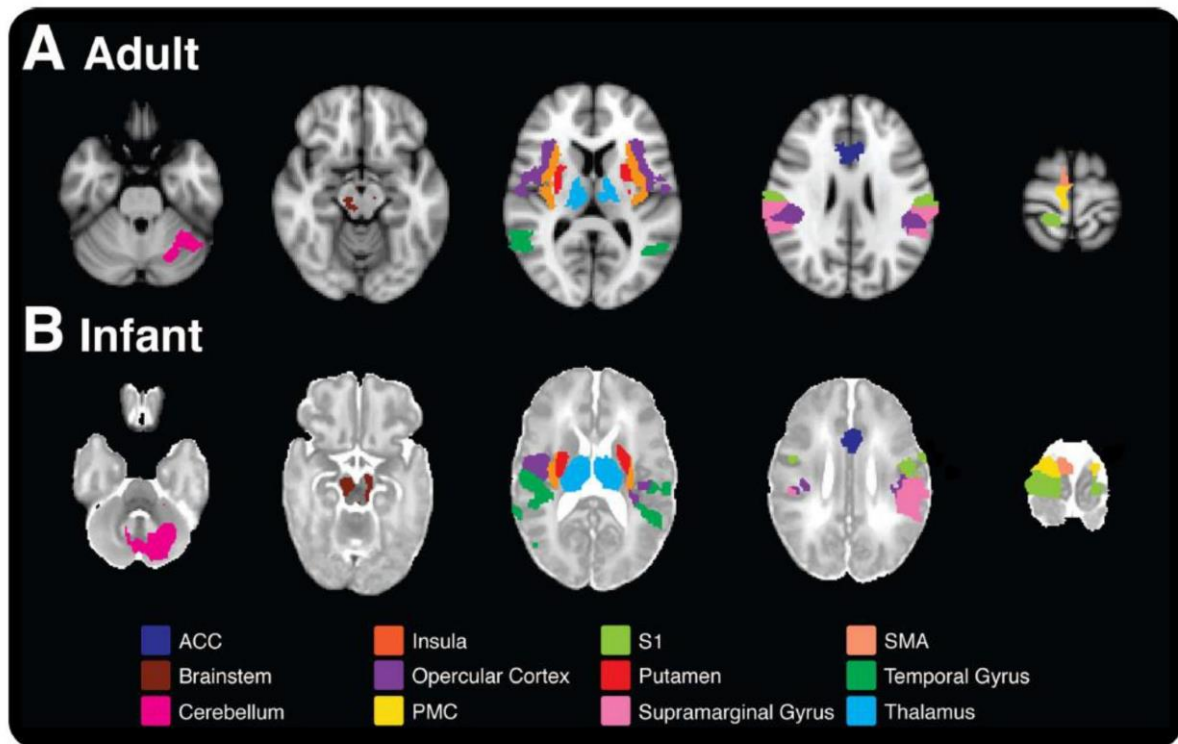


# General Introduction

Pain, even if generally preferred to be avoided, is an essential protective mechanism involved in individual survival. According to the last definition of the *International Association for the Study of Pain*, it is “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.” It is accompanied by sub-definitions, in particular the following: “verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a nonhuman animal experiences pain.” As stated, this concerns non-verbal humans such as babies, some disabled or elderly people, as well as animals. It is still an ongoing research topic, for example with a review highlighting neural and behavioral evidences of pain in insects only a year ago (Gibbons et al., 2022).

For human babies, despite pain as been reported almost a century ago in babies’ first week of life (Sherman, 1928), it has long been neglected. Indeed, babies pain has been denied until the 1980s, with surgeries routinely conducted without anesthesia, from heart surgery to circumcision (Porter et al., 1986, 1988). One can found scientific papers in the 1970s discussing the role of learning and memory in pain perception, assumed absent in babies, or the limited presence of babies’ reactions during invasive procedure, leading to a lack of evidence for babies pain in their point of view (Merskey, 1975; Poznanski, 1976). More broadly, babies were supposed to have an immature nervous system, not allowing them to perceive pain (Rodkey & Pillai Riddell, 2013). It started to change in the 1980s with parent activism and the development of pediatric pain research.

Now, there are evidences that pain perception emerges in fetal life, at about 20-22 weeks of gestation (Bellieni, 2019). In neonates, pain perception shares neural correlates similar to those observed in adults (Duff et al., 2020; Goksan et al., 2015, see Figure 1). However, clinical practices are slowly evolving, with one to 14 daily procedures for infants in neonatal intensive care unit with no systematic pain-relieving interventions (Campbell-Yeo et al., 2022), even if it is known that pain in early life has significant long lasting adverse effects on behavior, cognition, pain processing and health outcomes in childhood and even adulthood (Williams & Lascelles, 2020).



*Figure 1. Comparison of nociceptive-evoked brain activity in selected brain regions that are active in both adults (A) and infants (B). From Goksan et al., 2015.*

Current pain assessment tools in pediatric care are based on multiple physiological and/or behavioral items, such as heart rate, facial expressions, body movements, changes in sleep-wake state or attention, and crying (Eriksson & Campbell-Yeo, 2019). In these scales, cries are only evaluated by their presence and duration even though they are known to contain much more information (Barr, 2000), and that pain induced vocalizations have been proposed as a potential tool for pain measurement in young children (Levine & Gordon, 1982).

**In this introduction, I provide an overview of the emission/reception chain of crying, with a special focus on pain: how babies produce crying and information that provides, and how babies caregivers perceive it to provide an adapted response.**

## **I. Babies produce cries, a support of information**

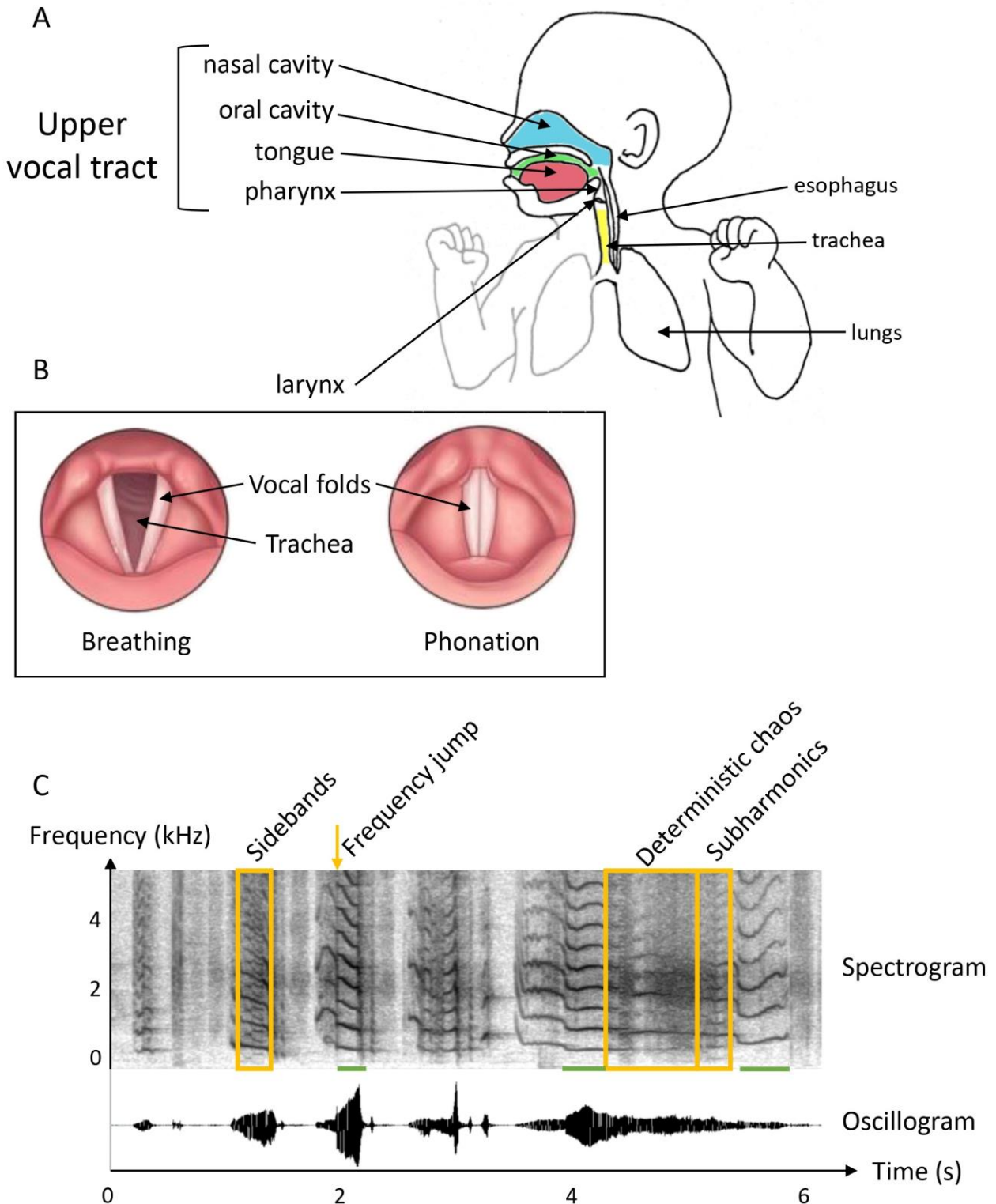
### **1. Cries production and acoustics**

Crying is the result of complex interactions between the central and peripheral nervous system, the respiratory system and a variety of muscles (Golub & Corwin, 1985). As most vocal signals, cries can be described in the source-filter theory framework (Taylor & Reby, 2010). During the

expiratory phase of breathing, the air is expelled from the lungs and travels up the trachea. It then passes into the larynx, which is made up of the vocal folds and the glottis. When the vocal folds are closed, the passage of air in this narrow tube leads to a drop in air pressure, causing the rapid opening and closing of the vocal folds. The vibrating vocal folds are the source of the sound. Both the air pressure coming from the lungs and the tension and length of the vocal folds can modulate the vibration frequency, defined as the fundamental frequency ( $f_0$ ) of the sound, which is responsible of its perceived pitch. Then, the sound travels in the upper vocal tract (pharynx, oral and nasal cavities, lips) and is filtered to produce resonance frequencies or formants (LaGasse et al., 2005; Soltis, 2004). The vocal folds may also vibrate asynchronously, with coupled or not frequencies. This leads to acoustic perturbations such as biphonation, subharmonics or deterministic chaos referred as nonlinear phenomena (NLP), which are responsible of perceptual roughness. Subharmonics are additional harmonics visible in the spectrum beneath  $f_0$  and/or between harmonics, result of the coupling between oscillators (for example collision of the two vocal folds). Two oscillators vibrating independently, non-harmonically in any ratio of frequencies, is called biphonation. Deterministic chaos is aperiodic vibration, characterized by the presence of broadband “noise” in the spectrum, at many different frequencies (Fitch et al., 2002; Mende et al., 1990; Titze, 2008; Wilden et al., 1998) (see Figure 2 for representation of baby’s vocal apparatus and acoustic characterization of a cry).

Cry production is ensured by the nervous system, particularly dependent on the 10<sup>th</sup> cranial nerve or vagal nerve. This nerve is involved in the autonomic control of heart, lungs and digestive tract, as well as well as sensory perception and motor control for the pharynx and larynx. An increase in the vagal outflow leads to an inhibition of the laryngeal muscles, and thus a decrease of the fundamental frequency. On the contrary, a decrease of the vagal tone is associated to laryngeal constriction and increased tension in the vocal folds, making irregular or asynchronous vibration of the vocal folds more likely to occur. In addition, the brainstem controls the shape of the upper vocal tract and thus can modulate the formant frequencies, and central brain structure like the hypothalamus or the amygdala are involved in cry initiation (LaGasse et al., 2005; Soltis, 2004).

Every change in these mechanisms can lead to abnormal cry production, thus cries can first be considered as a biomarker of good health, or in contrast of a medical problem (Corwin et al., 1996).



**Figure 2. Baby's vocal apparatus and cry acoustic characterization.** (A) Representation of the vocal apparatus and the esophagus. Above the larynx is the upper vocal tract. (B) Larynx with vocal folds in breathing (open) and phonation (closed) position. (C) Graphical representation of a cry. Lower part is an oscillogram representing sound amplitude over time. Upper part is a spectrogram representing sound frequency over time. This cry contains tonal parts, underlined in green, and nonlinear phenomena, framed in yellow and described above each one.



## 2. Cries as a biomarker

Birth cry is the first cry used as a biomarker. When a baby is born, one of the first actions is to cry. This marks the proper transition from fetal to extra-uterine life and is considered as a sign of good health (van Manen, 2016). Indeed, absence of crying at birth has been linked to a higher risk of pre-discharge mortality (Kc et al., 2020).

More generally, abnormal cries have long been described for a wide range of pathologies affecting the cry-production system: from peripheral causes like asymmetric vocal folds or abnormal vocal tract shape (unilateral cleft lip and palate; Etz et al., 2012), to brain damages linked to severe birth asphyxia, meningitis, hydrocephalus, encephalitis or Down syndrome (Corwin et al., 1996; Soltis, 2004). Cries have also been described as an early biomarker with a potential in detection and diagnosis, as in autism (Esposito et al., 2017) or for sudden infant death syndrome (Corwin et al., 1996; Robb et al., 2013). Abnormal cries may also have a prognostic value of developmental outcome, for example for preterm infants (Corwin et al., 1996; Shinya et al., 2014). This biomarker function continues to be developed in recent years with the rise of machine learning as a potential tool for detecting pathologies (Farsaie Alaie et al., 2016; Ji et al., 2021; Zayed et al., 2023).

Regarding pain, the presence of crying has been shown to be positively associated with acute pain (Helmer et al., 2020), but it does not seem to be a specific marker, air puff or cold stimulation eliciting crying as well (Maitre et al., 2017).

In addition to these biological aspects, cries are communication signals, designed to attract caregivers' attention. Crying provide various cues (Soltis, 2004), both static information linked to physical traits like identity, sex and body size, and dynamic information related to emotional and physiological variations (Aubin & Mathevon, 2020).

## 3. Cries as communication signals

### *1. A support of static information related to identity*

Apart from any medical condition, interindividual differences can be observed regarding the anatomical and morphological features of the vocal apparatus: length and stiffness of the vocal folds, length and shape of the vocal tract. This leads to differences in fundamental frequency parameters and formants, as it has been described in many terrestrial mammal species (Charlton et al., 2020).

In human babies, individual signatures have long been reported, for babies aged from a few days to several months. These interindividual differences are linked to fundamental frequency parameters (mean, maximum and its modulation), allowing classifiers to distinguish effectively various individuals (Gustafson et al., 1984; Gustafsson et al., 2013; Lenti Boero et al., 1998; Ringel & Kluppel, 1964). With age, cries become less noisy and more tonal (Fuamenya et al., 2015; Lockhart-Bouron et al., 2023, see Annex I) but  $f_0$  parameters remain stable. This was first shown in a 3 months longitudinal follow-up of one given baby (Lind & Wermke, 2002) and recently confirmed by a longitudinal study on 24 babies, with correct classification of babies identity based on cries sets recorded at mixed ages (Lockhart-Bouron et al., 2023). This high reliability of  $f_0$  parameters extends beyond the first few months of life, with babies cries pitch being predictive of infant voice pitch at 5 years old (Levrero et al., 2018), and infant voice pitch linked to the adult's one (Fouquet et al., 2016).

In human babies, as in adults, there is no clear relationship between body size and frequency parameters. According to the allometric principle, bigger individuals are assumed to produce lower  $f_0$  vocalizations (Taylor et al., 2016). Lighter infants have higher frequency parameters compared to heavier ones (Lenti Boero et al., 1998), but this result is not replicated,  $f_0$  features decreasing only marginally with body size increase (Wermke & Robb, 2010)

Moreover, individual acoustic features are not linked to the baby's sex, with no acoustic differences between baby girls and baby boys cries (Reby et al., 2016). In adults, voices show a strong sexual dimorphism with men having lower voices than women, related to testosterone level (Cartei et al., 2014). This dimorphism is easily captured by adult listeners and despite no such pattern in human babies cries, it leads to strong sex stereotypes with high-pitched cries being more likely to be attributed to baby girls than baby boys (Reby et al., 2016).

This strong information on baby's identity in cries, reliable across time, makes it thus critical to control when looking at other features encoded in cries (Gustafson et al., 2017). Perception of these individual signatures will be addressed in III.1 of this introduction.

### *2. A support of dynamic information related to need or distress*

In addition to acoustic individual profiles, changes in the emotional or physiological state lead to modulations at each level of cry production (brain, larynx, vocal tract or lungs), thus influencing vocalizations (Briefer, 2020). Two conceptual frameworks are used to describe these dynamic modulations: cries as distinct types or as a graded signal.

Because of the different circumstances that can trigger crying, it was initially described as distinct cry types related to discrete causes such as hunger cry, discomfort cry, pain cry, sleepy cry, pleasure cry or attention cry (Müller et al., 1974; Wasz-Höckert et al., 1964a; Zeifman, 2001). This concept of distinct cry types is very popular in the general public, with the belief that babies have their own language. The most popular is the « Dunstan Baby Language », based on the personal experience of its creator, which argues that babies have a secret and universal language based on “words”, and proposes a method for learning this language. As they claim on their website, they have reached “a global audience of over 100 million viewers in more than 20 countries” (*Learn the Dunstan Baby Language*, 2022). Numerous studies describe cry types, based on their acoustic properties (Scheiner et al., 2002) and more recently using classification methods (Ji et al., 2021). With machine learning algorithms, excellent classification rates have been demonstrated, from 81% (Sharma et al., 2019) to 98% (Rezaee et al., 2023) for classifications across 5 cry types. Despite rigorous and elaborate methods in these studies, there are limitations regarding the cry databases used. The two most common are the *Donate a Cry* (Rezaee et al., 2023; Sharma et al., 2019) and the *Dunstan Baby* database (Franti et al., 2018; Nadia Maghfira et al., 2020; Osmani et al., 2017), which are composed of cries for 0-2 years old and 0-6 months old babies respectively, from 5 distinct causes (hungry, sleepy, burping, belly pain and discomfort). Most studies tend to classify cries regardless of the baby’s age, therefore exposed to a substantial bias. Moreover, the identity of the baby from whom each cry comes is not provided, so it cannot be ruled out that some individuals are recorded only at a certain age or in a certain context, resulting in an unbalanced dataset. Thus, the good results obtained using these databases may be linked to significant biases related to the age or individual characteristics of the recorded babies (Gustafson et al., 2017; Ji et al., 2021). To address these biases, a longitudinal study has been conducted in the ENES lab, recording 24 babies at 15 days, 1.5 months, 2.5 months, and 3.5 months after birth. Based on the parental behavior that stopped the cry, three main contexts were labelled (discomfort, hunger, isolation). When controlling for the baby’s age and identity, Random Forest model was unable to classify cry context over chance, indicating no robust differences among cries associated with each cause (Lockhart-Bouron et al., 2023, see Annex I).

An alternative way of describing cries is to consider it as a graded signal (Soltis, 2004), reflecting the baby’s level of need or distress. This supposes that higher distress levels are linked to more severe cry acoustics, and has been particularly described in the case of painful situations. Cries recorded in such conditions, like routine blood withdrawal, are less phonated,

partially voiced or voiceless (Lenti Boero et al., 1998), which today would be described as nonlinear phenomena. They are linked to the physiological modulations a baby experiences in pain, with arousal of the autonomic nervous system and a diminution of the vagal tone (Porter et al., 1988). It leads to increase in subglottal pressure, laryngeal constriction and increased tension in the vocal folds and thus to irregular or asynchronous vibration of the vocal folds, resulting in nonlinear phenomena (Fitch et al., 2002; Tokuda, 2018). Similar acoustic features are present in infant distress vocalizations of other terrestrial mammals (Lingle et al., 2012) and may be a way to generate unpredictability to prevent habituation from listeners (Taylor et al., 2016). When experiencing higher level of pain, babies produce cries with higher occurrence of nonlinear phenomena. For example, cries during most invasive procedures of circumcision show fewer harmonics and greater variability in the fundamental, in addition to be longer and more frequent (Porter et al., 1986). The same pattern is found in relation to the baby's experience during blood sampling, a more common and still relevant procedure, when pain is assessed using the *Douleur Aiguë du Nourrisson* scale. Cries for low pain levels are harmonic, while biphonation and chaos appear at intermediate levels. High pain levels show large zones of chaos without a clear fundamental frequency (Facchini et al., 2005). Similar results are also found for cries elicited by two different vaccines. The more painful injection sequence, determined with behavioral scales (Ipp et al., 2009) is associated with more acoustic roughness, i.e. less voiced, with less harmonic, more variable  $f_0$  and more occurrence of chaos (Koutseff et al., 2017). Nonetheless, as there is no extensive description of the nonlinear phenomena present in cries, this will be addressed in Chapter II. The gradual aspect of acoustic properties is also observed in nonverbal vocalization of simulated pain in human adults (Raine et al., 2019). In opposition to this gradual increase of nonlinear phenomena, fundamental frequency value does not seem to be correlated with pain levels (Koutseff et al., 2017) but may represent an alarm threshold when a high level is reached (Bellieni et al., 2004).

To sum up, there are accumulating evidences in favor of the “graded cry” hypothesis, but this does not necessarily require the rejection of anything that resembles the identification of a context, particularly if it has clinical relevance such as assessing the presence or absence of pain.

### *3. Interaction between static and dynamic information*

After describing these two types of information conveyed by crying, one can wonder how they interact, whether they coexist, influence or disturb each other.

First, regarding the reliability of individual signatures in different contexts, they have been observed in low distress contexts, like pulling the baby's hair (Ringel & Kluppel, 1964), hunger (Gustafson et al., 1984) or discomfort during bathing (Gustafsson et al., 2013). To my knowledge, only one study investigated the stability of f0 across different contexts (hunger, pain and manipulation) and found mixed evidences depending of the individual (Lenti Boero et al., 1998). In human adults, inter-individual differences are shared between speech and nonverbal vocalizations (Pisanski et al., 2020). In some other species, these individual signatures are found shared across call types, for example in red deers (Reby et al., 2006) or cattle (A. Green et al., 2019). However in bonobos, even if shared across call types, individual vocal signatures show a fluctuating reliability, with calls used in high-arousal contexts supporting the strongest signature (Keenan et al., 2020). More surprisingly, multiple vocal signatures specific to each call type have been found in zebra finches, a highly vocal social songbird (Elie & Theunissen, 2018). In babies cries, the interaction between pain and individual signatures will be addressed in the Chapter I of this thesis.

Secondly, regarding the encoding of dynamic information, it may be baby specific, with each baby developing a personal strategy to code the cause of crying, of shared between individuals. In low-distress contexts, this hypotheses of baby specific encoding has been tested, with no evidence regarding the acoustic signal (Lockhart-Bouron et al., 2023). For the expression of pain, converging evidences come from numerous studies on different individuals, in favor to a shared expression of pain, and this will be further investigated in Chapters I and II.

**In the first part of this introduction, I emphasized the role of cries as a signal conveying various information, linked to their production mechanisms. According to the very definition of a signal, it implies to be received and interpreted by someone. In this second part, I present the main receivers of baby signals, human adults, and how interacting with babies and cries transforms them.**

## **II. Babies caregivers: mothers, fathers and others**

Becoming a parent brings neural and physiological changes that most often provide the motivation to care for the baby. These changes have been first and most described in mothers, as they are the main caregiver in almost all mammal species, and in a large part of families in our modern society.

### **1. Mothers: primary caregivers in the animal reign and in our society**

#### *1. Early hormonal changes*

A cascade of hormonal secretions takes place from the start of pregnancy, in particular involving prolactin and oxytocin, enabling maternal behavior to be established and maintained (Rogers & Bales, 2019; Russell et al., 2001). Oxytocin, which is involved in attachment processes in general, whether romantic, in friendships or between parents and offspring, has been extensively studied (Feldman, 2017). This hormone is released during childbirth and breastfeeding, and in the longer term, repeated interactions with the child increase its production (Rilling, 2013). Due to the numerous receptors present in cerebral areas of the limbic network involved in parental care (ventral tegmental area, nucleus accumbens, insular cortex, amygdala; which will be presented in more detail in II.1.3), oxytocin modulates the activity of this network. It is involved in reward, emotionality and motivation, and thus associated with mother-infant attachment (Feldman, 2016; Kim et al., 2016; Rajhans et al., 2019). This link was stronger emphasized with intranasally administration of oxytocin during listening to infant crying. Brain activity was reduced in the amygdala, and increased it in the bilateral insula and inferior frontal gyrus, suggesting that oxytocin favors responsiveness to infant crying, by lowering activity in anxiety and aversion circuits, and increasing activity in areas involved in empathy (Riem et al., 2011).

#### *2. Long lasting brain morphological changes*

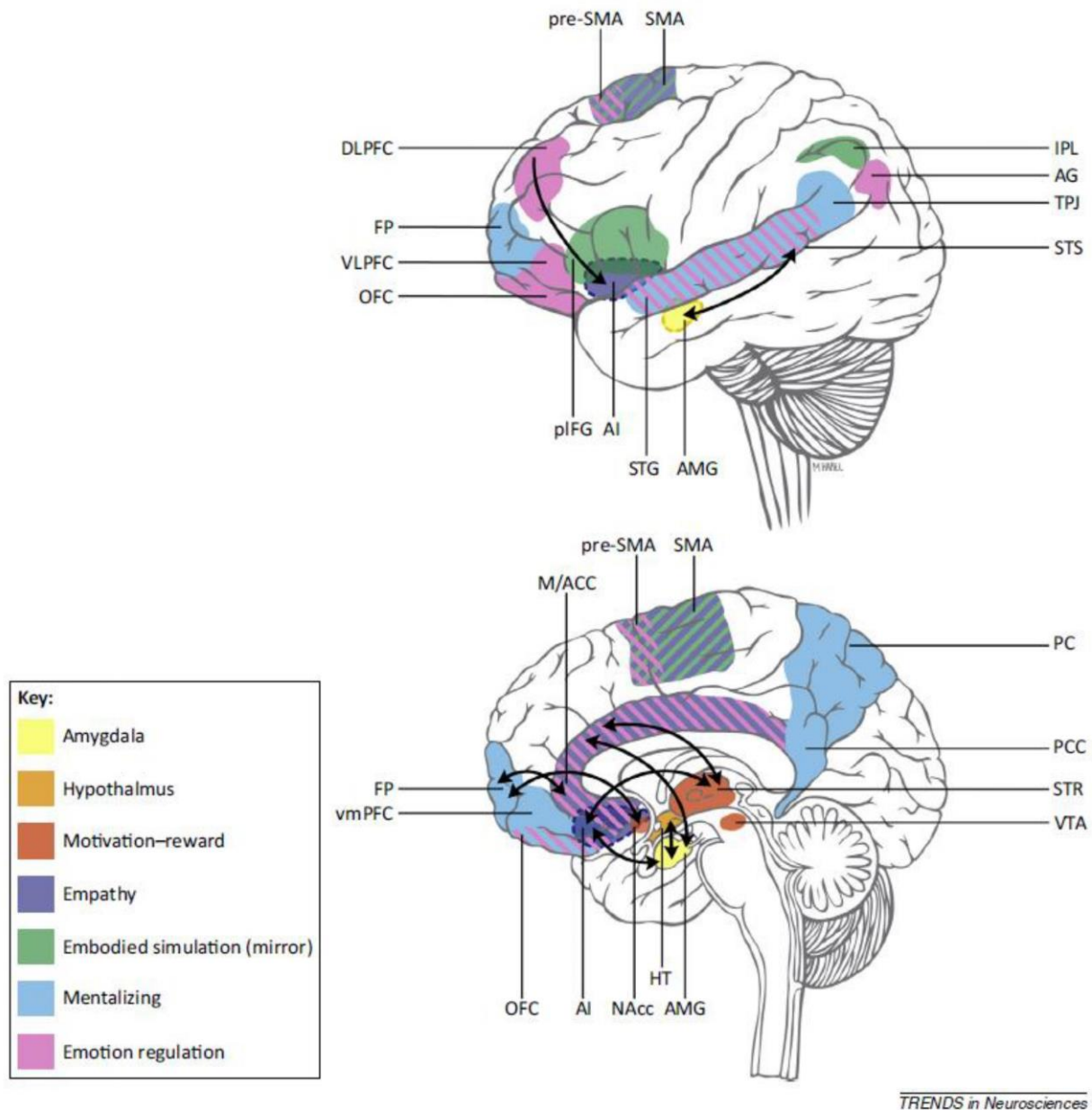
In addition to these hormonal changes, there are also morphological changes in the brain, mainly a reduction in grey matter volume (Martínez-García et al., 2021a). The volume reduction during pregnancy is located in regions of the default mode network (frontal and temporal areas, precuneus, left insula, anterior cingulate cortex, left hippocampus and parahippocampal regions) (Hoekzema et al., 2017). One explanation put forward for these reductions in grey matter is to prepare mothers-to-be for the stress and pain of childbirth, by promoting low-order brain functions that provide resilience (Martínez-García et al., 2021a). In the early post-partum,

grey matter volume is reported to increase (Kim et al., 2010, 2018), but it decreases again in the late post-partum and this reduction persists 2 years after birth (Hoekzema et al., 2017). This reduction is even observed 6 years after the baby's birth, emphasizing the long lasting aspect of these changes (Martínez-García et al., 2021b). These changes are supposed to be linked to babies' cues processing, allowing a reallocation of resources towards babies' signals, and development of parental care. Indeed, when exposed to babies cues, 30% of the voxels that respond specifically to the mother's own baby are located in the brains areas which lost volume during pregnancy (Hoekzema et al., 2017). More broadly, larger morphological changes in mothers predict more positive perception and attachment to their baby (Martínez-García et al., 2021a).

### *3. Integration of infant cues, especially cries*

Perception of offspring cues by a mammalian caregiving network has been first described in female rodents. During pregnancy and pups care, increase in oxytocin and prolactin production sensitizes the mesolimbic dopamine circuits, via the medial pre-optic area (MPOA) of the hypothalamus, which enhances maternal reward when caring. This leads to dopamine release in the nucleus accumbens (NAcc) and amygdala ensuring mothers' motivation and vigilance, in parallel to suppressing aversion to infant cues (Feldman, 2015). Oxytocin sensitizes these circuits in term of activity, connectivity and susceptibility to structural reorganization, making postpartum a time of high brain plasticity (Feldman, 2016).

In human, parental caregiving network comprises this mammalian caregiving network, connected in addition with insulo-cingulate and frontotemporal networks enabling both top-down and bottom-up processes. Ruth Feldman proposed an organization based on different networks (see Figure 3): the empathy network (anterior insula and cingulate cortex), enabling parental resonance with infant emotions, the mirror network (inferior parietal lobule IPL, inferior frontal gyrus IFG, supplemental motor area SMA) which permits that parents represent infant action in their brain, a mentalizing network (superior temporal gyrus/sulcus STS/STG, precuneus, posterior cingulate cortex PCC, temporo-parietal junction TPJ, and ventro-medial prefrontal vmPFC) supporting the ability for parents to infer the infant's intentions, and an emotion regulation network (frontopolar cortex, medial orbito-frontal cortex mOFC) allowing parental inhibition and the selection of appropriate action. Compared to parenting in mammals, this may permit a flexibility of the human parenting, implementing cultural, multigenerational and social patterns (Feldman, 2016).



**Figure 3. The human parental caregiving network.** The amygdala, hypothalamus and motivation subcortical network are implicated in mammalian caregiving. The empathy network includes the dorsal anterior cingulate cortex (ACC), anterior insula (AI), and supplementary motor area (SMA), which resonate with physical pain and emotional distress of others. The embodied simulation (mirror) network comprises sensorimotor and pre-sensorimotor areas, inferior parietal lobule (IPL), and inferior frontal gyrus (IFG), and is involved in perception–action coupling, action understanding, and imitation. The mentalizing network comprises temporoparietal and frontal regions, including superior temporal sulcus/gyrus (STS/STG), temporal-parietal junction (TPJ), temporal pole (TP), precuneus, posterior cingulate cortex (PCC), and ventromedial prefrontal cortex (vmPFC), and subserves mental-state understanding and perspective-taking. The emotion-regulation network supports multitasking and executive control, and includes the dorsolateral prefrontal cortex (dlPFC), medial orbitofrontal cortex (mOFC), middle frontal gyrus (MFG), and frontopolar cortex. From Feldman, 2015.



Regarding specific perception of auditory cues, a recent meta-analysis synthesized studies on infant cry perception until January 2018 (Witteman et al., 2019). As any sound, cries travel through the outer, middle and inner ear, where the variations in air pressure (the sound) are translated into neural activity. The signal is transferred to the brain stem, the thalamus and then the cortex (Bear et al., 2016). Regarding cortical integration, cry perception first involves the auditory processing circuit in the superior part of the temporal lobe from the primary auditory cortex (Heschl's gyrus (HG) and the middle part of the STG) to the associative areas processing the semantic information (in the STG, MTG and, in between, the STS) (Hickok & Poeppel, 2007). This allows identification of the sound signal as a cry, and assessment of the level of encoded distress. Specifically, the STG may play a role in the processing of the acoustic properties of the cry, such as its pitch and timbre, and may support auditory processing of emotional prosody (Witteman et al., 2012). Meanwhile, cry listening engages a dorsal pathway including inferior frontal gyrus IFG, the right premotor cortex and bilateral SMA involved in auditory processing too, potentially by motor simulation of incoming auditory information (Lima et al., 2016). A second circuit shifts attention towards salient sensory events such as cries, functioning as a "neural alarm signal" (Rilling, 2013). This involves the dorsal anterior thalamus, a multisensory hub, and the limbic system through the amygdala and posterior cingulate cortex PCC (Leech & Sharp, 2014). This circuit interacts with a third set of fronto-insular regions involved in both emotional and cognitive empathy. The dorsal anterior insula, the mid cingulate cortex MCC and the TPJ focus attention on emotions conveyed by the voice, and allow enhanced processing of emotional information (Zhang et al., 2019). Frontal regions such as the IFG and dorso-medial PFC are involved in more cognitive aspects of empathy (Amodio & Frith, 2006; Hartwigsen et al., 2019), labelled as mirror and mentalizing network by (Feldman, 2015). Finally, the basal ganglia, particularly the caudate nucleus and the putamen, part of cortico-striatal motor loops are involved with the SMA in parental vigilance, planning and initiation of the parental response, such as some routine behaviors of parenting (Booth et al., 2007; Provost et al., 2010).

As informed by electroencephalography, magnetoencephalography and local field potential studies, activations occur sequentially in the previous described order, after an initiation in the periaqueductal grey (PAG) in the brainstem, which may be considered as an early detector of infant vocalizations (Parsons et al., 2014; Young et al., 2017).

## 2. Fathers: more and more involved in babies care

In the animal reign, paternal investment in caregiving is quite common in birds and fish, but only 3 to 5% of mammal species exhibit paternal caregiving in nature, mainly those who are monogamous. It is observed in some rodent species, like the prairie vole or the Mongolian gerbil, and is rare in non-human primates, mainly observed in Callitrichid monkeys, which include marmosets and tamarins. In captivity, more mammal species show paternal caregiving suggesting the existence of a neural system for paternal behavior in mammal males, with evidence emphasizing the role of MPOA and subcortical limbic circuits in rodent males, as shown in females (Feldman, 2019; Rilling & Mascaró, 2017).

In our modern Western society, human fathers have become more involved in recent years, even if the distribution of care is far from balanced, starting with the taking of paternity and parental leave, which remains limited (Sponton, 2022). However, paternal investment has shown beneficial effects for the fathers themselves with development of a collaborative social style, for the mother-father partnership, enhancing the emotional bond (Feldman, 2019), and for the children, associated with better social, emotional and cognitive outcomes (Sarkadi et al., 2008).

Even if fathers do not go through the physiological upheavals of pregnancy, childbirth and lactation, the close proximity to their pregnant or lactating partner, and then the contact with the newborn after birth leads to hormonal and brain changes comparable to mothers' (Rajhans et al., 2019). The main hormonal change observed is a decreased in testosterone in fathers compared to childless men. It starts during their partner pregnancy and is considered as a shift in resources from mating to parenting. Fathers with greater declines in testosterone level are more empathic toward their infant's cries, and both mothers and fathers report more postpartum investment, commitment and satisfaction (Saxbe et al., 2017). In the opposite way, fatherhood leads to an increase in prolactin and oxytocin levels. Prolactin levels increase when hearing infant cries, and make fathers more responsive to cries (Rajhans et al., 2019). Interaction with their partner and infant increases oxytocin levels but with a differentiate effect compared to mothers. While oxytocin is associated with displays of affection and warmth toward their infant in mothers, it correlates with stimulatory but not affectionate touch in fathers (Feldman et al., 2010). The causal effect of oxytocin on motivation to care and empathy for children has been studied by administrating it intranasally. This increases activity in brain areas such as caudate nucleus, anterior cingulate cortex ACC and visual cortex involved in reward, empathy and attention, when viewing pictures of their own child (Li et al., 2017). Nonetheless, it is worth

noting that hormonal changes are presented separately, as in most studies, although they may interact with each other and even with other hormones to collectively influence parenting behaviors (Rajhans et al., 2019).

Brain morphological changes has been less investigated in fathers compared to mothers. No change are measured during the partner pregnancy (Hoekzema et al., 2017), but there is a reduction of cortical volume and thickness of the right precuneus in the early post-partum compared to before pregnancy. The more this reduction is, the stronger the brain activation while viewing pictures of their own baby (Paternina-Die et al., 2020).

When presented to infant cues, involvement of similar networks are shown in fathers compared to mothers: an embodied simulation network (anterior insula, ACC, SFG), close to the empathy network describe in mothers, grasping other attention and emotional resonance, a mentalizing network (STS, mPFC) providing accurate interpretation of infants' social cues, an emotion regulation network (IFG, OFC) and a subcortical parenting network (caudate nucleus, putamen, thalamus, amygdala) ensuring parental vigilance and preparation to action (Provenzi et al., 2021). Compared to mothers, fathers tend to show greater activity in regions involved in social-cognitive and semantic processing (STS, IFG, temporal pole and angular gyrus) and less activation in limbic regions like the amygdala (Abraham et al., 2014; Atzil et al., 2012; Wittman et al., 2019).

One study tried to disentangle the biologic difference from the childcare experience between mothers and fathers, by looking to brain activity in reaction to infant videos viewing, in heterosexual primary caregiver mothers, heterosexual secondary caregiver fathers and homosexual primary caregiver fathers. All homosexual fathers were living in a two-parent family, had a child through a surrogate mother and had raised their child without the mother's intervention since the child's birth. Primary caregiver fathers showed joint activation in amygdala, like primary caregiver mothers, and in the STS like secondary caregiver fathers. There was no difference in masculinity or femininity between heterosexual and homosexual fathers, suggesting that type and amount of contact with the child in the early postpartum period shape the perception of babies' cues. This hypothesis was supported by the aspect that time spent alone caring at their infant was correlated with amygdala-STS connectivity in all fathers (Abraham et al., 2014).

### 3. Nonparents and alloparents in our cooperative breeding species

Fathers involvement in infant care shows that pregnancy is not necessary to promote active parental behavior. In our society, the importance of fathers is increased by the fact that couples generally live apart from their families that could otherwise help in childcare (Rilling & Mascaró, 2017). Nonetheless, biological parents are not the only ones who provide care for children, and even if they are less studied, there are other ways of raising children. Indeed, other members of the social group (alloparents) can help one or both parents rearing their infant, making the human species a cooperative breeding species (Hrdy, 2007). Alloparents can be genetically related (siblings, aunts and uncles, grandparents) or not (foster parents, professional caregivers), and may or may not be parents themselves. Alloparenting is also described in around 3% of mammal species (prairie voles, dwarf hamsters, Callitrichids for examples), with a positive association with oxytocin expression (Rogers & Bales, 2019).

In an evolutionary perspective, alloparenting has been proposed to participate in *Homo Erectus* dissemination in Africa. Indeed, human babies are very immature at birth compared with other species, displaying only 25% of the adult brain size (40% in chimpanzees, 70% in *Macaca*) (Coqueugniot et al., 2004), and remaining dependent for many years. Alloparents help to distribute caregiving load, thus permitting slow maturation and progressive independency acquisition for offspring, and for parents to move and keep a short interbirth interval (Hrdy, 2007; Kenkel et al., 2017).

Alloparenting is also considered as a way to practice and be prepared for parenthood (Hrdy, 2007). For example, in rats, repeated exposure to pups induces increase expression of maternal-like behaviors (Kenkel et al., 2017). In non-parents, exposure to infant cues leads to activation of brain areas close to the parental caregiving network, including motor, mirror and limbic areas and specific sensory systems, visual or auditory depending of the stimuli used (Bos et al., 2010; Lenzi et al., 2013). This reactivity to infant cues seems linked to oxytocin too with intranasal administration leading to an increase in attraction to infants' faces, decrease in amygdala activation and increase in insula and IFG activation in nulliparous women (Kenkel et al., 2017; Riem et al., 2011). When compared to parents, nonparents show higher brain activation in the caudate nucleus, and lower activation in brain areas of empathy (anterior insula), emotion regulation (orbitofrontal cortex), mirror (SMA) and mentalizing (precuneus) networks. This could be interpreted as non-parents having a tendency to initiate action in response to infant signals, but being less effective in processing these signals emotionally and cognitively to provide an adapted response (Parsons et al., 2017; Witteman et al., 2019).

Thus, humans seem to have the ability to provide care to babies, even nonbiological parents (Glasper, 2019), but how this ability is shaped by nonparental experience remains unclear and will be addressed in Chapters II and III.

**In the second part of this introduction, I gave an overview of babies' caregivers and their general perception of babies' cues. The last part of this introduction will focus on how static and dynamic information are perceived by these caregivers. Indeed, appropriate perception of babies cues is essential both for infants and parents health, with maladaptive perception been linked to alteration of bonding, higher risk of postpartum depression and even to a higher risk of infant neglect or abuse (Barr, 2014).**

### **III. Cries perception and modulating factors**

#### **1. Perception of static information**

Identifying one's own newborn is the basis of parent offspring recognition highlighted in many mammal species. This ability is particularly relevant in species when mothers and pups experienced early separations so that the mother gets to feed, or when the risk of confusion between filial and nonfilial pups is high, like in high-density colonies. (Linossier et al., 2021; Martin et al., 2022). These situations remain rare in humans, but can be found for example in shared rooms in maternity wards, where mothers describe waking up preferentially for their baby's cries from the first days of life (Formby, 1967). Moreover, by being familiar with their own baby's cries, parents may be more sensitive to detect intra-individual variations linked to the baby's physiological and emotional state.

This recognition of one's own baby was first identified in mothers since day one of the baby's life (Valanne et al., 1967), regardless of the mother's age, the method of delivery nor the method of feeding (Formby, 1967; Morsbach & Bunting, 1979). It relies of a redundant set of acoustic parameters (duration, fundamental frequency, peak frequency in the spectrum, signal-to-noise ratio) that makes individuality recognition robust to acoustic degradation, like re-recording cries across an open field or filtering the sound in selected frequency bands (Gustafson et al., 1984, 1994). In fathers, it initially seemed that this ability was weaker, with only 45% of fathers achieving correct recognition of their 30 day old infant, while 80% of mothers succeeded (J. A. Green & Gustafson, 1983). After controlling for the time spent caring at their baby, fathers spending at least 4 hours a day with their infant are in fact as good as mothers (Gustafsson et al., 2013). This role of experience has been further emphasized when looking at the development of this ability in mothers. Indeed, they become more and more accurate, from 40% to 80% between the first and third day postpartum. Multiparous mothers with at least two older children are also better (Bouchet et al., 2020). In addition, this ability to recognize one given baby has also been shown in nonparents with a training/testing paradigm, where they are assigned to one given baby and asked to learn to recognize him/her. They are able to recognize this given baby above chance, after a small exposure of three 7-seconds cry bouts. Experience in babies care and exposure are again critical, with previous babysitting experience and listening to more cry segments leading to a better recognition (Bouchet et al., 2020).

A few studies investigated the neural correlates of this baby recognition, comparing brain activations when listening to one's own infant cry to other infant cry. In a small sample of 11 mothers, listening to own infant cries led to more activation in the dorsal ACC, the right insula,

the right occipital fusiform to lingual gyrus and left posterior supramarginal gyrus (Laurent & Ablow, 2012). In a larger cohort of 95 primiparous mothers, own baby cry listening was associated with stronger activation of the right fronto-insular cortex. In addition, several other areas described in the human caregiving network (precuneus, STS, SMA) were also more activated but did not survive correction for multiple statistical comparisons (Hipwell et al., 2015). This can be summarized as higher activity in brain regions involved in emotional and cognitive empathy. A meta-analysis on the perception of visual cues in mothers also provides information on this network specialization, with viewing stimuli of own versus unfamiliar children leading to more activation in brain areas involved in vigilance, emotion regulation, mentalizing and preparation to action (respectively caudate body, amygdala and other limbic structures, STG and precentral gyrus) (Paul et al., 2019). These stronger activations in the parental caregiving network are associated with higher sensitivity to infant cues (frontal pole, IFG, frontal operculum), harmonious interactions (hippocampus, precuneus) (Musser et al., 2012), and positive parenting (MTG, hypothalamus, thalamus, caudate) (Kim et al., 2015). To my knowledge, only one fMRI study investigated brain activations specific to own baby cry in fathers, and concluded to no difference compared to other baby cry (Li et al., 2018). However, there are several limitations in this study (only one own infant cry per participant, same unfamiliar cry for all participants rated as more aversive by an independent sample of listeners, no correct distinction between own and unfamiliar cries), that makes the results difficult to generalize.

To sum up, this ability to recognize one given baby is shared between parents and nonparents and learned quickly. This seems to imply stronger brain activity in the human caregiving network but evidences remain limited. Moreover, every studies documented this ability based on cries recorded in low distress contexts, mainly hunger (Morsbach & Bunting, 1979; Valanne et al., 1967) or mild-discomfort (Bouchet et al., 2020; Formby, 1967; Gustafsson et al., 2013), which are the most common situations in real life. As detailed in part I.3.3 of this introduction, there is no clear evidence of acoustic consistency of individual information across dynamic contexts, neither there is evidence if the ability to recognize one given baby is conserved in other situations, especially when the baby is feeling pain. These questions will be addressed in Chapters I and III.

## 2. Perception of dynamic information

### *1. Cry types versus graded level of distress*

Regarding the perception of crying causes, some studies first tested if adult listeners can distinguish different cry types, with mixed results. One shows failure of distinct cry types recognition (Sherman, 1928), but it is not reported if the tested nurses had some experience in infant care, and baby's mothers are not tested (Illingworth, 1955). Studies from another group show that childless nurses, some working with children, are able to correctly classify 67% of cries across 4 contexts (Wasz-Höckert et al., 1964a). Apart from nurses, men and women manage to recognize crying contexts as well, with experienced participants (parents or working in pediatric care) performing better than inexperienced ones (Wasz-Höckert et al., 1964b). However, the cries used in these studies come from babies at different ages, with no explicit control on the baby's identity, and only the six best copies are selected for testing, all of that could bias the results.

When assessing the graded perception of distress in cries, it seems to be shared by all adults. Qualitative judgment of cries shows similar patterns in parents and nonparents, tuned by parental experience (J. A. Green et al., 1987). Rated distress levels, either expressed distress in cries or felt distress by listeners, show no difference regarding the listeners' sex, parental status or experience in coding cries (Esposito et al., 2015; Wood & Gustafson, 2001; Yoo et al., 2019). For both parents and nonparents, cries of older babies are assessed as more intense when comparing 1 and 6 month old babies (Leger et al., 1996). This perception is linked to specific acoustic features: longer cries, with shorter pauses between cries, more subharmonics and dysphonation in cries (which refers to nonlinear phenomena) are rated as more aversive and expressing more distress (Gustafson & Green, 1989; Qiaobing Xie et al., 1993; Wood, 2009). More precise role of nonlinear phenomena has been emphasized for perceived distress in puppy whines. Adding synthetic chaos to whines increases the puppy's perceived distress by human listeners, and listeners with puppies extensive caregiving experience (breeders, veterinarians) are also sensitive to added sidebands and subharmonics leading to more perceived distress too (Massenet et al., 2022). Finally, perceived pitch shapes the perceived distress, with higher pitched vocalizations being rated as expressing more distress (Reby et al., 2016). However, this may be more be a bias than a relevant information especially when assessing distress in nonhuman species, with no clear difference in fundamental frequency between low and high distress cries, and high pitched vocalizations (bonobo ones) being systematically rated as expressing more distress than low pitched (chimpanzee ones), despite being recorded in various



contexts (Kelly et al., 2017). It is also worth noting that, in addition to being biased by the pitch, the perception of distress is influenced by sex stereotypes. At lower pitch, adult men rate cries as expressing more distress when attributed to baby boys compared to the same cries presented as belonging to baby girls (Reby et al., 2016).

One study investigated the neural correlates sustaining this perception, showing that high-distress cries, compared to low distress ones, are associated to reduced activation in mirror and mentalizing regions of the human caregiving connectome (bilateral STG, right MTG, left IPL, right superior occipital gyrus, and left precuneus) (Montoya et al., 2012).

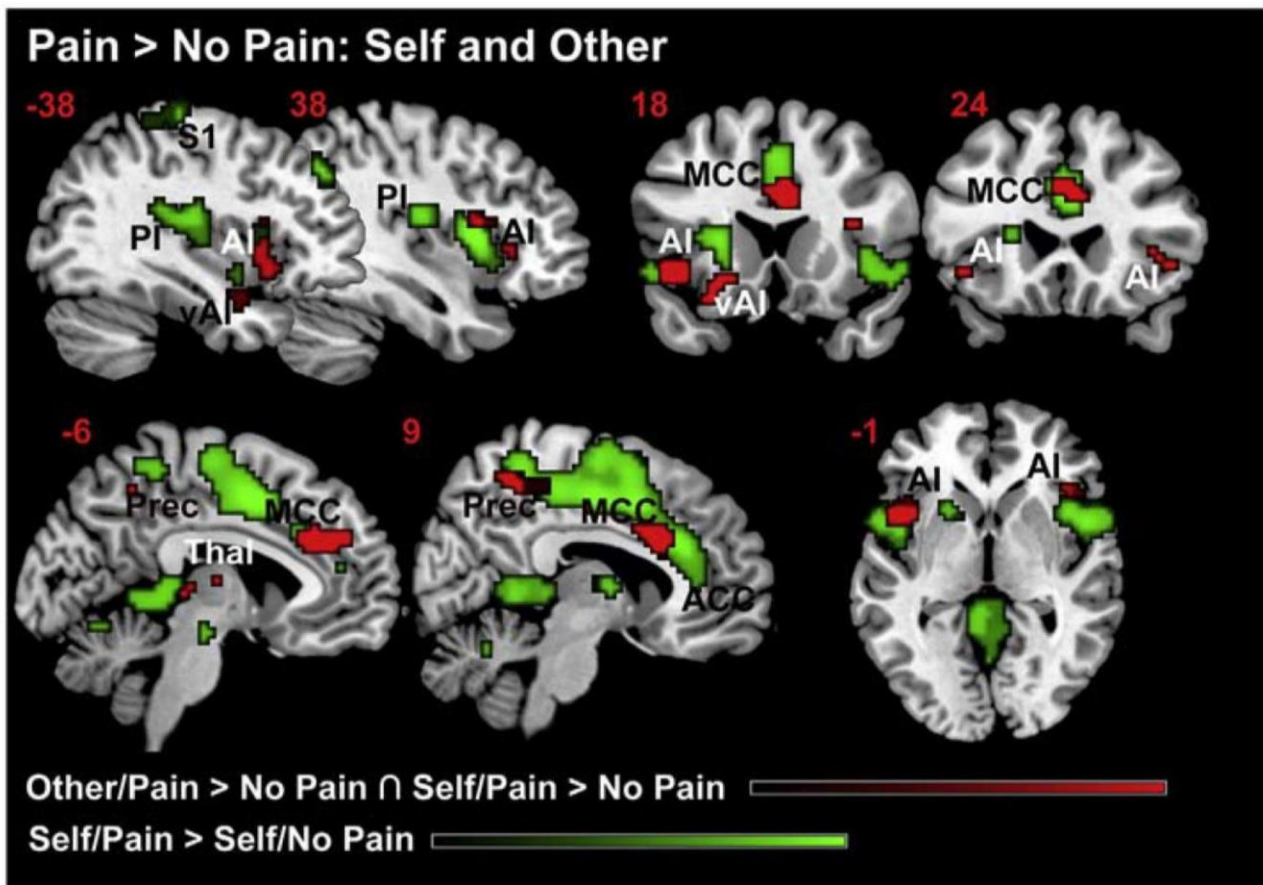
This graded distress perception influences listeners' behavioral response, with shorter latency to act while listening cries evaluated as expressing more distress. Caregiving context is associated with this perception of distress in establishing the response, with listeners waiting significantly longer to act when told that the infant needed a nap (Wood & Gustafson, 2001). However, these graded perceptions and responses may be incomplete, particularly in the case of pain, where a more decisive interpretation is required, for example to determine whether or not to administer an analgesic.

## *2. Facing babies' and others' pain*

The ability to distinguish pain cries from distress cries produced by other stressors has been shown in parents (Chóliz et al., 2012; Koutseff et al., 2017; Porter et al., 1986) but this is not consistent. For example, it requires information on the contexts in which cries are recorded to enable this recognition for children under 8 months of age (Chóliz et al., 2012). Moreover, there is contradictory evidence with absence of significant recognition of pain in a sample of parents and nonparents, without any difference between these two participant populations (Lindová et al., 2015). When present, this recognition seems to be linked to acoustic features specific to pain in cries, with cries from more invasive procedure during circumcision being described as louder, higher-pitched, more rapidly repeated and noisier (Porter et al., 1986). During this surgery, parents rate cries from more invasive procedures as more urgent. In the same way, higher pain intensity is linked to higher pain ratings when evaluating adult vocalizations simulated by trained actors (Raine et al., 2019). However, finer difference in cries elicited by two vaccines, even if characterized by different acoustic roughness level, are not captured by the baby's parents (Koutseff et al., 2017). No gender difference has been reported for this pain perception (Koutseff et al., 2017), but older people may be less accurate, as shown for overall

recognition of cries (Lindová et al., 2015), in line with other results on emotion perception in adult nonverbal vocalizations (Amorim et al., 2021). In addition, it is not known whether childless adults are able to identify pain in cries, and for parents, if they have a finer perception of their own child pain compared to unfamiliar infants and which acoustic features, particularly the nonlinear phenomena, enable their perception of pain in cries. These questions will be addressed in Chapter II.

While pain cries have been reported as eliciting the greatest discomfort, highest levels of unpleasantness, arousal and lack of control in listeners (Chóliz et al., 2012), there is no study to date investigating the neural perception of pain in cries. Nonetheless, facing babies' pain through cries listening can be linked to work on empathy for pain. Empathy can be defined as a sense of knowing the experience of another person with cognitive, affective and behavioral components (Goubert et al., 2005). It has been extensively studied by confronting people to others' pain to evoke an empathic response. Experiencing self-pain is associated to brain activations of a so-called pain matrix, where the principal regions are the primary and secondary somatosensory cortices (S1, S2), the thalamus, the insula, the ACC, and the medial prefrontal cortex (mPFC) (Peyron et al., 2000). This pain matrix is hierarchized in three sub matrices linked to the nociceptive, attentional and affective components of pain respectively (Garcia-Larrea & Peyron, 2013). One of the first study on empathy for pain by Tania Singer compares brain activations while receiving a painful stimulation, to those when the participant's partner received the painful stimulation. Empathy for pain, i.e. when the partner received the painful stimulation, is associated with the affective, but not the sensitive part of the pain matrix (Singer et al., 2004). A meta-analysis further synthesizes various studies on empathy for pain, showing that it involves a core network of bilateral anterior insular cortex and medial/anterior cingulate cortex, which overlaps directly with experienced pain (Lamm et al., 2011, see Figure 4). Empathy for pain can be elicited in different ways: abstract visual information about the other's state as mentioned above specifically recruits areas involved in the mental representation of self and other (precuneus, vmPFC, superior temporal cortex and TPJ), while viewing body parts in painful situations activates brain areas involved in action understanding (inferior parietal/ventral premotor cortices) (Jackson et al., 2005; Lamm et al., 2011). Closer to cries listening, hearing pain-related exclamations increases brain activity in STG, MTG, S2, thalamus and left insula (Lang et al., 2011), that is, areas involved in auditory processing and empathy for pain.



**Figure 4.** *Common and distinct activation when observing others in pain, and experiencing pain oneself.* Areas of common activation include AI, MCC/ACC, Precuneus and Thalamus (conjunction of other- and self-related activations, color-coded in red); distinct activations for self-related responses only are observed in posterior insula (PI), primary somatosensory cortex (S1), and in large parts of medial and anterior cingulate cortex (MCC/ACC; color-coded in green). From Lamm et al., 2011.

Additional neuroimaging studies may provide clues to pain processing in babies cries. Indeed, pain cries are characterized by acoustic roughness, which is also present in other natural and artificial alarm signals. This roughness induces increased activity in the bilateral anterior amygdala and primary auditory cortices (Arnal et al., 2015) and synchronization in large-scale brain networks involved in aversion processing (Arnal et al., 2019). Pain perception in cries will be further investigated in Chapter III.

### 3. Facing others' pain: specific case of healthcare professionals

One population particularly exposed to babies', and more generally other's pain is healthcare professionals. Empathy is often viewed as a basis of care and medicine, based on both bottom-

up processes like affect sharing, and top-down processes linked to perspective taking, emotion understanding and emotion regulation (Decety, 2020). Empathic care has shown beneficial effects for the patients, with more accurate diagnoses, better medical outcomes, satisfaction and adherence to the treatments. How healthcare professionals communicate can even influence the patients pain, with empathetic comments reducing the perceived pain (Fauchon et al., 2017). The effects on the health of professionals are more complex. Indeed, repeated exposure to pain in pediatric nurses is linked to higher empathy but also higher risk of secondary trauma, burnout and compassion fatigue, especially at the start of their career (Decety, 2020; Latimer et al., 2017). In an opposite way, higher empathy is also linked to more efficiency and satisfaction for professionals, and even suggested as having a protecting role against burnout (Zenasni et al., 2012a).

Daily exposure to the pain of others also impacts the ability of professionals to assess that pain, with mixed evidence again. Some have advanced that health professionals underestimate the patients' pain, allowing them to cope with their own distress and regulate their aversive reaction (Goubert et al., 2005). Workload and fatigue are suggested causes, leading to reduced attentional and cognitive resources (Jackson et al., 2015), but a recent study on intensive care nurses shows a robust pain recognition across day times and between the beginning and end of their 12-hour shifts (Schmidt et al., 2023). On the contrary, some studies show that pediatric nurses are more accurate in pain evaluation compared to allied health control, scoring higher infant pain indicating that they may have a better knowledge of infant pain cues, especially for low-intensity pain when fewer cues are available (Latimer et al., 2011, 2017).

This may be sustained by differential neural correlates of others' pain perception linked to their expertise. While viewing others' pain is associated with increased activity in the anterior insula and the ACC in control participants, expert health professionals show increased activation in the prefrontal cortex and the TPJ involved in emotion regulation (Cheng et al., 2007; Coll et al., 2017). These differences in processing occur at a very early stage, with one event-related potential study showing a suppression of the negative arousal component at 110ms over the frontal cortex and ACC in professionals compared to controls (Decety et al., 2010). Pediatric nurses show the similar pattern of decreased activity in the anterior insula, but also decreased activation of the inferior frontal and medial prefrontal cortices (Jackson et al., 2017), suggesting that expertise refinement of pain perception may be linked to the type of patients they care for (Tremblay et al., 2018). Pain assessment in professional caregivers, in the light of parental expertise in babies cries perception, will be investigated in Chapter II and III.

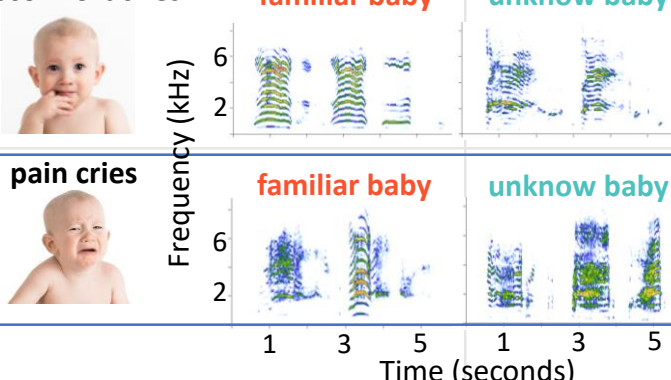
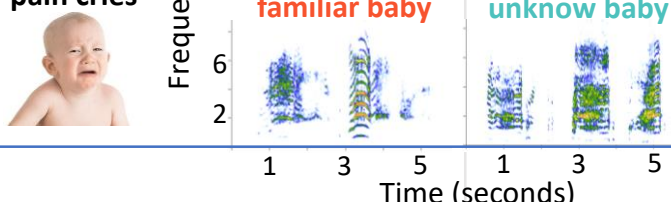
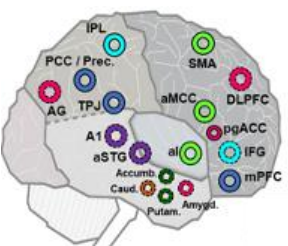
**To sum up, I gave an overview in this introduction of the emission/reception chain of crying: babies produce cries which support both static and dynamic information, which is perceived by adult listeners, mothers, fathers and other caregivers, especially professional pediatric caregivers.**

This thesis will address the following questions (see summary on the next page):

- Chapter I: How pain interacts with the individual information present in babies cries? Is the baby vocal signature shared, weakened or absent in pain cries?
- Chapter II: How adults learn to identify pain in cries? Which factors modulate the ability to identify pain in cries? Does familiarity with a given baby, experience (parental or professional) in babies care and younger age make adults better in recognizing pain in cries? On which acoustic parameters relies this identification of pain in cries?
- Chapter III: What are the neural correlates of individuality and pain perception in babies cries? How sex and parenthood shape the brain connectome engaged when listening to babies cries? How familiarity and dynamic context are processed in expert participants? With a different specialization between parents and professional pediatric caregivers, both experts in babies cries?

I will use a combined approach with psychoacoustic experiments, further transferred in an MRI scanner to access the neural correlates. All studies use cries of 2-month-old babies recorded before the beginning of this thesis (Koutseff et al., 2017). Babies are recorded in two different contexts: during undressing, bathing and dressing at their home (no pain condition), and during routine vaccination at the doctor's office (pain condition).

Two additional studies I participated in appear in the annexes: the study in Annex I addresses recognition of cry causes other than pain, and the one in Annex II details factors shaping the brain connectome engaged in cries listening.

<p><b>discomfort cries</b></p> 	<p><b>Individual vocal signature</b> Familiar babies are recognized by parents and non-parents based on discomfort cries</p>
<p><b>pain cries</b></p> 	<p><b>Chapter I: Is this individual signature also found in pain cries?</b></p>
<p><b>Physiological state</b> Pain cries are longer, louder, harsher and rougher Parents identify a pain state by listening to their baby's cries</p>	 <p>Cries listening by adults involve activation in a large-scale brain networks (auditory, cognitive, attention, emotion and mirroring networks)</p>
<p><b>Chapter II: How adults learn to identify pain in cries?</b> II.1: Is parenthood necessary? II.1: Is it easier for a familiar baby? II.2: Does it decline with aging? II.3: How non-linear phenomena in cries modulate this pain identification?</p>	<p><b>Chapter III: What are the neural correlates of individuality and pain perception in babies cries?</b> III.1: How sex and parenthood shape the brain connectome engaged when listening to babies cries? III.2: How familiarity and pain context are processed in expert participants?</p>

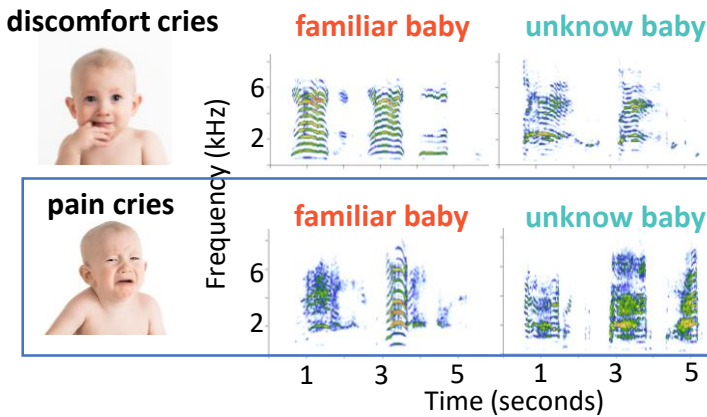


# Chapter I: Pain signaling takes over identity cues in baby distress cries



# Graphical abstract: Pain signaling takes over identity cues in baby distress cries

Siloé Corvin, Camille Fauchon, Hugues Patural, Roland Peyron, David Reby, Frédéric Theunissen, Nicolas Mathevon

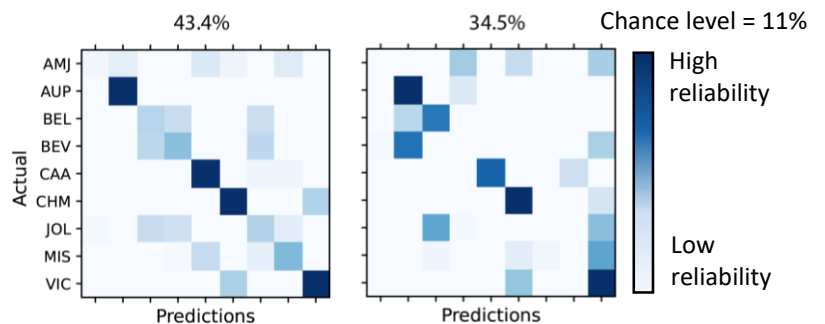
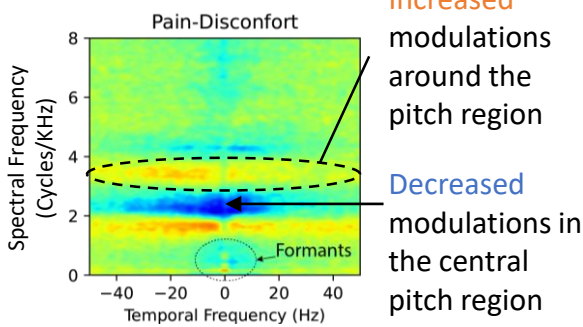


**Individual vocal signature**  
Familiar babies are recognized by parents and non-parents based on discomfort cries listening

**Is this individual signature also found in pain cries?**

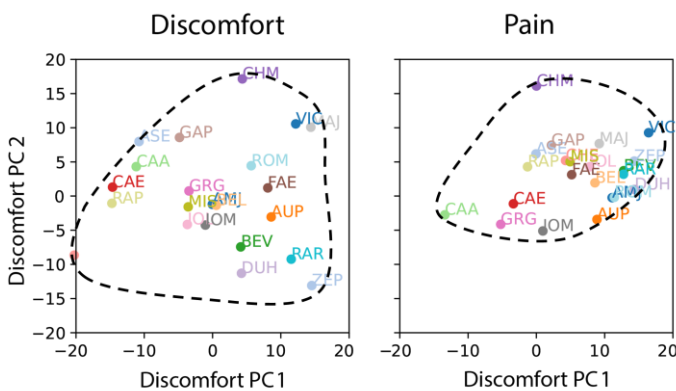
**Methods:** we combined acoustic analysis, machine learning and playback experiments.

## Results

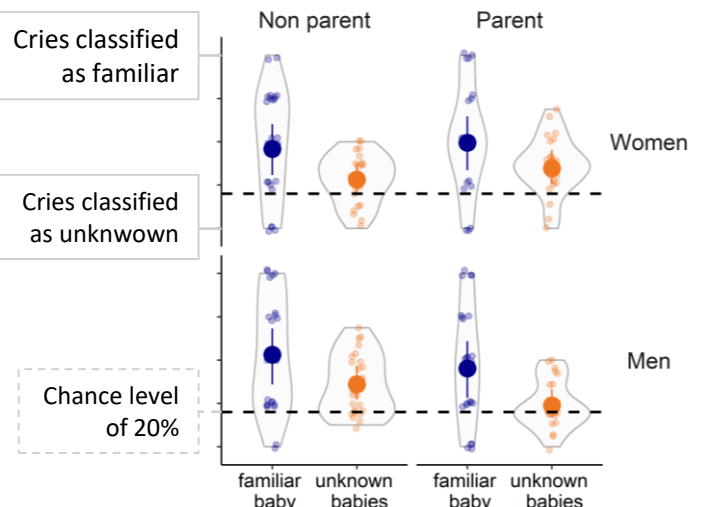


**B. Individual signatures are less reliable in pain cries than in discomfort cries.** LDA classifier trained on discomfort cries and tested either on discomfort cries (left panel) or pain cries (right panel).

### A. Pain cries have more variable pitch.



**C. The acoustic space of pain cries is shrunk compared to discomfort cries.** Average Modulation Power Spectrum for each baby is plotted in a 2D acoustic space define by the first two principal component coefficients of discomfort cries.



**D. Identifying a familiar baby by their pain cries is challenging for human listeners.**

**Conclusion:** The baby's identity is still encoded in pain cries, but it is weaker than in discomfort cries. As the rearing of young humans is notoriously cooperative, it may be useful for the baby in pain to become less identifiable and therefore more likely to attract any caregiver, familiar or not.

## Chapter I - Pain signaling takes over identity cues in baby distress cries

First, we combined acoustic analysis, machine learning and playback experiment to investigate whether pain interfere with static information on the baby's identity contained in cries. This chapter is in preparation for *Current Biology*.

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### **Abstract**

Decoding the signals emitted by the baby is essential to parental care. Baby cries convey static information related to individual identity as well as dynamic information related to the baby's emotional and physiological state. Can these informative messages be transmitted synchronously and independently or do they interfere with each other? Here we show that the individual vocal signatures carried by discomfort cries converge in pain cries towards a common expression of pain by babies, at the cost of a loss of individuality. Our acoustic analysis show that pain cries, compared with discomfort cries, are mainly characterized by a more unstable source. This unstable source is likely to fragilise both source- and filter-related cues to identity. Machine learning analyses and psychoacoustic experiments reveal that the baby's identity is still encoded in pain cries, but that it is weaker than in discomfort cries. Our results are consistent with idea that the costs of failing to signal distress outweighs the cost of weakening cues to identity.

## **Introduction**

Babies' cries soliciting parental care are generally triggered by pain, discomfort, hunger or separation from parents or other caregivers (Lingle et al., 2012). While some of the information conveyed by these cries is fairly stable over time and linked to the idiosyncratic characteristics of the sender, such as their age, size, weight and the anatomy of their vocal tract ("static information" or "vocal signature" allowing a given baby to be identified), other information is labile and relates to the current emotional and physiological state ("dynamic information" signalling the baby's immediate needs) (Koutseff et al., 2017). Parents or other caregivers adjust the quantity and quality of care provided to their baby according to this information (LaGasse et al., 2005; Soltis, 2004). Previous studies have shown that they also quickly learn to identify their baby by their cries, become better at detecting dynamic variations in the cries, and judge more accurately their baby's current emotional and physiological state than those of other babies (Corvin et al., 2022).

Studies with animals have examined the constancy of an individual vocal signature between different vocalizations. The results vary from species to species. In zebra finches (*Taeniopygia guttata*), for example, whose vocal repertoire includes many different call types emitted in a variety of contexts and with a variety of functions, each call has characteristics that allow to identify the individual caller (Elie & Theunissen, 2018). However, these individual vocal signatures are not transferable between call types and it is not possible to identify an individual from one type of call by using the acoustic criteria for individuality found in another type of call. A given individual therefore has as many vocal signatures as call types in its repertoire. In mammal species such as the red deer (*Cervus elaphus*) or the cow (*Bos taurus*), the coding of static information bearing the identity of the individual is shared across different vocalizations bearing different dynamic information (Reby et al., 2006), such as vocalizations with positive and negative valence (A. Green et al., 2019). In these species, variations in dynamic information have little effect on static information, which remains stable. In other species, the reliability of the individual vocal signature can vary between vocalisations. This is the case for the bonobo's vocal repertoire, where calls emitted in contexts of high-arousal are more individualized than vocalisations emitted in contexts of low arousal (Keenan et al., 2020). In the bonobo, the acoustic gradation that codes for dynamic information (i.e. the individual's level of excitation) is accompanied by a variation in the static information that supports vocal individuality.

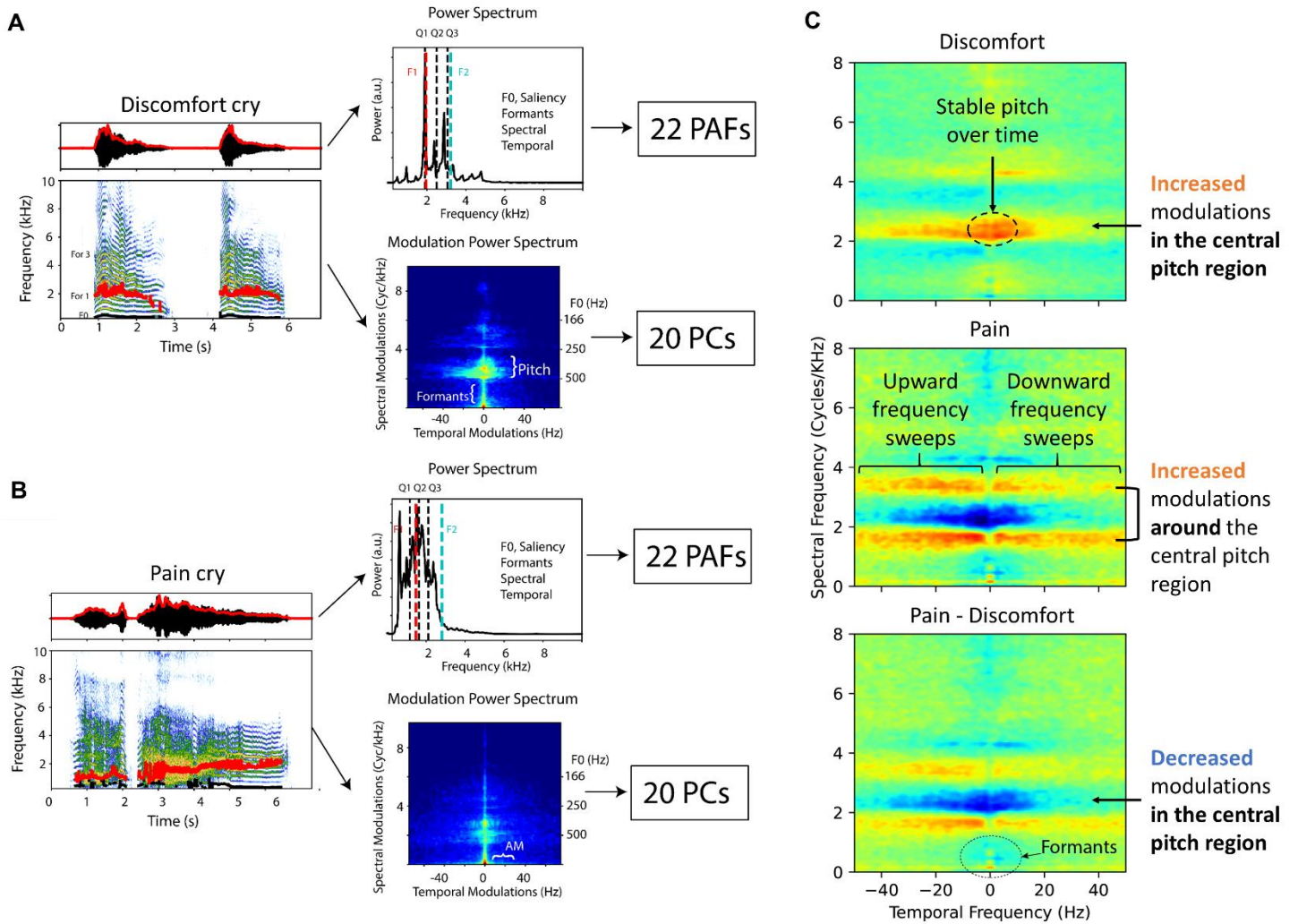
In humans, the fundamental frequency of the adult voice (pitch) is a reliable marker of individuality, which is preserved in verbal and nonverbal vocalizations (Pisanski et al., 2020). It is known that the fundamental frequency varies predictably during the development of an individual and stabilises in adulthood (Fouquet et al., 2016; Levrero et al., 2018). However, little is known about how static information and dynamic information interfere in human vocalisations. In the case of infant cries, a reliable individual vocal signature is present in discomfort cries (emitted during bathing (Bouchet et al., 2020; Gustafsson et al., 2013) or when the baby is hungry (Lockhart-Bouron et al., 2023; Morsbach & Bunting, 1979; Valanne et al., 1967)), but it is not known whether this signature is also found in cries provoked by pain. One hypothesis is that a signature common to all of a baby's cries would make it easier to identify the baby in all circumstances, increasing the motivation of the parent or any other caregiver to react to never previously-heard cries emitted by their baby. An alternative hypothesis is that by making the baby less identifiable, a difference in individual signature - or a reduction in its reliability - in their pain cries would increase the probability of engaging the response of any nearby adult, a strategy which could be well suited to emergency situations.

Here we test these hypotheses by examining whether the static information that enables a baby to be identified by their cries recorded in a discomfort context is preserved in cries elicited by a pain context. We first quantify the reliability of this information in both emission contexts using classifiers trained either with discrete acoustic parameters or with Modulation Power Spectra. We then test the reliability of classifiers trained on one type of cry (discomfort or pain) in identifying babies from the other type of cry. Finally, we conduct psycho-acoustic experiments to assess the ability of adult listeners - women and men, parents and non-parents - to recognize an assigned baby from their pain cries after familiarization based on their discomfort cries.

## **Results**

### **Pain cries have more variable pitch**

We recorded each baby (N = 22; 2 months old) under two conditions (Koutseff et al., 2017): during bathing, undressing or dressing by the parents at the baby's home ("discomfort cries") and during a vaccination session at the doctor's office ("pain cries"). We isolated 284 cry sequences from these raw recordings (4 sequences of pain cries and between 2 and 19 sequences



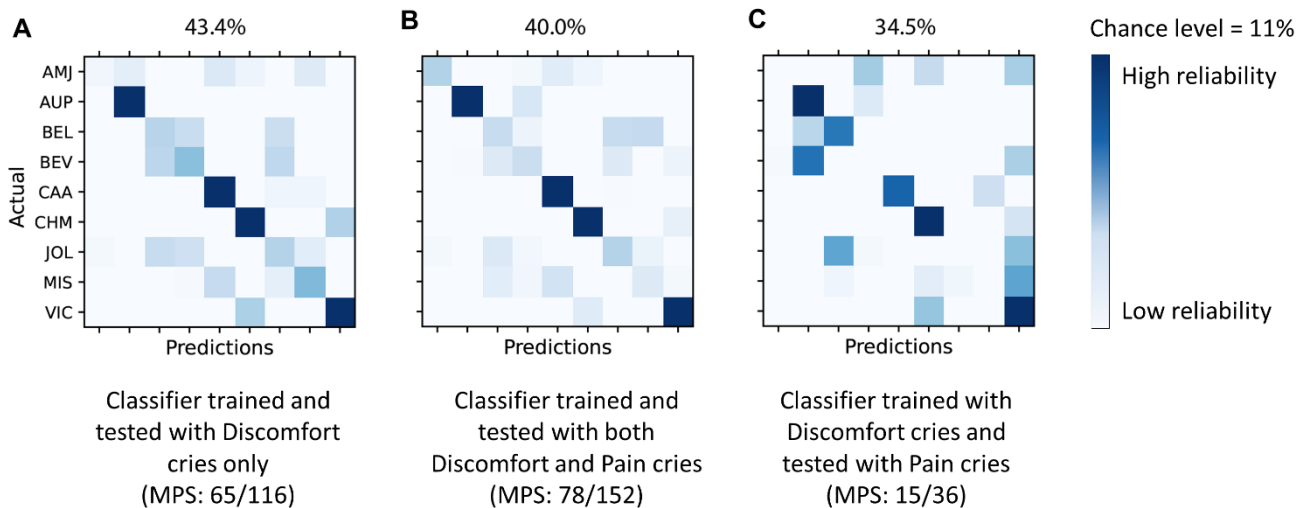
**Figure 1. Pain cries have more variable pitch.** Example of cries from one baby in the Discomfort (A) and Pain (B) conditions and extraction of acoustical features. Left panels. The vocalization is depicted as an oscillogram (top) and spectrogram (bottom). In the oscillogram, the sound pressure waveform is shown as a black line and its amplitude envelope with a red line. The time varying fundamental and time-varying first formant are shown on the spectrogram with black and red lines, respectively. Right panels. A total of 22 predefined acoustic features (22 PAFs) are extracted from the measures obtained from the amplitude envelope, the power spectrum, and the time-varying fundamental and formants. The modulation power spectrum (MPS) is obtained by calculating and averaging the amplitude of the 2D Fourier Transform of spectrogram in 1s windows. The first 20 principal components (PCs) of the MPS are also extracted as acoustical features. (C) Average modulation power spectrum (MPS) for discomfort, pain and the difference between the pain and discomfort conditions. The average difference is obtained from pair-wise differences in log power (db) of the average MPS in the pain condition minus the log power of the average MPS in the discomfort condition. The overall pair-wise average is obtained from the 22 babies in the acoustic database. In the pain condition, the modulations that are associated with pitch (and pitch quality) are greatly reduced (blue region around 3 cyc/kHz), whereas the spectral modulations around this central pitch region are enhanced (red regions).

of discomfort cries per baby; average duration of sequences =  $6.3 \pm 1.1$  s), and described their acoustic structure using 22 Predefined Acoustic Features (PAFs, characterizing the amplitude envelope, power spectrum, fundamental frequency -pitch- and formants), and the Modulation Power Spectrum (MPS (Singh & Theunissen, 2003), characterizing the power of the signal as a function of temporal and spectral modulations; see Methods; Fig. 1A and 1B).

While the mean pitch is not significantly different between discomfort and pain cries (Mixed-effects linear model, Wald Test  $z = 1.634$   $p = 0.102$ ), discomfort cries have a more stable pitch than pain cries whose pitch extends over a wider range and is more modulated (Fig. 1C, Discomfort panel: the central region in red near 3 cyc/KHz indicates a pitch around 330 Hz; Fig. 1C, Pain panel: the red regions around the 3 cyc/kHz blue region highlight that the range of pitches increased  $\sim$  from 250 to 580 Hz, with corresponding additional increases in rapid frequency modulation power for those extreme values of pitch -20 to 20 Hz). Pain cries are also marked by wider amplitude modulations (Fig. 1C, Pain panel: temporal modulations power along the x axis, i.e. with 0 cyc/kHz). In addition, pitch saliency is significantly lower in pain cries, meaning that they are on average more noisy and less tonal than discomfort cries (Mixed-effects linear model,  $dSal = -0.1 \pm 0.06$  (2SE);  $z = -3.364$ ;  $p = 0.001$ ).

### **Individual signatures are less reliable in pain cries than in discomfort cries**

We quantified the possibility of identifying babies from their cries using cross-validated supervised classifications with machine learning algorithms. The classifiers were tested and trained with the Modulation Power Spectra (MPS). The MPS was chosen as a feature space because it captures all of the joint spectral and temporal structure present in the sound signals without making *a priori* assumptions on what constitutes informative features. In addition, by being phase invariant, the MPS is also insensitive to the order of these features outside of its window of analysis. Contrary to spectrograms, MPS across exemplars for particular conditions (e.g. baby in discomfort) can be averaged: spectral-temporal features found in all cries will add up whereas they would get smoothed away in the average spectrogram. Figure 2 shows the confusion matrices illustrating the correct classification probabilities obtained with linear discriminant analyses. The cries were correctly attributed to the emitting babies in  $43.4 \pm 9.2\%$  (mean  $\pm$  2SE) of cases when the classifier was trained with discomfort cries and then tested with different cries but recorded in the same discomfort context (Fig. 2A; cries from 9 babies for which we had at least 10 samples of discomfort cries; chance level = 11%; see Methods for details). This result confirms the presence of a well-defined individual signature in discomfort



**Figure 2. Individual signatures are less reliable in pain cries than in discomfort cries.** Linear Discriminant Analysis (LDA) based on the MPS. Nine babies for which we had at least 10 samples of discomfort cries were used. The graphs represent the confusion matrices for the 9 different babies obtained with cross-validation. The classifier was either trained and tested with discomfort cries only (A), with both discomfort and pain cries (B), or trained on discomfort cries then tested on pain cries (C). Correct classification drops when trained on discomfort cries and tested on pain cries.

cries. When the classifier was trained and then tested with a mix of discomfort and pain cries, the reliability of the classification decreased (mean  $\pm$  2SE = 40.0%  $\pm$  7.9; Fig. 2B), suggesting that pain cries carry less individual information than discomfort cries. The identification of the crying babies became significantly weaker when the classifier had to assign identity to pain cries when it had been trained with discomfort cries (mean  $\pm$  2SE = 34.5%  $\pm$  15.8; Fig. 2C). For all three combinations of training and test data sets, the level of correct classification was significantly higher than chance (Fisher's exact test,  $p < 3.0e-06$ ; see details in Supplementary Table 1), highlighting that pain cries nevertheless retain a certain amount of information about the baby's identity. To confirm this analysis, we tested the performance of other classifiers (quadratic discriminant analysis QDA and Random Forest RF) which gave similar results (Supplementary Table S1).

To specify the acoustic features carrying the individual signatures, we then trained new LDA, QDA and RF classifiers using either the 22 Predefined Acoustic Features or a subset of 10 PAFs retaining only the spectral features of the cries (see Methods for a list of parameters). These approaches using the PAFs gave lower classification values than those using the MPSs, which is not surprising since the MPSs represent the spectro-temporal structure of the signal more

holistically than a set of discrete acoustic parameters (see Supplementary Fig. S2 and Supplementary Table S2). However, similar to what we obtained with the MPSs, the performance of the classifier using the 22 PAFs and trained with discomfort cries dropped from 35.6% when tested with other discomfort cries to 17.4% when tested with pain cries (Fisher's exact test for independence  $p=0.0001$ ). These performances are similar to those obtained by the classifier using the 10 selected PAFs, suggesting that the most salient acoustic features characterizing the information for baby identity are contained in the spectral shape of the cry, its tonality (pitch salience), and the fundamental (pitch) and its modulations (30.7% of correct classification when tested on discomfort cries using the 10 selected PAFs; see supplementary Fig. S2 and Table S2).

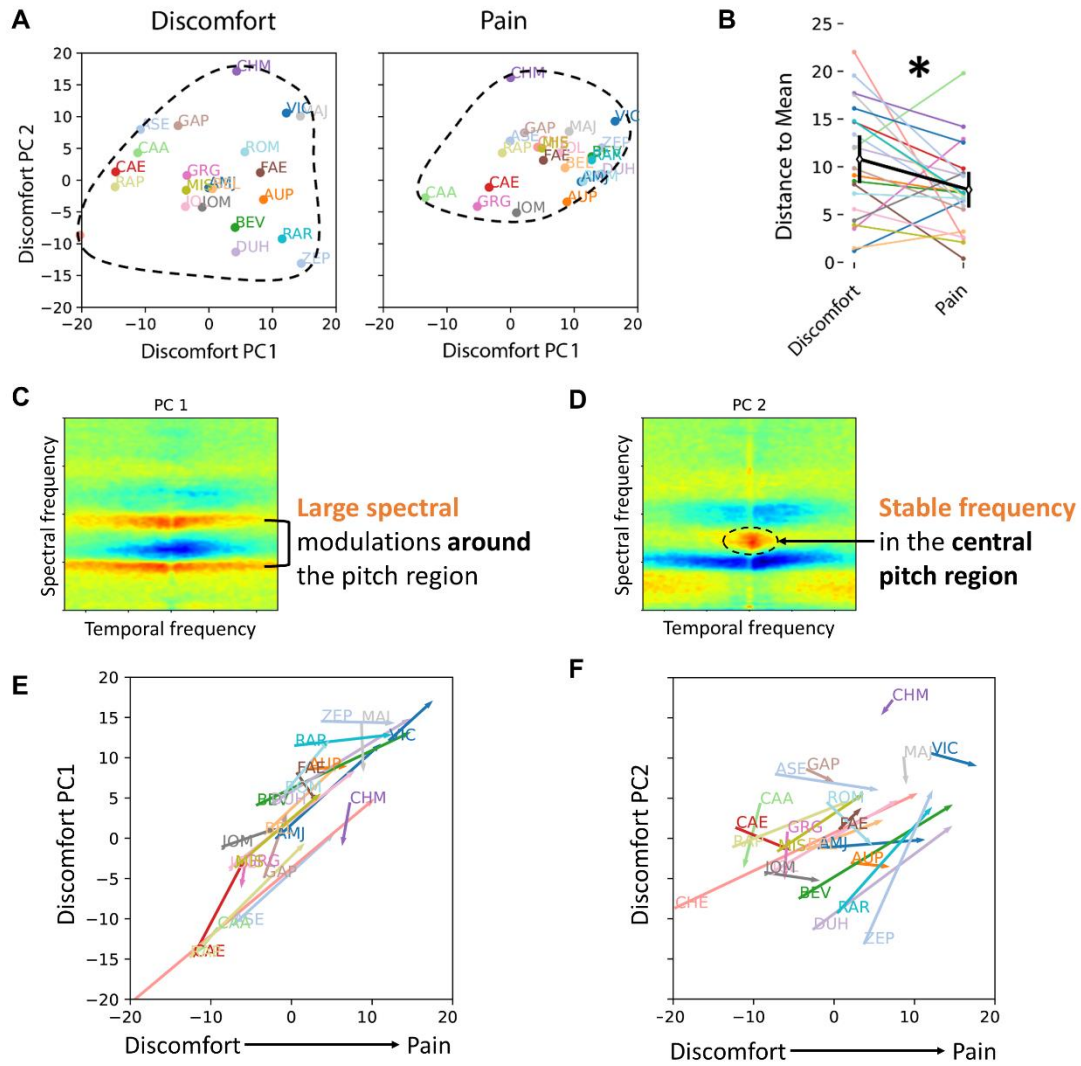
### **The acoustic space of pain cries is shrunk compared to discomfort cries**

Figure 3A shows the average positions of each baby's discomfort cries (Fig. 3A left) and pain cries (Fig. 3A right) in a two-dimensional space defined by the first two Principal Components of the Modulation Power Spectra in the discomfort condition (these two PCs capture 55% of the variability between discomfort cries, and are equivalent to linear discriminant functions describing the best acoustical subspace for discriminating baby identity using discomfort cries; see Methods for details of this MPS dimensional reduction). As can be seen by comparing the distribution of discomfort cries and pain cries (respectively the left and right panels of Fig. 3A), the pain cries occupy a smaller area in the acoustic space than the discomfort cries. This observation is consistent with the result of the classifiers we reported earlier: it is more difficult to discriminate between babies on the basis of their cries of pain than by using their cries of discomfort.

We quantified this contraction of the acoustic crying space in the pain condition by calculating the distance between the average position of each baby's cries in the 2D acoustic space and the centroid (average position) of all the babies' cries. As shown in Figure 3B, this distance decreases significantly in the pain condition for the vast majority of babies, which highlights the greater homogeneity of pain cries between babies (mean distance in the discomfort condition =  $10.80 \pm 2.50$  (2SE); mean distance in the pain condition =  $7.61 \pm 1.87$  (2SE); paired t-test  $D = 3.19$ ;  $t(21) = 2.251$ ;  $p = 0.0352$ ).

To test whether pain cries could still encode an individual signature but along acoustic dimensions distinct than those obtained from discomfort cries, we repeated the previous





**Figure 3. The acoustic space of pain cries is shrunk compared to discomfort cries.** (A) Individual signature in the acoustic space of discomfort cries is degraded in pain cries. The average modulation power spectrum (MPS) for each baby is plotted in a 2D acoustic space defined by the first two principal component coefficients (PC1, PC2) of discomfort cries, in the discomfort and pain condition. The pain condition results in a shift of PC1 towards higher values as well as a reduction of the acoustic space spanned (dotted circles). (B) The distance between the average position of each baby's cries and the centroid decreased significantly in the pain condition. (C) and (D) The two first Principal Component PC1 and PC2 derived from the Modulation Power Spectra. (E) Trajectories in acoustic space of each baby cries from average discomfort (base of arrow) to average pain (arrowhead). The x-axis is the single discriminant function in the MPS that best separates cries obtained in the discomfort condition from cries obtained in the pain condition. The y-axis are the positions in the first principal component obtained from the average MPS per baby in the discomfort condition. The first acoustic dimension that best discriminates the identity of the babies in the bath condition is very similar to the best acoustic dimension that separates discomfort from pain cries. (F) A large fraction of the information that is available along discriminant dimension for the identification of the baby identity in the discomfort condition is lost in the pain condition. Similar representation of each baby cries in the acoustic space as 3E, the y-axis being the positions in the second principal components derived from the MPS. The spread of the data points is reduced as one goes from discomfort to pain.

analysis in a space where the two dimensions corresponded to the first two principal components of the MPS of pain cries and no longer discomfort cries (see Supplementary Fig. S3). While this approach optimized the discrimination of babies recorded in the pain condition, we did not observe any significant variation in the occupation of the acoustic space between the discomfort and pain conditions (mean distance to the centroid in the discomfort condition =  $8.30 \pm 1.73$ ; mean distance to the centroid in the pain condition =  $9.77 \pm 2.13$ ;  $t(21) = -1.141$ ;  $p = 0.2666$ ).

### **The main acoustic dimension carrying individuality is similar to the one separating discomfort cries from pain cries**

Figure 3 (panels C and D) shows how the two Principal Components PC1 and PC2 derived from the Modulation Power Spectra capture the variability of discomfort cries between different babies. The first PC (PC1, Fig. 3C) is characterized by broad spectral modulations framing the pitch. This means that inter-individual differences between cries are particularly explained by variations in pitch modulation (i.e., some babies produce cries whose pitch varies little over time, while others modulate the pitch of their cries more strongly). As we reported in the first part of the results, variations in pitch modulation are also an essential dimension of the difference between discomfort and pain cries. Figure 3E illustrates this correlation between the PC1 dimension separating individual babies (Y-axis) and the dimension separating discomfort cries from pain cries (X-axis). On the figure, each baby is represented by an arrow, the base of which indicates the average position of its discomfort cries and the tip the average position of its pain cries. The arrows are essentially oriented along the diagonal axis of the graph, highlighting a strong correlation between the two axes of the graph (correlation between the X and Y coordinates of the discomfort cries:  $r = 0.899$ , Fisher's exact test  $p = 1.295e-08$ ; correlation for the pain cries:  $r = 0.903$ ,  $p = 8.933e-09$ ;  $N = 22$  babies). It is therefore remarkable that the coding of individual identity is to a good extent along the same dimension as the coding of the discomfort versus pain context.

The second Principal Component (PC2, Fig. 3D) that best discriminate discomfort cries between babies is characterized by a constriction of the central region of the pitch (red region) and by an inhibitory band (blue) highlighting a reduction in spectral modulations. This means that the inter-individual differences are based on differences in the absolute value of the pitch (i.e. each baby will emit their cries with an own average pitch value). As shown in Figure 3F, there is also some correlation between the PC2 dimension separating individual babies (Y axis)

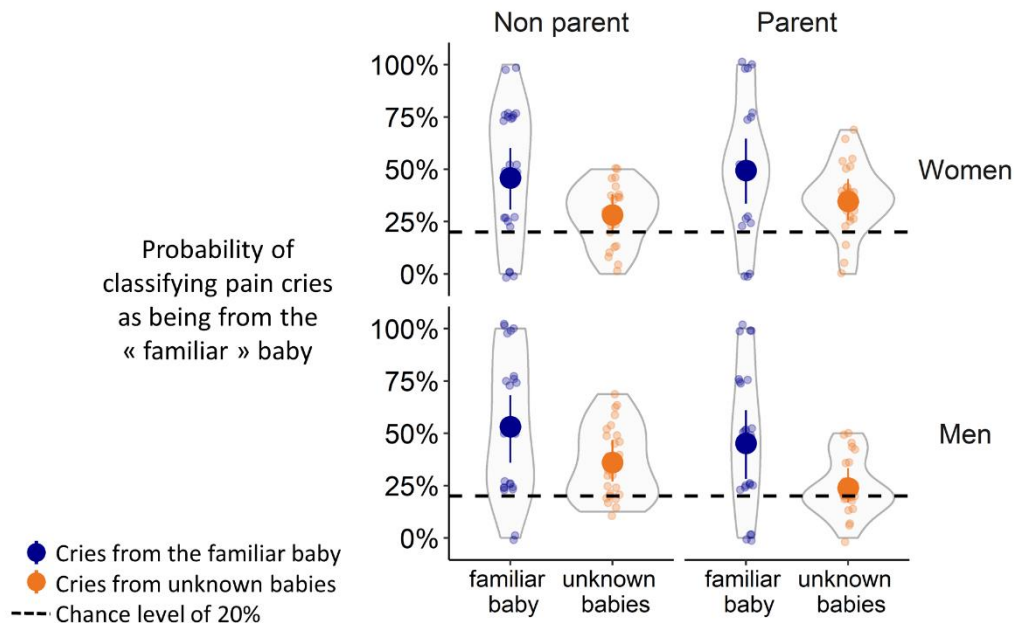
and the dimension separating discomfort cries from pain cries (X axis) but it is much weaker (correlation between the X and Y coordinates of the discomfort cries:  $r=0.382$   $p=0.07913$ ; correlation for the pain cries:  $r=0.468$   $p=0.02791$ ). In addition, although the distribution of the orientation of the arrows indicating the trajectories followed by each baby from their discomfort cries to their pain cries is more random than for PC1, it nevertheless shows a reduction in the dispersion of cries when moving from the discomfort context to the pain context (distance from the mean for the discomfort condition =  $6.03 \pm 1.93$  (2SE); for the pain condition =  $3.75 \pm 1.30$  (2SE); difference = 2.280;  $t(21) = 2.282$ ;  $p = 0.033$ ). Much of the information available along this second dimension to discriminate babies in the discomfort condition is thus lost in the pain condition.

### **Identifying a familiar baby from their pain cries is challenging for human listeners**

We tested whether adult listeners are able to extract information about a baby's identity from their pain cries. Participants ( $N = 100$ ) first listened to discomfort cries from a "familiar" baby (two training sessions one day apart, 5 different cries from the same baby per session, different cries between sessions). A few hours later (mean delay =  $6.4 \pm 4.4$  h, min-max = 3-22.6), the participants listened to 20 different pain cries, including 4 cries from their "familiar" baby and 16 cries from unknown babies (2 boys, 2 girls; see Methods for details), which they had to classify as either "familiar" baby or "unknown" baby.

The tested listeners were able to identify their familiar baby from their pain cries significantly better than chance (Bayesian mixed model, median of the posterior for correct recognition 48.5%, 95% CI [35.1, 59.8], chance level of  $4/20=20\%$ ; Fig. 4). Despite a relatively high false positive rate (cries from unknown babies considered to be from the familiar baby; 30.8% (95% CI [24.3, 38.8]), familiar babies were 17.7% more likely to be identified than unknown babies (95% CI [1.7, 30.6]). We found no significant difference in this ability to recognize the familiar baby between women and men (-1.4% [-13.3, 11.3]), nor between parents and non-parents (-2.2% [-14.5, 11.4], Fig. 4). Mothers and non-parent men had a higher probability of false-positive errors than fathers, with 10.6% [1.7, 19.5] and 12.1% [2.4, 21.6] more errors respectively.

To compare the ability of human listeners with that of a machine learning algorithm, we trained an LDA classifier with the MPS by faithfully reproducing the experimental design used with humans (i.e. 10 training cries per familiar baby and 20 cries of pain – 4 from the familiar baby



**Figure 4. Identifying a familiar baby by their pain cries is challenging for human listeners.** Results of the playback test. Circles represent the individual data and solid disks the medians of the posteriors distributions, with bars indicating the 95% CI. The dotted lines indicate the 20% chance level. Subjects were able to recognize a familiar baby from pain cries when they had previously listened only to discomfort cries, but with a high false-positive rate. The ability to identify a familiar baby from pain cries was independent of the listener's sex and parenting experience.

and 16 from unknown babies – for the test phase). The performance obtained with the classifier was similar to that shown by humans (mean  $\pm$  2SE: classifier  $49.4 \pm 6.6$  % versus posteriors for human recognition  $48.2 \pm 12.3$  %). These results suggest that adult listeners are remarkably efficient at capturing the information contained in the set of spectro-temporal features of crying.

## Discussion

In this study, we show that the individual acoustic signature carried by human baby cries emitted in a context of simple discomfort is only partly preserved in cries recorded in a painful context. Pain cries are therefore less individually signed than discomfort cries, making it more difficult to identify a given baby by its cries.

The presence of an individual vocal signature in discomfort cries is an established fact, and can be explained by idiosyncratic characteristics of both the sound source (values of the fundamental frequency of the cry) and the vocal tract (length and shape of the tract) (Gustafsson

et al., 2013). Previous studies have thus shown that mothers recognize their own babies by their cries of discomfort (Morsbach & Bunting, 1979; Valanne et al., 1967). This ability is acquired through exposure to the baby in the first few days after birth (Bouchet et al., 2020). If they are caring for their baby, fathers are as good as mothers at identifying them by their cries (Gustafsson et al., 2013), and non-parents become able to identify an assigned baby after a short exposure (Bouchet et al., 2020). In the present study, we again demonstrated the importance of learning to identify a baby using their cries. Intriguingly, our results highlight a convergence of these individual signatures in the acoustic space of cries when looking at pain cries. This suggests that babies share, to some extent at least, the same ways of expressing pain through their cries. This “universal coding” of pain comes at the expense of the coding of individual identity.

The fact that the principal component PC1 that best characterizes the individual signatures carried by discomfort cries in the acoustic space of cries is similar to that separating discomfort cries from pain cries may seem surprising. Rather, it was expected that the acoustic dimensions coding for static information (individual signatures) would be different from those coding for dynamic information (distress level). This result suggests two hypotheses. Firstly, the strength of individual signatures in discomfort cries, illustrated by the wide dispersion of babies on the PC1 acoustic dimension, may reflect small variation in the morphology of the vocal apparatus (larynx and vocal tract) of each individual. A second hypothesis is that not all babies are similarly affected in our condition of mild discomfort (bathing), creating *de facto* acoustic differences between individuals in this context. In either case, this variability may be blurred in pain cries as the vocal apparatus is pushed towards extreme and features specific to distress (e.g. unstable source) take over the available acoustic space.

However, the individual signature carried by discomfort cries is not limited to the PC1 acoustic dimension. Primarily linked to the fundamental frequency of the cry (perceived as the pitch of the voice), the second dimension PC2 also plays an important role. Previous research has shown that this acoustic parameter is an essential marker of sender identity, and that it is highly stable: the pitch of a baby’s discomfort cries predicts the pitch of its voice at the age of 5 (Levrero et al., 2018), and even in adulthood (Fouquet et al., 2016). In adults, differences between individuals’ mean fundamental frequencies are preserved between speech types (Pisanski et al., 2021) and in non-verbal vocalizations (Pisanski et al., 2020). In painful situations, babies experience excitation of the autonomic nervous system and a decrease in their vagal tone (Porter et al., 1988; Soltis, 2004). These changes result in increased tension in the structures of the

vocal tract (intrinsic contraction of the larynx and tension of the vocal folds) which have an impact on the fundamental frequency of the cry (Branco et al., 2007; Porter et al., 1988). Moreover, as a result of irregular or asynchronous vibration of the vocal folds (Fitch et al., 2002; Tokuda, 2018), the fundamental frequency of the cry as perceived by a listener (i.e. the pitch) is modified by the presence of nonlinear acoustic phenomena characteristic of pain cries (deterministic chaos, biphonation and subharmonics) (Anikin et al., 2021; Koutseff et al., 2017). Not only these nonlinear phenomena, which are inherently less stable and thus likely to fragilize source-related cues to identity, but they can also lead to “pseudoformants” that will also weaken the production and perception of filter-related cues to identity.

The number of false positives (i.e., cries from unknown babies mistakenly attributed to the assigned baby) is an interesting element to take into account. In previous studies that also tested recognition of babies by their cries, the proportion of false positives was around 20%. In other words, when an adult hears a cry of discomfort from an unknown baby, they declare it to be their baby around 1 in 5 times (17% in parents (Gustafsson et al., 2013) and 23% in non-parents (Bouchet et al., 2020) tested with cries of discomfort; 21% in mothers tested with cries of hunger (Valanne et al., 1967); 25% in mothers tested with a mix of cries of hunger and pain (Wiesenfeld et al., 1981)). Our results show that the proportion of false positives rises to 30% when a baby is identified solely on the basis of pain cries. The loss of individual information in pain cries therefore accompanies an increase in false positives. Identifying stranger babies as own when in doubt gives a margin of safety to the baby-caregiver communication system, reducing the risk of failing to respond in a situation where promptness to respond is paramount to the baby’s survival. This communication trade-off, in which the ability to identify a baby decreases with increasing distress could represent an ecological advantage in the context of the cooperative breeding characteristic of the human species (Hrdy, 2007). Any potential caregiver, parent or non-parent, will essentially receive “pain” information that will be little noised by the baby’s “individual identity” information, which may encourage cooperation.

From a methodological point of view, our study illustrates the interest of considering a holistic description of the acoustic structure of signals rather than a description by discrete variables, when we are interested in the quantity of information carried by signals. Thus, classifier results are better when they work on the basis of modulation spectra than when they are based on a set of pre-defined parameters. The modulation spectrum representation of sound better captures signal-specific features.

However, our study has a number of limitations. The first is the limited number of pain cries available for each baby (only 4 pain cries per individual). Pain cries were recorded during vaccine injections, and it was obviously not possible to induce them over a prolonged period. For both classifier training and playbacks with human participants, we took the precaution of considering only babies for whom we had at least 10 different discomfort calls. This avoided over-fitting the classifiers and the opportunity for participants to learn. However, the limited number of pain cries per baby allowed only a partial representation of the range of cries potentially emitted by each baby. It is possible, for example, that cries emitted in a more painful context would be even less individually signed. It is however important to note that pain cries are typically rare, thus giving little opportunity for caregivers to learn the voice of individual babies during their development. From this perspective, it appears adaptive to favor the expression of distress and urgency in these contexts.

A second limitation is that participants only completed a short training session (10 short sequences of discomfort cries). This degree of exposure to cries is certainly much less than that actually experienced by parents in everyday life, where learning opportunities from their baby's cries are frequent and repeated. Our experimental protocol, in which participants listen to an assigned baby's cries from headphones, is also far from natural conditions where the baby's physical presence and the attachment bonds they develop with their caregivers certainly influence learning to recognize their cries.

**In conclusion, the present study shows that static information (vocal signatures) and dynamic information (stress level) compete in babies' cries as they are not encoded by fully independent acoustic features. Indeed, the emergence of distress-induced information in pain cries is at the expense of static cues to identity. While this may result from biomechanical constraints affecting sound production by a highly aroused, tensed vocal apparatus, it also makes sense from a survival perspective to favor the communication of urgency over identity in high distress contexts. This observation makes sense in the light of the cooperative nature of the human species: a baby in pain, having become less identifiable, should increase its chances of being rescued by any potential caregiver, related or not.**

**Authors contributions.** SC: conceptualization, methodology, investigation, formal analysis and data curation (psychoacoustic experiment), writing – original draft; CF: conceptualization, methodology, funding acquisition, writing – review & editing; HP: resources (cries recording), funding acquisition; RP: conceptualization, funding acquisition, writing – review & editing; DR: conceptualization, methodology, funding acquisition, writing – review & editing; FT: methodology, investigation, formal analysis and data curation (acoustic analysis and machine learning), writing – original draft; NM: conceptualization, methodology, writing – original draft, project administration, funding acquisition.

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**Declaration of interests.** The authors declare no competing interests.



## **STAR Methods**

### **Resource availability**

#### *Lead contact*

Further information and requests for resources and reagents should be directed to and will be fulfilled by the lead contact, Nicolas Mathevon (mathevon@univ-st-etienne.fr).

#### *Material Availability*

This study did not generate new unique reagents.

#### *Data and code availability*

- Dataset have been deposited on GitHub and will be publicly available as of the date of publication.
- The R code used to analyze the human subject's classification performance has been deposited on GitHub and will be publicly available as of the date of publication.
- The BioSound Python libraries used to extract the bio acoustical features (PAFs and MPS) and perform supervised classification are publicly available at Github (<https://github.com/theunissenlab/soundsig>) and includes with jupyter notebooks as tutorials (<https://github.com/theunissenlab/BioSoundTutorial>). A release version with DOI will be made at the time of publication.
- The custom code that uses BioSound to perform the acoustical and corresponding clustering and statistical analyses on this data set has been packaged as a separate set of jupyter notebooks. This python coded will be available on Github and a DOI for a frozen version will be generated at the time of publication.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

### **Experimental model and study participant details**

A total of 120 participants were recruited through the Prolific online platform ([www.prolific.co/](http://www.prolific.co/)). Once recruited, participants were redirected to the Labvanced online platform (<https://www.labvanced.com/>) (Finger et al., 2017) where the experiment was hosted. After completing the experiment, subjects were redirected to Prolific and paid at the recommended rate of 7.5 GBP per hour. All self-reported to have normal hearing.

Sixteen of them dropped out before the testing session, giving data for 104 participants. To ensure data quality in the context of online experiments, all submissions were manually screened for obvious cheating. Data from four participants were excluded because of abnormally long reaction time, responding always the same, or launching copies of the experiment leading to training on both assigned and stranger babies cries. Analysis were therefore done on 100 participants, who were distributed as follows:

- 50 participants were non-parents (N = 25 men, 25 women, mean age =  $23.1 \pm 4.2$  years);
- 50 participants were parents of at least one child younger than 2 years old (N = 25 fathers, 25 mothers, mean age =  $33.5 \pm 4.9$  years).

All participants lived in Europe. The majority of participants (90 out of 100) were Europeans. The remaining 10 participants were from a variety of countries (North America, South America, Africa, Middle East). Due to French legislation, no data on race or ethnicity was collected.

The experiment was approved by the local ethics committee (October 2019 – Comité d’Ethique du CHU de Saint-Etienne, Institutional Review Board: IORG0007394), and informed consent was obtained from all participants.

## **Methods details**

### *Sound recordings*

Cry recordings were extracted from a cry database previously built by the ENES Laboratory (Koutseff et al., 2017). Discomfort cries were recorded during bathing, undressing, or dressing by parents at the baby’s home. Pain cries were recorded during scheduled routine vaccination at the doctor’s office (N = 22 babies, 10 boys and 12 girls; age =  $60.3 \pm 3.4$  days on the vaccination day; delay between recording sessions of discomfort cries and pain cries for a given baby =  $6.9 \pm 3$  days, see (Koutseff et al., 2017) for a complete description of the recording parameters).

Using Audacity software ([www.audacityteam.org](http://www.audacityteam.org)), we isolated 284 cry sequences from these raw recordings (mean sequence duration =  $6.3 \pm 1.1$  s; 4 sequences of pain cry per baby and 2-19 sequences of discomfort cry per baby). We took care to isolate sequences without background noise such as adult voices, water flowing or door slamming.

The sound intensity of the cry sequences was normalized to 100% of the maximal amplitude using the “normalize” function of the tuneR R package ([cran.r-](http://cran.r-)

project.org/web/packages/tunerR/index.html). These sequences were used as stimuli during the experiment, and are referred to as “discomfort cries” and “pain cries”.

### *Acoustic analyses*

A total of 22 predefined acoustic features (22 PAFs) are extracted from the measures obtained from the amplitude envelope (mean, sd, skew, kurtosis, entropy, rms, max), the power spectrum (mean, sd, skew, kurtosis, entropy, Q1, Q2 or median, Q3), the time-varying fundamental (meanF0, MaxF0, MinF0, cvF0, pitch-saliency) and the average frequency of the first two formants (F1, F2). See (Elie & Theunissen, 2016) for additional details on how these values are calculated. In some analyses we restricted the 22 PAFs to a subset of 10 capturing the fundamental and spectral features (Q1, Q2, Q3, meanF0, MaxF0, MinF0, cvF0, pitch-saliency, F1, F2).

The modulation power spectrum (MPS) is obtained by calculating and averaging the amplitude of the 2D Fourier Transform (FT) of log of the spectrogram in 1s ( $1s=6sd$ ) gaussian windows. The spectrogram was calculated using a gaussian window with a width in the frequency dimension set at 50 Hz ( $50Hz = 6sd$ ), in what is often referred to as a narrow-band spectrogram. Before taking the 2D FT the log spectrogram of each baby cry by normalized by its maximum dB value and, after this normalization, minimum values were bounded at -50 dB. The MPS estimated from this normalized log spectrogram is insensitive to the overall rms of the sound and simply captures the overall presence of structure characterized by relative power in specific joint spectral-temporal modulations. Because the MPS is high dimensional, it was projected to a subspace determined by its first 20 principal components (PCs). These PCs are equivalent to the linear discriminant functions that describe the best acoustical subspace for discriminating baby identity, assuming equal and diagonal covariance matrix. The first 2 PCs captured 55% of this between baby MPS variance in the discomfort cries. The first PC (PC1) captures a spread of the spectral-temporal modulations around the central pitch region and is strikingly similar to the difference in average MPS observed between discomfort and pain (compare Fig. 2B, PC1, with Fig. 1C, Pain-Discomfort). The second PC (PC2) captures a sharpening of the central pitch region associated with more stable pitch (i.e. continuous) at the corresponding fundamental frequency. The inhibitory (blue) band shown for lower spectral modulations will also result in higher PC2 coefficient values for cries that lack power in these lower frequency modulations, which correspond to higher value of the pitch fundamental.

All the acoustic parameters were estimated using the BioSound python package (<https://github.com/theunissenlab/BioSoundTutorial>).

To visualize the individual signature of the baby cries and how this signature changes in the two conditions, we plotted the average MPS represented by its first two principal component coefficients (PC1, PC1) in the two conditions. To quantify this reduction in individual signature, we estimated the distance of each MPS to the average across babies in this 2D acoustic space. We repeated the analysis but by calculating the PCs in the Pain condition instead of the discomfort condition and this finding acoustic dimensions optimized to separate babies from their cries in the Pain condition.

### *Supervised Classification*

Linear Discriminant Analysis (LDA) was used to assess the discriminability of the baby identity based on acoustic features. Nine babies for which we had at least 10 samples of discomfort cries were used. Posterior probabilities obtained in cross-validation were represented with confusion matrix. This LDA was done using either the 22 predefined acoustic features (PAFs), limited to a subset of 10 spectral features or the Modulation Power Spectrum (MPS). We reported the number of correctly classified stimuli in cross-validation. Cross-validation was performed using 10 folds when the fitting and test set of baby cries were taken from the same condition(s) (i.e. discomfort and/or pain). When the fitting and testing set were from different conditions, here discomfort and pain respectively, we used all the data in the discomfort condition for fitting and all the data available in the pain condition for testing. Analyses were repeated using Quadratic discriminant analysis (QDA) and Random Forest Classifiers (RF). LDA, QDA and RF were performed using Python scikit-learn package (1.2.2). Additional custom python code was used to perform the cross-validation and, as needed, dimensionality reduction of the feature space to ensure robustness. This supervised classification code is also part of the BioSound package (<https://github.com/theunissenlab/BioSoundTutorial>). A Fisher exact test was performed to directly compare the number of baby cries in the cross-validation set whose identity was correctly identified to the number expected by chance given the total sample size. Fisher exact tests were also used to compare classification performance under different conditions, again based on the number of babies correctly classified and the sample size in each condition.

### *Psychoacoustic experiment*

The experimental procedure included two successive training sessions over two days followed by a test session a few hours later (Corvin et al., 2022) (mean delay from the end of the second training session to the beginning of the test session =  $6.4 \pm 4.4$  h, min-max = 3-22.6). During the training sessions, participants listened to discomfort cries from their assigned, “familiar” baby (5 different cries per session; different cries between sessions). During the test session, participants listened to 20 different pain cries, including 4 pain cries from their “familiar” baby and 4 pain cries from 4 unknown babies (2 boys, 2 girls), presented in random order.

The discomfort cries used as stimuli in the training sessions came from the 9 babies (3 boys, 6 girls) for whom we were able to extract at least 10 discomfort cry sequences. In order to diversify the identity of the babies, the pain cries used as stimuli in the test session were extracted from the recordings of the 22 babies (i.e. from the complete databank). Randomization of stimuli among the tested listeners was performed using an R script implementing the “sample” function.

At the beginning of each training session, participants were given the following instruction: “You are going to hear several cries of one baby, who will be named YOUR baby for the rest of this study”. Then, the participants’ task during the test session was to decide whether each cry they heard was produced by their “familiar” baby or by an unknown baby. The playback experiment was designed to elicit 20% “yes” responses (4 out of 20 cries from the familiar baby) and 80% “no” responses (16 out of 20 cries from unknown babies). Participants were unaware that the cries were from different contexts (discomfort cries for training and pain cries for testing). To avoid decision bias, participants did not know how many cries came from their assigned baby or how many different babies they were listening to.

## **Quantification and statistical analysis**

### *Acoustic features*

We used mixed effect statistical modeling to assess differences in acoustical features between cries produced either in the discomfort or pain condition. The response variable was the acoustic feature. The fixed effects were baby’s sex and condition and their interaction, and the random effect was the intercept for each baby. We used Wald test to assess whether the coefficients for the fixed effects were significantly different from zero. The mixed effects statistical modeling was performed using the `mixedlm()` function from the Python package *statsmodels* (v0.13.5).

*Psychoacoustic experiment*

Statistical analyses were performed in R (v4.2.2) using Bayesian mixed models fitted with the brms R package (Bürkner, 2017). The advantages of using the Bayesian approach are multiple, including its high flexibility, quantification of uncertainty in estimates, and intuitive interpretation of confidence intervals (Kruschke & Liddell, 2018; Kruschke, 2014). Response scores were modeled using a logistic function (Bernoulli family). The outcome variable was the binary “yes/no” response that participants gave when asked whether or not the cry belonged to their assigned baby. The baby status (familiar or unknown), participants’ sex and parental status (parent or non-parent) were included in the model as fixed factors. Participant identity and familiar baby identity were included as random factors. Random slopes were defined using the Watanabe-Akaike information criterion for model selection (WAIC). The structure of the model in R compact notation was: `rated_baby_status ~ real_baby_status x parentality x sex + (real_baby_status + parentality|babyID_ref) + (real_baby_status|subjectID)`. 3000 iterations were run over two MCMC chains (Markov chain Monte Carlo) with the first 1000 iterations of each chain used to adjust the algorithm. To improve convergence when modeling response scores, we specified mildly informative priors (distribution (0,1), chance level at 20%). Results were summarized as medians of the posterior distributions and 95% credible intervals (CIs). Credible intervals for estimates above the chance level indicate a credible effect given the observed data and model structure (Kruschke & Liddell, 2018). Similarly, when contrasting two conditions, CIs excluding the null value can be inferred to indicate a credible difference between the conditions.

**Supplemental information**

**Supplementary tables**

Type	Features	LDA Correct	QDA Correct	RF Correct	Tested	LDA Pval	QDA Pval	RF Pval	LDA Post	QDA Post	RF Post	LDA Post 2SE	QDA Post 2SE	RF Post 2SE
Discomfort/ Discomfort	MPS	65	55	51	116	6,81E-32	1,52E-22	3,20E-19	43,4	45,8	36,5	9,2	9,3	8,9
Mixed/ Mixed	MPS	78	77	79	152	2,41E-34	2,01E-33	2,81E-35	40	41,6	35	7,9	8	7,7
Discomfort/ Pain	MPS	15	12	15	36	2,72E-06	0,00033807	2,72E-06	34,5	29,1	28,2	15,8	15,1	15

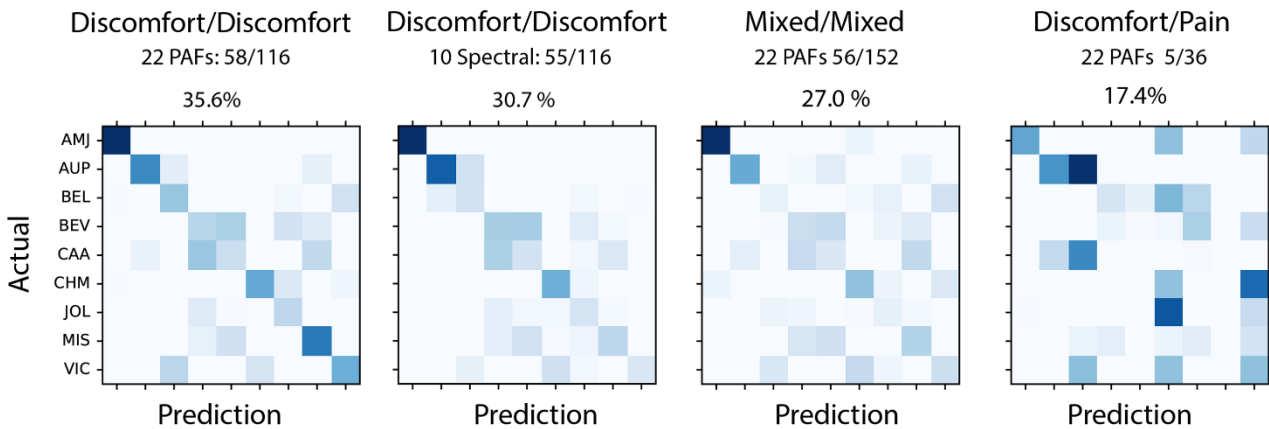
***Table S1. Machine learning results based on the Modulation Power Spectrum (MPS), related to Figure 3A. Results of the Linear Discriminant Analysis (LDA), the Quadratic discriminant analysis (QDA) and Random Forest Classifiers (RF) with 3 different training/testing sets: Discomfort/Discomfort, Mixed/Mixed or Discomfort/Pain.***

Type	Features	LDA Correct	QDA Correct	RF Correct	Tested	LDA Pval	QDA Pval	RF Pval	LDA Post	QDA Post	RF Post	LDA Post 2SE	QDA Post 2SE	RF Post 2SE
Discomfort/ Discomfort	PAFs	58	67	58	116	3,40E-25	6,09E-34	3,40E-25	35,59	46,48	35,58	8,89	9,26	8,89
Discomfort/ Discomfort	10 Spectral	55	57	65	116	1,52E-22	2,69E-24	6,81E-32	30,73	42,43	34,88	8,57	9,18	8,85
Mixed/ Mixed	PAFs	56	63	81	152	1,05E-16	1,04E-21	3,54E-37	27,05	35,63	32,08	7,21	7,77	7,57
Discomfort/ Pain	PAFs	5	11	8	36	0,37093716	0,00134559	0,04084098	17,42	24,42	19,03	12,64	14,32	13,08

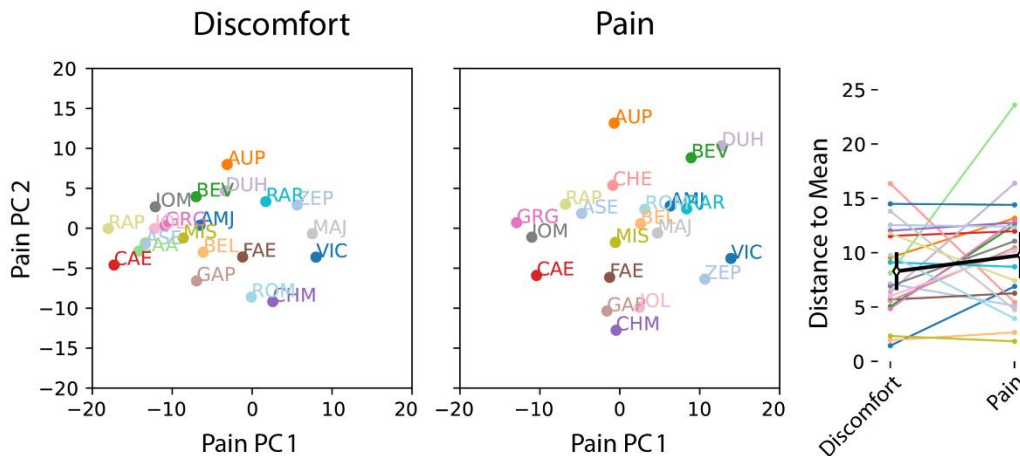
**Table S2. Machine learning results based on the Principal Acoustic Features (PAFs) or 10 selected spectral features, related to Figure S3. Results of the Linear Discriminant Analysis (LDA), the Quadratic discriminant analysis (QDA) and Random Forest Classifiers (RF), with 3 different training/testing sets: Discomfort/Discomfort, Mixed/Mixed or Discomfort/Pain.**



**Supplementary figures**



**Figure S2. Linear Discriminant Analysis (LDA) Results Based on PAFs, related to Figure 2.** LDA was used to assess the discriminability of the baby identity based on acoustic features. Nine babies for which we had at least 10 samples of discomfort cries were used. Confusion matrices of posterior probabilities obtained in cross-validation are represented. The 22 predefined acoustic features (PAFs) are used except for the second left panel where the acoustic features are limited to a subset of 10 spectral features. The title above shows the condition of the stimuli used in training/validation. The numbers on the second line show the number of correctly classified stimuli in the cross-validation. The percent indicated above each confusion matrix is the average of the “diagonal”.



**Figure S3. Variability in individual signatures are lower and not coded differently in the acoustic space of pain cries compared with discomfort condition, related to Figure 3.** We repeated the analysis shown in Fig. 2 but by calculating the PCs in the Pain condition instead of the discomfort condition and this finding acoustic dimensions optimized to separate babies from their cries in the Pain condition. In this representation, there is not difference in the extend of the acoustic area spanned ( $t(21)=-1.141$   $p=0.2666$ ).

## Chapter II: Pain perception in babies cries

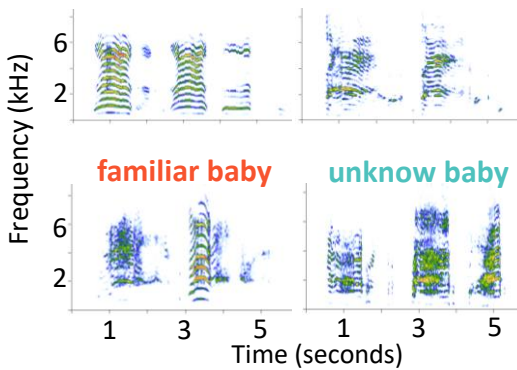
# Graphical abstract: Pain perception in babies cries

Siloé Corvin, Camille Fauchon, Roland Peyron, David Reby, Nicolas Mathevon

discomfort cries



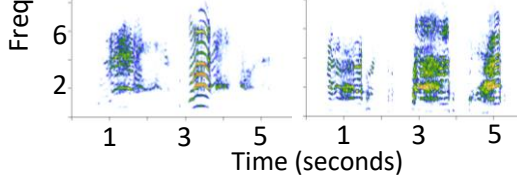
familiar baby      unknown baby



pain cries



familiar baby      unknown baby



## Emotional and physiological state

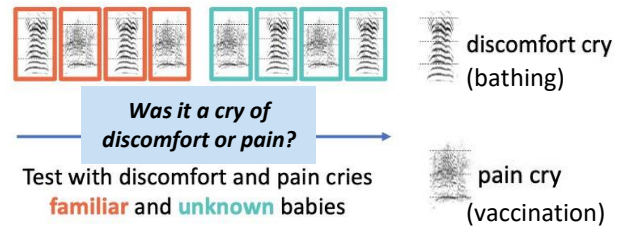
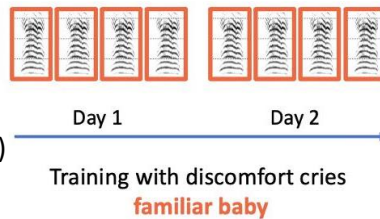
Pain cries are longer, louder, harsher and rougher  
Parents identify a pain state by listening to their baby's cries

*Does experience in babies care, familiarity with a given baby or younger age improve caregivers' ability to identify pain in cries?*

## Methods

Online experiment

363 participants (age 18-87) with various experience in babies care



## Results



No experience (no previous contact with babies; N = 50)

Poor recognition of cries context



Moderate experience (babysitting, younger siblings; N = 51)

Effective recognition of pain cries for a familiar baby



Strong experience parents (with > 5 years-old baby; N = 50)

Effective recognition of cries context for a familiar baby and of bath context for an unknown baby



Strong experience parents (with < 2 years-old baby; N = 52)

Effective recognition of cries context for both a familiar and an unknown baby



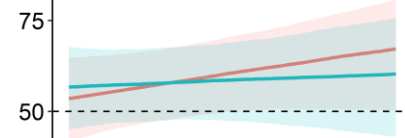
Strong experience non parents (professional caregivers; N = 31)

Effective recognition of cries context for a familiar baby and of bath context for an unknown baby

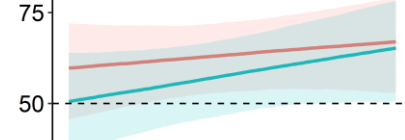
■ familiar baby      ■ unknown baby

50 % = chance level for context recognition (discomfort or pain)

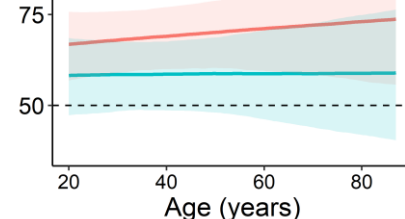
No experience



Past experience



Current experience



**A. Adults learn to identify pain in babies cries.**

**B. The ability to decode babies' cries does not decline with age**

**Conclusion:** Exposure through caregiving and/or parenting shapes the auditory and cognitive abilities involved in decoding the information conveyed by the baby's communication signals. This ability is maintained with age which comforts alloparents' role in babies caregiving.

## **II.1. Adults learn to identify pain in babies cries**

In this first study, we used playback experiments to investigate how experience in babies care and familiarity with a given baby shape the ability to identify pain in cries. This chapter has been published in *Current Biology*.

**Corvin, S., Fauchon, C., Peyron, R., Reby, D., and Mathevon, N. (2022). Adults learn to identify pain in babies' cries. *Current Biology* 32, R824–R825. [10.1016/j.cub.2022.06.076](https://doi.org/10.1016/j.cub.2022.06.076).**

In a side project presented in Annex I, we have extended this question to include causes other than pain (hunger, discomfort, isolation).

# Adults learn to identify pain in babies' cries

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eTOC blurb

Using playback experiments, Corvin et al. show that current parents of young babies are able to identify a baby's pain cries even if they have never heard this baby before, whereas inexperienced individuals are typically unable to do so. This shows how parenting shapes our ability to decode the information conveyed by babies' communication signals.

\*\*\*

Because the expression of pain in babies' cries is based on universal acoustic features, it is assumed that adult listeners should be able to detect when a crying baby is experiencing pain<sup>1-5,51-54</sup>. Here, we show that detecting that a baby's cry expresses pain actually requires learning through experience. Indeed, our psychoacoustic experiments reveal that adults with no experience of caring for babies are unable to identify whether a baby's cry is a pain cry induced by vaccination or a mild discomfort cry recorded during a bath, even when they are familiar with the discomfort cries from this particular baby. In contrast, people with prior experience of babies (parents or professional caregivers) identify a familiar baby's pain cries without having heard these cries before. Parents of very young children are even able to identify the pain cries of a baby who is completely unfamiliar to them. These results underline the extent to which exposure through caregiving and/or parenting shapes the auditory and cognitive abilities involved in decoding the information conveyed by the baby's communication signals.

In mammals, parental care is often accompanied by striking acoustic displays from the offspring<sup>55</sup>. These vocalizations -called "distress calls" or "cries"- are typically triggered by pain, discomfort, hunger, or separation from parents or other caregivers<sup>56</sup>. While some of the information carried by these calls is static and relates to individual characteristics of the emitter (sex, age, size), some is dynamic and related to their current emotional and physiological states (immediate needs)<sup>4</sup>. Caregivers can therefore acquire critical information by listening to these vocalizations, and the amount of parental care they will provide depends primarily on this information<sup>3,57</sup>.

The expression of pain is vital information that prompts caregivers to act<sup>58</sup>. Compared with signals of lesser distress, infant cries expressing pain are longer, louder, with more variable pitch, as well as harsher and rougher due to nonlinear phenomena (chaos, sub-harmonics, etc)<sup>6,59</sup>. Previous studies have highlighted the ubiquity of these pain-coding acoustic features in infant cries from a range of mammalian species, and suggested that caregivers are able to innately decode these universal acoustic properties<sup>5,510-513</sup>. However, recent research has shown that experience and familiarity can affect the perception of infant cries, both between and within species. For example, human listeners unfamiliar with bonobos and chimpanzees have a limited ability to range the emotional content of these apes' infant vocalizations, because humans rate these usually high-pitched calls according to the same scaling rule they use for human babies<sup>514</sup>. More crucially for our species, it is well-established that exposure

and familiarity improve the ability of human parents to recognize their babies from their cries, suggesting that experience shapes our ability to decode infant cries<sup>7,8</sup>. However, the factors driving human listeners' judgements and responses to baby cries have not been thoroughly explored<sup>2</sup>, and it is not known whether experience improves caregivers' ability to judge whether a baby's cry is expressing pain.

In the present study, we tested the hypothesis that having prior caregiving experience with babies facilitates the identification of cries expressing pain. We predicted that listeners with extensive prior exposure to baby cries (such as parents or baby care professionals) would be more successful at this task. We also predicted that listener familiarity with the cries of a given baby would facilitate the identification of their pain cries. To test this we recorded cries produced by babies in two contexts: mild-discomfort cries given during bathing at home and pain cries during a vaccination sequence in the paediatrician's medical office (Figure 1A), and then conducted psychoacoustic experiments with adult participants having different levels of experience with babies: individuals with no experience with babies (N = 25 men, 25 women), non-parents with moderate non-professional experience such as occasional babysitting or caring for younger siblings (N = 25 men, 26 women), parents with children at least 5 years old at the time of the experiments (N = 25 fathers, 25 mothers), parents with babies less than 2 years old (N = 25 fathers, 27 mothers), and non-parents with extensive professional caregiving experience (N = 1 man, 30 women).

The experimental procedure consisted of a training phase followed by a test phase (Figure 1B). During the training phase which occurred on two successive days, each participant heard 8 different discomfort cries (4 on each day) from the same assigned baby (mean duration of sequences =  $6.3 \pm 1.1$  seconds). Previous studies have established that adult listeners become familiar with an assigned baby's cries after a small number of short crying sequences, and quickly become able to recognize this familiar baby from their cries alone<sup>8</sup>. A few hours after the end of the training phase, each participant entered the test phase in which they listened to new cry sequences from their familiar baby (2 discomfort and 2 pain cries) and from an unknown baby (2 discomfort and 2 pain cries), and was asked to categorise each of these cries as "discomfort" or "pain" (see Supplemental information for methodological details).

The results show that listeners' ability to categorize baby cries as discomfort or pain depends on their prior and current experience with babies (Figure 1C, Table S1). Nonparents without experience with babies were unable to identify the two contexts better than chance (Bayesian mixed model, 54.3 % of correct recognition, 95 % CI [45.9, 62.3], 84.4 % of the posterior distribution PD above the chance level of 50 %). Nonparents with moderate experience showed a moderate ability to identify the crying context (57.3 % [49.0, 65.0], 96.2 % of PD > 50 %), only recognizing the pain cries of their familiar baby better than chance (65.3 % [51.8, 77.3]). In contrast, adults with strong experience with babies, either because they were parents or because they were pediatric care professionals, identified the crying context of their familiar baby better than chance (65.5% [56.4, 74.1], 71.2 % [61.7, 78.9] and 71.1% [60.2, 80.2] with 99.9, 100 and 100 % of PD > 50 %, respectively for parents of children older than five years of age, parents of younger babies, and professional pediatric caregivers). Remarkably, parents of younger babies were also able to identify the crying contexts of an unknown baby they had never heard before (64.2 % [53.8, 73.1], 99.5 % of PD > 50 %). Interestingly, we found that both parents of children older than five and non-parents with extensive experience performed at chance level in their ability to identify pain cries from an unfamiliar baby. This is consistent with observations indicating that experienced listeners can develop a resistance that decreases their sensitivity to acoustic cues of pain<sup>S3, S15, S16</sup>. We found no effect of listener sex (see Supplemental information for details of the results).

In short, our results indicate that having experience with babies facilitates the correct identification of pain condition through the use of acoustic information. The acquisition of this ability through exposure is likely supported by the neurobiological changes that accompany parenthood and, more generally, infant care<sup>9,10,S17,S18</sup>. From an evolutionary perspective, it is now well established that humans are cooperative breeders, which is rare among primates<sup>S19</sup>. Human baby cries have thus evolved in a network of emitters and listeners, including the core of the baby's family (the baby, mother, father and siblings) as well as other potential caregivers (e.g. grandparents and more distant relatives, unrelated individuals)<sup>S20,S21</sup>. Our study shows that it is through experience that these diverse caregivers become expert interpreters of the infants' cries, allowing them to efficiently identify, and thus appropriately respond to the encoding of pain in cries.



## Supplemental information

Supplemental information including experimental procedures, one table, references and sound files can be found with this article online at [XXX](#).

## References

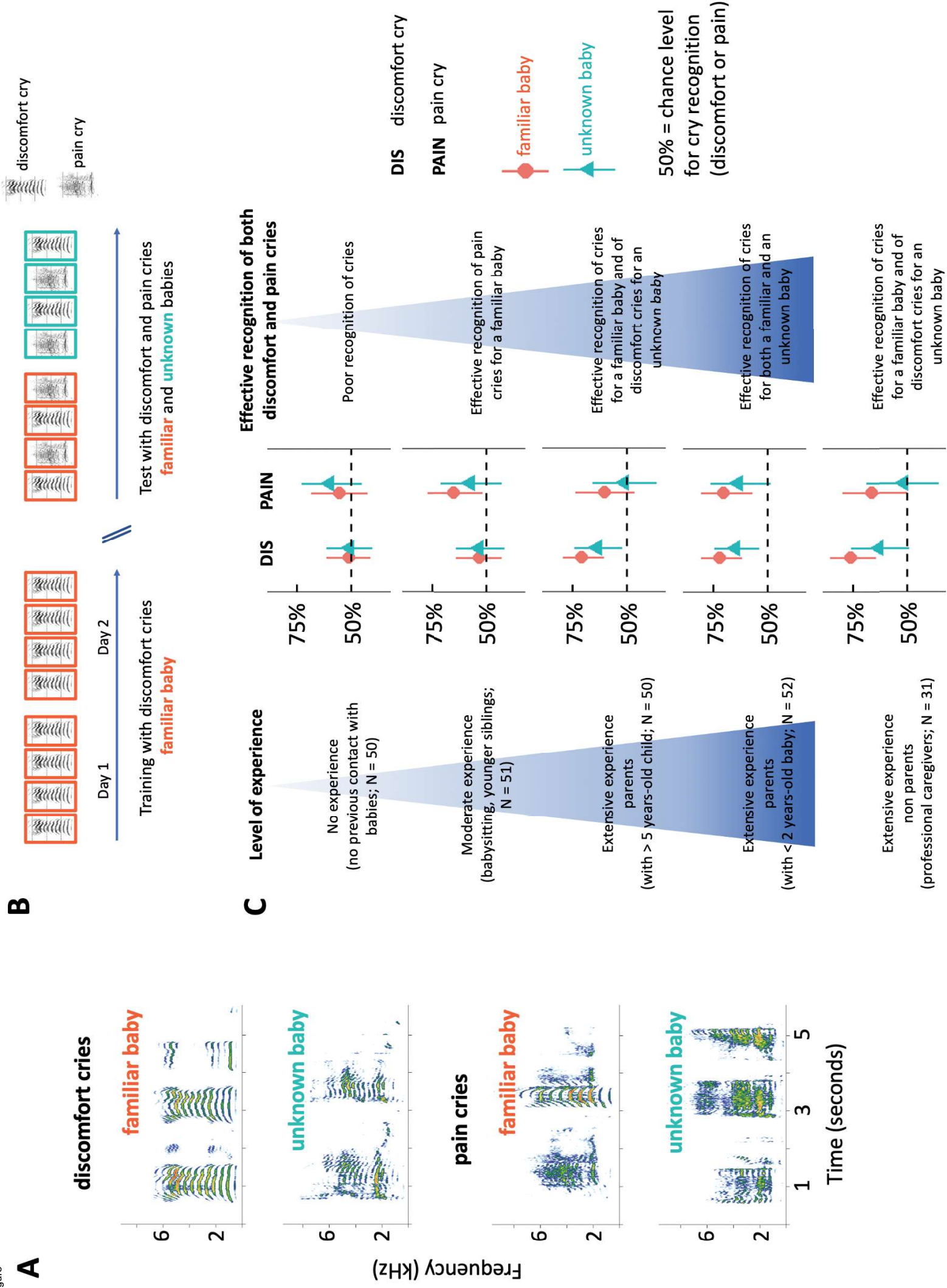
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## Declaration of Interests

The authors declare no competing interests.

## Figure Legend

**Figure 1. Playback experiment testing the ability of Human adult listeners to identify pain in a baby's cry.** (A) Examples of babies' cries used in the experiments. Pain cries differ from discomfort cries by being more chaotic (higher levels of roughness). The cries are from two different babies, highlighting the inter-individual differences (these sound files are available as Supplementary material). (B) Timeline of the experimental procedure. Adult subjects began by hearing discomfort cries from an assigned baby in two successive sessions (training sessions with a « familiar » baby; cries previously recorded while the baby was bathing; 8 different cry sequences from the same baby; duration of cry sequences =  $6.3 \pm 1.1$  seconds). In a second step, subjects listened to successive sequences of cries from either their familiar baby or an unknown baby (4 different sequences from each baby). The cries were either discomfort cries or pain cries (recorded during vaccination sessions). Subjects were asked to classify each cry as either « discomfort » or « pain » cry. The discomfort cries from the familiar baby were different between the training and test sessions. Familiar and unknown babies differed between the tested subjects. The order of presentation of the discomfort and pain cries was random, and the order of presentation of the familiar and unknown baby cries was balanced among the tested subjects (see Supplemental Information for details). (C) Results of the playback tests. Solid disks and triangles represent the medians of the posterior distributions, with bars indicating the 95% CI. The dotted lines indicate the 50% chance level. The ability of tested adults to recognize cries as cries of "discomfort" or "pain" depended on their experience with babies. Whereas inexperienced individuals randomly categorized both the familiar and unknown baby's cries, parents currently raising a baby correctly identified the cries in both cases. Overall, the ability to identify cry is improved by prior and current experience with babies.



**SUPPLEMENTAL INFORMATION**

	No experience	Moderate experience	Extensive experience: parents with > 5 years-old baby	Extensive experience: parents with < 2 years-old baby	Extensive experience: non-parents professional caregivers
Age: mean ± SD (min-max)	24.3 ± 5.4 (18-39)	24.2 ± 4.7 (18-38)	40.0 ± 5.6 (28-50)	32.3 ± 5.5 (20-40)	28.7 ± 6.7 (23-51)
Correlation between age and success	r=0.03; p=0.85	r=0.11; p=0.42	r=0.22; p=0.11	r=0.04; p=0.78	r=0.21; p=0.26
Nationality of participants	Average success in % (number of participants)				
Belgium	62,5% (2)		62,5% (1)		
Brazil		75% (1)			
Bulgaria			75% (1)	62,5% (2)	
Colombia				50% (1)	
Egypt			50% (1)		
Estonia				62,5% (2)	
France		50% (2)	58,3% (3)		62,5% (27)
Germany	50% (1)	37,5% (1)	75% (1)		
Hungary	75% (1)				
India	75% (1)	75% (1)		25% (1)	
Iran		87,5% (1)			
Ireland		75% (1)	70,8% (3)	62,5% (1)	
Israel				62,5% (1)	
Italy	54,2% (9)	55,4% (14)	57,5% (5)		75% (2)
Latvia				75% (1)	
Lithuania				87,5% (1)	
Luxembourg		50% (1)			
Morocco		75% (1)			
Netherlands			50% (2)	75% (2)	
Nigeria		62,5% (2)		75% (2)	
Pakistan		75% (1)	62,5% (1)		
Poland	50% (1)		62,5% (1)	60,4% (12)	
Portugal	54,2% (21)	52,1% (12)	51,8% (7)	43,8% (2)	75% (2)
Romania				75% (1)	
Russian Federation			75% (1)	87,5% (2)	
Serbia		25% (1)			
Spain	56,3% (2)	62,5% (5)	70% (5)	75% (1)	
Syrian Arab Republic		12,5% (1)			
Turkey	37,5% (2)	75% (1)			
Ukraine	37,5% (1)				
United Kingdom	47,2% (9)	57,5% (5)	60,3% (17)	71,1% (19)	
United States				87,5% (1)	
NA			100% (1)		

	Discomfort cries		Pain cries		Familiar baby (discomfort and pain cries)	Unknown baby (discomfort and pain cries)
	Familiar baby	Unknown baby	Familiar baby	Unknown baby		
Nonparents without experience with babies	54.3 [45.9 - 62.3]		P(δ>50) = 84.4%		53.3 [43.7 - 62.8] P(δ>50) = 75.8%	55.3 [45.1 - 64.6] P(δ>50) = 85.7%
	51.0 [42.4 - 59.7] P(δ>50) = 59.8%		57.7 [45.0 - 69.0] P(δ>50) = 89.7%			
	51.1 [41.0 - 61.2] P(δ>50) = 58.6%	50.8 [40.1 - 61.3] P(δ>50) = 56.5%	55.4 [42.3 - 68.3] P(δ>50) = 80.0%	59.9 [45.1 - 72.6] P(δ>50) = 91.1%		
Nonparents with moderate experience	57.3 [49.0 - 65.0]		P(δ>50) = 96.2%		59.4 [49.9 - 68.2] P(δ>50) = 97.4%	55.4 [45.1 - 64.6] P(δ>50) = 85.6%
	53.4 [44.5 - 62.0] P(δ>50) = 78.4%		61.3 [49.2 - 72.4] P(δ>50) = 96.9%			
	53.5 [43.1 - 64.1] P(δ>50) = 74.3%	53.3 [41.7 - 64.1] P(δ>50) = 71.8%	65.3 [51.8 - 77.3] P(δ>50) = 98.3%	57.6 [42.7 - 70.8] P(δ>50) = 84.8%		

Parents with child at least 5 years old	61.4 [53.3 - 69.3] P( $\delta > 50$ ) = 99.5%				65.5 [56.4 - 74.1] P( $\delta > 50$ ) = 99.9%	57.2 [46.8 - 67.1] P( $\delta > 50$ ) = 92.5%
	67.1 [58.7 - 74.7] P( $\delta > 50$ ) = 100%		55.8 [43.4 - 67.6] P( $\delta > 50$ ) = 83.8%			
	70.8 [60.6 - 79.2] P( $\delta > 50$ ) = 100%	63.7 [51.9 - 73.9] P( $\delta > 50$ ) = 98.8%	60.4 [46.3 - 73.5] P( $\delta > 50$ ) = 93.4%	51.2 [36.4 - 65.6] P( $\delta > 50$ ) = 56.9%		
Parents with baby under 2 years old	67.6 [59.6 - 74.8] P( $\delta > 50$ ) = 100%				71.2 [61.7 - 78.9] P( $\delta > 50$ ) = 100%	64.2 [53.8 - 73.1] P( $\delta > 50$ ) = 99.5%
	68.3 [59.8 - 76.0] P( $\delta > 50$ ) = 100%		66.8 [55.0 - 76.9] P( $\delta > 50$ ) = 99.5%			
	72.2 [61.7 - 80.8] P( $\delta > 50$ ) = 100%	64.7 [53.6 - 74.6] P( $\delta > 50$ ) = 99.5%	70.4 [57.1 - 80.7] P( $\delta > 50$ ) = 99.6%	63.7 [48.8 - 76.3] P( $\delta > 50$ ) = 96.5%		
Professional caregivers	64.1 [54.8 - 72.7] P( $\delta > 50$ ) = 99.7%				71.1 [60.2 - 80.2] P( $\delta > 50$ ) = 100%	57.2 [45.5 - 69.0] P( $\delta > 50$ ) = 88.4%
	69.5 [59.4 - 78.5] P( $\delta > 50$ ) = 100%		58.8 [45.0 - 71.6] P( $\delta > 50$ ) = 90.1%			
	76.3 [64.3 - 85.3] P( $\delta > 50$ ) = 100%	63.1 [49.1 - 75.7] P( $\delta > 50$ ) = 96.6%	66.4 [49.9 - 79.7] P( $\delta > 50$ ) = 97.4%	51.5 [35.5 - 68.6] P( $\delta > 50$ ) = 57.2%		

**Table S1. Age and nationality of participants and results of the analysis of participants' responses to the playback experiment.** Adult subjects listened to cries from either a familiar baby or an unknown baby. They were asked to classify each cry as either « discomfort » or « pain » cry. Bayesian mixed model: outcome variable = success in recognizing the context of crying (discomfort or pain); fixed factors = correct context (discomfort or pain), baby status (familiar or unknown), participant experience with babies (5 levels of experience; see Supplemental Experimental Procedures for details); random factors = participant identity and baby identity. Posteriors distributions of model parameters are summarized by their medians, 95% credible intervals, and the percentage of posteriors being above the chance level of 50%.

## **Supplemental experimental procedures**

### **Sound recordings**

Cry recordings were extracted from a cry database previously built by the ENES Laboratory<sup>4</sup>. Discomfort cries were recorded during bathing, undressing, or dressing by parents at the baby's home. Pain cries were recorded during scheduled routine vaccination at the doctor's office (N = 22 babies, 10 boys and 12 girls; age = 60.3 ± 3.4 days on the vaccination day; delay between recording sessions of discomfort cries and pain cries for a given baby = 6.9 ± 3 days). Two different vaccine were injected: a hexavalent DTPa-HBV-IPV/Hib vaccine (Infanrix Hexa®) and a 13-valent pneumococcal conjugate vaccine (Prevenar 13®). Cries were recorded with a microphone (Sennheiser MD42) placed at about 30 cm from the baby and connected to a portable digital audio recorder (Zoom H4n, sampling rate = 48 kHz, uncompressed .wav files). Using Audacity software (www.audacityteam.org), we isolated 284 cry sequences from these raw recordings (mean sequence duration = 6.3 ± 1.1 s; 4 sequences of pain cry per baby and 2-

19 sequences of discomfort cry per baby). We took care to isolate sequences without background noise such as adult voices, water flowing or door slamming.

To limit pseudoreplication of stimuli among the participants tested in the playback experiment, we retained only those babies for whom we had at least 10 sequences of discomfort cry and 4 sequences of pain cry ( $N = 9$ ; 3 boys, 6 girls). The sound intensity of the cry sequences was normalized to 100% of the maximal amplitude using the “normalize” function of the tuneR package ([cran.r-project.org/web/packages/tuneR/index.html](http://cran.r-project.org/web/packages/tuneR/index.html)). These sequences were used as stimuli during the experiment, and are referred to as “discomfort cries” and “pain cries”.

## Participants

Participants ( $N = 234$ ) were recruited through the online platform Prolific ([www.prolific.co/](http://www.prolific.co/)). They all reported normal hearing and were distributed as follows (mean age =  $30 \pm 8.2$  years, min-max = 18-51, Table S1):

- 50 participants were non-parents with no experience with babies (25 men, 25 women; mean age =  $24.3 \pm 5.4$  years, min-max = 18-39);
- 51 participants were non-parents, had never had a child, and had moderate, nonprofessional experience with babies, such as occasional babysitting or looking after younger siblings (25 men, 26 women; mean age =  $24.2 \pm 4.7$  years, min-max = 18-38);
- 50 participants were parents with children who were at least 5 years old at the time of the experiment (25 fathers, 25 mothers; mean age =  $40.0 \pm 5.6$  years, min-max = 28-50).
- 52 participants were parents with at least one child under 2 years old at the time of the experiment (25 fathers, 27 mothers; mean age =  $32.3 \pm 5.5$  years, min-max = 20-40);
- 31 participants were non-parents, had never had a child, and had extensive professional experience with babies (30 women, 1 man; mean age =  $28.7 \pm 6.7$  years, min-max = 23-51; mean duration of professional exposure to babies =  $5.2 \pm 5.4$  years, min - max = 5 months - 20 years).

All participants lived in Europe. The majority of participants (213 out of 234) were Europeans. The remaining 21 participants were from a variety of countries (India, North America, South America, Africa, Middle East).

Once recruited, participants were redirected to the Labvanced online platform (<https://www.labvanced.com/>) where the experiment was hosted. After completing the experiment, subjects were redirected to Prolific and paid at the recommended rate of 7.5 GBP per hour.

To ensure that participants were homogeneously motivated to participate in the test, we recruited regular users of the Prolific platform. On this platform, each participant is characterized by a Prolific score based on the approval/rejection ratio obtained during their participation in previous Prolific studies. When selecting subjects, we imposed a minimum threshold of 75/100 for this score. In the end, the average scores were much higher than this threshold, (around 99 for all groups tested), attesting to the high level of engagement of participants regardless of their category. Both the drop-out rate (number of participants who dropped out before the end/number of participants who started the study) and the time taken by participants to answer each question (reaction time) were similar between groups (drop-out rate: min-max = 14-18 %; reaction time: min-max = 2-3 seconds).

### **Experimental procedure**

The experimental procedure consisted of two successive phases: a training phase in which participants listened to the discomfort cries of an assigned baby, and a testing phase in which participants were asked to rate the cries of their assigned baby and those of an unknown baby as “discomfort cry” or “pain cry”. The timeline of the experiment is shown on Figure 1B.

At the beginning of their training session, participants received the following instruction: “You are going to hear several cries of one baby, who will be named YOUR baby for the rest of this study. YOUR baby is in the bath, it is uncomfortable, YOUR baby is crying.” Then they listened to a succession of four discomfort cries from their assigned baby. This training was repeated a day later, using four more discomfort cries from the same assigned baby.

Participants then performed their test session a few hours after the end of the second training session (mean =  $6.8 \pm 5.5$  h, range [3 - 29.3 h]). During the test, they listened to two successive sets of four cries: two pain cries and two discomfort cries presented in a random order. One of the two sets of cries came from their assigned, “familiar” baby. The other set of cries came from an unknown baby. The order of presentation of the two sets, familiar and unknown, was balanced among the participants. Before the start of each set of cries, participants were informed whether they would hear the cries of their assigned baby or an unknown baby. After each cry,

participants were asked to estimate in a two-alternative forced choice whether the cry they heard was due to discomfort or pain. Participants were not told how many cries of discomfort or pain they would listen to.

Each participant was trained and tested with different cries, which avoided the possibility of idiosyncratic acoustic characteristics biasing the results. Randomization of cry stimuli across participants was achieved using the “*sample*” function in R statistical software (<https://www.r-project.org/>).

In this study, we chose to train the subjects only with discomfort cries because this design corresponds to the most common situation in real life. Indeed familiarity is expected to be acquired in discomfort cries rather than pain cries, as caregiver will regularly hear a baby crying in discomfort (during bathing, nappy changing, etc.), whereas they should rarely hear a baby crying in pain.

### **Data analysis**

Participants’ responses were analyzed with a Bayesian mixed model using the Stan modeling language (*brms* R package, [cran.r-project.org/web/packages/brms/index.html](https://cran.r-project.org/web/packages/brms/index.html)). The outcome variable was success in recognizing the context of crying (discomfort or pain). Correct context (discomfort or pain), baby status (familiar or unknown), and participant experience with babies were included in the model as fixed factors. Participant identity and baby identity were included as random factors. Random slopes were defined using the Watanabe-Akaike information criterion for model selection (*WAIC*). To improve convergence and avoid overfitting, we specified mildly informative conservative priors. Posteriors distributions of model parameters were summarized by their medians and 95% credible intervals, reported as 95% CIs. The structure of the model in *brms* syntax was as follows: `success ~ baby_status x experience x correct_context + (baby_status + correct_context | subjectID + babyID_stim)`.

Furthermore, focusing on the four groups of participants with a balanced number of men and women (i.e., excluding the group of participants with high professional experience with babies that was predominantly composed of women), we tested the potential effect of participant sex using the following model: `success ~ sex * baby_status * experience * correct_context + (baby_status + correct_context | subjectID + babyID_stim)`. We found no effect of participants’ sex on the attribution of cry context (in contrast to men, women were 1.2 % more successful [-4.5, 6.8], 66.3 % of posterior distribution (PD) > 0).



**Ethical statement.** All experiments were approved by the local ethics committee (October 2019 – Comité d’Ethique du CHU de Saint-Etienne, Institutional Review Board: IORG0007394), and informed consent was obtained from all participants.

**Resource availability.** The distribution of the sound stimuli among the tested listeners, the code for the statistical analysis, the sound files used in the experiments, and any other material are available upon request ([mathevon@univ-st-etienne.fr](mailto:mathevon@univ-st-etienne.fr)).

**Authors contributions.** All authors conceived the original idea for this research and designed the experiments. SC conducted the experiments and analyzed the results. All authors helped shape the research, analysis and manuscript. SC and NM took the lead in writing the manuscript with the help of CF and DR. All authors provided critical feedback.

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## II.2. Old but attuned: The ability to decode babies' cries does not decline with age

In this second study, we kept the same experimental design to investigate whether listener age compromise the ability to identify pain and discomfort in babies cries. This chapter is in preparation for *Proceedings of the Royal Society B: Biological Sciences*.

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### **Abstract**

In our ageing cooperative breeder societies characterized by a considerable increase in life expectancy, old grandparents often take an important role in the upbringing of children, even providing care in newborn. However, the general ability to identify emotions is known to decline with advancing age. Does this loss of emotional sensitivity compromise the ability of the elderly to assess babies' needs? Here we show that regardless of age, prior experience with babies and familiarity with a given baby make adults better at discriminating pain from discomfort in a baby's cry. We also show that this ability tends to increase with age, and that even very old participants retain full performance. We suggest that the accumulation of exposure and experience with babies over a lifetime may counteract the effect of ageing. As such adults, and therefore grandparents, remain capable of judging whether a baby's cry signals real pain or mere discomfort, an essential skill for alloparenting.

**Keywords:** parenting, aging, cooperative breeding species, baby cry

## **Introduction**

In humans, it is common for people other than biological parents to look after children, taking part in their care and feeding. This alloparenting probably began with *Homo erectus* around 2 million years ago (Hrdy, 2016), and characterizes us as a cooperative breeding species. Alloparents may or may not be genetically related to the children they care for, and their positive impact has been widely demonstrated (Aubel, 2021; Chapman et al., 2023; Hrdy, 2007). In traditional societies, the presence of grandmothers is thus accompanied by better child survival and shorter intervals between pregnancies for mothers (Hawkes & Coxworth, 2013), whereas mothers with limited allomaternal support are more likely to abandon their babies at birth (Hrdy, 2007). Grandmothers' childcare support also plays a major role in modern societies: it helps to improve the child's social and academic functioning, and is particularly valuable when the mother is an adolescent (Zeiders et al., 2015).

Providing appropriate care for babies requires the ability to identify their needs by decoding the visual and vocal signals they emit. Previous studies have shown that aging makes adults less able to identify emotions (Amorim et al., 2021; Lima et al., 2014; Lindová et al., 2015; Malykhin et al., 2023). Recognition of emotional facial expressions and cognitive empathy decline with age (Beadle & de la Vega, 2019; Malykhin et al., 2023). It has also been shown that the ability to decode emotions in adult non-verbal vocalizations is affected by ageing (Lima et al., 2014) and decline sharply after the age of sixty (Amorim et al., 2021). In a study involving participants aged between 16 and 68, younger adults were better than older ones at identifying the context of infant vocalizations (Lindová et al., 2015). However, this study did not take into account the participants' previous experience in caring for babies, a crucial factor that modulates the ability to identify the level of pain encoded by cries (Corvin et al., 2022).

In the present study, we tested the hypothesis that the ability to decode baby cries decreases with age. We conducted playback experiment with participants aged 20 to 87 years, all in good health, to identify whether getting older is accompanied by an increase in difficulty in identifying whether a baby cry signals pain or simple discomfort. We also tested whether previous experience with babies could modulate this ability by comparing people who had never cared for a baby, others who had cared for a baby in the past, and others who were currently caring for a baby.

## **Methods**

### **Participants**

We tested a sample of 309 participants (mean age =  $41.1 \pm 17.2$  years, min-max = 20-87). Participants were recruited on the online platform Prolific ([www.prolific.co/](http://www.prolific.co/)), then directed to the online platform Labvanced (<https://www.labvanced.com/>) where the experiment took place. Once the experiment was completed, participants were paid at the recommended rate of 8.0 GBP per hour. All participants reported having normal hearing. They were distributed as follows (see Table 1 for details):

- 95 participants had no experience with babies (“no experience” group; 48 men, 47 women; mean age =  $39.2 \pm 17.6$  years, min-max = 20-76).
- 81 participants had cared for one or more babies in the past, more than 5 years ago (“past experience” group; 40 men, 41 women; mean age =  $51.1 \pm 18.6$  years, min-max = 20-87).
- 133 participants were currently looking after at least one baby under 2-years old (“current experience” group; 52 men, 81 women; mean age =  $36.4 \pm 13.2$  years, min-max = 20-72).

Age of the participants	20-29 years	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	> 80 years
Participants with no previous experience with babies (men; women)	20;18	6;5	7;5	6;5	6;5	3;4	0;0
Participants with past experience with babies (men; women)	5;6	5;7	12;6	6;5	5;6	6;6	1;5
Participants with current experience with babies (men; women)	16;38	18;29	6;7	5;5	6;4	1;3	0;0

***Table 1. Men and women participants to the playback experiment.***

### **Sound stimuli**

The recordings used to produce the stimuli for the playback experiment were extracted from the cry database of the ENES Bioacoustics Research Laboratory (Koutseff et al., 2017). Pain cries were recorded at the pediatrician’s office during a vaccination session (N = 22 babies, 10 boys and 12 girls; age =  $60.3 \pm 3.4$  days on the day of vaccination). Discomfort cries were recorded at the baby’s home during bathing, undressing or dressing by the parents (time

between recording sessions for discomfort cries and pain cries for a given baby =  $6.9 \pm 3$  days; for details concerning recording conditions see (Koutseff et al., 2017)).

These raw recordings were segmented into 284 cry sequences using Audacity software ([www.audacityteam.org](http://www.audacityteam.org)). We selected only those sequences with an excellent signal-to-noise ratio (mean sequence duration =  $6.3 \pm 1.1$  s; 4 sequences of pain cries per baby and 2-19 sequences of discomfort cries per baby). Furthermore, in order to limit pseudo-reproduction of stimuli in the playback experiment, we retained only those babies for whom we had at least 10 sequences of discomfort cries and 4 sequences of pain cries (N = 9; 3 boys, 6 girls; total = 150 sequences). The sound intensity of the stimuli was normalized to 100% of the maximal amplitude using the “normalize” function in the tuneR package ([cran.r-project.org/web/packages/tuneR/index.html](http://cran.r-project.org/web/packages/tuneR/index.html)).

## **Experimental procedure**

Once recruited, participants were asked to complete the Interpersonal Reactivity Index (IRI) questionnaire (Davis, 1980), whose perspective-taking sub-score characterizes cognitive empathy (Davis, 1983). Next, the experimental procedure consisted of two successive phases (same procedure as in Corvin et al., 2022, Chapter II.1): a training phase in which participants listened to the discomfort cries of an assigned baby, and a testing phase in which participants were asked to rate the cries of their assigned baby and those of an unknown baby as “discomfort cry” or “pain cry” (see Figure 1A). Each participant was trained and then tested with different cries, thus preventing idiosyncratic acoustic characteristics of individual babies from biasing the results. Randomization of cry stimuli was achieved using the “*sample*” function in R statistical software (<https://www.r-project.org/>).

At the beginning of the training session, participants received the following instruction: “You are going to hear several cries of one baby, who will be named YOUR baby for the rest of this study. YOUR baby is in the bath, it is uncomfortable, YOUR baby is crying.” Then they listened to a succession of four discomfort cries from their assigned baby. This training was repeated a day later, using four more discomfort cries from the same assigned baby. Participants then performed their test session a few hours after the end of the second training session (mean =  $6.7 \pm 5.6$  h, range [3 - 29.3 h]). During the test, they listened to two successive sets of four cries: two pain cries and two discomfort cries presented in a random order. One of the two sets of cries came from their assigned, “familiar” baby. The other set of cries came from an unknown

baby. The order of presentation of the two sets, familiar and unknown, was balanced among the participants. Before the start of each set of cries, participants were informed whether they would hear the cries of their assigned baby or an unknown baby. After each cry, participants were asked to estimate in a two-alternative forced choice whether the cry they heard was due to discomfort or pain. Participants were not told how many cries of discomfort or pain they would listen to.

### **Data analysis**

Statistical analyses were performed using Bayesian mixed models fitted with the brms R package (Bürkner, 2017). Response scores were modeled using a logistic function (Bernoulli family). 3000 iterations were run over two MCMC chains (Markov chain Monte Carlo), with the first 1000 iterations of each chain used to tune the algorithm. To improve convergence when modeling response scores, we specified mildly informative priors (distribution (0,1), chance level at 50%). Results are summarized as medians of the posterior distributions and 95% credible intervals (CIs), with one fitted value per year. The chance level was set at 50% as it was a two-forced choice (discomfort/pain) with a balance number of the two conditions. Credible intervals for estimates above the chance level indicate a credible effect, given the observed data and model structure (Kruschke & Liddell, 2018). Similarly, when contrasting two conditions, CIs excluding the null value can be inferred to indicate a credible difference between the conditions.

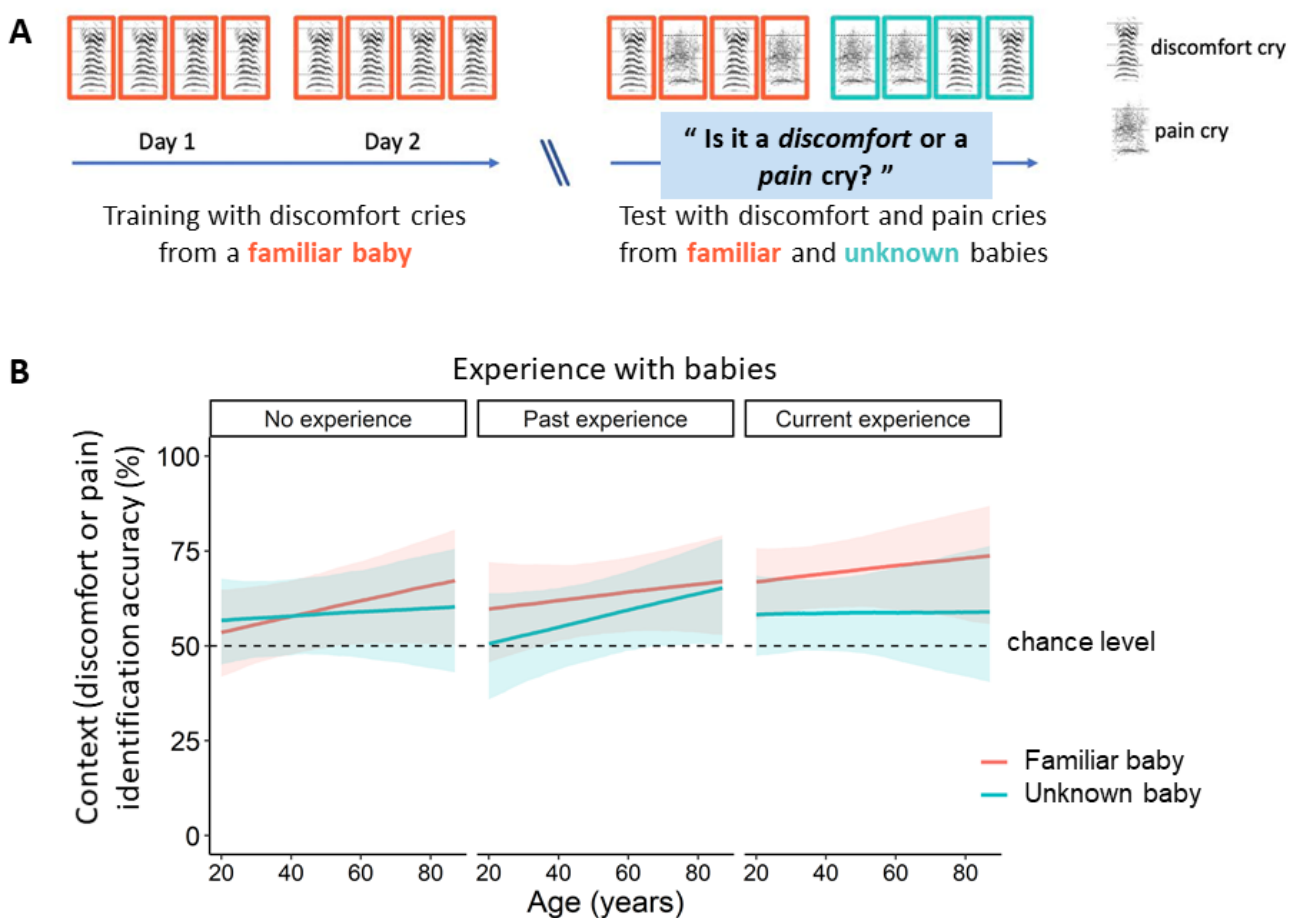
The outcome variable was success in recognizing the context of crying (discomfort or pain). The participant's age, experience with baby care, as well as the baby's status (familiar or unknown), were included in the model as fixed factors. The participant's identity and that of the baby were included as random factors. Random slopes were defined using the Watanabe-Akaike information criterion for model selection (WAIC). The structure of the model in brms syntax was as follows:

```
success ~ age x level_experience x baby_status + (1 | subjectID + babyID_stim)
```

To assess the effect of listener's sex, we added sex as a fixed factor in the previous model.

## Results

As shown in Figure 1B, the participants on average successfully identified the “discomfort” or “pain” contexts of crying and we observed no decline in this ability with the age of the participants (correct recognition = 61.5%, 95% CI [52.6, 69.6]; chance level = 50%). The recognition accuracy was 57.5% (95% CI [48.1, 66.1]) at the age of 20, and increases to 63.5% [54.1, 71.8] at age 70 (5.9% better, [-0.7, 12.4]). Regardless of age, participants were more successful in identifying the crying context when they heard a cry from their assigned (familiar) baby than a cry from an unknown baby (6.3% better, [1.2, 11.2]).



**Figure 1. Aging does not impair the ability to identify whether a baby cry expresses pain or simple discomfort.** A. The protocol consisted of two successive phases: a training phase in which participants listened to an assigned baby's cries of discomfort, followed by a testing phase (playback tests) in which participants had to classify cries from their assigned baby and other cries from an unknown baby as “cries of discomfort” or “cries of pain”. B. Results of the playback tests. Solid lines represent medians of posterior distributions and light areas 95% credible intervals. Dotted lines indicate the 50% chance level. The accuracy of identifying the context of cry emission (discomfort or pain) did not decrease with the age of the participants. Previous experience with babies improved participants' ability to identify the crying context for familiar babies.



Previous experience with babies improved participants' ability to identify the context of crying in familiar babies (recognition accuracy = 60.5% [50.1, 70.3], 63.4% [53.3, 72.4], and 70.4% [60.2, 79.1] respectively for participants with no experience with babies, those with previous experience, and those currently caring for a baby). At the age of 20, participants with no previous experience with babies were unable to identify the crying context of familiar baby (53.6% of accuracy, 95% CI [41.9, 64.9]). However, this category of participants performs better at the age of 60 (61.9% [50.6, 72.2]), and this progression is even more marked in the over-70s (65.6% [50.6, 77.9]). Participants aged 20 with previous experience of babies also failed to recognize familiar baby cries (59.7% [45.7, 72.1]). However, the performance of this category of participants becomes greater from the age of 35 (61.4% [49.9, 71.4]), and is even greater after the age of 70 (66.1% [53.6, 77.1]). Finally, participants currently caring for a baby under 2-years old were able to identify whether cries of a familiar baby have been emitted in a discomfort versus a pain context from the age of 20 with a predicted accuracy of 66.8% [57.0, 75.7]. This ability was maintained, with some progression, in the over-70s (recognition accuracy = 72.9% [57.1, 85.1]).

Participants with no experience of babies were never able to recognize the crying context in unknown babies (58.6% [47.4, 68.9]). We found the same result in participants with past experience of babies at the age of 20 (50.5% [35.9, 63.9]), but these people improved their performance after the age of 70 (61.7% [50.0, 72.8]). Finally, the age of the most experienced participants (with babies under two years of age) did not seem to influence their ability to identify the context of an unknown baby's cry.

Basal levels of empathy were higher for women compared to men for the IRI total score, and all subscores except the perspective taking one. IRI total score, perspective taking and empathic concern subscores were positively correlated with age (Pearson's correlation: respectively  $r=0.20$ ,  $r=0.26$ ,  $r=0.21$ ;  $p<0.001$ ) for both men and women. For all participants, there was no correlation between empathy scores and success in cry context identification, neither IRI total score (Pearson's correlation:  $r = 0.08$ ,  $p = 0.18$ ) nor perspective-taking subscore ( $r = -0.01$ ,  $p = 0.91$ ). Furthermore, the model including the participants' sex did not explain the data any better (WAIC of 3252.6 versus 3239.8 without) and suggested no difference between men and women (-0.3% [-5.6, 5.3]).

## **Discussion**

In this study, we showed that as adults age, they retain the ability to identify whether a baby cry is emitted in a context of simple discomfort or real pain. Our results demonstrate that experience in caring for babies is a predictor of this ability (Corvin et al., 2022, Chapter II.1).

Babies' cries are signals that carry information about the baby's identity and age ("static" information) and immediate needs ("dynamic" information) (Lockhart-Bouron et al., 2023; Mathevon, 2023). Knowing how to identify this information in the cry signal - in other words, being able to decode the information conveyed by the cry - is essential if caregivers are to provide appropriate care. Previous studies have shown that previous experience with babies considerably improves the ability to decode cries, both for static information (Bouchet et al., 2020) and for dynamic information (Corvin et al., 2022). For example, mothers who have already had several children learn to identify their newborn more quickly than primiparous mothers (Bouchet et al., 2020). Parents of young children and healthcare professionals working with babies are much better at identifying pain encoded in babies' cries than inexperienced people (Corvin et al., 2022). The results of the present study confirm this importance of experience and highlight its role throughout life.

Regardless of age, participants currently caring for a baby are the most able to determine whether a cry signals pain or simple discomfort, and therefore whether the baby needs immediate help or not. Not only is this ability not lost in the elderly, but it seems to strengthen, possibly as a result of experience gained over a lifetime. In the same vein, while young adults who have never had to care for babies are only marginally better than chance at identifying the context of a familiar baby's cry, older people who have had no direct experience of baby care are able to do so. This improvement in performance was also found in participants who had cared for a baby in the past. This beneficial effect of age on the ability to decode babies' cries could be explained by the fact that human adults are probably indirectly exposed to babies' cries throughout their lives via their social network (family, friends), the media, or on various occasions such as public transport journeys. It should be noted however that our sample of participants included a higher proportion of parents among the older participants. Indeed, those with no experience were necessarily non-parents, as were younger participants with more than 5 years' experience, mainly acquired through babysitting or looking after younger siblings. In contrast, older participants with past or current experience were almost all parents. It is possible that this favored the older people's ability to decode babies' cries.

Do our results mean that all older people are able to decode babies' cries? Probably not. Indeed, we cannot ignore the fact that advancing age is often accompanied by a decline in sensory and cognitive abilities, along with difficulties in perceiving and analyzing sensory stimuli from the environment (Heft & Robinson, 2017; Humes & Young, 2016; Mather, 2010). In this respect, our sample is certainly biased in favor of people who have retained most of their abilities. First of all, all participants reported normal hearing. While the oldest participants almost certainly had age-related hearing loss, this usually affects high frequencies, starting at around 2 kHz and becoming increasingly significant as the sounds approach 8 kHz (Großmann, 2023). As babies' cries are broadband signals extending over a wide frequency spectrum into the low frequencies (Koutseff et al., 2017), it is unlikely that our participants had issues hearing them. In addition, the perception of roughness, which is the main acoustic property characterizing pain in cries, is little affected by age-related hearing loss (Tufts & Molis, 2007). With regard to the potential impact of cognitive decline with age, participants were enrolled on Prolific© and had to be able to complete the experiment online, with three successive sessions. This involved regularly accessing their mailbox, following a link to the next session and following instructions. Being able to perform these tasks is highly likely to have selected people with conserved cognitive abilities. Furthermore, our results say nothing about the potential effects of age on the behavioral response to crying babies. We cannot rule out the possibility that the reaction to baby cries may be impacted by the age of the person. This impact could be positive - an older, more experienced person could possibly make better decisions than a younger one -, or negative - age could increase the stress associated with listening to a pain cry, or make the person less able to act promptly and appropriately.

In conclusion, our work underlines that experience in caring for babies is crucial for developing the ability to decode the information conveyed by cries and that this effect persists at advanced ages, as long as sensory and cognitive capacities are preserved. It would therefore be interesting to encourage cooperation, for example via multigenerational housing, so that old people can keep busy by looking after the children while the parents work.

**Ethics.** The experiment was approved by the local ethics committee (October 2019 – Comité d’Ethique du CHU de Saint-Etienne, Institutional Review Board: IORG0007394), and informed consent was obtained from all participants.

**Data accessibility.** The dataset and the R code for analyzing data will be available on Zenodo.

**Author contributions.** SC: conceptualization, methodology, investigation, formal analysis, data curation, writing – original draft; CC: methodology; RP: funding acquisition; DR: writing – review & editing, funding acquisition; CF: conceptualization, methodology, writing – review & editing, funding acquisition; NM: conceptualization, methodology, project administration, funding acquisition, writing – original draft.

**Conflict of interest declaration.** The authors declare no competing interests.

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### **II.3. Complementary experiment: How do nonlinear phenomena in babies' cries affect pain perception by human listeners?**

This study is an ongoing project, in preparation for a special issue in *Philosophical Transactions of the Royal Society B*, on the role of nonlinear phenomena in vocal communication. Here we investigate their role for pain perception in babies cries.

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#### **Abstract**

Nonlinear phenomena (NLP) are widely reported in the distress calls of infant mammals, including human baby cries. These phenomena are responsible for perceptual harshness, making calls unpredictable and difficult to ignore by caregivers. As such, NLP have been suggested to serve to signal heightened level of distress, grab the attention of caregivers and elicit them care. Nonlinear phenomena are extremely common in human babies' cries, and particularly in pain cries. Here, we test the predictions that NLP in human babies' cries is a vocal indicator of pain and that pain perception in adult listeners is correlated to the presence of NLP in these calls. First, comprehensive acoustic analyses conducted in both natural pain and non-pain cries (N = 304 cry sequences) reveal that pain cries are characterized by significantly more NLP, especially chaos and vibrato. Second, psychoacoustic experiments in which human listeners (N = 40) were asked to rate perceived pain level, further support these findings. Indeed, longer episodes of chaos and vibrato in natural cries are significantly associated with higher level of pain as judged by adult listeners. Therefore, our study provides the first evidence that NLP may signal pain to caregivers. Achieving a better understanding of the signaling function of NLP in babies' cries can critically improve pain assessment for pediatric care with the development of vocal-based tools.

## **Introduction**

Babies crying is an essential distress signal to elicit parental care, generally triggered by hunger, discomfort or pain (Lingle et al., 2012). The source of this acoustic signal is the vibration of the vocal folds in the larynx, defined as the fundamental frequency  $f_0$ , which is responsible of the perceived pitch (Golub & Corwin, 1985; Taylor & Reby, 2010). Although vocal fold vibrations are generally regular, there can be abrupt changes in the tonal structure of acoustic signals, leading to acoustic irregularities known as nonlinear phenomena (NLP) (Fitch et al., 2002; Wilden et al., 1998). Several types of NLP are described: frequency jumps, subharmonics, biphonation and deterministic chaos (Anikin, 2020). Frequency jumps are abrupt changes in the vocal fold vibration frequency (Riede et al., 1997). When one vocal fold vibrates as a multiple frequency to the second one, it leads to subharmonics, additional harmonics in an integer value of harmonics (e.g. 1:2, 1:3) visible in the spectrum beneath  $f_0$  and/or between harmonics. Two oscillators vibrating independently, non-harmonically in any ratio of frequencies, is called biphonation. It results in either sidebands (nonparallel fundamental frequencies and/or harmonics) or vibrato (unbroken  $f_0$  contour modulated in a sinusoidal manner) (Charlton, 2017; Wilden et al., 1998). Finally, deterministic chaos (hereafter chaos) is aperiodic vibration, characterized by the presence of broadband “noise” in the spectrum, at many different frequencies (Mende et al., 1990; Titze, 2008).

Cries are considered as a graded signal (Soltis, 2004) reflecting the baby’s level of need or distress, with higher distress levels being linked to more severe cry acoustics, particularly in the case of painful situations. Fundamental frequency value did not seem to be correlated with pain levels (Koutseff et al., 2017) but may represent an alarm threshold when a high level is reached (Bellieni et al., 2004). On the other hand, NLP are observed in painful conditions, like routine blood withdrawal, where cries were described as less phonated, partially voiced or voiceless (Lenti Boero et al., 1998). These acoustic features are linked to the physiological modulations a baby experiences in pain, with arousal of the autonomic nervous system and a diminution of the vagal tone (Porter et al., 1988). This leads to increase in subglottal pressure, laryngeal constriction and increased tension in the vocal folds and thus to irregular or asynchronous vibration of the vocal folds. It results in NLP (Fitch et al., 2002; Tokuda, 2018), which may be a way to generate unpredictability to prevent habituation from listeners (Taylor et al., 2016). As in adults (Raine et al., 2019), babies experiencing higher level of pain produce cries with more acoustic roughness, i.e. less voiced, with less harmonic, more variable  $f_0$  and

more occurrence of chaos (Koutseff et al., 2017; Porter et al., 1986). However, there is to date no extensive description of NLP presence and duration in non-painful and painful babies cries.

Despite these acoustic features specific to pain in cries, identifying pain through cry listening requires some experience in babies care, either parental or professional (Corvin et al., 2022). Perceived pitch shaped the perceived distress, with higher pitched vocalizations being rated as expressing more distress (Reby et al., 2016). NLP also seem to shape this perception with longer cries, with shorter pauses between cries, more subharmonics and biphonation in cries are rated as more aversive and expressing more distress (Gustafson & Green, 1989; Qiaobing Xie et al., 1993; Wood, 2009). However, the extensive separate role of each NLP has not been investigated in babies cries. More precise role of NLP has been emphasized for perceived distress in puppy whines. Adding synthetic chaos to whines increased the puppy's perceived distress by human listeners, and listeners with puppies extensive caregiving experience (breeders, veterinarians) were also sensitive to added sidebands and subharmonics leading to more perceived distress too (Massenet et al., 2022).

Here, we investigated with acoustic analysis and playback experiment which NLP characterize pain in natural babies cries, and how it shapes the perception of pain in cries by adult listeners. We predict that NLP in babies' cries is a vocal indicator of pain and that pain perception in adult listeners is correlated to the presence of NLP in these cries.

## **Methods**

### **Sound recording**

Cry recordings were extracted from a cry database previously built by the ENES Laboratory (Koutseff et al., 2017). Discomfort cries were recorded during bathing, undressing, or dressing by parents at the baby's home. Pain cries were recorded during scheduled routine vaccination at the doctor's office (N = 24 babies, 11 boys and 13 girls; age =  $60.3 \pm 3.3$  days on the vaccination day; delay between recording sessions of discomfort cries and pain cries for a given baby =  $6.8 \pm 3.3$  days, see (Koutseff et al., 2017) for a complete description of the recording parameters).

Using Audacity software ([www.audacityteam.org](http://www.audacityteam.org)), we isolated 304 cry sequences from these raw recordings (mean sequence duration =  $6.3 \pm 1.1$  s; 3-4 sequences of pain cry per baby and 2-19 sequences of discomfort cry per baby). We took care to isolate sequences without

background noise such as adult voices, water flowing or door slamming. Cries recorded during bathing are referred as “discomfort cries”, the first cry in response to the vaccine injection as “acute pain cry” and the second one, approximately 6 seconds later, as “residual pain cry”.

The sound intensity of the cry sequences was normalized to 100% of the maximal amplitude using the “normalize” function of the tuneR package ([cran.r-project.org/web/packages/tuneR/index.html](http://cran.r-project.org/web/packages/tuneR/index.html)).

### **Acoustic analysis**

Each cry sequence was manually labelled using Praat software (Boersma, 2001). On the cry sequences, single continuous vocal utterance produced on a single exhalation was labelled as a “cry”. Nonlinear phenomena were characterized by conducting a visual inspection of the spectrogram, combined with sequences listening. Onset and offset of the following phenomena were measured: chaos, subharmonics (sh), sidebands (sb) and vibrato (vib). Duration of each phenomena was normalized to the cry duration, and reported as relative duration. Frequency jumps (fj) onsets were measured.

### **Participants**

We tested a sample of 40 parents of at least one child under 2 years old (20 mothers, 20 fathers, mean age =  $33.3 \pm 5.1$  years, mean child age =  $11.6 \pm 5.9$  months). Participants were recruited on the online platform Prolific ([www.prolific.co/](http://www.prolific.co/)), then directed to the online platform Labvanced (Finger et al., 2017) (<https://www.labvanced.com/>) where the experiment took place. Once the experiment was completed, participants were paid at the recommended rate of 8.0 GBP per hour. All participants reported having normal hearing.

### **Experimental design**

Once recruited, participants were asked to provide their demographic data. Next, the experimental procedure consisted of listening to 60 cry sequences, randomly selected from the 3 conditions (discomfort, acute pain, residual pain). For each condition, the 20 cry sequences came from 20 different babies in the database in order to maximize the ecological validity of



the results. Cry sequences were presented in a randomized order across conditions using Labvanced randomization tool.

At the beginning of the session, participants received the following instructions: “Now you will listen to baby cries and rate their level of pain. After listening to a cry, move the cursor on the sliding scale. You can rate from 'no pain and no distress' to 'the worst pain imaginable'. The mark on the scale corresponds to the 'pain threshold': the transition from distress to pain. You can replay by clicking on the play/pause button.” Then, participants had to answer after each cry to the question “How does this baby feel?” using a scale from “No pain and no distress” (coded as 0), to “Worst pain imaginable” (coded as 100). A mark on the scale corresponding to 40/100 was representing the “pain threshold”. Participants were not informed about the three conditions there were listening to.

### **Statistical analysis**

Statistical analyses were performed in R (v4.2.2). To describe the cries acoustic features across the three conditions, Kruskal-Wallis tests and Dunn post-hoc tests were used for quantitative continuous variables (cry duration, NLP relative duration) and logistic regression for binomial variables (presence/absence of each NLP). Playback results were analyzed using Bayesian mixed models fitted with the brms R package (Bürkner, 2017). The outcome variable was the pain rating re-coded from 0 to 1 and modeled using zero-one-inflated beta distribution (Ospina & Ferrari, 2012). The cumulated cry duration on the sequence was included as fixed factor. We used two different models with either the presence of each NLP or its relative duration as fixed factors. Participant and baby identity were included as random factors. The structures of the model syntaxes were:

```
pain_rating ~ cry_duration + chaos_presence + fj_presence + sh_presence + sb_presence +  
vib_presence + (1|subjectID + babyID)
```

```
and pain_rating ~ cry_duration + chaos_relative_duration + sh_relative_duration +  
sb_relative_duration + vib_relative_duration + (1|subjectID + babyID)
```

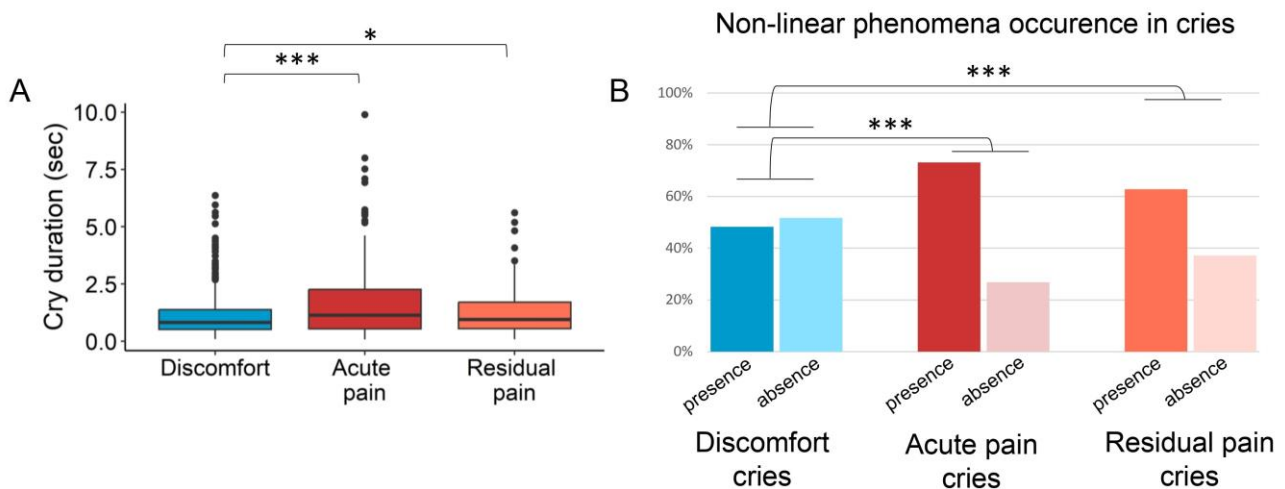
4000 iterations were run over four MCMC chains (Markov chain Monte Carlo) with the first 500 iterations of each chain used to adjust the algorithm. Results were summarized as medians of the posterior distributions and 95% credible intervals (CIs). When contrasting two

conditions, CIs excluding the null value can be inferred to indicate a credible difference between the conditions (Kruschke & Liddell, 2018).

## Results

### Acute pain cries are longer and characterized by deterministic chaos

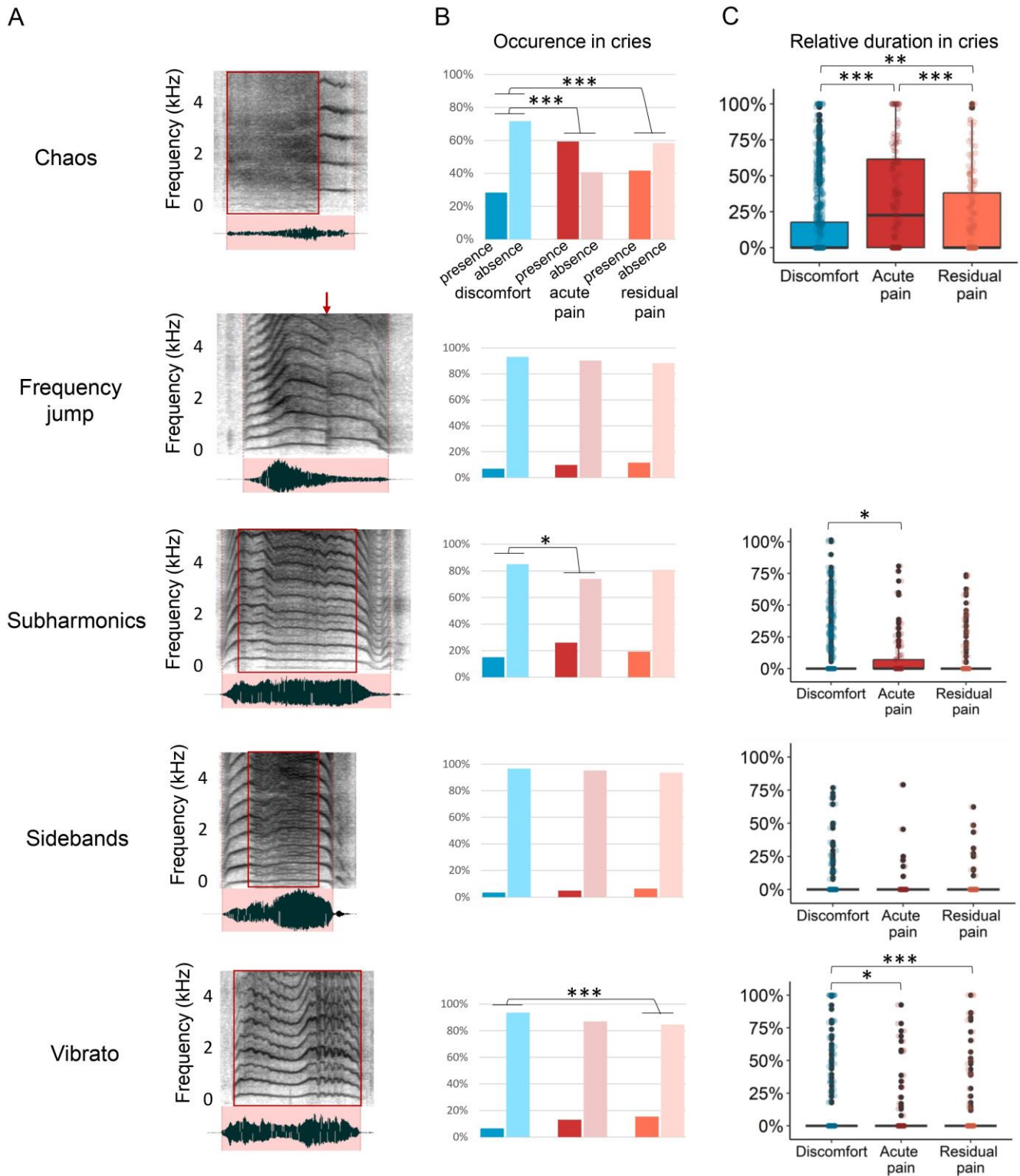
From the 304 cry sequences, 1099 cries were labelled: 820 discomfort cries, 123 acute pain cries and 156 residual pain cries. Acute pain cries lasted on average  $1.8 \pm 1.9$  seconds (mean  $\pm$  s.d., min = 0.1s, max = 9.9s), while residual pain cries lasted  $1.2 \pm 1.0$  s (min = 0.1s, max = 5.6s) and discomfort cries  $1.1 \pm 0.8$  s (min = 0.1s, max = 6.4s). Condition significantly affected the cry duration ( $H(2) = 13.707$ ,  $p < 0.001$ ; Kruskal-Wallis test). Pairwise comparisons showed that acute and residual pain cries were significantly longer than discomfort cries (respectively  $p < 0.001$  and  $p = 0.031$ , Dunn post-hoc tests; Figure 1A). Nonlinear phenomena were present in 73% of acute and 62% of residual pain cries, which was significantly more than in discomfort cries (48%; Logistic regression Wald tests,  $p < 0.001$ , Figure 1B).



**Figure 1. Acute pain cries are longer and contain more nonlinear phenomena.** A. Cry duration for the three conditions.  $*p < 0.05$ ,  $***p < 0.001$  for Dunn post-hoc tests. B. Nonlinear phenomena occurrence in cries for the three conditions.  $***p < 0.001$  for logistic regression Wald tests.

Examples of each nonlinear phenomenon are presented on Figure 2A, with their occurrence (Fig. 2B) and relative duration in cries (Fig. 2C). Chaos was the more frequent NLP, present in 34% of cries. Subharmonics were present in 17% of cries, vibrato and frequency jumps in 8%, and sidebands in 4% of cries. Regarding the three conditions, chaos was present in 59% of acute

and 42% of residual pain cries, which was significantly more frequent than in discomfort cries (28%;  $p < 0.001$ , logistic regression Wald tests). Normalized to the cry duration, chaos occupied  $34 \pm 36$  % of acute pain cries (min-max = 0-100%),  $20 \pm 29$  % of residual pain cries (min-max = 0-100%) and  $13 \pm 25$ % of discomfort cries (min-max = 0-100%). This relative duration was significantly different across conditions ( $H(2)=59.420$ ,  $p < 0.001$ ), longer in acute pain cries compared to residual pain and discomfort cries ( $p < 0.001$ , Dunn post-hoc tests), and for residual pain cries compared to discomfort cries ( $p = 0.001$ ). Subharmonics occur significantly more in acute pain cries (26% versus 15%;  $p < 0.013$ , logistic regression Wald test) and last longer ( $p = 0.016$ , Dunn post-hoc test) than in discomfort cries. Vibrato episodes occur significantly more in residual pain cries than in discomfort cries (15% versus 6%;  $p < 0.001$ , logistic regression Wald test), with their relative duration being significantly different across conditions ( $H(2)=15.489$ ,  $p < 0.001$ ). Vibrato lasted significantly longer in acute and residual pain cries compared to discomfort cries (respectively  $p = 0.021$  and  $p < 0.001$ , Dunn post-hoc tests). There was no significant difference between conditions for frequency jumps and sidebands, either regarding their occurrence nor relative duration.



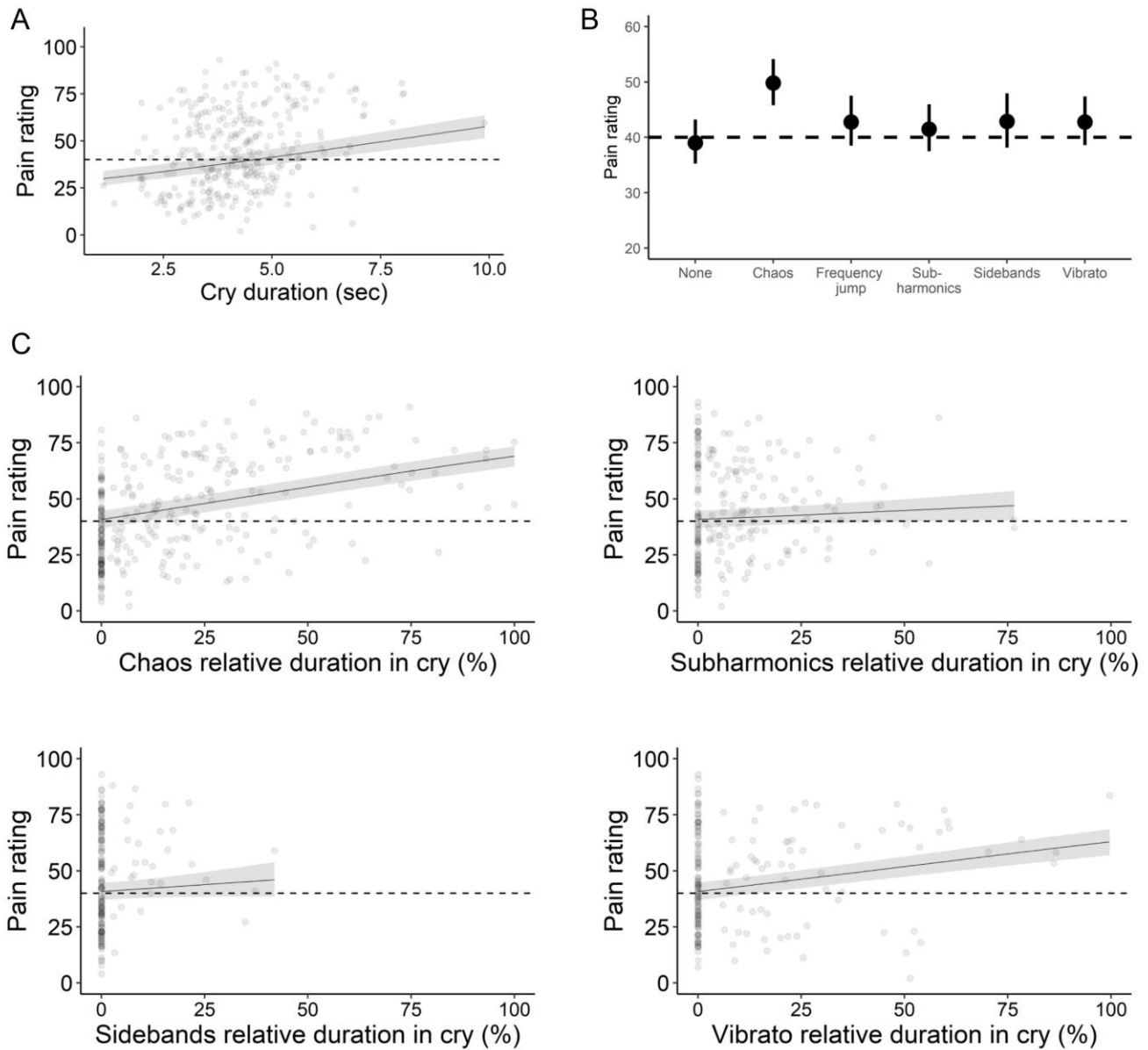
**Figure 2. Occurrence and relative duration in cries for each nonlinear phenomenon: chaos, frequency jumps, subharmonics, sidebands and vibrato.** A. Oscillogram and spectrogram of each NLP example. The pink area on the oscillogram represent the cry. The red frame or arrow on the spectrogram indicates the nonlinear phenomenon. B. Occurrence of each NLP in cries, for the three conditions. \* $p < 0.05$ , \*\*\* $p < 0.001$  for logistic regression Wald tests. C. Relative duration of each NLP. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  for Dunn post-hoc tests.

### **Cry duration, chaos occurrence and duration, and vibrato duration increase the pain ratings**

As shown in Figure 3A, in absence of any nonlinear phenomena, the estimated pain rating for the minimal duration of cry in the cry sequence (1.12 seconds) was 29.9/100 (95% credible interval CI [26.4, 34.0]). This estimated rating increases to 59.5/100 [51.3, 63.7] for the maximal duration of cry (9.9 seconds), which was 27.5 points higher than the shortest cries (95% CI [21.1, 33.8]).

For the mean cry duration of 4.3 seconds (Figure 3B), the estimated pain rating was 39.0/100 [35.3, 43.2] in the absence of any NLP. At this fixed duration, the presence of chaos in the cry sequence increases by 10.8 points (95% CI [8.7, 12.9]) the pain ratings. The presence of the other nonlinear phenomena increases only marginally the pain ratings, with respectively 3.8 [1.6, 6.0], 2.4 [0.6, 4.4], 3.9 [1.0, 6.8] and 3.7 [1.6, 5.9] points higher for frequency jumps, subharmonics, sidebands and vibrato.

As shown in Figure 3C, the second model estimated the separate effect of each NLP relative duration reported to the cry duration, except for frequency jumps which are discrete events. Estimated pain ratings were 28.2 points higher [24.4, 32.1] for cries with 100% of chaos, compared to those without chaos. Cries completely occupied by vibrato were rated 22.1 points higher (95% CI [17.0, 27.2]) than those without vibrato. Subharmonics and sidebands in cries only increase marginally the pain ratings. Cries with the maximal duration of subharmonics (77%) were rated 6.2 points higher [0.3, 11.9], only slightly above those without NLP, while those with a maximal duration of sidebands (42%) were rated 5.2 points higher [-1.6, 12.0] which indicate no credible difference.



**Figure 3. Cry duration, chaos occurrence and duration, and vibrato duration increase the pain ratings.** A. Effect of cry duration, estimated without NLP. B. Separate effect of each NLP, estimated for the mean cry duration. C. Effect of chaos (upper left), subharmonics (upper right), sidebands (lower left) and vibrato (lower right) relative duration in the natural range of each NLP relative duration, estimated in the absence of other NLP, for the mean cry duration. A, C. Solid lines represent medians of posterior distributions and light areas 95% credible intervals (CI). Light circles correspond to one cry sequence. B. Solid disks represent the medians of the posterior distributions, with bars indicating the 95% CI. All panels. Dotted lines indicate the 40% pain threshold.

### **Conclusions and perspectives**

In this study, we showed that pain cries are longer and characterized by significantly more NLP. Chaos is the more frequent NLP in cries, occurs significantly more and lasts longer in pain than in discomfort cries. Its duration is also significantly longer in acute pain cries, just after the vaccine injection, than in residual pain cries. In addition, subharmonics are more frequent and longer in acute pain cries, while vibrato is more frequent and occupies longer duration in residual pain cries than in discomfort cries.

Secondly, parents of babies under two years old rated longer cries as expressing more pain than shorter ones, with presence of chaos increasing their ratings. Cries occupied by longer episodes of chaos and vibrato were also rated as expressing more pain than those without NLP, while longer episodes of subharmonics and sidebands did not impact their pain ratings. Overall, this shows that parents ratings of pain are consistent with acoustic features specific to pain in cries, namely longer cry, chaos and vibrato duration.

In our study, all participants were parents of young babies, thus experts in babies care. Key role of expertise for distress and pain assessment has been emphasized in previous studies. For example, adults with no experience in babies care were not able to identify pain in cries (Corvin et al., 2022, Chapter II.1). When asked to rate distress in puppy whines, breeders and veterinarians had a more fine-grained evaluation than the general population, relying their ratings on chaos but also on sidebands and subharmonics (Massenet et al., 2022). Thus, it will be interesting to investigate in non-experienced adults how NLP shape their evaluation of pain in cries, or in other words which information they are missing in pain cries, making them unable to identify pain in these cries.

In synthetic puppy whines with complete control of the present NLP, a ceiling effect has been highlighted when chaos occupied more than 50% of the whines. More surprisingly, perceived distress was reduced for longer episodes of subharmonics and sidebands (Massenet et al., 2022). In our study, we found the opposite with cries containing longer episodes of chaos and vibrato being rated as expressing more. In addition, we did not find any effect of subharmonics presence nor duration, whereas this characterized more acute pain cries. With our sample of natural cries, it is hard to say if listeners missed this information, or if our limited sample of cries makes us unable to highlight a difference. This limitation could be overcome by using synthetic cries. Indeed, there is now tools to create synthetic sounds and adding chosen type and duration of NLP (Anikin, 2019), thus enabling a precise assessment of each NLP role in pain rating.

In conclusion, our study provides evidence that NLP signal pain to caregivers. Achieving a better understanding of the signaling function of NLP in babies' cries can critically improve pain assessment for pediatric care with the development of vocal-based tools. Using synthetic cries with manipulation of NLP presence and duration will help to further assess their fine role in pain evaluation.

**To sum up this second chapter, it shows that pain identification ability is gain through experience in babies care, either parental or professional, and does not seem to decline with listener's age. Familiarity with a given baby makes adults better at discriminating pain from discomfort in a baby's cry. Then, acoustic chaos and vibrato characterize pain in cries and drive pain perception.**



Chapter III: Neural correlates of  
individuality and pain perception in  
babies cries

### **III.1. Preliminary study: Parenthood modulates the brain connectome engaged when listening to baby cries**

When listening to a baby cry, various brain regions work together to apprehend the amount of distress expressed and implement a response to the infant's solicitations. Here we analyzed this brain connectivity in men and women, parents and non-parents, by playing them cries expressing different levels of pain. This study has been conducted before the beginning of my thesis, and led to the questions addressed in Chapter III.2. It is currently in preparation and I participate in the writing. A detailed summary is provided here, and the complete draft is in Annex II.

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## **Introduction**

The cry of a baby is one of the most emotionally evocative signals for parents and other caregivers. Despite research indicating that this signal activates various cerebral networks, including those of vigilance and empathy processing, there is still limited understanding of the functional connectivity within and between these networks. Additionally, the impact of parenting experience and sex on brain network connectivity remains largely unexplored. In the present study, we explore the brain connectome engaged when listening to baby cries and determine the effect of parenthood and sex on the organization and activity of this connectome. We tested the hypothesis that parental experience results in increased specialization of the brain connectome mobilized when listening to babies' cries. Furthermore, we predicted that the brain response to cries with the most acoustic roughness - a marker of pain level - is more specific in adults, with stronger emotional empathy.

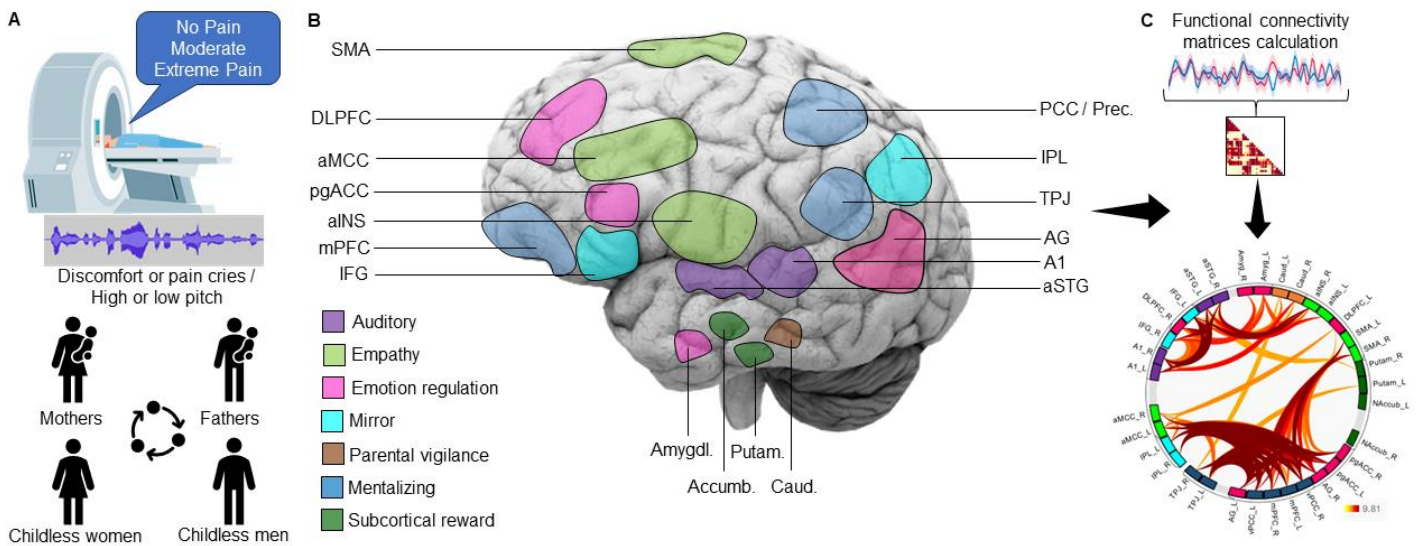
## **Methods**

Eighty individuals took part in the study: 40 parents (20 fathers; 20 mothers) and 40 age/sex-matched healthy non-parents. Parents had at least one baby aged from 28 days to 2 years at the time of the experiment. It was verified for non-parents that they were not in contact with a baby on a regular basis (i.e., midwife, pediatrician, nanny, person with babysitting experiences or being in contact with a baby in their close circle were excluded).

Cries were from 20 2-month-old babies (10 boys; 10 girls) previously recorded in two conditions (Koutseff et al., 2017): during bathing (discomfort condition) and routine vaccination (pain condition, “reaction cry” only, first 6 seconds after the injection). Using Praat software, two editions of each cry were created, with pitch fixed either at 360 or 500 Hz.

In the MRI scanner, participants listened to 80 cries from the four sub-conditions (i.e., bath and vaccine cries with a pitch fixed at 360 or 500 Hz) in a randomized order. After cry listening, they rated the level of pain expressed by the cry on a scale from 1 to 3: 1 = No pain, 2 = Medium pain, 3 = Extremely painful (Fig. 1A).

BOLD activity was modeled using a general linear model (GLM) with two regressors of interest: the cry stimuli (12s) and the rating phase (3s). The four cry conditions (bath 360 or 500 and vaccine 360 or 500) were also incorporated into the model. Two parametric modulators to the cry regressor in the GLM: the roughness of the cry (PC1 value) and the pitch (360 or 500 Hz).



**Figure 1. Overview of the experimental procedures and brain connectome related to cries decoding.** A. Experimental procedure. B. The adult brain connectome of baby’s cry perception, set of brain regions (17 bilateral areas) considered here to be involved in processing sound distress signal from babies. They are organized in 7 networks named auditory, empathy, emotion regulation, mirror, parental vigilance, mentalizing and subcortical reward networks. C. Computing functional connectivity between this set of regions of interest allow us to construct individual and sub-group average connectivity matrices, and to calculate the number of links between and within the 7 networks of interest.

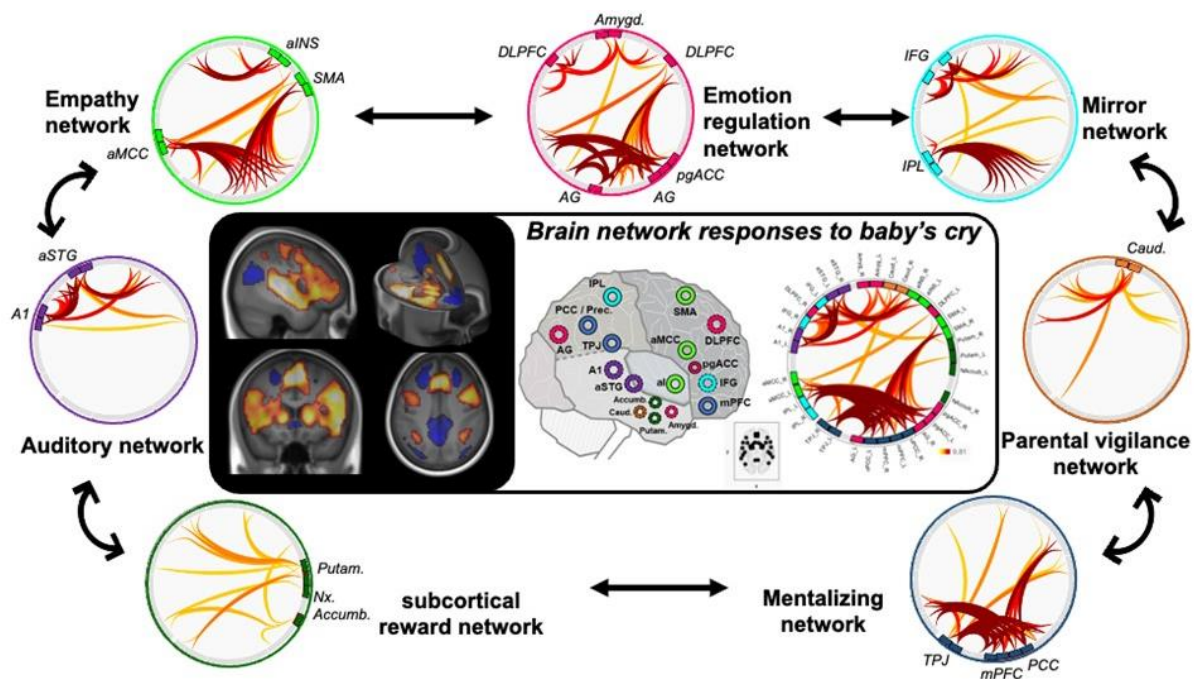
AG: Angular Gyrus; aINS: anterior insula; aMCC: anterior Mid Cingulate Cortex; amygd.: amygdala; Caud.: caudate nucleus; DLPFC / dmPFC: dorso lateral / medial prefrontal cortex; Hipp.: hippocampus; IFG: inferior frontal gyrus; IPL: Inferior Parietal Lobule; Nx. Accumb.: nucleus accumbens; PCC: Posterior Cingulate Cortex; pgACC: perigenual Anterior Cingulate Cortex; Putam.: putamen; SFC: superior frontal gyrus; SMA: Supplementary Motor Area; TPJ: Temporo-Parietal Junction; L, left; R, right.

The individual functional connectivity matrix was formed from the 34 cortical and subcortical nodes of the parental brain network, significantly activated by infant cries (Fig. 1B). By measuring the synchronization of the BOLD signal between brain regions, the connectivity analysis aimed to highlight the functional relationships between the brain areas activated by hearing baby cries (Fig. 1C).

## Results

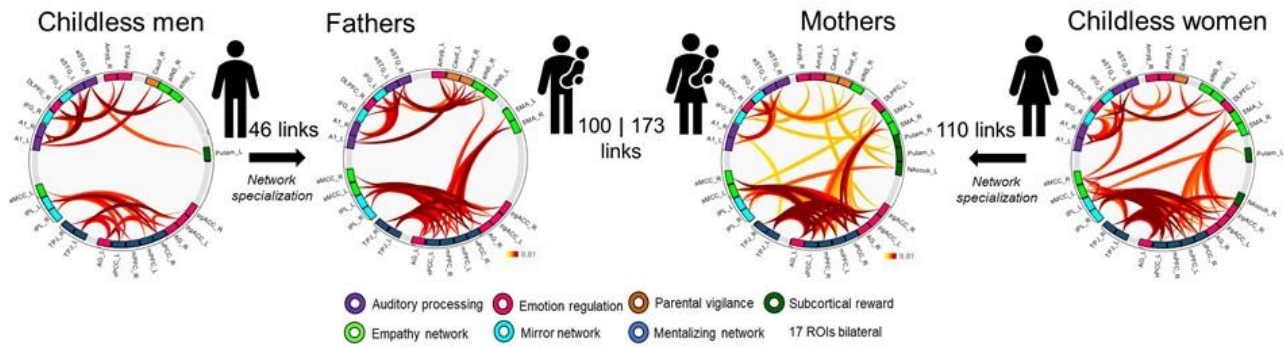
In all participants, listening to cries were associated with activity changes and higher functional connectivity within several brain networks including: 1) *the auditory network*, marked by strong functional connectivity between the primary auditory cortex (A1) and the anterior superior

temporal gyrus (aSTG); 2) *the empathy network*: anterior insula (ant INS), anterior mid cingulate cortex (aMCC), supplementary motor area (SMA); 3) *the emotion regulation network*: amygdala (Amyg), dorsolateral prefrontal cortex (dlPFC), the angular gyrus (AG), and the pregenual anterior cingulate cortex (pgACC); 4) *the mirror network* (cognitive evaluation): inferior frontal gyrus (IFG) and inferior parietal lobule (supramarginal rostro-dorsal (IPL)); 5) *the parental vigilance network*: caudate nucleus (Caud.); 6) *the mentalizing network*: temporo-parietal junction (TPJ: supramarginal ventro-caudal), medial prefrontal cortex (mPFC), precuneus and posterior cingulate cortex (Prec/PCC); and 7) *the subcortical reward network*: putamen (Putam) and accumbens nucleus (Nx. Accumb.). These brain areas are related to various processing aspects of vocal emotions and may be considered as the adult brain connectome of baby's cry perception (Fig. 2).



**Figure 2. Brain activations and functional networks associated with listening to baby's cries in adults.** This included a strong functional connectivity between these regions in 7 sub-networks involved in auditory processing, empathy and mirror processes, mentalizing, emotion regulation, subcortical reward and parental vigilance.

While the same seven cerebral networks were involved in all listeners, sex and parenthood shaped functional connectivity in these networks (Fig. 3).



**Figure 3. Sex and parenthood shaped functional connectivity in response to cries listening.** The functional connectomes differ between the four groups of subjects. Those of parents of both sexes show specialization with a higher number of significant connections (links) compared with childless adults.

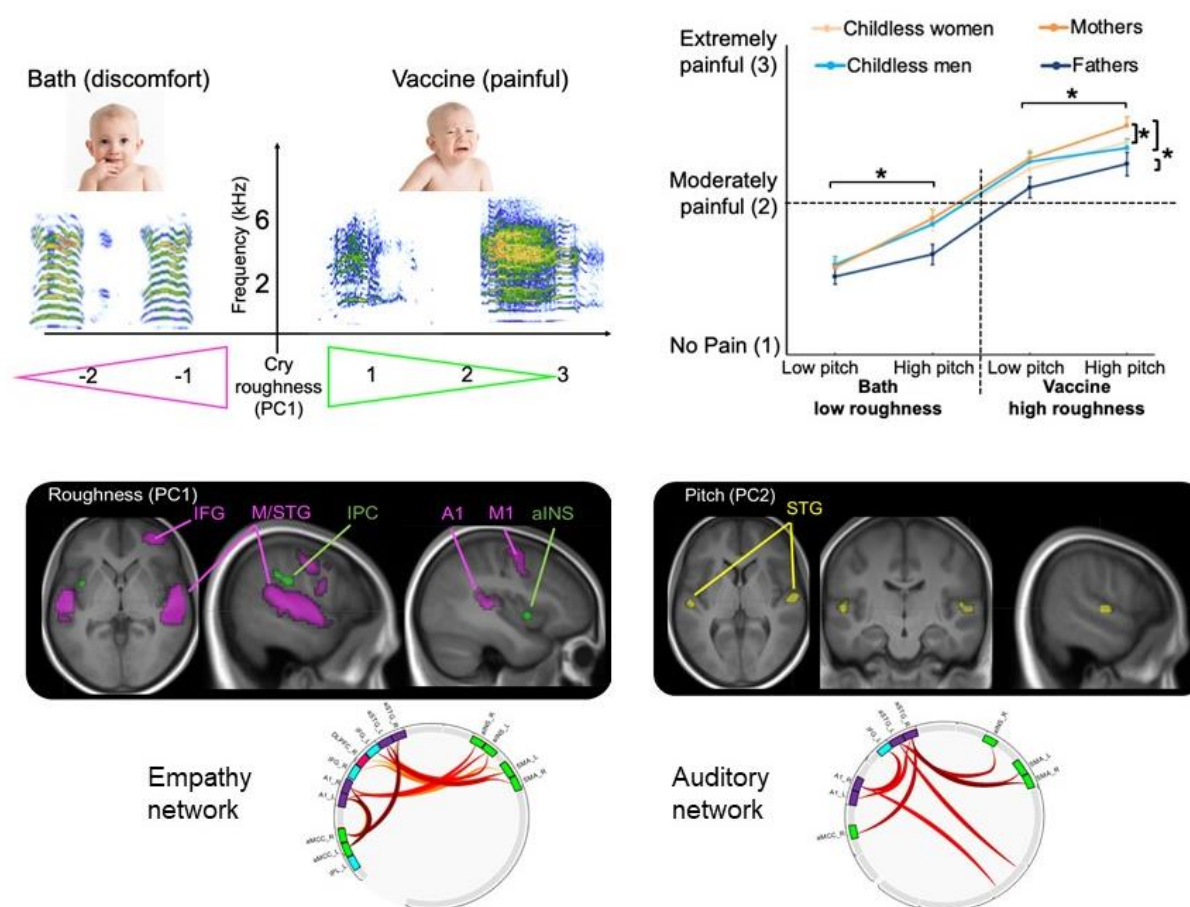
Specifically, listening to cries mobilized the amygdala nuclei less in fathers than in other adults. Mothers showed higher activity in subcortical regions (amygdala, putamen, hippocampus, caudate nucleus), higher connectivity in subcortical reward network and lower functional connectivity in auditory network compared to fathers.

In addition, parents exhibited greater global connectivity in this connectome than non-parents. Particularly, childless men showed higher activity in the prefrontal cortex, anterior insula and IFG, and weaker functional connectivity in the emotion regulation, mentalizing and empathy network compared to fathers. Childless women showed higher connectivity in the empathy network and lower in the mentalizing one compared to mothers. This suggests a shift from aversive and emotional reaction in nonparents to a more cognitive processing in parents.

Regarding pain ratings, there was a significant effect of the cry recording condition for all participants (Fig. 4). Pain ratings were lower for bath cries (mean  $\pm$  SD = 1.67  $\pm$  0.02) than for the vaccination cry (2.26  $\pm$  0.02). The effect of cry's pitch was also significant, and pain ratings were higher for cries fixed at 500 Hz than for cries at 360 Hz. Fathers had lower pain ratings than other participants in both high pitch and vaccine conditions, whereas mothers showed higher pain ratings to vaccine condition compared to childless females. At the condition level, acoustic roughness was higher in pain cries than in discomfort cries. At the cry level, higher index of roughness in the cries was associated with higher levels of pain rated by the participants. In addition, higher roughness in cries was associated with increased activity in the bilateral anterior insula and the inferior parietal cortex, decreased activity in the bilateral auditory association cortex (M/STG, A5), premotor areas (M1) and dorsolateral and inferior



right frontal cortex (DLPFC, IFC) and higher functional connectivity between empathy areas. On the other hand, changes in pitch value significantly correlated with bilateral brain activity in a restricted cluster of the STG including the primary auditory area and the lingual gyrus, and higher functional connectivity within the auditory network (Fig. 4). Mothers showed higher activity linked to roughness in the mid temporal gyrus and the caudate nucleus, and higher connectivity between brain regions involved in auditory, emotional regulation and parental vigilance, compared to fathers.



**Figure 4. Pain cries, characterized by acoustic roughness, are rated as more painful and recruited the empathy brain network.** Listening of rougher cries was associated with stronger brain activity in the bilateral anterior insula and the inferior parietal cortex (in green), whereas lower roughness was associated with activity in the bilateral auditory association cortex, premotor areas, and the right dorsolateral and inferior frontal cortex (in purple). The cry average pitch, a poor marker of pain, mainly recruited auditory areas (superior temporal gyrus, in yellow).

### **Conclusion and perspectives**

This study provides the first general framework of cerebral functional connectivity in response to baby cries and the information they carry, and highlights the importance of parental experience and sex in the brain response to these critical sound signals. Babies cries listening leads to brain activity and functional connectivity between regions in 7 sub-networks involved in auditory processing, empathy and mirror processes, mentalizing, emotion regulation, subcortical reward and parental vigilance. In addition, evoking pain through babies cries listening involves the empathy network and the anterior insula, a key region in empathy for pain.

In the next study (Chapter III.2), we investigate how recognition of a familiar baby, additionally to pain perception, modulates activity in brain regions involved in general babies cries perception. In light to previous studies showing that cries identification may be challenging for non-parents (Chapter II.1), we restrict our investigations to parents of babies under 2-year-old. Moreover, we aim to compare this parental expertise to a professional one, by recruiting childless women working in pediatric care.



## **III.2. Familiarity and pain context shape neural processing of babies cries in expert participants**

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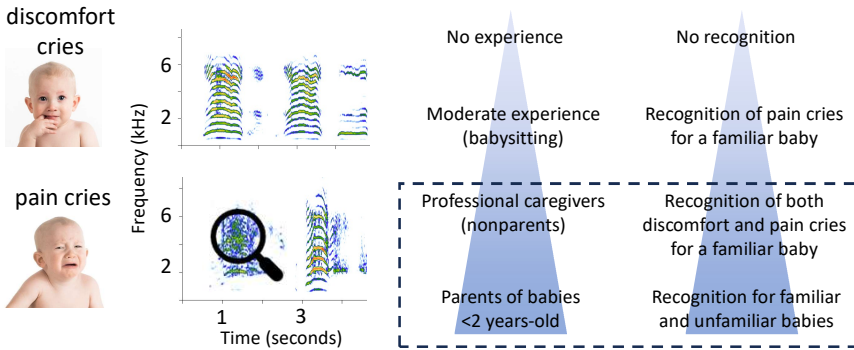
### **Abstract**

Babies crying is an essential signal to elicit parental care, conveying both information on the baby's identity and the baby's current physiological state. While general brain processing of these babies' cues is well described, integration of distinct information contained in cries remains unknown. In this fMRI study, we investigated the neural correlates of familiarization and pain identification through cries listening in 60 expert participants (parents of young children and women working in pediatric care). Participants managed to recognize one given baby's cries by engaging brain areas involved in voice recognition, even if pain disrupts this ability. Identification of the contexts for which the cry was generated (i.e., pain or discomfort) was more difficult and involve high-level non-specific cognitive processing. This difficulty was not compensated by either the participant's sex or experience. Similar performance to these tasks were observed in parents as well as healthcare professionals. Thus, cries are likely to be integrated as a complex vocal communication signal by these experts in babies care, rather than as a basic aversive alert.

# Graphical abstract: Familiarity and pain context shape neural processing of babies cries in expert participants

Siloé Corvin, Isabelle Failenot, David Reby, Nicolas Mathevon, Roland Peyron, Camille Fauchon

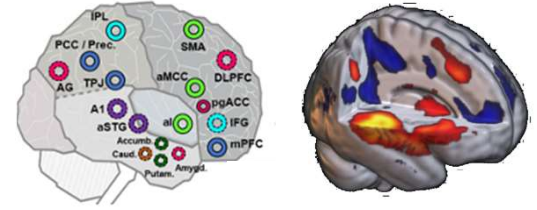
## Background: adults learn to identify pain in babies cries



1. Pain cries are longer, louder, harsher and rougher

2. Effective recognition of both discomfort and pain cries increase with experience in babies care

## 3. Cries listening involve activation in a large-scale brain networks (auditory, cognitive, attention, emotion and mirroring networks)



**Aim: What are the brain correlates of pain identification for familiar and unfamiliar babies in experts?**

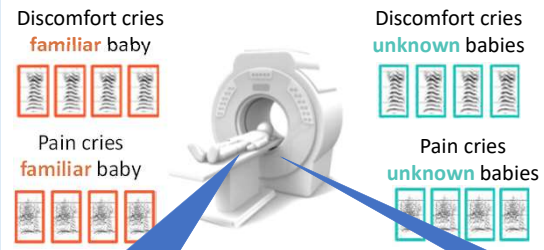
We hypothesized that familiar cries would recruit brain networks involved in memory and associative processing.

## Methods

Day 1: Training with discomfort cries familiar baby

Day 2: Test with 64 cries, 4 conditions

Bayesian mixed models and BOLD contrasts



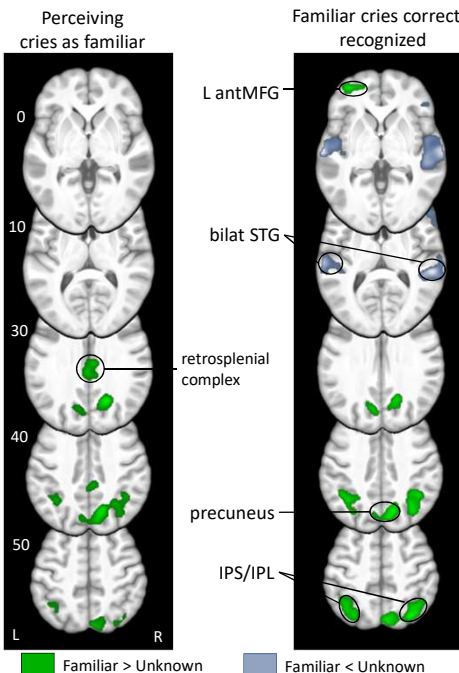
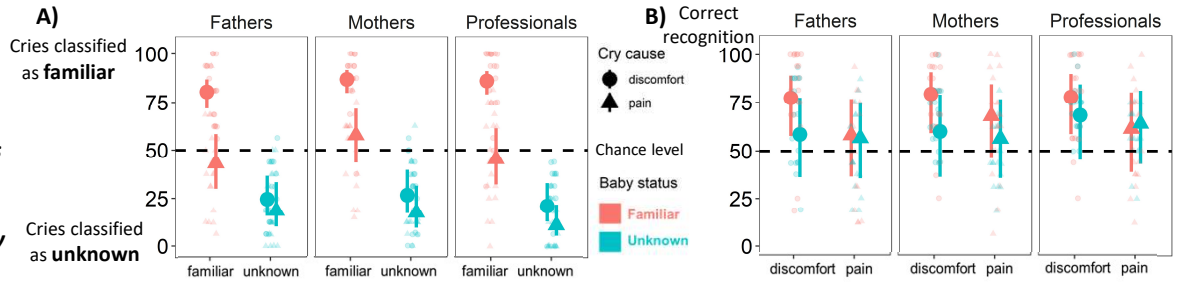
20 mothers  
20 fathers



20 childless women working in pediatric care

## Results

4. A) Listeners recognized well their familiar baby based on discomfort cries, but not based on pain cries. They correctly rejected cries of unknown babies; B) Only discomfort cries from the familiar baby were correctly recognized above chance.



## Conclusion

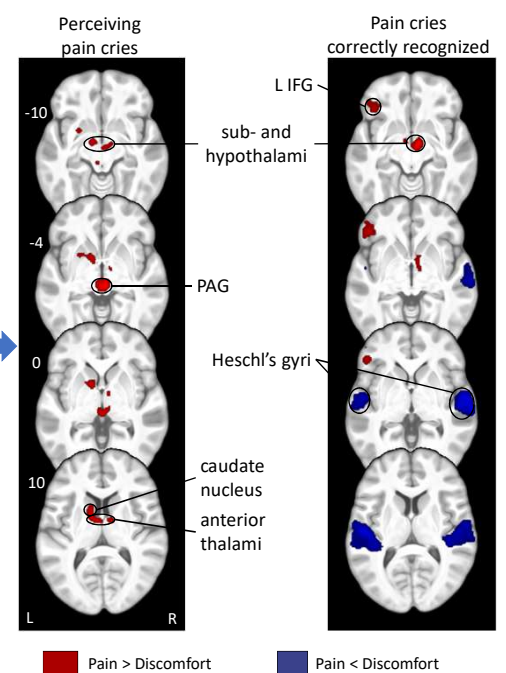
Cries contain strong information on baby's identity, allowing expert listeners to recognize one given baby, but pain disrupts this recognition (Fig 4A). Familiarity with a baby engages brain areas known to be involved in familiar voice recognition (precuneus, IPL; decreased in STG; Fig 5).

Despite acoustic specificity, identifying pain in cries is difficult for experts in babies care (Fig 4B). It leads to an increase in BOLD activity in associative areas (IFG) and decreased in primary auditory areas (Heschl's gyri; Fig 6).

Performances and general brain processing of information are similar in all groups.

Thus, cries are likely to be integrated as complex vocal communicative signal rather than a more basic aversive alert by adult experts in babies care.

IPS: inferior parietal sulcus; IPL: inferior parietal lobule; IFG: inferior frontal gyrus; MFG: middle frontal gyrus; PAG: periaqueductal grey matter; STG: superior temporal gyrus



5. Correct recognition of the familiar baby activated brain areas involved in perspective-taking, emotion regulation and familiar voice recognition (all subjects).

6. Pain recognition involved high-level processing (all subjects).

## **Introduction**

Babies crying is an essential signal to elicit parental care. It is generally triggered by pain, discomfort, hunger or separation from parents or other caregivers (Lingle et al., 2012; Soltis, 2004). These cries contain both static information on the baby's identity (Gustafson et al., 1984; Lockhart-Bouron et al., 2023), stable over time, and dynamic one linked to their current physiological state (Koutseff et al., 2017; Porter et al., 1986). Among dynamic information, pain is particularly relevant to detect, in order to provide adapted care. Identifying baby's identity and his physiological state are performed with varying difficulty by adult caregivers. Individual vocal signature, specific to each baby, is linked to fundamental frequency parameters responsible of perceived pitch. This allows a reliable identification of one given baby based on low-distress cries (i.e. hunger (Morsbach & Bunting, 1979; Valanne et al., 1967) or mild-discomfort during bathing (Bouchet et al., 2020; Gustafsson et al., 2013)). This baby recognition is strong and reliable, acquired in the first days of the baby's life. Fathers perform as well as mothers when they spend time caring for their babies (Gustafsson et al., 2013), and even nonparents can quickly learn to recognize a given baby by listening to his/her cries (Bouchet et al., 2020). However, pain cries are characterized by more unstable pitch and more acoustic *roughness* which disrupts adults' ability to recognize one given baby (Chapter I). However, this perceived roughness characterizing pain is essential for adults to identify it as such, even though this requires experience in caring for babies. Indeed, adults with no experience at caring for babies are unable to identify pain in cries, while professional caregivers can identify pain for a baby they are familiar with. Parents of young babies are even able to identify pain for unfamiliar babies (Corvin et al., 2022, Chapter II.1; Koutseff et al., 2017).

Decoding and interpreting cries involves complex brain processes in the listener to provide an adapted behavioral response (Feldman, 2015; Witteman et al., 2019). General integration of cries involves first auditory processing in the temporal lobe from the primary auditory cortex (Heschl's gyrus (HG) and the middle part of the superior temporal gyrus (STG)) to the associative areas processing the semantic information (in the STG, mid temporal gyrus (MTG) and, in between, the superior temporal sulcus (STS)) (Hickok & Poeppel, 2007). A second circuit shifts attention towards arousing sensory events such as cries, functioning as a "neural alarm signal" (Rilling, 2013). This involves the dorsal anterior thalamus, a multisensory hub, and the limbic system through the amygdala and posterior cingulate cortex (PCC) (Leech & Sharp, 2014). This circuit interacts with a third set of fronto-insular regions involved in both emotional and cognitive empathy. The dorsal anterior insula, the mid cingulate cortex (MCC)

and the temporo-parietal junction (TPJ) focus attention on emotions conveyed by the voice, and allow enhanced processing of emotional information (Zhang et al., 2019). Frontal regions such as the inferior frontal gyrus (IFG) and dorso-medial prefrontal cortex (dmPFC) are involved in more cognitive and conscious aspects of empathy (Amodio & Frith, 2006; Hartwigsen et al., 2019), labelled as mirror and mentalizing network (Feldman, 2015). Finally, the basal ganglia, particularly the caudate nucleus and the putamen, part of cortico-striatal motor loops are involved with the supplementary motor area (SMA) in parental vigilance, planning and initiation of the parental response, such as some routine behaviors of parenting (Booth et al., 2007; Provost et al., 2010). These activations occur sequentially in the described order. The midbrain periaqueductal gray (PAG) plays a central role in the descending control of vocalization across vertebrates, and is also centrally involved in the first step of auditory-vocal integration of babies vocalizations (Parsons et al., 2014; Young et al., 2017). Compared to mothers, fathers tend to show greater activity in regions involved in social-cognitive and semantic processing (STS, IFG, temporal pole and angular gyrus) and less activation in limbic regions like the amygdala (Abraham et al., 2014; Atzil et al., 2012; Fauchon et al., in prep, Chapter III.1; Witteman et al., 2019).

Brain regions involved in cry processing are well described, but there is no evidence on how static and dynamic information in cries can modulate their activities. A few studies investigated the neural correlates of baby recognition, comparing brain activations when listening to one's own baby cry to other unknown baby cry. In mothers, listening to own baby cries leads to more activation in brain regions involved in emotional and cognitive empathy (ACC, right insula and fronto-insular cortex and left posterior supramarginal gyrus) (Hipwell et al., 2015; Laurent & Ablow, 2012). Only one fMRI study investigated brain activations specific to own baby cry in fathers, and concluded to no difference compared to other baby cry (Li et al., 2018). However, there are several limitations in this study (only one own baby cry per participant, same unfamiliar cry for all participants rated as more aversive by an independent sample of listeners, no correct distinction between own and unfamiliar cries), that make the results difficult to generalize. Regarding integration of dynamic information, high distress cries listening, compared to low distress cries, is associated with decreased activity in bilateral STG, right MTG, left IPL, right superior occipital gyrus, and left precuneus (Montoya et al., 2012). In a recent study, higher roughness in cries has been linked with the same deactivation in auditory associative cortices (MTG/STG), in addition to increased activity in the bilateral anterior insula and the inferior parietal cortex (Fauchon et al., in prep), which are known to be involved in

empathy for pain (Lamm et al., 2011; Singer et al., 2004). Acoustic roughness induces differential integration in parents, with greater activity in the mid temporal gyrus (A5) and caudate nucleus in mothers than in fathers (Fauchon et al., in prep, Chapter III.1).

Professional caregivers shared some of parents' ability for pain identification (Corvin et al., 2022, Chapter II.1), but there is only few evidence on how they integrate babies cues. In a study asking to rate baby pain based on video clips, pediatric nurses score higher baby pain indicating that they may have a better knowledge of baby pain cues, especially for low-intensity pain when fewer cues are available (Latimer et al., 2011, 2017). While viewing others' pain is associated with increased activity in the anterior insula and the ACC in control participants, adult health professionals showed increased activation in the prefrontal cortex and the TPJ involved in emotion regulation (Cheng et al., 2007; Coll et al., 2017). Pediatric nurses showed the similar pattern of decreased activity in the anterior insula, but also decreased activation of the inferior frontal and medial prefrontal cortices (Jackson et al., 2017), suggesting that expertise refinement of pain perception may be linked to the type of patients they care for (Tremblay et al., 2018).

In this study, we investigated how information on the baby's identity and pain in cries influence brain responses in 60 expert healthy adults. We expect recognition of familiar baby to be based on activations in fronto-parietal brain areas (IFG, supramarginal gyrus). We also expect pain perception in cries to be linked with higher activity in empathy brain areas (anterior insula, ACC) and decreased activation in primary auditory regions. We focused on experts in babies care, both parents and professional caregivers, as pain recognition is known to be difficult for other adults (Corvin et al., 2022, Chapter II.1). We expect more cognitive and less limbic integration in fathers compared to mothers. Compared to parents, we expect professional caregivers to show greater activity in brain regions involved in mentalizing processes and less activity in regions related to emotional resonance when listening to crying.

## **Methods**

### **Participants**

Sixty adults took part in the study: 40 parents (20 fathers, mean age  $\pm$  SD = 35.6  $\pm$  4.7, [29-43]; and 20 mothers, mean age  $\pm$  SD = 32.2  $\pm$  4.7, [25-41]) and 20 childless women but working in pediatric care (mean age  $\pm$  SD = 28.4  $\pm$  5.4, [21-44]). The repartition was balanced across two

recruitment sites between Saint-Etienne and Lyon hospitals (30/30; 13/7 mothers, 9/11 fathers, 8/12 professionals). Participants were recruited from the community using poster board and email to the university and hospital staff, and in collaboration with the pediatric departments of Saint-Etienne and Lyon hospitals. All participants gave written informed consent to the study approved by the local Ethics Committee (CHU de Saint-Etienne 2021, Comité de Protection des Personnes Ouest V, France, n° ID RCB 2021-A02270-41) and received an 80€ compensation for their participation. They were all right-handed and reported no history of psychiatric, neurological, hearing disorder, depression or anxiety. They were additionally screened for depression and anxiety with Beck Depression Inventory (Beck et al., 1988) and Spielberger State-Trait Anxiety Inventory (Spielberger et al., 1970), respectively. Their basal empathy level was assessed using the Balanced Emotional Empathy Scale (BEES) (Mehrabian, 1996) and the Inter-Personal Reactivity Index (IRI) (Davis, 1980). In addition, parents took the Postpartum Bonding Questionnaire (PBQ) (Brockington et al., 2006; Demanche et al., 2022) and the professionals the Jefferson Scale of Physician Empathy (JSPE) (Zenasni et al., 2012b). All parents had at least one baby aged under 2 years at the time the experiment (mean age  $\pm$  SD =  $13.6 \pm 5.5$  months, [2.5-23]), and had up to 3 more older children. They reported spending  $5.8 \pm 1.7$  hours a day caring at their baby, excepting the time when the baby is asleep ( $5.0 \pm 1.2$  [3-7] for fathers,  $6.5 \pm 1.7$  [3-10] for mothers). There were 4 couples in the 40 parents. All mothers reported to be their baby primary caregiver, as well as 15% of fathers (3/20), and one father reported a balanced involvement in caregiving. Parents reported a cumulative experience in babies care of  $3.0 \pm 2.9$  years ( $2.3 \pm 1.4$  for fathers,  $3.7 \pm 3.8$  for mothers). None of the mothers was breastfeeding at the time of the experiment. Professionals were all childless and working in pediatric care at the time of the experiment: 1 medical student, 7 childcare assistant and 12 childcare nurses. They were working with babies for  $5.3 \pm 4.8$  years, spending  $9.5 \pm 2.8$  hours caring at babies on their working days. None of the parents were working in pediatric care.

### **Stimuli and acoustic characterization**

Cry recordings were extracted from a cry data database previously built by the ENES laboratory (Koutseff et al., 2017). Discomfort cries were recorded during bathing, undressing, or dressing by parents at the baby's home. Pain cries were recorded during scheduled routine vaccination at the doctor's office (N = 22 babies, 10 boys and 12 girls; age =  $60.3 \pm 3.4$  days on the vaccination day; delay between recording sessions of discomfort cries and pain cries for a given

baby =  $6.9 \pm 3$  days, see (Koutseff et al., 2017) for a complete description of the recording parameters).

Using Audacity software ([www.audacityteam.org](http://www.audacityteam.org)), we isolated 284 cry sequences from these raw recordings (mean sequence duration =  $6.3 \pm 1.1$  s; 4 sequences of pain cry per baby and 2-19 sequences of discomfort cry per baby). We took care to isolate sequences without background noise such as adult voices, water flowing or door slamming.

To limit pseudo replication of stimuli, we retained only the babies for whom we had at least 10 sequences of discomfort cry and 4 sequences of pain cry ( $N = 9$ ; 3 boys, 6 girls; age =  $59.4 \pm 3.4$  days; 150 cry sequences). Due to poor identity (Chapter I) or pain (Corvin et al., 2022, Chapter II.1) recognition rate in previous playback experiments, one of this 9 babies was not used as “assigned” baby.

The sound intensity of the cry sequences was normalized to 100% of the maximal amplitude using the “normalize” function of the tuneR R package ([cran.r-project.org/web/packages/tuneR/index.html](http://cran.r-project.org/web/packages/tuneR/index.html)), and audio files were saved at a binary rate of 705 Kbits/s with Audacity for compatibility with Eprime 2.0 software.

For each stimulus, mean roughness (proportion of modulation spectrum within the roughness range of amplitude modulation 30-150 Hz) was calculated with soundgen 2.6.0 R package (Anikin, 2019).

## **Experimental design**

The experiment took place on two days, with a training/testing paradigm. The first day, participants listened to discomfort cries from their assigned, “familiar” baby (6 different discomfort cries, named “training cries”). They were given the following instruction: “You are going to hear several cries of one baby, who will be named YOUR baby for the rest of this study”.

The second day, participants performed the test session within the MRI scanner. Cries were delivered through high-quality headsets (MR compatible earphones S14, Sensimetrics Corporation, MA, USA). Participants had first a recall of the training cries, presented in a different randomized order compared to the first day. After, they received the instructions for the task and practice it on the training cries (they were aware that it was discomfort cries from

their assigned baby). This first part took place during the anatomical scan and audio volume was adjusted after if necessary, to provide an optimal listening despite the scanner noise.

Then, fMRI acquisitions start and participants performed the test part on 64 cries divided equally into 4 conditions:

- 4 discomfort cries from the assigned baby, presented 4 times each: 16 cries. To avoid the possibility of idiosyncratic acoustic characteristics biasing the results, none of these cries were present in the training cries.
- 4 pain cries from the assigned baby presented 4 times each: 16 cries
- 4 discomfort cries from 4 unknown babies: 16 cries
- 4 pain cries from 4 unknown babies: 16 cries

Each stimulus consisted in a cry played twice (cumulated duration: mean  $\pm$  SD = 13.2  $\pm$  2.3 seconds [8.2-18.8]) and, immediately after, participants answered to two questions displayed on a screen: “YOUR baby?” and “Pain?”. They had 3 seconds per question, to answer “Yes” or “No” using two response buttons (site 1: model Lumina LU400-PAIR, Cedrus Corporation, USA; site 2: 4 buttons diamond response pad P904, Current Design, PA, USA). The first answer to each question as well as the answer time was recorded. Rating time was followed by a silence of a pseudo-randomized duration (range 5-11 seconds) to avoid anticipation effects.

The presentation order of the 64 stimuli was pseudo-randomized across 4 sessions of 8.5 min to control that the delay between two identical conditions stay under 128 seconds (see detail in Table 1), due to the high pass filter applied (see fMRI statistical analysis).

Session A	Session B	Session C	Session D
stranger1.pain.1	assigned.pain.1	assigned.discomfort.1	stranger2.discomfort.4
assigned.discomfort.2	stranger2.pain.2	stranger3.pain.3	assigned.pain.3
assigned.pain.3	stranger2.discomfort.1	stranger2.pain.4	assigned.discomfort.4
stranger4.discomfort.1	stranger3.discomfort.2	stranger1.discomfort.3	assigned.discomfort.1
stranger2.pain.1	assigned.pain.2	assigned.discomfort.2	stranger1.discomfort.4
assigned.discomfort.1	stranger3.pain.2	stranger1.pain.4	assigned.pain.1
assigned.pain.4	stranger1.discomfort.1	stranger2.pain.3	assigned.discomfort.3
stranger3.discomfort.1	stranger4.discomfort.2	stranger2.discomfort.3	assigned.discomfort.2
stranger3.pain.1	assigned.pain.3	assigned.discomfort.3	stranger4.discomfort.4
assigned.discomfort.4	stranger1.pain.2	assigned.pain.2	assigned.pain.2
assigned.pain.3	stranger2.discomfort.2	stranger1.pain.3	assigned.discomfort.4
assigned.pain.1	assigned.discomfort.1	stranger3.discomfort.3	stranger4.pain.4
stranger4.pain.1	assigned.pain.4	assigned.discomfort.4	stranger3.discomfort.4
assigned.discomfort.3	stranger4.pain.2	assigned.pain.1	assigned.pain.4
assigned.pain.4	stranger1.discomfort.2	stranger4.pain.3	assigned.discomfort.3
assigned.pain.2	assigned.discomfort.2	stranger4.discomfort.3	stranger3.pain.4

**Table 1.** Pseudo-randomization of the 64 stimuli across the 4 fMRI sessions.



The session order was pseudo-randomized across participants. Between the second and third session, participants had a recall of their familiar baby listening again to the training cries.

The association between the familiar baby and the 4 unknown babies was unique to each participant, achieved using the “sample” function in R statistical software (<https://www.r-project.org/>). For a given familiar baby, training and testing cries vary across participants. To avoid decision bias, participants did not know how many cries came from their assigned baby or how many different babies they were listening to, nor how many pain or discomfort cries there was.

E-Prime 2.0 software (Psychology Software Tools, Inc.) was used to play the cries, display the instructions and ensure the synchronization of stimuli onset and the acquisition of ratings.

### **Behavioral analysis**

Statistical analyses were performed in R using Bayesian mixed models fitted with the brms R package (Bürkner, 2017). Response scores were modeled using a logistic function (Bernoulli family). 3000 iterations were run over two MCMC chains (Markov chain Monte Carlo) with the first 1000 iterations of each chain used to adjust the algorithm. To improve convergence when modeling response scores, we specified mildly informative priors (distribution (0,1), chance level at 50%). Results were summarized as medians of the posterior distributions and 95% credible intervals (CIs). The chance level was 50% for each question, as it was a two-forced choice (yes/no) with a balance number of the two conditions (assigned/unknown or pain/discomfort). Credible intervals for estimates above the chance level indicate a credible effect given the observed data and model structure (Kruschke & Liddell, 2018). Similarly, when contrasting two conditions, CIs excluding the null value can be inferred to indicate a credible difference between the conditions.

For the assigned baby recognition, the outcome variable was the binary “yes/no” response that participants gave when asked whether or not the cry belonged to their assigned baby. The baby status (familiar or unknown), the cry cause (pain or discomfort) and the participants’ group (father, mother or professional) were included in the model as fixed factors. Participant identity and familiar baby identity were included as random factors. Random slopes were defined using the Watanabe-Akaike information criterion for model selection (WAIC). The structure of the model in brms syntax was:

```
rated_baby_status ~ real_baby_status x real_cause x group +  
                    (real_baby_status + real_cause | subjectID + assignedID)
```

In a very similar way for the cause recognition, the outcome variable was the success at recognizing correctly the crying context. The baby status, the cry cause and the participants' group were also included in the model as fixed factors. Participant identity and baby's identity were included as random factors. After selection of random slopes, the structure of the model in brms syntax was:

```
success_cause ~ real_baby_status x real_cause x group +  
                (real_baby_status + real_cause | subjectID + babyID_stim)
```

In addition, for identity recognition, we calculated for each assigned baby its correct recognition, and how unknown were mistaken as being the assigned baby. We did this analysis for discomfort and pain cries and represented it with confusion matrices.

In addition, for context recognition, we calculated for discomfort and pain cries the correlation between correct identification and the roughness of each audio stimulus.

### **MRI data acquisition**

All participants underwent a magnetic resonance imaging in a 3T MR system (Prisma Siemens, Erlangen, Germany, EU) with a 64-channel head/neck coil.

A T1-weighted anatomical MP-RAGE image (TR = 2000 ms; TE = 2.19 ms, flip angle 8°, 192 sagittal slices with 0.9 mm isotropic voxels, matrix 256 × 256) was acquired at the beginning of the experiment.

Four BOLD runs of 8 min 26 seconds each were acquired using an interleaved gradient echo-planar imaging sequence (TR = 2200 ms, TE = 30 ms, isotropic voxel of 3.0 mm, flip angle 90°, 40 axial slices/volume, with a GRAPPA acceleration factor of 2). Orientation of slices was around the AC-PC plane but to avoid the artefact of magnetic susceptibility due to the sinuses, the plane was tilted to -10°.

A gre-field sequence with identical geometrical parameters and echo spacing than the BOLD sequence was acquired to correct spatial distortions in the BOLD data.

### **MRI data pre-processing**

Dicom images were converted to nifty in BIDS format using Heudiconv (Halchenko et al., 2023). The first 5 volumes were discarded of the following processes.

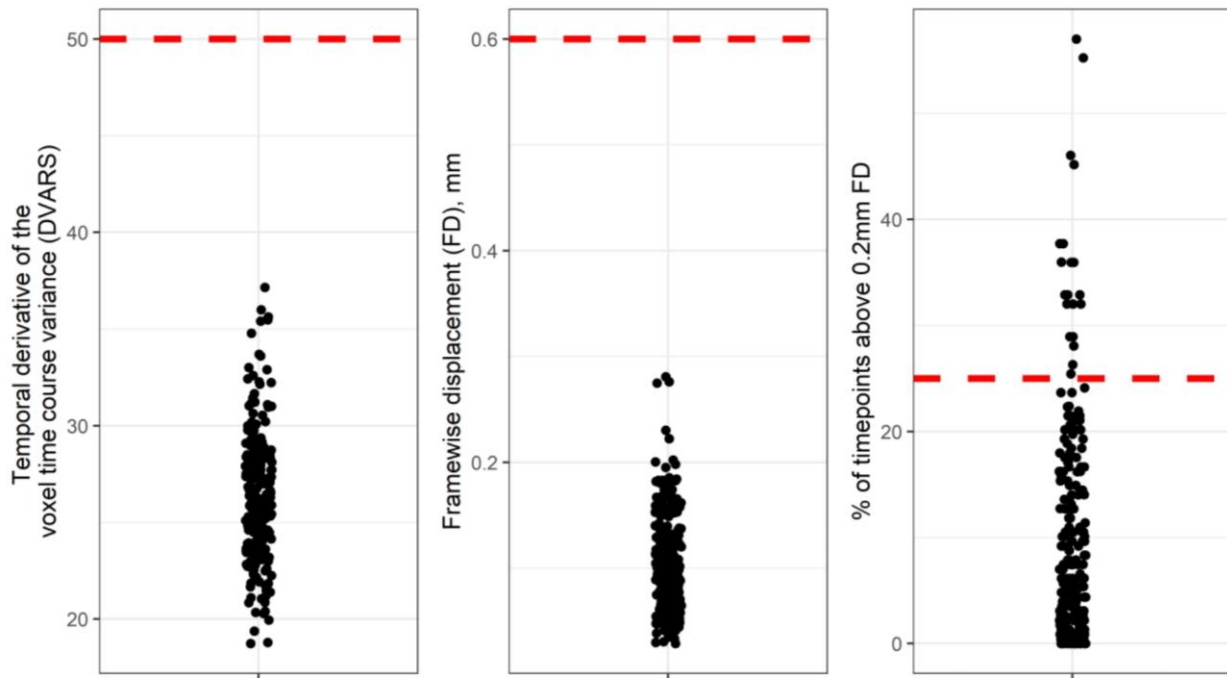
Data were then processed using fMRIPrep 21.0.2, 22.0.0 and 22.0.2 (Esteban et al., 2018, 2023) (RRID:SCR\_016216). Preprocessing are detailed in supplementary data (copy of the fmriprep output) and briefly described hereby.

Anatomical T1w image was segmented in cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) and normalized towards the MNI152NLin6Asym template.

BOLD images were corrected for BO inhomogeneity using fieldmap and for head movements; slice-time corrected and coregistered to the T1w image and normalized to the MNI template. Automatic removal of motion artifacts using independent component analysis (ICA-AROMA (Pruim et al., 2015)) was performed after spatial smoothing with an isotropic Gaussian kernel of 6mm FWHM. Resulting “non-aggressively” denoised runs were resampled and were spatially smoothed again with an isotropic kernel of 5mm FWHM, so that they were globally smoothed at 8mm.

### **MRI quality check**

All data were evaluated with the MRI Quality Control tool (MRIQC 22.0.6, Esteban et al., 2017) to exclude any low quality data. Average framewise displacement (FD) and standardized DVARS were used as the main quality control measures for the functional sessions. Sessions were excluded if FD value exceeded 0.6 mm, or if more than 25 % of a participant’s time points were above 0.2 mm FD, or if the temporal derivative of the voxel time course variance (DVARS) reflected more than 5% BOLD signal change (equivalent to a DVARS\_nstd from MRIQC of over 50) (Raiser et al., 2020). No run showed a FD value above 0.6 mm, or a DVARS\_nstd above 50. Twenty sessions distributed among 11 participants had at least 25% of the volumes showing a FD above 0.2mm (Figure 1). The three participants (two mothers, one father) for which 3 or 4 sessions out of 4 were low quality were excluded for functional analysis. For the eight others (5 mothers, 2 fathers, 1 professional), individual statistical analyses were done without the one or two low quality runs.



**Figure 1.** *MRI quality check metrics for functional sessions. The red dotted lines represent the thresholds for run exclusion.*

Data from the sixty participants were recorded on two sites with the same 3T MR system with a balanced repartition across sites. To ensure that there was no machine effect, we run a statistical comparison on the contrast representing overall cry listening. Comparison between participants recorded on the two sites resulted in no significant difference.

### **fMRI statistical analysis**

Analyses were done using SPM12 (Wellcome Trust Centre for Neuroimaging, UK). A within-subject general linear model (GLM) design matrix was built and incorporated the 4 functional sessions (or 2 or 3 for subjects having low quality runs as mentioned in the MRI quality check section). Four different models were computed and the specific regressors of interest are detailed below. For each model, four regressors of no interest described 1/ the rating phases (6s following the displaying of the 16 questions “YOUR baby?” / “Pain?”); 2/ the motor responses to all questions (32 onsets of 1s); 3&4/ the time-course of the CSF and WM as saved in the confounds file of fMRIPrep output. Regressors were convolved with the canonical hemodynamic response function (HRF) and its time-derivative except the regressors of no-interest 3&4. A high pass filter with a cut off of 128 s was applied to remove low-frequency

signals, caused by physiological noise as well as by physical (scanner-related) noise, which are a main source of autocorrelation.

#### *Analysis contrasting conditions*

Four regressors of interest were defined, corresponding to the four conditions of our factorial design: pain of the familiar baby (FP), discomfort of the familiar baby (FD), pain of unknown babies (UP) and discomfort of unknown babies (UD). Onset and duration of each trial matched the onset and duration of the audio stimulus. Analyses focused on the contrasts assessing the difference between pain and discomfort (FP+UP)-(FD+UD), between familiar and unknown babies (FP+FD)-(UP+UD), between familiar and unknown babies for pain cries FP-UP and between pain and discomfort for the familiar baby FP-FD.

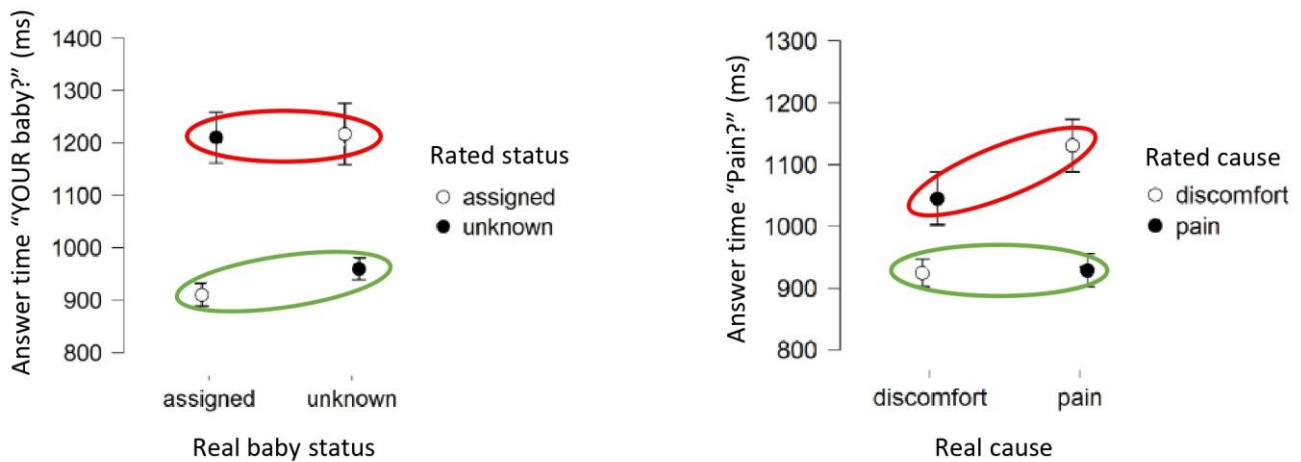
#### *Analysis based on successful recognition*

For this analysis, only successful trials were included in the regressors of interest, giving to each trial a weight depending of the subject confidence when answering each question. To do so, we used answer time (time between the beginning of the displaying of the question and the subject answer) as a proxy for confidence. Indeed, successful answers were given on average more quickly than wrong ones, for each question (ANOVA, interaction between real and rated status:  $F=65.7$ ,  $p<0.001$  for the “YOUR baby?” question;  $F=23.4$ ,  $p<0.001$  for the “Pain?” question; see Figure 2).

We constructed 2 index (ID & Cause) that could be used as regressors in the GLM. First, to deal with normal data, each answer time was summarized by its decile in the whole distribution of each subject (value from 1 to 10).

Then we assigned to each trial two values, one linked to the question “YOUR baby?” (ID) and the other to the “Pain?” one (Cause). When the subject gave the wrong answer, the value was 0. Otherwise, the absolute value ranged from 1 (long answer time, 10<sup>th</sup> quartile) to 10 (short answer time, 1<sup>st</sup> quartile), thus giving more weight for successful trials recognized quickly. For ID value, the sign was positive when the trial corresponds to a familiar cry correctly assessed and negative when the trial was an unknown cry correctly rejected. The Cause value associated

to the “Pain?” question was constructed in the same manner: positive values associated to correct recognition of pain, and negative values to the correct rejection of discomfort.



**Figure 2.** Correct answers were given significantly quicker than incorrect ones. Answer time are circled in green for correct answers and in red for incorrect ones. The interaction between real and given status was significant (ANOVA:  $F=65.7$ ,  $p<0.001$  for the “YOUR baby?” question;  $F=23.4$ ,  $p<0.001$  for the “Pain?” question). Means and standard errors are represented.

We had drawn inspiration from (Mumford et al., 2023) to construct the GLM where the cry stimuli were defined by 3 parametric modulators. The main regressor (‘cries’) correspond to all cry stimuli with a constant duration corresponding to the minimal stimuli duration (8 seconds). The first modulator was the real duration of each stimulus, centered on the mean stimuli duration. The second and third modulator were respectively the ID value and the Cause value. These three parametric modulators were not orthogonalized because they have low collinearity.

Analyses focused on the contrasts assessing the correct recognition of the baby identity (ID: contrast ID\_correct) and the correct recognition of the cause of the cry (cause modulator: Cause\_correct). For example, the ID modulator contrast (at 1) will show more activity when listening to the familiar baby than to the unfamiliar ones, when correctly identified and especially when the subject is confident in the given response.

#### *Analysis based on given responses, regardless of the listened condition*

We also defined a GLM with 2 regressors of interest representing the given response to each question, regardless of the listened condition. The ID index range from -10 (cry quickly assessed as being from an unknown baby) to 10 (cry quickly assessed as being from their

familiar baby), and the Cause index from -10 (cry quickly assessed as a discomfort cry) to 10 (cry quickly assessed as a pain cry). The GLM contain a main regressor ‘cries’ with 3 parametric modulators: centered real duration of the cry, ID index and Cause index. The two contrasts of interest were ID\_eval, showing more activity when the cry was assessed as being from the familiar baby compared to when assessed as being from an unknown one, and Cause\_eval linked to pain labelling versus discomfort labelling.

#### *Analysis linked to acoustic roughness*

Same structure was used to model the variability of the neural response linked to the acoustic roughness (see Stimuli and acoustic characterization for the value definition). The main regressor was the cry stimulus (8 second duration), with two parametric modulators: the actual duration and the mean roughness of the stimulus, both centered on their mean across all stimuli. The analyses were focused on the contrast assessing the roughness effect (Roughness).

#### *Group analysis*

Second-level one-sample T-tests were performed to assess the brain activity within the entire group (57 subjects after exclusion of 3 participants due to low quality data) related to the contrasts described in the 3 models above.

Group comparisons were performed to assess the effect of listener’s sex (comparing mothers and fathers) and the kind of experience in babies care, either parental or professional (comparing mothers and professionals). Intergroup BOLD contrasts were computed with two-sample t tests.

The resulting SPM maps were thresholded at  $p < 0.001$  and clusters that survived FWE correction for multiple comparisons  $p < 0.05$  were reported. Anatomical regions were labeled using the HCPex atlas (Glasser et al., 2016; Huang, 2022) and, for location under the thalamus not segmented in the HCPex atlas, we used the atlas created by (Krauth et al., 2009). Activations were visualized on the average T1 image across all subjects.

T values of the chosen peaks presented in tables were extracted for each subject. These values were compared across groups and correlated with subject accuracy and several personal traits (IRI total score and subscores, BEES score, PBQ score).

## **Results**

### **Personality traits: Fathers had lower basal levels of empathy**

The BEES average score was significantly lower in fathers ( $42 \pm 24$ ) compared with mothers ( $74 \pm 17$ ) (ANOVA post-hoc test,  $p < 0.001$ ). In the same way, IRI scores were significantly lower for fathers than for mothers (total score: fathers  $64 \pm 12$ , mothers  $75 \pm 9$ ; fantasy subscore: fathers  $15 \pm 5$ , mothers  $21 \pm 4$ ; empathic concern subscore: fathers  $18 \pm 4$ , mothers  $24 \pm 3$ ; ANOVA post-hoc test, respectively  $p = 0.001$ ,  $p < 0.001$  and  $p < 0.001$ ; no difference in perspective taking and personal distress subscores). There was no significant difference between mothers and professionals.

Participants took the IRI questionnaire two times: at the first visit and just after the MRI session. Their perspective-taking subscore was in the normal range at the two time points but significantly higher after the MRI session (paired samples t-test:  $p < 0.005$ ).

There was no significant difference in the Parental Bonding Questionnaire between mothers and fathers ( $6.8 \pm 4.1$  in mothers,  $9.8 \pm 6.3$  in fathers, the norm being below 26; t-test:  $p = 0.081$ ). There was no significant difference either in JSPE total score between childcare assistants and childcare nurses (total score:  $114.4 \pm 4.4$  for childcare assistants,  $120.3 \pm 6.5$  for childcare nurses; Mann-Whitney test:  $p = 0.052$ ). The JSPE compassionate subscore was significantly higher for nurses than for childcare assistants ( $36.3 \pm 3.6$  for childcare assistants,  $40.3 \pm 3.5$  for childcare nurses; Mann-Whitney test:  $p = 0.046$ ).

### **Behavioral results**

#### *Familiar babies were successfully recognized based on discomfort cries*

Participants recognized successfully 66.5% [59.9, 73.6] the cries coming from their assigned familiar baby (chance level of 50%), and correctly rejected cries from unknown babies (20.2% [14.7, 28.5] being mistaken as coming from the familiar baby, Figure 3). Cry cause interfered with this correct recognition: 84.4% [78.5, 88.7] of assigned baby discomfort cries were correctly identified, but only 48.7% [37.7, 61.7] of the pain cries, which was not above the chance level. However, pain cries from unfamiliar babies were more likely to be rejected than those of the familiar baby (32.8% [22.9, 41.2] more likely rejected). These results suggest that pain in cries interferes with assigned baby recognition.

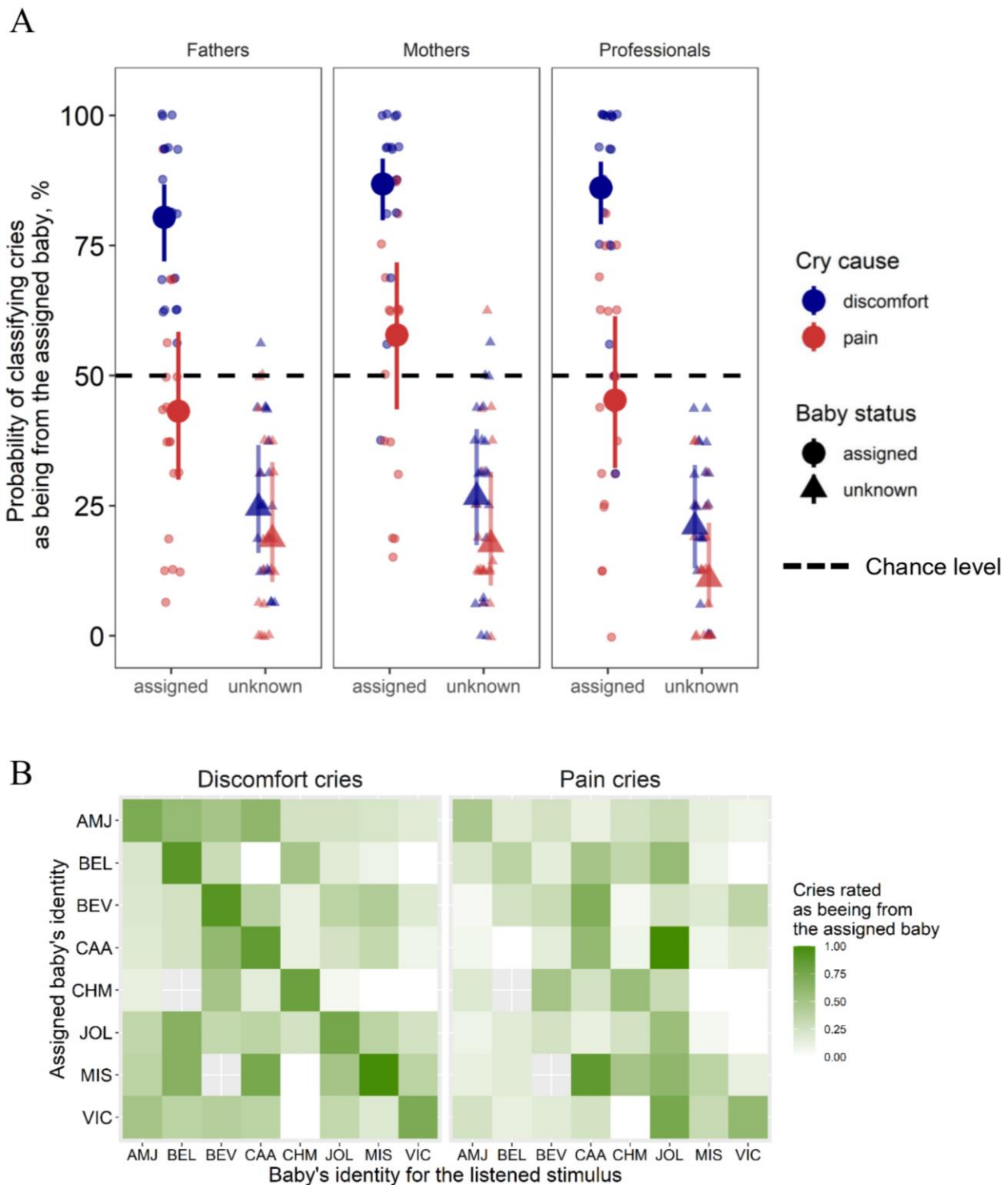


All 3 groups of participants recognized successfully their assigned baby's cries, with 61.8% [52.6, 71.1], 72.4% [63.5, 80.1] and 65.7% [57.0, 74.6] for fathers, mothers and professionals respectively. Mothers were better than fathers (10.3% [0.7, 19.6]) but not than professionals (6.4% [-2.9, 15.5]).

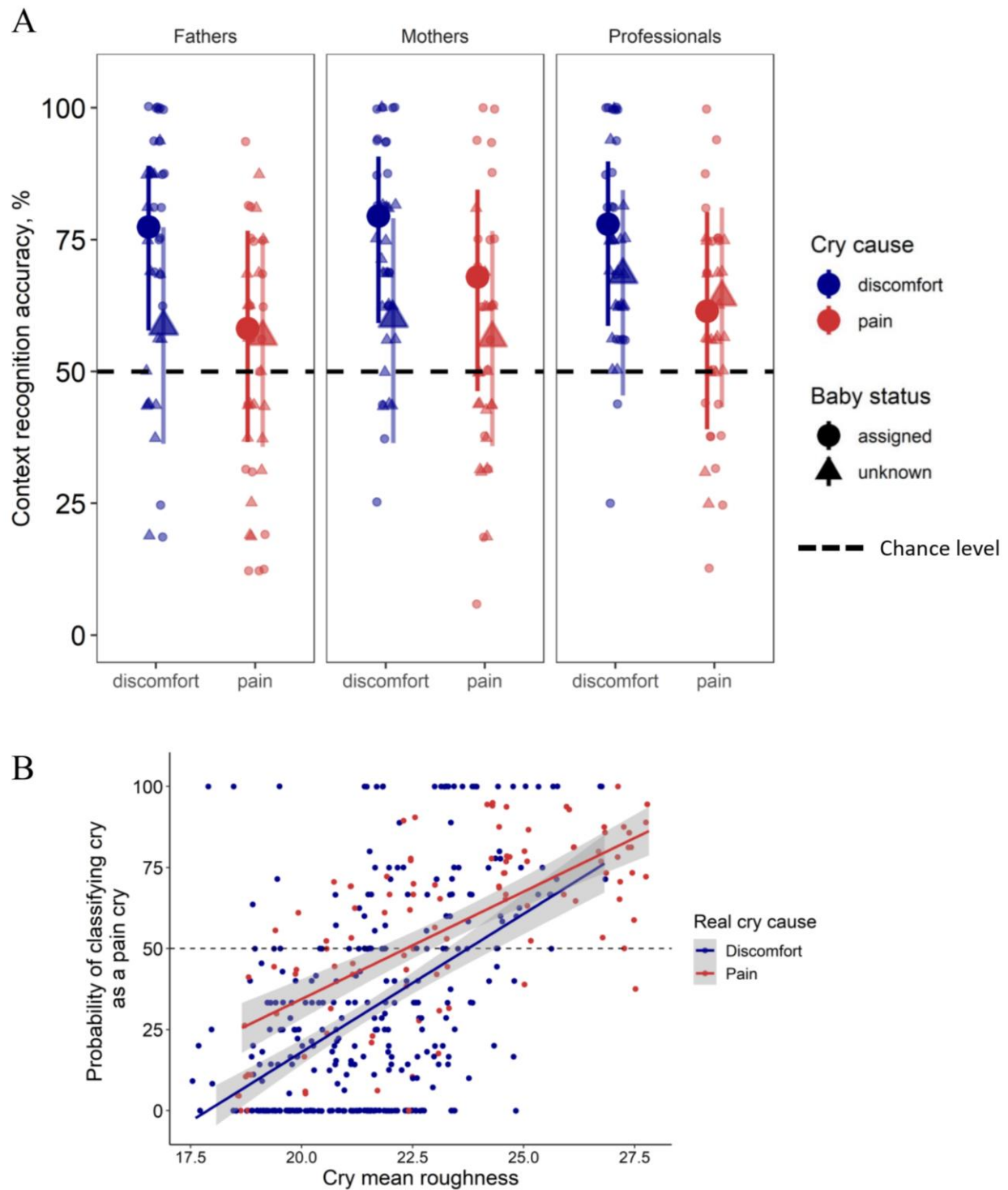
*Cry cause identification was difficult, driven by cry roughness*

When participants assessed whether cries were pain cries or not (Figure 4A), they were slightly above the 50% chance level with 65.3% [50.7, 76.9] of correct recognition. Seventy percent (70.1% [50.9, 84.1]) of discomfort cries were successfully rejected, but only 60.7% [41.1, 77.7] of pain cries were correctly identified, which was not above the chance level. Both professionals and mothers recognized cries cause above the chance level but not fathers, with respectively 67.6% [53.2, 79.0], 65.7% [51.3, 77.6] and 62.5% [47.0, 74.8] of correct recognition. However, there was no statistical difference between the groups. Being familiar with one baby's cries made participants better at identifying cry cause, with cries from the assigned baby being 9.4% [3.6, 15.1] more successfully identified than those from unknown babies.

Pain cries were characterized by more acoustic roughness than discomfort cries (Mann-Whitney:  $p < 0.001$ ). Cries with more roughness were more likely to be classified as pain cries (significant correlation Pearson's  $r = 0.59$ ,  $p < 0.001$ ). Figure 4B shows that this is the case for both discomfort ( $r = 0.50$ ,  $p < 0.001$ ) and pain cries ( $r = 0.67$ ,  $p < 0.001$ ).



**Figure 3. Adult listeners recognized very well their familiar baby based on discomfort cries, but not based on pain cries.** (A) Solid disk and triangles represent the medians of the posterior distribution, and bars the 95% credible intervals (CI). Small shapes represent the individual data. The dotted line indicates the 50% chance level. Participants showed 84% [79,89] of correct recognition based on discomfort cries, but only 49% [38,62] based on pain cries listening. They correctly rejected cries of unknown babies (20% [15,29] of false-positive), either discomfort and pain cries. (B) Confusion matrices for discomfort and pain cries. Strong green on the diagonal correspond to a correct recognition of the assigned baby, which drops in pain cries compared to discomfort cries.

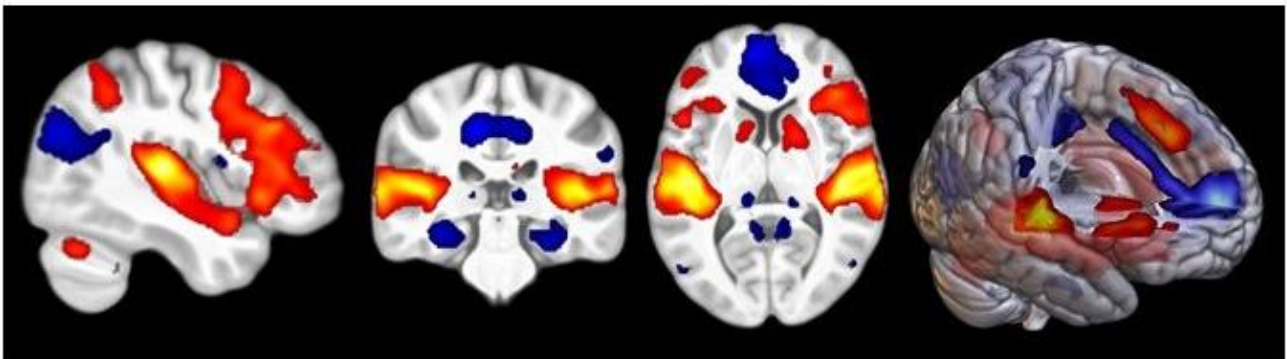


**Figure 4. Cry cause was correctly recognized only for assigned baby’s discomfort cries, and driven by cry roughness.** (A) Solid disk and triangles represent the medians of the posterior distribution, and bars the 95% credible intervals (CI). Small shapes represent the individual data. The dotted line indicates the 50% chance level. Participants correctly recognized 70% [51, 84] of discomfort cries, but only 61% [41, 78] of pain cries. (B) Cries characterized by more roughness were more likely to be classified as pain cries. The overall positive correlation was significant (Pearson’s  $r=0.59$ ,  $p<0.001$ ), for both discomfort (Pearson’s  $r=0.50$ ,  $p<0.001$ ) and pain cries (Pearson’s  $r=0.67$ ,  $p<0.001$ ). Each dot is an audio stimulus.

## fMRI results

### *Cries listening involved activation in distributed brain regions*

Regardless of the condition, cries listening compared to the baseline led to bilateral increase of BOLD activity in brain areas previously described in a meta-analysis on cry perception (see Wittman et al., 2019): bilateral STG, anterior insulae, frontal areas (IFG, MFG, post mSFG), angular gyri, caudate nuclei, cerebellum and substantia nigra. Decreased BOLD activity was observed bilaterally in parahippocampal cortices, cingulate cortices, ant mSFG, lateral occipital, thalami (medial pulvinar) and precuneus (Figure 5).

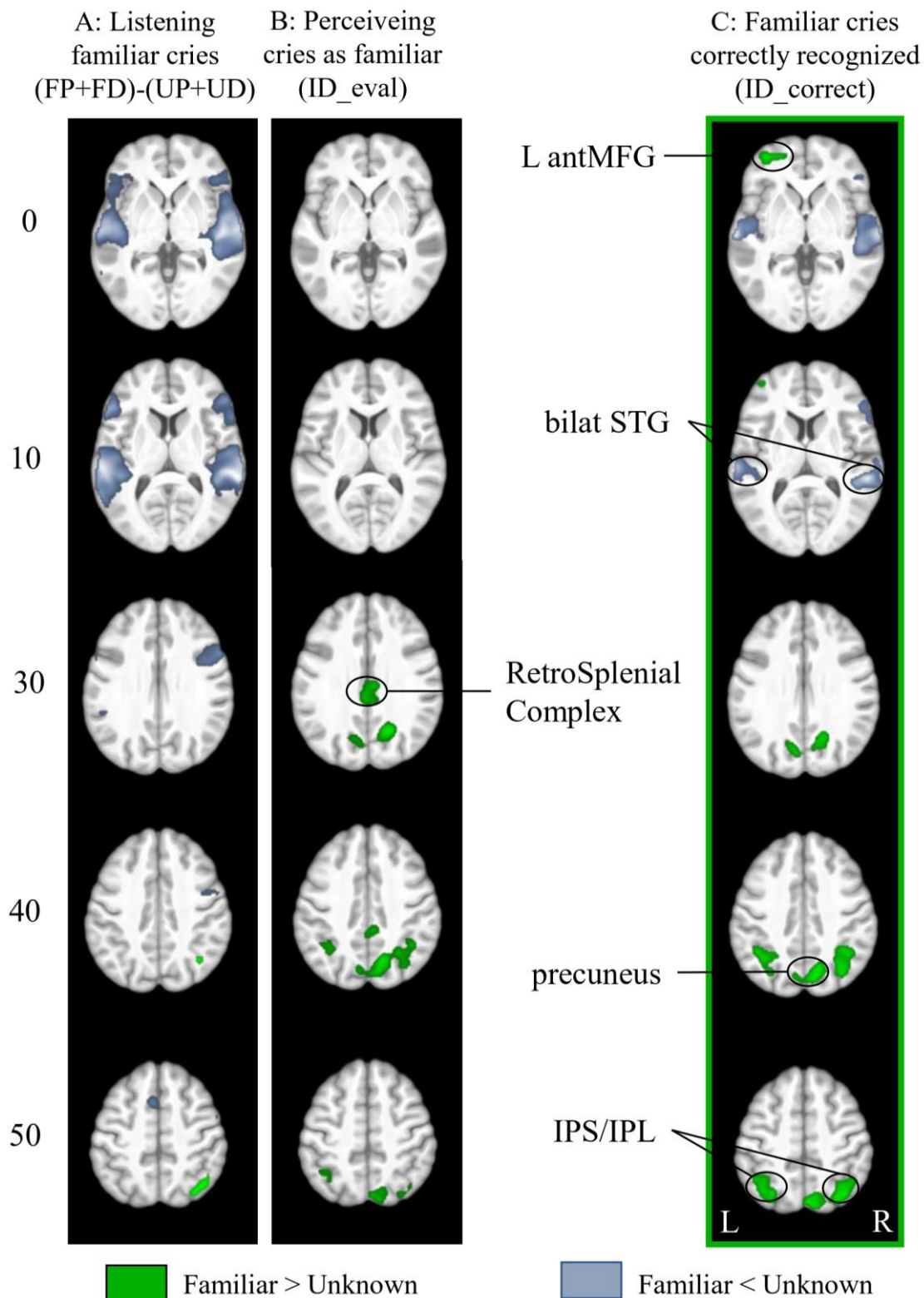


**Figure 5.** *Cries listening involved activation in distributed brain regions (including auditory, cognitive, attention, emotion regulation and mirroring brain networks). BOLD activations (in orange) were observed bilaterally in the STG, anterior insula, frontal areas (IFG, MFG, post mSFG), angular gyri, caudate nuclei, cerebellum and substantia nigra. Decreased BOLD signal (in blue) was observed bilaterally in parahippocampal cortices, cingulate cortices, ant mSFG, lateral occipital, thalami (medial pulvinar) and precuneus (FWE corrected at the voxel level,  $p < 0.001$ ).*

### *Familiar baby recognition*

Correct recognition of the familiar baby, compared to correct rejection of unknown babies (contrast ID\_correct), was associated with increased BOLD activity in the Inferior Parietal Sulcus (IPS) bilaterally, the precuneus and the left anterior Middle Frontal Gyrus. On the contrary, correct rejection of unknown babies was associated with increased BOLD activity in bilateral STG, right STS and left planum temporale (Figure 6C, peaks detailed in Table 2).

Listening to familiar cries, regardless of their perception (contrast (FP+FD)-(UP+UD)) was associated with increased activation in the right IPS (T peak=3.91; MNI coordinates 38, -62, 42; Figure 6A). The perception of cries as familiar, independent of the listened condition (ID\_eval) led to activations in the same brain clusters than correct recognition: IPS bilateral and precuneus, and an extra cluster was found in the retrosplenial complex bilaterally (T peak=5.19; 8, -20, 28; Figure 6B).



**Figure 6. Familiar babies cries activated brain areas known to be involved in perspective-taking, emotion regulation and familiar voice recognition.** BOLD modulations are represented (A) depending of the listened stimulus, (B) depending of the response given by the participant, or (C) when the baby status is correctly recognized. For this last model, BOLD activations (in green) were found in the inferior parietal sulcus bilaterally, the precuneus and the left anterior middle frontal gyrus. Deactivations (in grey) were mostly found in auditory areas (bilat STG).

Cluster p(FWE- corr)	Volume (cm <sup>3</sup> )	T (chosen peaks)	Peak MNI coordinates			HCPex areas	Macroanatomical locations
			x	y	z		
<b>Familiar &gt; Unknown</b>							
0.000	17.71	5.45	32	-70	46	IP1 (PFm, PGs)	R post IPS/IPL
		5.10	8	-76	44	POS2 (7PL, DVT)	R precuneus
0.000	6.73	4.65	-38	-58	44	IP2/PFm (MIP/IP1, LIPd)	L IPS / IPL
0.022	2.17	5.08	-38	52	4	a9-46v (a10p, p47r)	L ant MFG
<b>Familiar &lt; Unknown</b>							
0.000	16.6	6.65	50	-6	-10	STSda/TA2 (STGa)	R STG & STS middle
		6.06	68	-18	4	A5 (TPOJ, A4, STSdp)	R STG & STS post
0.000	9.22	6.51	-66	-18	0	A5 (A4, PBelt, PSL, TPOJ)	L STG, planum temporale
		4.93	-56	2	-10	A5/STSda (STGa/TA2)	L STG
0.013	2.46	4.41	54	36	6	IFSa (44, 45)	R IFG

**Table 2. Significant clusters for the contrast ID\_correct.** For each cluster, peaks have been selected to indicate the areas included in the cluster. The areas shown in brackets indicate the extent of the cluster, and are sometimes partially activated.

### Context recognition

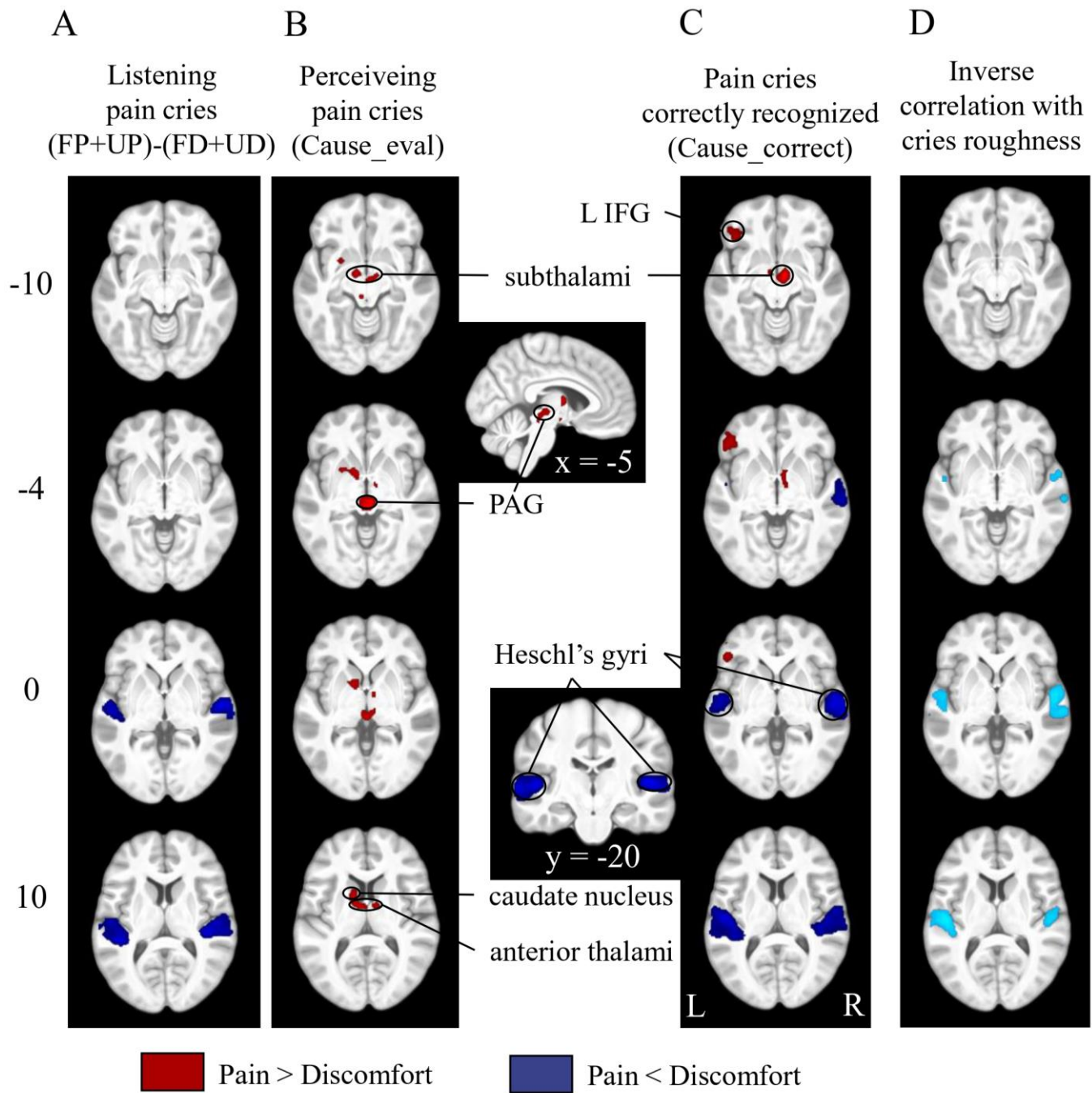
Listening to pain cries, regardless of their perception (contrast (FP+UP)-(FD+UD)) was associated with decreased BOLD activity in bilateral Heschl's gyri (Left: T peak = 5.56; MNI coordinates -52, -16, 7; Right: T = 6.59; 54, -14, 4; Figure 7A).

Identifying cries as pain cries, regardless of the listened condition (Cause\_eval) led to activations in the anterior thalamus, subthalamus and caudate nucleus (Figure 7B, peaks detailed in Table 3).

Correct recognition of pain cries, compared to correct rejection of discomfort cries (contrast Cause\_correct), was associated with increased BOLD activity in the left Inferior Frontal Gyrus and the Peri-Aqueducal Grey matter. On the contrary, correct rejection of discomfort cries was associated with increased BOLD activity in bilateral Heschl's gyri (Figure 7C, peaks detailed in Table 3).

Regardless of the cry context, BOLD activity was negatively correlated with cry roughness in bilateral Heschl's gyri (Left: T = 7.37; -50, -18, 8; Right: T = 6.92; 54, -16, 4; Figure 7D).





**Figure 7. Pain recognition involved high-level processing.** Listening pain cries (A) was associated with decreased BOLD activity in auditory areas (Heschl's gyri). Perceiving cries as pain cries (B) was associated with increased BOLD activity in the thalamus, subthalamus and caudate nucleus. When the stimulus was correctly recognized (C), BOLD activations were found in the left Inferior Frontal Gyrus and the PAG. Deactivations were found bilaterally in Heschl's gyri. The same deactivations were found in correlation to increased roughness in cries (D).

Cluster p(FWE -corr)	Volume (cm <sup>3</sup> )	T (chosen peaks)	Peak MNI coordinates			HCPex / Morel areas	Macroanatomical locations
			x	y	z		
<b>Pain &gt; Discomfort (Cause_correct)</b>							
0.041	1.69	6.07	8	-6	-10	subthalamus	
0.013	2.26	4.25	-48	34	-2	45 (47l, p47r)	L IFG (ventral et ant)
<b>Pain &lt; Discomfort (Cause_correct)</b>							
0.000	10.79	7.46	-50	-16	6	MBelt (A1, pBelt)	L Heschl's gyrus, planum temporale
0.000	11.22	7.37	54	-14	4	PBelt (MBelt, A4, A1)	R Heschl's gyrus, planum temporale
<b>Pain &gt; Discomfort (Cause_eval)</b>							
0.008	2.84	5.42	4	-26	-4	PAG	
		4.25	10	-10	-8	STh	Subthalamus
		4.16	10	-4	10	Morel: Thalamus VApc ; HCPex: VLa	Anterior thalamus
0.008	2.85	3.24	-9	-10	-11	STh	Subthalamus, hypothalamus
		4.35	-12	2	10	Caudate nucleus	
		4.26	-5	-4	10	Morel: thalamus AV/VApc; HCPex: AV	Anterior thalamus

**Table 3. Significant clusters for the contrasts Cause\_correct and Cause\_eval.** For each cluster, peaks have been selected to indicate the areas included in the cluster. The areas shown in brackets indicate the extent of the cluster, and are sometimes partially activated.

#### Other results

No differences were found between mothers and fathers, or between mothers and professionals, for any of the contrasts of interest. Comparisons between familiar and unknown babies for pain cries listening (FP-UP) and between pain and discomfort for the familiar baby (FP-FD) showed no significant activations. There was no significant correlation between peaks value and subject's performance, nor personal traits regarding empathy or parental bonding.



## **Discussion**

In the present study, we investigated how experts in babies care integrate static (familiarity) and dynamic (pain) information contained in babies cries. Our results show that, after a short period of familiarization with discomfort cries of a given baby, adult listeners were able to identify this familiar baby based on listening to other discomfort cries, as shown in previous studies (Bouchet et al., 2020; Gustafsson et al., 2013). This recognition was lost when listening to pain cries, even more than previously shown (Chapter I). Participants successfully rejected cries which were not from their familiar baby, with an expected false-positive rate (see Figure 3). Identifying the crying contexts was more difficult, and participants only identified above chance discomfort for their familiar baby, on which they have been trained (see Figure 4). In a previous study both professionals and parents recognized pain for their familiar baby (Corvin et al., 2022, Chapter II.1). Parents were even able to identify pain and discomfort for an unknown baby. These results were not replicated here, showing firstly that the task asked to the participants was more difficult: it combined two different questions and lasted around 45 minutes in an MRI scanner. The identification abilities of experts are therefore labile and decrease while difficulty increases.

Cries listening led to general activation in distributed brain regions (including auditory, cognitive, attention, emotion regulation and mirroring brain networks; see Figure 5) as previously described (Witteman et al., 2019), as well as reduced brain activity in the default mode network (parahippocampal and cingulate cortices, precuneus, ant mSFG) reflecting attention grasping and increased cognitive load (Jenkins, 2019; Raichle, 2015). Recognition of the familiar baby, regardless of the crying context, was associated with significant increased BOLD activation in the Inferior Parietal Sulcus bilaterally, the precuneus and the left anterior Middle Frontal Gyrus, and decreased activity in auditory areas (see Figure 6). Precuneus and IPS activations were close to those observed in previous studies for mothers listening to their own baby's cry (Hipwell et al., 2015; Laurent & Ablow, 2012). More interestingly, our results were very similar to patterns described when contrasting familiar and unfamiliar adult voices listening, in particular when voices were learned during the experiment (Blank et al., 2014; Kriegstein & Giraud, 2004; Zäske et al., 2017). As cries are a general distress signal, these results can be put into perspective with fMRI studies on empathy for pain, comparing empathy for a loved one (familiar) to a stranger. In a recent study, viewing a loved one experiencing experimental pain had been linked to higher brain activity in the precuneus and the right-lateralized inferior parietal lobe including the supramarginal and angular gyrus (Oliva et al.,

2023). This may be close to our precuneus and IPS observed activations, but the absence of the exact MNI coordinates makes it hard to confirm, especially as these activations were not reported in previous studies with similar designs (Cheng et al., 2010; Mazzola et al., 2010).

Identification of pain in cries did not lead to the expected activations on brain areas involved in empathy for pain (anterior insula, ACC) (Lamm et al., 2011; Singer et al., 2004), but instead to increased activity in the IFG and subcortical structures (thalami, subthalami, hypothalami, PAG; see Figure 7). Frontal activity reflects high level processing involved in emotion regulation, potentially linked to the expertise of listeners, as seen in physicians expert in acupuncture while viewing body parts pricked by a needle, compared to naive participants (Cheng et al., 2007). Subcortical structures, particularly the PAG, may be involved in adult responsiveness to babies signal, to rapidly mobilize wider cortical circuits, as shown in some rodent studies (Parsons et al., 2014; Young et al., 2017). Pain identification was also associated with decreased activity in primary auditory areas (Heschl's gyrus, planum temporale), as alarm screams compared non-alarm screams (Frühholz et al., 2021) or high-distress cries compared to low-distress cries (Montoya et al., 2012), representing a shift from low level sensory processing to high level cognitive processing. In addition, neither pain identification nor roughness processing in babies cries have shown involvement of brain regions associated with aversion like other rough acoustic signals (Arnal et al., 2015, 2019).

From a methodological point of view, we used four different models to explain our data: depending on the listened condition, of the given response, for correct recognition only or linked to acoustic roughness. We obtained consistent results across these different models, with models taking the subject response into account being more informative. This highlight both robustness of our results and relevance of our models based on the participants' given response. Fathers showed lower basal levels of empathy, but there were no sex-differential brain activations (comparison between mothers and fathers). There was no difference either linked to the nature of the experience in babies care (parental or professional, comparing mothers and professional pediatric caregivers). Interestingly, studies focused on identifying the context of baby cries (painful or not) even showed very limited number of activations (Fauchon et al., in prep, Chapter III.1). In the present study, the familiarity recognition task that has been added may have limited the contribution of the brain in identifying pain in cries. Accordingly, from a psychophysical point of view, it seems that the identification task of the cry has made the identification of pain difficult. Such a difficulty is likely to have limited the number of brain activations and possibly also, to have limited them to subcortical areas. It would be of interest

to complete these activity analyses with functional connectivity analysis, to investigate if sex or experience fine-tuned the processing of information in cries between the relevant brain areas involved (Fauchon et al., in prep, Chapter III.1).

**In conclusion, this third chapter shows that babies cries listening leads to brain activity and functional connectivity between regions in 7 sub-networks involved in auditory processing, empathy and mirror processes, mentalizing, emotion regulation, subcortical reward and parental vigilance. Parental experience and sex shape the brain response to these critical sound signals. Processing information in babies cries is difficult, even for adults with a strong experience in babies care. Familiar baby recognition and pain recognition involve brain areas part of mirror and mentalizing networks, corresponding to cognitive aspects of empathy, known to be involved in voice recognition and high-level cognitive processing. Thus, cries are likely to be integrated as complex vocal communicative signal rather than a more basic aversive alert by adult experts in babies care.**

### **Supplementary methods**

Results included in this manuscript come from preprocessing performed using fMRIPrep 21.0.2, 22.0.0 and 22.0.2 (Esteban et al., 2018, 2023) (RRID:SCR\_016216), which is based on Nipype 1.8.5 (Esteban et al., 2022; Gorgolewski et al., 2011) (RRID:SCR\_002502).

#### *Preprocessing of B0 inhomogeneity mappings*

Fieldmap images were used to estimate B0 nonuniformity map (or fieldmap) was estimated from the phase-drift map(s) measure with two consecutive GRE (gradient-recalled echo) acquisitions. The corresponding phase-map(s) were phase-unwrapped with prelude (FSL 6.0.5.1:57b01774).

#### *Anatomical data preprocessing*

The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al., 2010), distributed with ANTs 2.3.3 (Avants et al., 2008) (RRID:SCR\_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 6.0.5.1:57b01774, RRID:SCR\_002823 (Zhang et al., 2001)). Volume-based spatial normalization to two standard spaces (MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.3.3), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: ICBM 152 Nonlinear Asymmetrical template version 2009c (Fonov et al., 2009) [RRID:SCR\_008796; TemplateFlow ID: MNI152NLin2009cAsym], FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model (Evans et al., 2012) [RRID:SCR\_002823; TemplateFlow ID: MNI152NLin6Asym].

#### *Functional data preprocessing*

For each of the 4 BOLD runs found per subject, the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL 6.0.5.1:57b01774 (Jenkinson

et al., 2002)). The estimated fieldmap was then aligned with rigid-registration to the target EPI (echo-planar imaging) reference run. The field coefficients were mapped on to the reference EPI using the transform. BOLD runs were slice-time corrected to 1.06s (0.5 of slice acquisition range 0s-2.12s) using 3dTshift from AFNI ((Cox & Hyde, 1997) RRID:SCR\_005927). The BOLD reference was then co-registered to the T1w reference using mri\_coreg (FreeSurfer) followed by flirt (FSL 6.0.5.1:57b01774 (Jenkinson & Smith, 2001)) with the boundary-based registration (Greve & Fischl, 2009) cost-function. Co-registration was configured with six degrees of freedom. Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions (Power et al., 2014)) and Jenkinson (relative root mean square displacement between affines (Jenkinson et al., 2002)). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al. 2014 (Power et al., 2014)). The three global signals are extracted within the CSF, the WM, and the whole-brain masks.

The BOLD time-series were resampled into standard space, generating a preprocessed BOLD run in MNI152NLin2009cAsym space. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Automatic removal of motion artifacts using independent component analysis (ICA-AROMA (Pruim et al., 2015)) was performed on the preprocessed BOLD on MNI space time-series after removal of non-steady state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6mm FWHM (full-width half-maximum). Corresponding “non-aggressively” denoised runs were produced after such smoothing. Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos, 1964).

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# General discussion

The aim of my thesis was to investigate how adults perceive information contained in babies cries, especially cries produced in a painful condition, and how being familiar with one given baby, or with babies in general, shapes this perception. As many mammalian vocal signals, two types of information are described in cries (Aubin & Mathevon, 2020): static information related to the baby's identity, and dynamic one reflecting the baby's physiological state. I was particularly interested by the interactions between these two kinds of features, combining psychoacoustic and neuroimaging approaches. Before the beginning of this thesis project, there were multiple evidences that baby's identity was reflected by the fundamental frequency parameters (see I.3.1 in the General Introduction), thus allowing a given baby to be identified through cries listening. These parameters are stable in the first months of life (Lockhart-Bouron et al., 2023) and linked to the voice pitch at infant and adult ages (Fouquet et al., 2016; Levvero et al., 2018). Baby recognition was shown for parents and nonparents, always based on mild-discomfort cries listening and possible even for very short exposures (Bouchet et al., 2020; Gustafsson et al., 2013). On the other hand, dynamic information on pain was linked to acoustic roughness, i.e. less voiced and harmonic cries with the presence of nonlinear phenomena, parents being able to rate pain for their own baby (Koutseff et al., 2017).

First, I showed that pain cries are characterized by a more variable pitch, with a less defined fundamental frequency and more frequency modulations than discomfort cries (Chapter I; see the results summary figure on page 146 for a synthesis). This leads to a reduction of static information supported by pain cries, making more difficult to recognize one given baby based on pain cries. Both machine learning classifiers and human subjects show similar recognition performance, showing that listeners are able to capture the acoustic information present in cries. While recognition of a familiar baby based on discomfort cries is sensitive to experience in babies care, it seems to reach a plateau for pain cries, nonparents being as good as parents. However, this identity recognition based on pain cries listening is difficult, participants showing lower recognition rate, and higher false-positive rate than studies based on discomfort cries listening. In addition, in a more difficult task when asked to identify the crying contexts simultaneously, I observed a complete loss of this identity recognition ability (Chapter III.2). Overall, when focused on experts in babies care, recognition of a familiar baby on both discomfort and pain cries engages brain areas known to be involved in voice recognition: bilateral IPS, precuneus, and left anterior MFG, associated with decrease in auditory areas (Chapter III.2). This shows that static information on one's individual voice are already perceived as such in babies cries, at least by expert listeners.



Another way of understanding these results is to consider them not as a loss of individual information and disturbance of the familiarization process, but as a convergence of the expression of pain in cries. Indeed, I showed that the acoustic space occupied by various babies' discomfort cries is shrunk for pain cries, i.e. pain cries for various babies are more similar than discomfort ones (Chapter I). The acoustic features characterizing pain in cries are nonlinear phenomena, mainly chaos for acute pain cries (here just after the vaccine injection), and vibrato-like frequency modulations for residual pain cries, a short delay after (Chapter II.3). Recently, these same acoustic features have been highlighted in Congolese baby cries (Cornec, 2023), showing that pain expression in cries is shared even in very different cultural contexts. Knowing this shared expression of pain in cries, supported by specific acoustic features, I investigated how adults identify this information.

Surprisingly, adults with no experience in babies care, thus unfamiliar to babies cries, were totally unable to identify pain in cries. Identification ability was progressively gained through experience in babies care, either parental or professional. Despite the shared aspect of pain expression, being familiar with one baby, even through a very brief exposure, still makes easier to identify pain for this given baby for adults with a moderate experience. More experienced adults, i.e. parents with babies under two years-old, were able to recognize pain in cries even for a baby who was completely unfamiliar (Chapter II.1). This shows that parents' ability to identify pain is generalizable to totally unfamiliar babies, even if they may use their baby as a reference. Professionals, on the other hand, who have accumulated experience with many different babies, are no better at generalizing and recognizing pain in unfamiliar babies. For parents, pain evaluation is closely linked to acoustic features specific to pain cries, with increased pain ratings when chaos and vibrato episodes are longer in cries (Chapter II.3). However, even in experts in babies care, this ability is not so robust, reduced in a more difficult paradigm (Chapter III.2). Interestingly, for cry causes other than pain, causes are almost impossible to identify. Indeed, in a recent study where I did the playback experiments, we showed that there are no acoustical differences between hunger, isolation and discomfort cries. Neither machine learning algorithms nor human listeners managed to correctly identify the cry causes. Being a parent, and being familiar with the cries of the baby on whom they were being tested did not help to identify the causes of crying (Lockhart-Bouron et al., 2023, see Annex I). When asked to identify pain compared to discomfort, brain areas engaged in expert participants (IFG and subcortical structures) are not pain-specific, but rather marks the task difficulty engaging high-level processing (Chapter III.2). Interestingly, when restricted to cries recorded

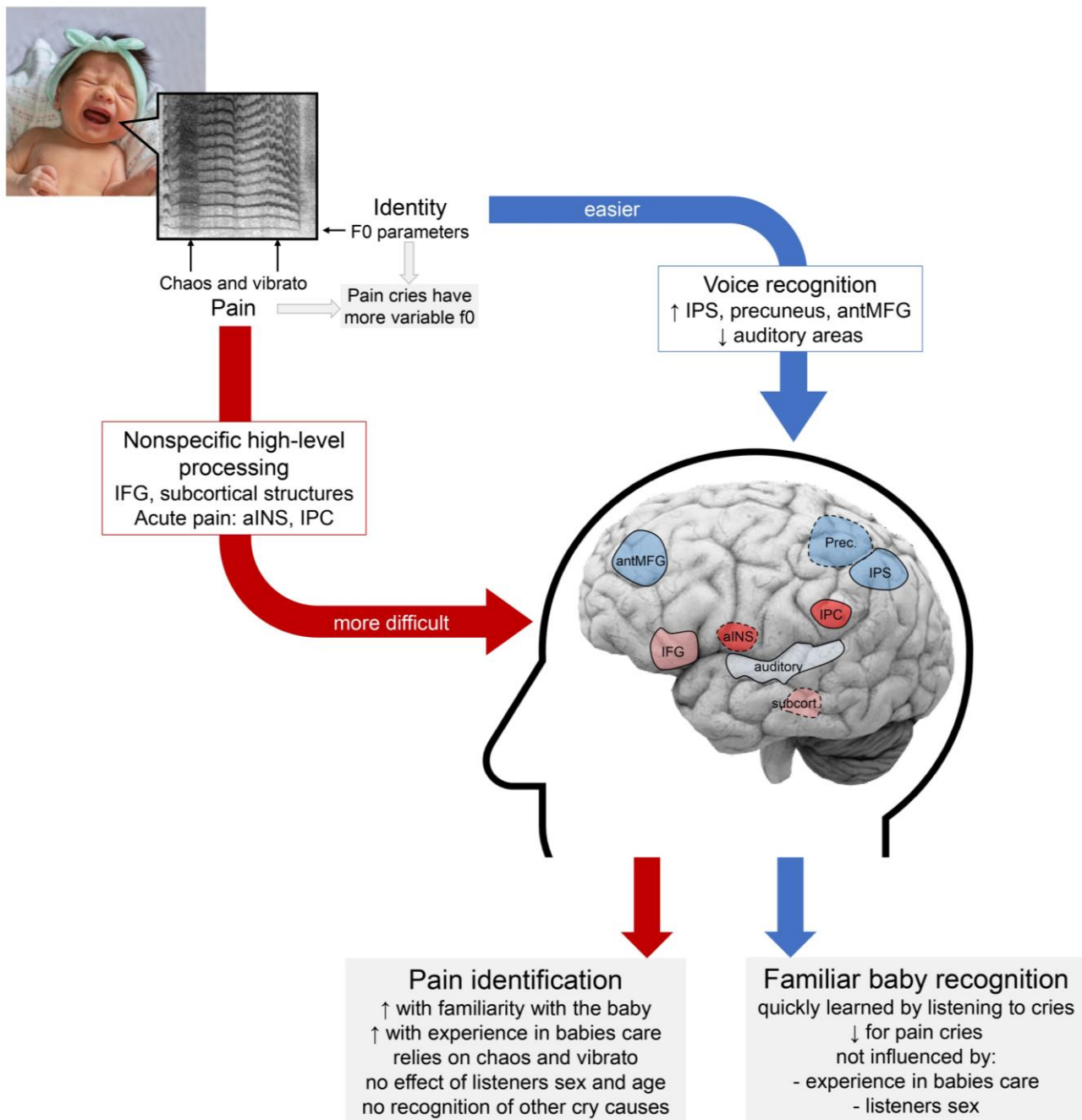
just after the vaccine injection, thus expressing more acute pain and characterized by more acoustic roughness (particularly more chaos and subharmonics), acoustic roughness was linked to more connectivity in the empathy network, and more BOLD activity in the inferior parietal cortex and the bilateral anterior insula, known to be involved in empathy for pain (Chapter III.1, Annex II). On the other hand, pitch value correlated with more activity and connectivity in the auditory network. Thus, there is a need to use quite intense stimuli to evoke pain through cry listening.

From this first stage of my thesis, we can conclude that acoustic decoding performs well for baby identification and less well for the physiological state leading to crying. This is particularly true for non-experts in babies care. These unexpected results could be explained by the fact that the acoustic areas of the brain first filter identity information in cries before their physiological correlates. Compared with everyday life, identifying pain by listening to cries in our experimental conditions has limitations, as these are non-ecological conditions. Once the brain has been alerted by the acoustic signal, there is usually a sequence involving the visual pathways more closely to ascertain what is happening. This second stage is perhaps involved or more specialized in detecting "what" is happening, as there is now evidence that auditory information allows to detect "who" is crying.

In addition, another important aspect addressed in my thesis is how experience in babies care shapes the ability of cry identification. In chapter I, I showed that experience does not influence the ability to recognize one given baby based on pain cries listening, the residual acoustic information being captured by parents and non-parents. On the contrary, experience in babies care is mandatory to identify pain in cries (Chapter II.1). This can be linked to the specialization through parenthood of the brain connectome engaged by cry listening, or to learned shortcut for entering the connectome. Parents exhibited greater global connectivity in this connectome than non-parents, with a shift from aversive and emotional reaction in nonparents to a more cognitive processing in parents (Chapter III.1), which may enable them to process the information conveyed by cries more effectively. Nevertheless, parenthood is not the only way to gain experience in babies care, with positive effects of experience through caring for younger siblings, grandchildren, or even for nonrelated babies in the case of professional caregivers (Chapters II.1, II.2 and III.2). These healthcare professionals, not having babies on their own, had similar performances and brain activity than parents (Chapters II.1 and III.2), showing that biological parenthood is not mandatory to be an adapted caregiver. In addition to this qualitative aspect, there are also effects over time. While parents of children above 5 years old are less

accurate at identifying pain than those who have babies under two, adults who are still engaged in caregiving show as good abilities, which are maintained regardless of their age (Chapter II.1 and II.2). This emphasized that we are a cooperative breeding species, the quantity and quality of time spent caring for babies being a more decisive factor than biological parenthood, enabling a large number of adults to provide adapted care. Taken together, these profiles suggest that there is a large place for learning in the final performance.

Alongside this question of experience, I also investigated the sex-related effects in cries identification. Indeed, there is a strong belief in the general population that certain abilities are the results of “maternal instinct” (Borovska, 2015). There are in fact some sex-differences regarding the brain processing: the amygdala nuclei were less activated by cry listening in fathers than in other adults, which may reflect a downregulation of their aversive reaction induced by cries. Mothers showed higher functional connectivity in the subcortical reward network, whereas fathers showed higher connectivity in the auditory network (Chapter III.1). However, regarding identification of either baby’s identity or crying contexts in cries, there was almost no difference between men and women (all chapters). There was no difference either in brain activations while processing this information (Chapter III.2). Moreover, for the observed differences, it is not possible to determine whether they are due to biological sex differences, or to the gendered division of tasks in childcare. In my samples of participants, all mothers were primary caregivers, and almost all fathers were secondary caregivers. Besides the difference in the amount of time spent caring for children, the nature of their investment may also differ, for example with more affectionate contact for mothers and more stimulatory contact in fathers (Feldman et al., 2010). Their perceptions can also be quite gender-specific, with, for example, a father in our participants reporting a balanced investment while his wife does not. This division of tasks is likely to play a decisive role in the observed differences between men and women, given the studies that have been carried out on homosexual fathers, who are primary caregivers, showing similar patterns of brain activity and connectivity compared to mothers (Abraham et al., 2014).



**Results summary.** From production (upper left) to perception (lower right) of information in cries related to baby's identity (blue) and pain (red). For brain areas, light red: related to identification of all pain cries; deep red: restricted to acute pain cries; blue: increased activity linked to familiar baby recognition; white: decreased activity linked to familiar baby recognition. aINS: anterior insula, antMFG: anterior middle frontal gyrus, f0: fundamental frequency, IFG: inferior frontal gyrus, IPC: inferior parietal cortex, IPS: inferior parietal sulcus, Prec.: precuneus, subcort.: subcortical structures (PAG, caudate nucleus, anterior thalami and subthalami).

### *Open questions*

This work leads to new questions. First, we showed that experience in babies care is a key element to learn to recognize pain in babies cries. It would be interesting to determine whether training focused on the acoustic properties present in pain cries could replace, or supplement, the experience gained through care or parenthood. This could, for example, be proposed to parents-to-be in anticipation of the arrival of their child. Secondly, all studies were performed using cries of healthy full-term babies, without any serious medical history. Pain cries were recorded during routine vaccination, which leads to acute pain. It will be of interest to investigate if our findings can be generalized to other painful situations, and for other populations, for preterm babies or babies with a medical condition, a patient profile more likely found in pediatric care units.

In more fundamental perspectives, we now have a fMRI database of 140 adults scanned during cries listening, with extensive acoustic characterization of these cries (fundamental frequency, roughness, presence and duration of nonlinear phenomena...). This will allow to investigate in detail the neural correlates of the integration of this different acoustic information. In addition, a parallel question of this thesis was to investigate pain perception, overcoming the nociceptive sensory aspect by evoking pain through the auditory channel. We obtained limited but promising results, acoustic roughness being linked to anterior insula activation when listening to acute pain cries. We could use more explicit auditory signals, such as the screams emitted by women giving birth without an epidural, as recorded by the ENES team (Valente et al., in prep), or synthetic cries (Anikin, 2019) with added episodes of chaos and vibrato to enhance their perception of pain. Finally, I did not find any difference in brain activations linked to the nature of experience, when comparing mothers and childless women working in pediatric care. It would be interesting to carry out functional connectivity analyses on these data, to find out whether there are differences in the temporal relationships between the regions of interest, which could mark a different refinement of the brain connectome engaged by cries listening.

### *Implications for babies care*

This work provides knowledge about the information conveyed by cries. In day-to-day life, it provides parents with the information they need to provide appropriate care. Decoding cries is a learning process, so it is normal not to know what to do, or even to be lost at first. The more time you spend caring for your baby, the more you learn. Parents will learn to recognize their

child's voice, and become "specialists" in it. Recognizing pain is more difficult, but again they will learn. There is no acoustic information on the other causes of crying, so there is no pressure to put on this side, and all the business around it is to be avoided. Education programs focusing on other aspects have already shown good results, enabling a reduction of visits to pediatric emergency departments for crying complaints (Barr et al., 2015) and, more importantly, a reduction in hospitalizations for abusive head trauma (Barr et al., 2018). It would be necessary to define parents' expectations and questions to find out what they need.

With regard to pain management in pediatric care, my work has shown that parents are very effective at identifying pain, sometimes more so than the professionals themselves, even for an unfamiliar baby. It is therefore particularly important to involve parents, in collaboration with the medical team (nurses, physicians), in pain management of newborns (Balice-Bourgeois, 2020). This collaboration is appreciated by the nurses who use it, who feel that parents have the best information about their baby's needs, and appreciate the collaborative approach to individualizing pain management for newborns (Axelin, 2015). This collaboration is particularly relevant as parents can be involved in the solutions to be applied: oral sucrose administration, breastfeeding, skin to skin contact (Campbell-Yeo et al., 2022). In intensive care unit, pain assessment may be more difficult, particularly for intubated and mechanically ventilated infants (Elias et al., 2014). However, it is still beneficial to involve parents in care, particularly for parents themselves, to help them to learn to parent, which may be difficult in these intensive care units (Skene et al., 2012). In addition, it would be interesting to use what we know about acoustic features specific to pain in cries. For example, a detector of nonlinear phenomena (chaos, subharmonics, vibrato) may be a useful tool to detect and monitor acute pain in pediatric care.

Lastly, I showed that many other caregivers can be involved and perceive the information conveyed by crying in an adapted way, in addition to biological mothers who are often the primary caregiver. Fathers are the most involved and studied, and show similar abilities to mothers when they spend time looking after their babies. Children raised by fathers involved in collaborative coparenting show better emotion regulation and social collaboration skills (Abraham, 2017), and are better at handling conflict with respect and empathy (Feldman et al., 2013). This involvement in care also benefits the fathers themselves, with daily paternal caregiving being associated with the development of a collaborative social style, which may be beneficial in their personal and professional life (Feldman, 2019). Fathers' involvement should therefore be encouraged, first and foremost by taking the paternity leave to which they are

entitled. More specifically, it has been shown that the type of paid leave reserved for fathers, lasting several months and used in part outside the mother's leave, is most likely to encourage men's involvement in parental and domestic tasks (Sponton, 2022). In addition to the parents, grandparents can also be involved, with beneficial effects for the children (Amorim, 2019). Other non-parent adults can also get involved, and even become experts when involved in intensive baby care. For non-parents, this could be a way of practicing parenting (Hrды, 2016). Put together, all these points show that there are multiple ways to rear a child.

**In conclusion, this work shows that babies cries are a complex communicative signal, rich in information. Information on baby's identity is encoded through the fundamental frequency parameters, which are more variable in pain cries. In addition, pain in cries is encoded by nonlinear phenomena. Decoding this acoustic information is learned with experience and time spent caring for a baby, enabling everyone to find a legitimate place in baby care.**





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# Annex I: Infant cries convey both stable and dynamic information about age and identity

Lockhart-Bouron, M., Anikin, A., Pisanski, K., **Corvin, S.**, Cornec, C., Papet, L., Levrero, F., Fauchon, C., Patural, H., Reby, D., & Mathevon, N. (2023). Infant cries convey both stable and dynamic information about age and identity. *Communications Psychology*.

In this study, I conducted the playback experiments to investigate whether adults are able to recognize other causes than pain in babies cries.

## Infant cries convey both stable and dynamic information about age and identity

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What information is encoded in the cries of human babies? While it is widely recognized that cries can encode distress levels, whether cries reliably encode the cause of crying remains disputed. Here, we collected 39201 cries from 24 babies recorded in their homes longitudinally, from 15 days to 3.5 months of age, a database we share publicly for reuse. Based on the parental action that stopped the crying, which matched the parental evaluation of cry cause in 75% of cases, each cry was classified as caused by discomfort, hunger, or isolation. Our analyses show that baby cries provide reliable information about age and identity. Baby voices become more tonal and less shrill with age, while individual acoustic signatures drift throughout the first months of life. In contrast, neither machine learning algorithms nor trained adult listeners can reliably recognize the causes of crying.

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Crying during infancy is an innate survival mechanism that evolved in humans and many other animals to maintain proximity to and obtain care from caregivers<sup>1–5</sup>. Commonly triggered by isolation, hunger, discomfort or pain, human infant cries are characterized by specialized acoustic features such as severe roughness under extreme distress<sup>6</sup>. Acoustic features of infant distress vocalizations share similarities across terrestrial mammals, from rodents, dogs and deer to primates, including humans<sup>2</sup>. This shared acoustic structure almost certainly arose from the shared adaptive function of a cry: exploiting the hearing sensitivities of listeners to elicit aid<sup>7–9</sup>. Indeed, human baby cries consistently and cross-culturally lead to interventions such as holding or feeding that can be critical to an infant's welfare<sup>10,11</sup>.

Despite the universality and tremendous biological relevance of the human infant cry, there remains little consensus on what information cries can convey<sup>4</sup>. For example, the remarkably common question “why is my baby crying?” returns hundreds of thousands of contradictory results from online search engines. To the same question, the *Web of Science* returns a large number of scientific articles and books dating back more than a century. Despite this enormous interest expressed by the general public and scientific community, it remains unclear whether human baby cries encode their ostensible cause, and whether adult listeners can correctly decipher this cause. While such a capacity could benefit both the caregiver and the infant<sup>4</sup>, it may be trumped by selection pressure to preserve stable vocal indices of identity in babies' cries that likely increased infants' chances of survival throughout human history<sup>12</sup>.

Traditionally, infant cries were thought to represent acoustically distinct cry types, each associated with a discrete cause such as birth cries, pain cries, hunger cries, pleasure cries, startle cries, and attention cries<sup>13,14</sup>. Early studies suggested that mothers and trained nurses could identify such cry types without additional contextual cues<sup>14,15</sup>. However, recent research suggests that identifying discrete information related to the cause of a cry is not so straightforward. For example, while parents can discriminate between highly distinct cry contexts, such as pain versus mild discomfort<sup>6</sup>, discrimination is substantially degraded for cries that share a similar level of distress<sup>16</sup>. Moreover, it has been shown experimentally that an adult listener's ability to classify a cry as communicating pain or discomfort is highly dependent on their prior experience with infants<sup>17</sup>.

Although these previous studies suggest that it is difficult to identify the cause of a cry by ear, it is commonly believed, especially by the general public, that parents can discern why their baby is crying just by listening. Books on parenting echo this belief, while countless websites offer recipes to decipher babies' cries. Some non-academic sources even suggest that babies' cries are a “language” made up of phonemes whose meaning can be learned, and mobile applications proposing to decode babies' cries are becoming increasingly popular, despite a lack of fundamental scientific evidence to support their veracity. Moreover, researchers have yet to test the hypothesis that each baby may develop his or her own coding strategy for the cause of crying, as we test here. The question of whether baby cries encode information about their cause has therefore not yet been effectively answered.

Besides experiments testing whether human listeners can decode baby cries, recent attempts to develop automated methods to detect context-specific cry types, including pathological cries for clinical applications, have also produced mixed results<sup>18–20</sup>. A number of studies using various methods of acoustic analysis followed by machine learning have shown that it is possible to distinguish cries expressing strong pain from cries due to another cause. For example, cries were categorized with 71.68% reliability by analyzing visual features extracted from spectrograms of cries

caused by pain versus non-pain stimuli<sup>21–23</sup>. In contrast, few studies have tested whether crying can categorically encode the most common types of distress experienced by infants such as hunger, separation, or simple discomfort. A major reason for this is the difficulty of obtaining databases with a sufficient number of well-documented cry recordings in these everyday contexts, for babies of a given age, and with enough replicates per baby<sup>20</sup>. Most studies testing whether cries carry information about their cause have therefore been conducted on a limited number of cry databases (see<sup>24</sup> for an overview). Problematically, most of the used datasets include a mixture of cries from healthy and sick or disabled babies, or babies with a high pathological risk. For example, The *Baby Chillanto* database<sup>24</sup> lists five types of cries including “deaf”, “asphyxia”, “normal”, “hungry”, and “pain”.

Few cry databases are focused solely on healthy babies. One exception, the *Donate a Cry* dataset<sup>25</sup>, is still relatively undocumented<sup>20</sup>. Using only 150 baby cries from this database, a previous study<sup>26</sup> classified five cry types (“hunger”, “attention seeking”, “lack of ease”, “stomach issue”, “unidentified reasons”) with 81.27 % reliability. However, in addition to the very small sample of cries, the fact that the babies included in the database ranged between 0 and 2 years of age makes the result of the study difficult to interpret, as age may explain substantial variance in cry acoustics. A similar bias is found in another study<sup>27</sup> where the authors, despite having obtained good classification scores, also mixed cries from babies of very different ages (1–22 months; 320 cries extracted). The *Dunstan Baby* database<sup>28</sup> is another database of cries traditionally used to test cry classification methods, and was established for commercial purposes. The database contains a limited number of cries recorded at different ages (between 1 day and 6 months), classified into five categories defined without scientific validation (« Neh » hungry, « Eh » Pain/burp-me, « Ow » sleepy, « Airh » Pain, and « Heh » discomfort). After a meticulous review of the cries available in this database, some authors<sup>29</sup> were able to extract only 400 s of usable audio recordings (83 cries from 39 babies; see also<sup>30</sup>). They obtained excellent recognition scores for all five cry causes. As the authors point out, however, the small number of cry recordings they used increases the risk of overfitting in the learning models. Using the same database but different analysis methods, other studies<sup>31,32</sup> obtained comparable results. However, the problem of mixing cries from babies of different ages, and the fact that it is probably not the same babies who were recorded longitudinally, makes the interpretation of these results very difficult. Another recurrent problem with available databases of infant cries is that the identity of the babies is often not known. It thus cannot be excluded that some cries in certain categories may have been produced by the same babies, leading to pseudo-replication issues and falsely inflating recognition accuracy.

Taken together, the search for automatic methods to identify the causes of baby cries cannot be considered to have been successful to date. This is not because acoustic analysis and machine learning methods are inefficient—on the contrary, they are now particularly elaborate. Rather, a key problem is that modern analytical methods have not been previously applied to a large and well-controlled corpora of cry recordings. Here, we present a dataset containing cries from a cohort of babies recorded systematically and longitudinally at multiple ages during the first months of life and whose causes of crying have been labeled in a bottom-up, systematic manner. With this material, we can test whether a baby develops its own way of encoding information about the cause of crying.

A parallel body of literature describes the human infant cry as largely divorced from context<sup>33</sup>. Instead, some researchers argue, variations in cry acoustics reflect the baby's level of distress regardless of cry cause. According to this “graded cry” hypothesis,

more extreme distress levels predict increasingly severe cry acoustics, as observed in other primate species<sup>8</sup>. For example, human infant cries are often characterized by nonlinear phenomena that arise from aperiodic vibration of the vocal folds and that contribute to the perceived roughness of vocalizations<sup>34,35</sup>. Such roughness increases with distress, for example in cries produced during a vaccination compared to during a bath<sup>6</sup>. Infant cries also show an acute spike in their fundamental frequency ( $f_0$ , perceived as pitch) when distress levels reach an upper threshold<sup>36</sup>, likely due to excessive vocal fold tension. Perception experiments show that adult listeners associate these acoustic variations with the ostensible level of distress or pain experienced by the crying infant<sup>6,16,37</sup>, offering converging support for the graded cry hypothesis.

The ongoing debate surrounding whether human infant cries dynamically encode discrete causes is further complicated by salient individual differences in cries across babies, which researchers have often failed to control for in acoustic analyses (see<sup>38</sup> for discussion). Indeed, cries have long been known to differ acoustically from one baby to another<sup>12,38</sup>, and we have experimental evidence of the ability of parents and naive listeners to recognize specific infant calls very reliably<sup>39,40</sup>. This is why it is critical to control for baby identity when testing whether baby cries communicate their cause. Individual vocal signatures in babies' cries have most consistently been tied to individual differences in  $f_0$  (pitch)<sup>41</sup> and are already present by 3 months of age<sup>42</sup>. Remarkably, individual differences in  $f_0$  remain stable across the human lifespan, from infancy to childhood<sup>43</sup> and from childhood to adulthood<sup>44</sup>, suggesting that the human voice may function as a stable biomarker of identity, beginning already at birth. If baby cries have been shaped by selection to provide reliable indexical information about the infant, such as their sex, age, and identity, we can expect some degree of stability and predictability in cry acoustics within individual babies.

Although  $f_0$  is known to differ across babies<sup>42</sup>, standardized fine-grained acoustic analyses of cry signatures are lacking<sup>1,4</sup>. It thus remains unknown how much variance in cry acoustics can be explained by static traits such as sex and age. Because sexual dimorphism of the vocal anatomy does not emerge until puberty in humans<sup>45</sup>, we do not expect sex differences to be present in baby cry acoustics. Indeed, in a previous study, we found no difference between the pitch of female and male baby cries<sup>42</sup>. A previous study<sup>46</sup> also points out that sex does not directly predict variance in cries, though peripheral estradiol concentrations (a baby-specific characteristic) do predict infant vocal performance. In the present study, we did not investigate hormone levels, but we did test for effects of sex and age. While we did not predict sex differences, we do expect that babies' cries will evolve with age. Indeed, expansion of the vocal apparatus, developmental maturation of neurocognitive capacities, and progressive changes in parent-infant communication strategies may all contribute to age-related vocal changes in the first months of life<sup>5</sup>. At the same time, anatomical constraints and selection pressure for indexical signaling may lead to stability in individual cry signatures during early ontogeny, for example, to facilitate parent-infant recognition, bonding, and to allow parents to familiarize themselves with the cries of their infant allowing them to extract dynamic cues to cry context or urgency<sup>4,39</sup>. Evidence for within-baby stability in cry signatures would also raise the possibility that contextual cues in infant cries may be specific to each infant, a hypothesis that has yet to be tested.

In this longitudinal study, we test for acoustic variability and stability in human baby cries, both across infants and across the first 4 months of each infant's life. We test the predictions that babies have individual cry signatures and that these individual cry signatures do not differ between the sexes and remain stable with

age. We also test the prediction that there are consistent acoustic differences between baby cries caused by different events. To achieve these objectives, we audio recorded 24 male and female babies during several continuous 48-h sessions in their homes at 15 days, 1.5 months, 2.5 months, and 3.5 months after birth. We classified cries into three key contexts (hunger, isolation, or discomfort), relying mainly on the parental behavior that ceased the cry, which also corresponded to the parental evaluation of cry cause in 75% of cases. Crying bouts were segmented into 39201 individual cries, from which we measured ecologically relevant acoustic parameters including fundamental frequency (perceived as pitch), perturbation and noise parameters, roughness, and duration. These cries and their associated metadata have been collated into a database available online: *EnesBabyCries1* (see Methods and Supplementary Data). Using mixed models and machine learning, we tested whether these acoustic characteristics vary as a function of cry cause and whether this information is universally coded or specific to each baby. To verify the robustness of the results we derived from our acoustic analyses, nearly 250 male and female adult listeners judged the causes of these cries in two psychoacoustic perception experiments involving either an implicit or explicit training phase.

Combining longitudinal naturalistic recordings of human baby cries across contexts, fine-grained acoustic analysis, machine learning, and psychoacoustic experiments with human listeners, we answer long-standing questions about the encoding and decoding of evolutionarily relevant information in human infant cries: Are infant cries sexually dimorphic? Which acoustic parameters contribute to individual cry signatures? Are cry signatures stable across the first 4 months of life? Does the acoustic structure of baby cries differ by cause, either universally or within infants? And finally, to what extent can adult listeners assess the cause of babies' cries when trained on a specific infant?

## Methods

The research was performed under the authorizations 18CH085, no.IDRCB 2018-A01399-46 (recordings of cries) and IRBN692019/CHUSTE (psycho-acoustic experiments) and approved by the French national human ethics committee: *Comité de Protection des Personnes*. The study, including sample characteristics, design, procedures, and outcome measures was preregistered on <https://clinicaltrials.gov/> under no. NCT03716882. The preregistration did not specify the hypotheses or the full analysis plan. Informed consent was obtained from all parents. Parents consented to public sharing of the cry-data. The playback experiment was approved by the local ethics committee (*Comité d'Éthique du CHU de Saint-Etienne*, Institutional Review Board: IORG0007394), and informed consent was obtained from all participants.

**Acoustic recording.** To obtain recordings of infant cries in real-life contexts, we selected 30 families recruited during their stay in the maternity ward of the University Hospital of Saint Etienne and living in the vicinity of Saint-Etienne, France. Mothers were visited by a pediatric resident (MB) during working hours on one of the 3 days of their stay in the maternity ward and invited to take part in the research project. Key inclusion criteria included full-term childbirth and eutrophy. We therefore did not include babies with intrauterine growth retardation, antenatal or established neurological pathologies at birth, perinatal asphyxia, encephalopathy, known antenatal pathology or those born from a multiple pregnancy. As five families withdrew from the study and one more baby was not recorded due to technical issues, our final sample included 24 babies (10 girls and 14 boys) from 24 families (Table 1). The sex of the babies was given by the parents and was

**Table 1 Biological data of 24 recorded babies.**

Baby ID	Birthdate (dd/mm/yy)	Sex (M/F)	GA (weeks)	DW (CS/V)	Apgar at 5 min	BW (g)	BH (cm)	BHC (cm)	Deafness Screening results	Pg	N B	F-Ch
RBO1	12/10/18	M	38	CS	10	3615	51	35	NL	1	1	1
KA02	16/10/18	M	39	CS	10	3805	52	37	NL	1	1	1
BS03	16/10/18	F	38	CS	10	3415	50	35	NL	3	2	2
TM04	19/10/18	M	37	V	10	2135	42	32	NL	2	2	2
TA05	23/10/18	F	40	V	10	3395	50	33	NL	1	1	1
BR07	26/10/18	M	39	CS	10	3710	51	35.5	NL	2	2	2
PA08	06/11/18	M	38	V	10	2710	48.5	33	NL	2	2	2
LC10	11/11/18	F	39	V	10	3245	50	33	NL	1	1	1
CA12	01/01/19	F	37	V	10	2995	49	34.5	NL	2	2	2
GL13	06/01/19	M	40	V	10	3865	48.5	35	NL	1	1	1
PJ14	06/01/19	F	41	V	10	3510	51	35.5	NL	2	1	1
BR15	14/01/19	F	39	V	10	2910	47	33	NL	1	1	1
TL16	07/01/19	M	40	V	10	3170	50.5	31	NL	1	1	1
XM17	20/01/19	F	40	V	10	3895	51	34	NL	1	1	1
PE18	22/12/18	M	38	V	10	3235	49	35.5	NL	5	3	3
SA20	29/01/19	M	40	V	10	3580	50.5	34.5	NL	2	2	2
ML21	26/02/19	M	41	V	10	3600	52.5	33.5	NL	2	1	1
HA22	28/02/19	F	39	V	10	3285	MD	35	NL	1	1	1
SB23	27/02/19	M	39	V	10	2675	47	33	NL	2	2	2
PB24	02/03/19	M	38	V	10	2790	47	32	NL	1	1	1
LC26	03/04/19	M	41	V	10	3595	51	35	NL	2	2	2
PA27	03/04/19	F	39	V	10	3100	50	35	NL	2	2	2
BM29	31/08/19	M	39	V	10	3900	52	35	NL	1	1	1
MR30	23/10/19	F	39	V	10	3265	48	35.5	NL	1	1	1

dd day, mm month, yy year, M male (boy), F female (girl), GA gestational age, DW delivery way, CS cesarean section, V vaginal delivery, BW birth weight, BH birth height, MD missing data, BHC birth head circumference, NL normal, Pg number of pregnancies for the mother, B number of birth for the mother, F-Ch number of children for the father.

consistent with their civil status. We collected no data on race nor ethnicity.

Recordings were conducted inside each family's private home during several 48-h sessions at 15 days, 1.5 months, 2.5 months, and 3.5 months following birth. Because of variations in parental availability and the well-known decrease in the frequency of infant crying with age<sup>1</sup>, some babies could not be recorded at each of the four ages (Supplementary Table 1). We thus obtained recordings from 17 infants at 15 days, 24 infants at 1.5 and 2.5 months, and 12 infants at 3.5 months.

We used automated sound recorders equipped with omnidirectional microphones (Song-Meter SM4 Acoustic Recorder®, Wildlife Acoustics, Inc., Concord, MA, USA). The acoustic recorder was placed in the baby's room at a height of 1.2–2.1 meters and at a distance of 1–4 meters from the baby to ensure a high signal-to-noise ratio. Recordings were made at 44.1 kHz with a 16-bit resolution and saved as WAV files. In total, we obtained around 3600 h of audio recording (24 babies \* 4 recording sessions—21 missing recording sessions \* 48 h).

**Parental questionnaire on cry causes.** During each 48-h recording period, parents completed a form indicating, for each crying sequence produced by their baby, the onset time of the cry, the potential cause identified for the cry, the action(s) taken to stop the cry, and the action that was ultimately effective. Parents chose from the following causes: hunger, isolation, physical discomfort (such as fever, cold temperature, full diaper), pain, and unknown. There was also an option for parents to indicate a cry cause that was not listed via an open response comment box. In 75% of the cases, the action that stopped the crying matched the parental assessment of the cry cause (for example, parents indicated “hunger,” and feeding their child did indeed stop the cry). When the parent's assumed cause did not match the action that stopped the cry, we coded the cause of the cry based on that

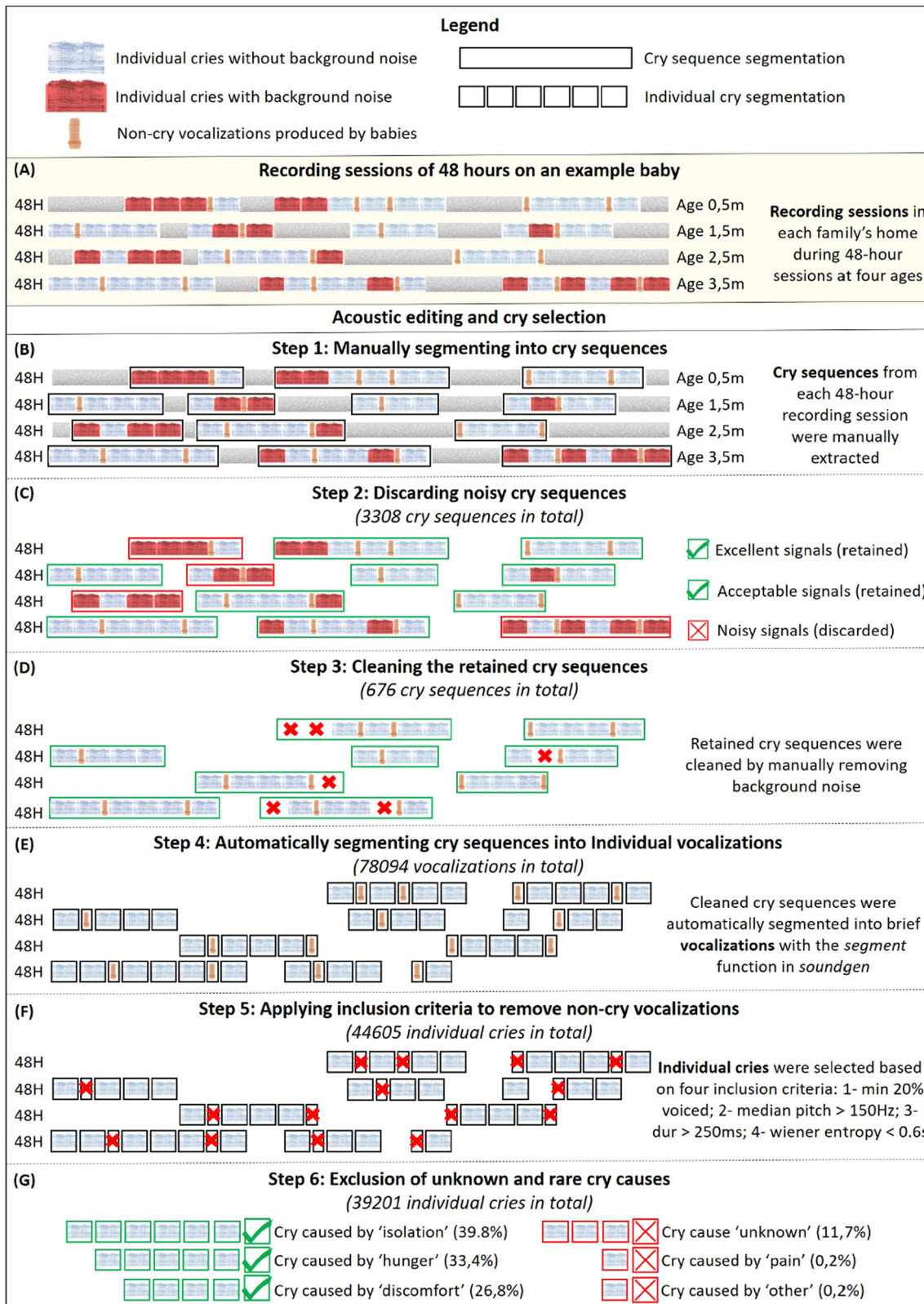
action and not on the parental assessment. We made this choice to increase the reliability and objectivity of labeling cry causes.

**Extraction of cries.** Cries were selected and edited following a six-step process (see Fig. 1). In step 1, we manually extracted audio cry sequences from each 48-h recording session using Praat software version 6.1.16<sup>47</sup>. Each cry sequence corresponded to a single questionnaire entry completed by the parents, and thus to a single crying bout and cause. We obtained 3308 cry sequences, which were then classified by their acoustic quality in step 2 as: (1) excellent signals with no interfering environmental noise; (2) acceptable signals with only short durations of interfering noise; and (3) highly noisy signals. Noise was identified as any overlapping background sound, corresponding in most cases to parental voices or distant sounds, for example from televisions or music. Only sequences classified as excellent or acceptable were retained for subsequent editing (total: 676 cry sequences from 24 babies; average sequence duration  $49 \pm 74$  s, range 1–73 s). In step 3, any cry sequences with short durations of noise were cleaned by manually cutting out those bits of background noise, resulting in clean, spliced cry sequences.

In step 4, to standardize cry signals for acoustical analysis, the 676 clean cry sequences were automatically segmented into 78094 vocalizations with the *segment* function in *soundgen* 2.0.0<sup>48</sup>. We looked for segments that were a minimum 50 ms in duration, separated from other cries by at least 100 ms. More details on the segmentation algorithm are available in the documentation of the *soundgen* function *segment*, and the R code for segmentation is provided in the supplements (scripts.zip, file prep.R).

In step 5, we removed all non-cry vocalizations produced by infants (e.g., unvoiced grunts, coughing), thus retaining only cries, operationalized as at least partly voiced episodes of vocalizing that were different from steady background noise and that satisfied the following four conditions: (1) minimum 20% voiced; (2) median pitch > 150 Hz; (3) duration > 250 ms;





and (4) Wiener entropy < 0.6. These inclusion criteria yielded the lowest rate of false positives (2% of non-cry vocalizations) in a randomly drawn sample of 100 selected and 100 rejected cry syllables. The automatic segmentation resulted in a total of 44605 cries across infants and ages.

Finally, in step 6, we removed cries classified by parents as having been caused by pain (95 cries) and those classified as

“other” (e.g., fear, fatigue, colic, excessive noises, awakened; 76 cries), as these responses each represented less than 0.2% of all cries. We also removed cries labeled with an “unknown” cause (11.7% of cries). The three major cry causes (isolation, hunger, and discomfort) were thus represented by 15609 (39.8%), 13095 (33.4%), and 10497 (26.8%) cries, respectively, with an average duration of 860 ± 590 ms (range 0.220–12 s). The final sample for



**Fig. 1 The six steps of the cry selection and editing process.** **A** Recordings were conducted inside each family's private home during several 48-h sessions at 15 days, 1.5 months, 2.5 months, and 3.5 months following birth. Cries were then selected and edited following a six-step process: **(B)** step 1: manual extraction of audio cry sequences; **(C)** step 2: only sequences classified as excellent (no interfering environmental noise) or acceptable (only short durations of interfering noise) were retained; **(D)** step 3: retained sequences were cleaned by manually cutting out the remaining bits of background noise; **(E)** step 4: Automatic segmentation, resulting in cry segments of 50 ms minimal duration separated from other cries by at least 100 ms; **(F)** step 5: Removal of non-cry vocalizations; **(G)**: step 6: removal of cries classified by parents as having been caused by pain and those classified as "other" (less than 0.2% of all cries). Only recordings obtained in step 6 were used for the present study. The *EnesBabyCries1* database contains the recordings after step 3 (*EnesBabyCries1A*) and after step 5 (*EnesBabyCries1B*). The database is available online at <https://osf.io/ru7na/> (see Supplementary Data for a description of the database).

acoustic and statistical analysis included 39201 cries (Supplementary Table 1).

We used short cries as our unit of acoustic and statistical analysis, justified by two important factors. First, recordings were taken in real-life environments, wherein background noise was inevitable and needed to be removed to ensure high-quality audio for robust acoustic analysis. Cry sequences were thus manually cut to remove background noise (steps 2–3), resulting in spliced cry sequences. Second, by measuring acoustic parameters over an entire sequence, we would have introduced a greater degree of acoustic variation, making it difficult to assess the contributions of individual acoustic parameters.

The cries collected for this study are now available in the form of a new cry databank (*EnesBabyCries1*, Supplementary Data). This bank contains two sets of recordings (*EnesBabyCries1A* and *EnesBabyCries1B*). *EnesBabyCries1A* contains the sequences of recordings from step 3 (i.e., after removal of noisy parts). *EnesBabyCries1B* contains the cries from step 6 (after segmentation and selection of the cries; these cries are the ones used in the present research). This databank is anonymized. No clues to the identity of the baby have been retained in the recordings. The metadata accompanying the cries are: (1) the age of the recorded baby; (2) the baby's biological sex; (3) the cause of the cry as stated by the parent; (4) the parental action that ended the cry. We obtained parental permission to make these recordings and information public. The databank *EnesBabyCries1* is available here: <https://osf.io/ru7na/>.

**Acoustic analysis.** The acoustic structure of each of the 39201 cries was represented by ten key acoustic variables. The choice of these variables was based on a large body of research in animal communication and the human voice sciences, implicating these acoustic variables as markers to speaker identity, speaker physical traits, and/or motivation and emotion<sup>9,49–51</sup>. A key acoustic parameter in human nonverbal vocal communication is fundamental frequency, perceived as voice pitch, which is highly individual and stable between individuals<sup>(44)</sup>, and yet also dynamic within individuals and thus critical in the communication of effect and emotion<sup>52</sup>. We hence included the following acoustic parameters: *Median Pitch* (median fundamental frequency  $f_0$ , given in hertz) as a measure of central tendency that is more robust to noise in pitch tracking than is the mean pitch and *Pitch IQR* (interquartile range of  $f_0$ , in Hz), which was used instead of standard deviation or range as such measures are less sensitive to noise (i.e., incorrectly measured pitch in some voiced frames). The overall proportion of frames that are voiced was also included as it can distinguish between mostly tonal whine-like cries and wheezy or breathy vocalizations, but also because measures of voice quality were calculated specifically for voiced frames (*Voicing*, scaling from 0 to 1). Voice quality or "timbre", understood as any acoustic characteristics that distinguish between two voices at the same intensity and pitch, was captured by several acoustic variables including *Spectral centroid* (median spectral centre of gravity of voiced segments, in Hz), which

indicates how much energy is present in high versus low frequencies and distinguishes between bright or shrill and relatively "dark" voices. Finally, several acoustic parameters were measured to describe tonal versus noisy vocalisations: *Entropy* (median Wiener entropy, scaling from 0 to 1), *Harmonics-to-noise ratio* (measure of harmonicity, in decibels), *Jitter* (short-term disturbances in  $f_0$ , given as a percentage), *Shimmer* (short-term disturbances in the amplitude of the sound signal, given as a percentage), and *Roughness* (median proportion of modulation spectrum of voiced segments within the roughness range of amplitude modulation 30–150 Hz, given as a percentage). Working with short cries, temporal structure cannot be captured, apart from one obvious descriptive—cry *Duration* (in seconds). Amplitude (loudness) of cries could not be computed because the recording distance (microphone to baby) was not perfectly standardized. Acoustic measurements were performed in *soundgen 2.0.0*<sup>48</sup>, except for *jitter* and *shimmer*, which were measured in Praat<sup>47</sup>.

**Statistical analysis of cry features.** Each acoustic variable was normalized to a mean of 0 and SD of 1 within each baby. The acoustic differences between cries according to their apparent cause (hunger, discomfort, or isolation) and baby age were assessed with multivariate Bayesian mixed models fit in R with the *brms* package, version 2.17.0<sup>53</sup>. Because multiple vocalizations were extracted from the same sequences of crying, we also included a random intercept per crying sequence, as well as per baby. The model was:  $m\text{vbind}(\text{duration}, \text{entropy}, \text{HNR}, \text{jitter}, \text{pitch\_iqr}, \text{pitch\_median}, \text{roughness}, \text{shimmer}, \text{spectralCentroid}, \text{voiced}) \sim \text{cause} * \text{age} + (\text{cause} * \text{age} | \text{baby}) + (1 | \text{sequence})$ .

We used a Random Forest classifier, *randomForest* package in R, version 4.7-1<sup>54</sup>, with the same 10 acoustic predictors and with stratification per cause (i.e., without over-representing more common causes) to predict cry cause from acoustics using machine learning. Two-thirds of the available observations were used for training, and one-third for testing. Crucially, we trained our models on cries from one set of recording sessions and tested them not only on different cries but also on cries taken from different recording sessions. Because cries from the same recording session may share not only the same internal baby's state but also background noises and other confounds, training, and testing on different sessions ensures that the model learns the categories of interest (causes of crying, babies' identities, etc.) rather than session-specific acoustic signatures. The Random Forest algorithm is stochastic, and the training sample was chosen at random; therefore, we ran each model 100 times with different training and test sets and summarized its performance by median accuracy and 95% coverage intervals.

Considering the large dataset of cries (39201 cries), it was essential to develop an effective method to visualize similarities across cries based on various categories such as individual babies, age groups, or cry causes. The crux of this problem is obtaining a reliable and intuitive measure of similarity across cries. To solve this issue, we present a method based on dynamic time warping

(DTW) of frame-by-frame acoustic features (fundamental frequency, harmonicity, etc.). To reduce the dimensionality of the resulting distance matrix, we use the state-of-the-art algorithm of Uniform Manifold Approximation and Projection (UMAP) implemented in R with the *uwot* package version 0.1.11<sup>55</sup>. UMAP is conceptually similar to traditional unsupervised methods for dimensionality reduction, such as principal components, multidimensional scaling, and more recent techniques like tSNE, but UMAP uses rigorous mathematical methods of topological analysis, preserves global structure and within-cluster distances, and scales well to very large datasets, as recently demonstrated in complex comparative analyses of animal vocal acoustics<sup>56</sup>. Importantly for our purposes, UMAP accepts a pre-calculated distance matrix as input, which in this case was the output of dynamic time warp; calculating this matrix only once is much faster than using DTW as a distance metric inside UMAP, making it possible to analyze tens of thousands of sounds without the need for cluster computing.

**Playback experiments.** Two independent samples of 146 adult listeners (36 mothers, 37 fathers, 38 non-mother women, 35 non-father men; mean age  $\pm$  sd = 28.0  $\pm$  6.4 years, range 18–40 years) and 102 adult listeners (26 mothers, 25 fathers, 24 non-mother women, 27 non-father men; mean age  $\pm$  sd = 27.1  $\pm$  5.6 years, range 18–40 years) took part in playback Experiments 1 and 2, respectively. Participants were recruited on the online recruitment platform *Prolific*<sup>57</sup>, where they were redirected to the online testing platform *Labvanced*<sup>58</sup> on which the experiments were designed and hosted. Participants were paid for their time at the recommended rate of 7.5 GBP per hour.

For these perception experiments, we selected cries from 1.5-month-old babies who produced at least 36 cries longer than 0.7 s for each context. By eliminating shorter cries, we aimed to ensure that listeners have sufficient acoustic information from each cry. We focused on a single age group because, as our analyses show, individual cry signatures change with age. Only seven male infants and one female infant met these criteria and thus, to avoid possible confounding effects of biological sex, we used only the cries of male infants as playback stimuli (total of 2430 cries; mean duration  $\pm$  sd = 1.34  $\pm$  0.51 s, range [0.80, 5.70]). For implicit training in Experiment 1, we prepared two series of 12 cries for each cry cause (hunger, discomfort, isolation), resulting in six sets per participant, with all cries emitted by the same baby. For explicit training in Experiment 2, we prepared one set of 69 cries, with 23 cries per cause. For the testing phase of both experiments, we prepared one set of 30 cries, with 10 cries from each cry cause. Training and testing sessions involved cries from the same baby, with different cries in the training versus testing sessions, in order to maximize the ecological validity of our results. Stimuli were fully randomized within sessions. All listeners completed a short questionnaire indicating their age, gender, and whether they were biological parents. To control for potential experience with babies' cries among nonparents, all participants reported their experience with infants, including whether and how often they currently have contact with and/or have cared for babies aged less than 2-years.

Both experiments consisted of a training phase and a testing phase. In Experiment 1, listeners were implicitly familiarized with the cries of a single baby. They assessed the level of either hunger, discomfort or isolation of the baby from its cry using a sliding scale ranging from *Not at all* to *Extremely*. Examples of discomfort included cold, fever, and full diaper, whereas isolation was defined as the infant seeking contact or attention. This task ensured that listeners were actively attending to cries for maximal familiarization via implicit training. In the subsequent test

session, listeners indicated whether each cry was due to hunger, discomfort, or isolation in a three-alternative forced-choice task. In Experiment 2, listeners were explicitly trained on the cause of a subset of cries. For each cry in this training phase, listeners indicated if the cry was due to hunger, discomfort, or isolation in a three-alternative forced-choice task, after which they received explicit feedback regarding the actual cause of the cry. They were informed that their goal was to use this explicit feedback to learn to recognize the cause of baby cries in a forthcoming test. The final 30 trials, which included cries the participants had not heard during the training phase, were considered the testing phase.

Unaggregated, trial-by-trial responses in both psychoacoustic experiments were analyzed using Bayesian mixed models fit with the *brms* package<sup>53</sup>. Cry cause, number of previous exposures to cries from the same recording session (*nSameSession*), participant sex, and parental status (parent or nonparent) were included as fixed factors, while participant and baby identity were included as random factors. Fixed factor interactions and random slopes were defined using WAIC, Watanabe-Akaike information criterion<sup>59</sup> for model selection. The model structure was as follows:

$$\begin{aligned} \text{success} \sim & n\text{SameSession} + \text{sex} + \text{cause} + \text{parentality} \\ & + \text{cause} : \text{parentality} + \text{sex} : \text{parentality} \\ & + (1|\text{subjectID} + \text{babyID}) \end{aligned}$$

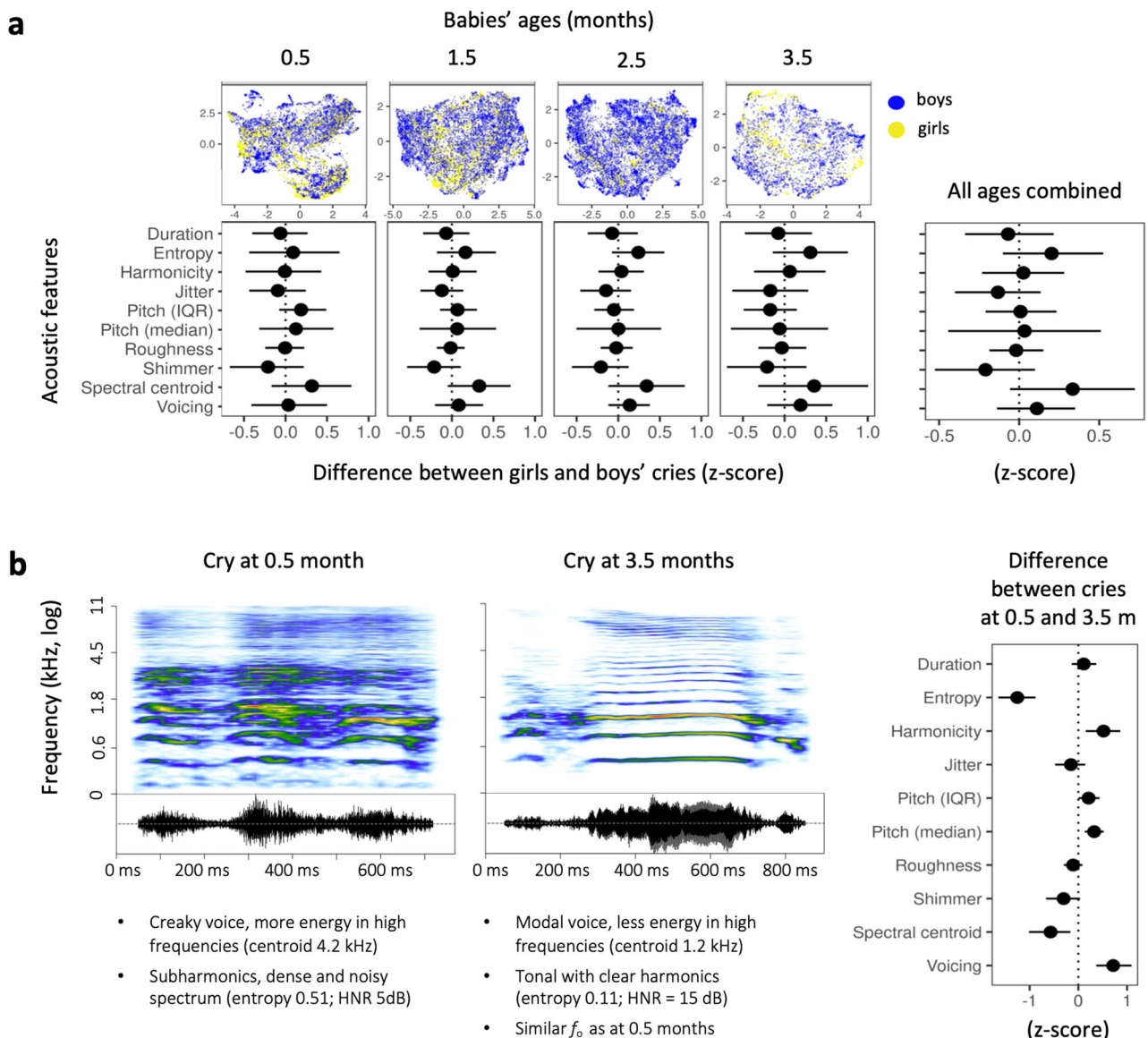
**Reporting summary.** Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

## Results

**Acoustic encoding of sex and age.** We first tested whether individual cries, regardless of cry context, carry acoustic information about the vocalizing infant's sex and age based on ten acoustic predictors known to be important in human and animal nonverbal communication: average fundamental frequency (median pitch) and its interquartile range (pitch IQR), entropy, roughness, spectral centroid, harmonicity, jitter, shimmer, duration, and voicing (see Methods for a detailed description of the measured acoustic variables and their justification; see also<sup>49–51</sup>). Together, these acoustic parameters capture the most biologically and perceptually relevant cry characteristics including voice pitch and its variability, voice quality, and duration.

Multivariate Bayesian mixed models did not reveal any consistent acoustic differences between the cries of infant boys and girls, either overall or for any specific age group (Fig. 2a), corroborating previous work on 3-month-old babies<sup>42</sup>. While infant cries did not differ between sexes, we found consistent acoustic changes in cries as babies grew older (Fig. 2b). Notably, cries became considerably more tonal with age, as evidenced by an increase in the harmonics-to-noise ratio (average increase per month of age: 0.17 SD, 95% CI [0.05, 0.29]) and a very rapid drop in the entropy of cries (–0.42 SD per month [–0.55, –0.29]). With each additional month of age, we also observed an increase in the proportion of voiced frames (0.24 [0.12, 0.36]) and a slight increase in cry fundamental frequency (herein, pitch) (0.11 [0.04, 0.17]), whereas spectral centroid became lower with each month of ageing (–0.19 [–0.34, –0.05]).

Taken together, we show that human infants gradually shift from producing mainly noisy and shrill cries to producing more tonal and melodious cries from birth to nearly 4-months of age (Fig. 2b). However, accurate estimation of actual age from a single cry of any given baby was low. Indeed, a Random Forest classifier (randomForest R package<sup>54</sup>; see Methods), using the same ten acoustic predictors, could recognize a baby's age group with a moderate accuracy of about 40% [35, 43], with an Odds Ratio to



**Fig. 2 Sex and age information in human baby cries. a** Absence of a sex signature. Top: The distribution of baby boys' and girls' cries ( $N = 39201$ ) in two-dimensional UMAP acoustic spaces shows strong acoustic similarities between the cries of both sexes, emphasizing the lack of sex differences in human baby cries (each dot represents one cry, acoustic spaces are obtained using UMAP, see Methods). Bottom: No acoustic descriptor varied between sexes, either for each age independently or for all ages combined (multivariate Bayesian mixed models, medians of posterior distributions with 95% CI). **b** Cry acoustics change systematically with age in the first 4 months of life. Left: Example spectrograms of two cries recorded from the same baby boy at 0.5 and 3.5 months of age, illustrating changes in key acoustic characteristics over this time (50 ms Gaussian window, frequency in kHz on a bark-spaced scale). Right: Changes in acoustic predictors from 0.5 to 3.5 months of age, showing that acoustic indices of roughness decreased with age, while those indicating tonality increased (multivariate Bayesian mixed models, medians of posterior distributions with 95% CI;  $N = 24$  babies, 39201 cries).

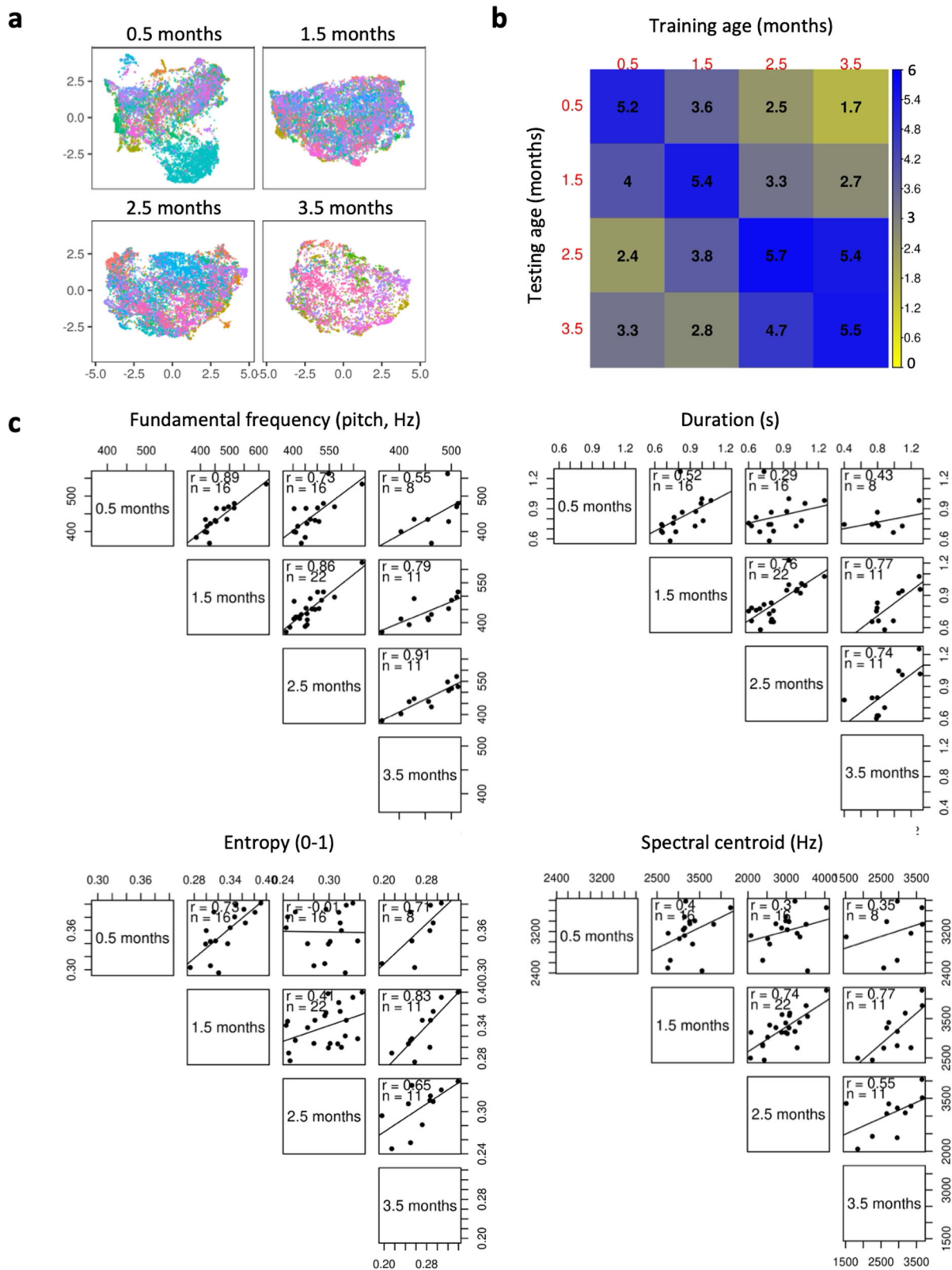
chance of 2.0, 95% CI [1.6, 2.2] [odds for model 40/(100-40) = 0.66; odds for random guessing 25/(100-25) = 0.33; 0.66/0.33 = 2].

This lack of robust age signatures may be explained by strong inter-individual variation across infants. As a next step, we therefore precisely analyzed individual signatures in cries and their development in early ontogeny.

**Acoustic encoding of baby identity.** We observed individual cry signatures across infants. A Random Forest model using the same ten acoustic predictors but normalized across all observations instead of within each baby achieved an accuracy of ~28% (95% CI [23, 31]) when discriminating among all 24 babies from a

single cry and across all ages. This is much better than chance (OR = 8.7 [6.8, 10.2]), and also constitutes a high rate of recognition from an ecological perspective, wherein infant recognition in real life would almost never involve having to identify one newborn baby from among two dozen others. Moreover, this is also a very conservative estimate as the model relies on only a fraction of the available acoustic predictors in infant cries, and cries from the same recording session never appeared in both training and test sets. All ten acoustic characteristics noticeably contributed to individual recognition of babies by Random Forest models, but median pitch was the top predictor. These results, therefore, support the hypothesis that babies' cries carry idiosyncratic acoustic characteristics that define an individual signature unique to each baby<sup>12,38</sup>. Further corroborating this result,





we observed some clustering by baby identity at each age in an unsupervised UMAP projection, a two-dimensional representation of the acoustic similarity between the analyzed cries (Fig. 3a).

Our results also show that individual signatures of human infants remain relatively stable throughout the first months of life. Indeed, models trained on cries recorded at a given age can still identify individual babies if tested with their cries recorded at

other ages (Fig. 3b). Nevertheless, we observed developmental drift in cry signatures: the greater the difference in baby age between training and test datasets, the less reliable the model's recognition of infant identity (Fig. 3b). This indicates that cry signatures, while specific to each baby and relatively stable throughout early ontogeny, nevertheless change to some degree with age.

**Fig. 3 Individual vocal signatures in baby cries.** **a** Distributions in 2D acoustic spaces of baby cries with each color representing an individual baby identity suggest idiosyncratic vocal properties at each age ( $N = 39201$  cries including 4580–12399 cries per age, 327–4140 cries per baby; acoustic spaces obtained with UMAP, see Methods). **b** Accuracy in classification of baby identity using a machine-learning classifier. The test-retest matrix shows the accuracy of classifying cries by baby identity with Random Forest models trained on cries from one age group and tested on either the same or a different age group (odds Ratio to chance; 1 = no better than chance), showing that recognition is highest in the same-age group, even though training and testing are performed on cries from different recording sessions. The dataset includes 15540 cries of six babies who were recorded at all four ages. Columns show the training-age group, and rows show the testing-age group. The greater the difference in age between training and testing, the less accurately the model can recognize the identity of a given baby. **c** Scatterplots showing the drift in individual babies' acoustic characteristics over the first 4 months of life. While acoustic characteristics change with age, they do so consistently for each baby (one data point = one baby). Not all babies were recorded at all four ages, so sample sizes vary across age groups, shown as  $n$  within each scatterplot. The strength of pairwise relationships between the same vocal parameter at two different ages is shown in each scatterplot as the  $r$  correlation coefficient.

This cry signature drift may be the result of how individual babies' voices change over time. However, because our results show that intra-individual cry acoustics remain stable throughout early development, we show that these ontogenetic changes largely follow a predictable trajectory for a given infant. For example, a baby whose cries are already high-pitched at 0.5 months of age relative to other babies retains relatively high-pitched cries at 3.5 months of age (Fig. 3c).

**Acoustic encoding of cry cause.** Finally, we tested whether the context in which cries were produced can be determined from the acoustic characteristics of cries. Our results show that hunger, discomfort, and isolation cries do not differ systematically in their acoustic structure and thus cannot be effectively segregated by cause when pooling the cries of all babies at all ages. Indeed, a Random Forest supervised classifier achieved an out-of-sample accuracy of only 36% (OR to chance = 1.1, 95% CI [1.0, 1.2]), indicating that there are no statistically robust acoustic differences among cries produced in each context. Using the cause of crying indicated by the parents in the questionnaire, instead of the action that stopped crying, produced nearly identical results with a classification accuracy of 35%, 95% CI [33, 36]. This is not meaningfully different from 36% [33, 38] based on the cause that stopped crying.

Including age group as a predictor in Random Forest classifiers, or training and testing the models within the same age class, failed to raise cry cause recognition accuracy above chance level (31% to 37%, OR to chance between 1.0 and 1.2 in each age group; Fig. 4a). Furthermore, after training Random Forest models on each age group and testing them on the same and other age groups, the accuracy of cry cause recognition did not improve with age and remained close to chance within each age group (Fig. 4b).

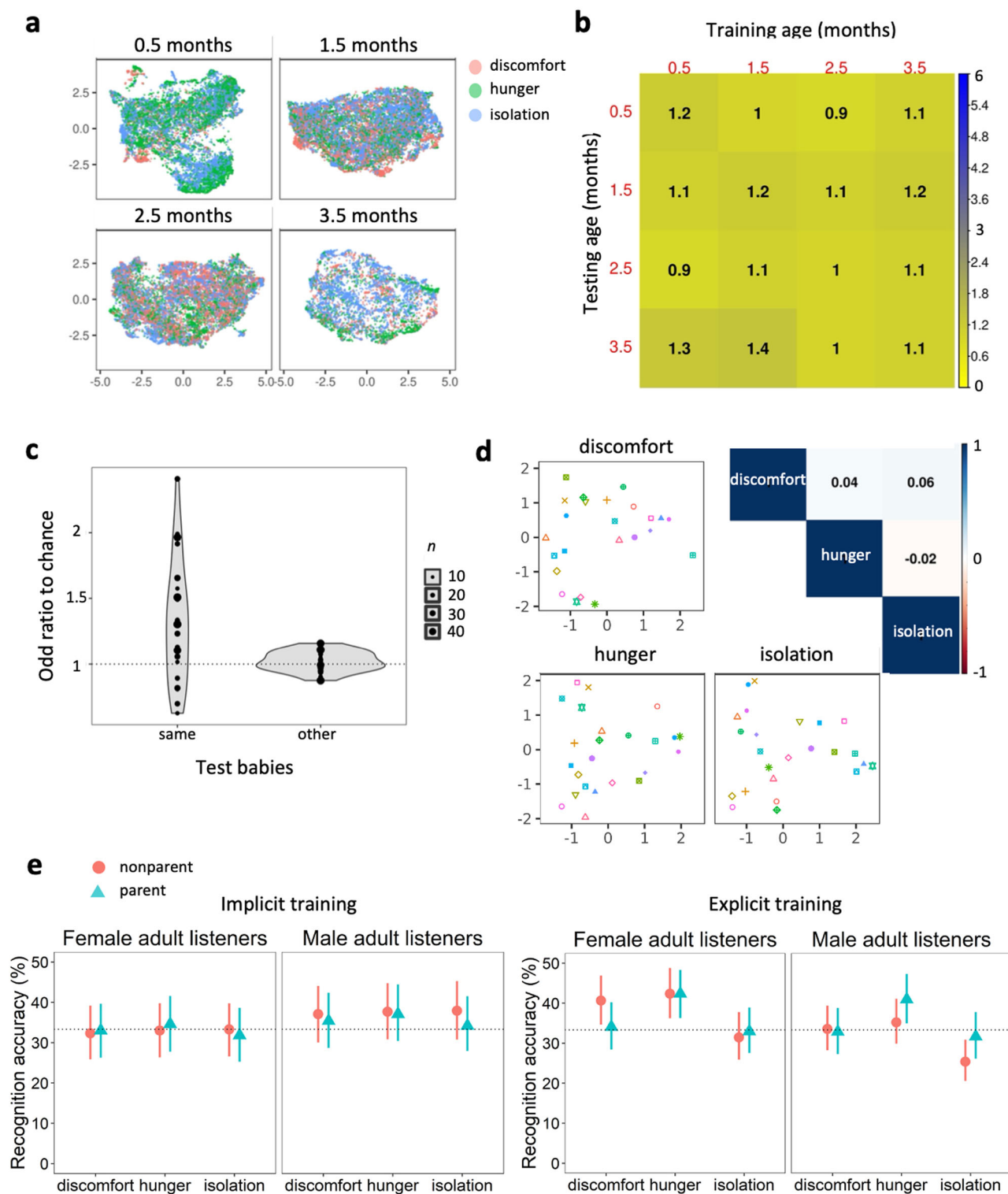
Our results corroborate previous findings that human babies have individual cry signatures. This raises the possibility that the cries of each baby may be characterized by a unique acoustic "code" linked to the specific cause of their cry. If so, we would predict more consistent acoustic differences between cries of hunger, discomfort, and isolation within each baby than across all babies. We did not find support for this. The recognition accuracy of a Random Forest model trained with the same ten acoustic predictors increased only slightly, from 36% [33, 38] to 43% [36, 50], after the inclusion of the baby's identity as another predictor of cry cause (OR boost from 1.1 [1.0, 1.2] to 1.5 [1.1, 2.0]). This small performance improvement might be partly attributed to differences in the distribution of causes of crying across babies. Therefore, we also trained a Random Forest classifier to recognize the cause of crying using cries from only a single baby, and then tested how well this model could detect the cause of crying either in the same baby or in all other remaining babies. Using ten acoustic parameters and age group as predictors, the average out-of-sample recognition accuracy of cry cause remained low at 38% [17, 65] (OR = 1.2 [0.4, 3.2]) for the same focal baby ( $n = 22$

babies recorded in all contexts), similar to when classifying cries of non-focal babies (34% [30, 54], OR = 1.0 [0.9, 1.2]; Fig. 4c).

We also tested the possibility that several babies might share a similar acoustic strategy to code for cry cause, a strategy that may not be universal to the entire group, but rather shared by sub-groups of babies within the larger sample. To test this, we calculated distance matrices showing the acoustic similarity between all possible (276) pairs of 24 babies in each of three cry causes, using fitted values of baby-specific acoustic signatures from the Bayesian mixed model predicting acoustics from context (Fig. 4d). If sub-groups of babies share similar strategies, these distance matrices should be correlated, with specific baby pairs showing stronger acoustic similarities than other pairs across cry contexts. This was not the case: the strongest correlation between pairs of distance matrices was negligible ( $r = .06$ ; Fig. 4d).

**Decoding of cry cause by human listeners.** Our acoustic modeling shows that baby cries do not vary across hunger, isolation, or discomfort contexts in a large pool of naturalistic cry recordings. However, the absence of evidence is not necessarily evidence of absence, and we thus set out to corroborate this null result by conducting two psychoacoustic perception experiments to test whether human listeners can gauge the causes of infant cries. In the first experiment, parents and nonparent men and women ( $n = 146$ , mean age  $28 \pm 6.4$ ) were implicitly trained and familiarized with the cries of a specific infant by rating cry intensity, and then tasked with classifying new cries from the same infant by their cause (see Methods; to limit pseudo-replication, we used the cries of seven different babies; each participant was assigned one of these seven babies). The overall recognition accuracy of cry cause in a logistic multilevel model was 34.8% (95% CI [29.4, 40.2]), which is no different than chance. We found no differences in performance between parents and non-parents ( $-0.9\%$  [ $-4.4, 2.7$ ]) and little to no difference between men and women (3.6% [ $-0.2, 7.3$ ]; Fig. 4e). In this experiment, nonparent men and women reported similar rates of prior experience with infants (women 39%, men 46%).

In the second experiment, a different sample of parents and nonparents ( $n = 102$ , mean age  $27.1 \pm 5.6$ ) were explicitly trained with a cry classification task designed to mimic the Random Forest classifier used in our machine learning procedures. Listeners were again presented with cries from a single infant and tasked with classifying each cry by its ostensible cause. Unlike experiment 1, however, here listeners were provided with explicit feedback after each trial indicating the actual cause of the cry, before classifying new cries from the same infant by their cause (see Methods). The overall recognition accuracy of cry cause was again at chance level: 35.4% [31.7, 39.1]. While we found no effect of parental status (1.0% [ $-2.5, 4.6$ ]), women performed slightly better than did men in identifying cry cause (4.0% [0.3, 7.6]) (Fig. 4e). Given that in this second experiment, more nonparent women reported prior experience with infants (66%) than did



nonparent men (37%), this effect could be largely driven by sex differences in experience with babies' cries in this sample of listeners. Indeed, we found that while mothers performed no better than did fathers (1.3% [-3.8, 6.3]), nonparent women performed better than did nonparent men (6.7%, [1.7, 11.7]). Controlling for the number of previous exposures to cries from the same cry session had no apparent effect on recognition accuracy (odds ratio = 1.01 [1.00, 1.02]).

The results of our perception experiments thus show that, like machine learning algorithms, human listeners cannot consistently

recognize the cause of crying from short recordings of human infant cries produced in the three most common contexts, regardless of their parental status or sex, and not even after brief training.

**Discussion**

Our study demonstrates that baby cries are not sexually dimorphic, that they bear an individual signature established by an array of specific acoustic features that drift systematically with

**Fig. 4 Baby cries do not encode or communicate their cause.** **a** Projections of baby cries in two-dimensional acoustic spaces (UMAP) show poor clustering by crying context: discomfort ( $n = 10497$  cries), hunger ( $n = 13095$ ), and isolation ( $n = 15609$ ). **b** Accuracy of context classification using a machine-learning classifier shows that cry cause recognition is around chance for all train-test combinations. The test-retest matrix shows the accuracy of classifying by context with Random Forest models trained on cries from one age group and tested on either the same or a different age group (Odds Ratio to chance; 1 = no better than chance), for cries of six babies recorded at all four ages. **c** Accuracy of predicting the context of crying from acoustics with Random Forest models trained with the cries of one baby and tested on the same versus other babies. Dot size indicates the number of recording sessions in a model. For a few babies, cry cause is recognized above chance when a model is trained and tested on different sessions from the same baby, but with high uncertainty due to a limited amount of data per baby (best classification: OR = 2.2 [0.9, 4.8]). There is no transfer of information to non-focal babies. **d** Left and bottom: The acoustic distances between babies do not form clusters within each cry context, suggesting an absence of groups of babies sharing the same coding strategies. Top right: Distance matrices per context are not correlated. **e** Performance of adult listeners in classifying the cries of an assigned baby by context after an implicit training session (left panels,  $n = 14892$  trials from 146 listeners) and after an explicit training session (right panels,  $n = 10098$  trials from 102 listeners). Markers represent fitted values from a logistic mixed model (medians of posterior distribution and 95% CI; chance level 33.3%), where blue triangles indicate parents, and red circles indicate non-parents. To limit pseudo-replication, we used the cries of seven different babies. For each listener, we chose different cries for training and testing sessions.

age, and that they do not communicate robust information about their cause, at least not within our very large sample of brief individual cries. We show this using acoustic analyses and modeling of nearly 40,000 human baby cries recorded longitudinally along the first 4 months of life from 24 infants in distinct real-life contexts, paired with playback experiments on adult listeners that confirm an inability in both parents and nonparents to consistently identify the most common cause of cries produced by a familiar baby, even after training.

**No significant difference between boys' and girls' cries.** The absence of vocal cues to sex in the cries of babies confirms previous observations in older infants. Indeed, the pitch of cries in infants aged 3 months has been shown to be independent of their sex<sup>42</sup>, in accordance with similarities in voice pitch between older boys and girls until puberty<sup>60–63</sup>. Here, we extend this observation over a span of 4 months in early ontogeny, from 15 days to 3.5 months postpartum, and to a larger set of acoustic descriptors. We show that none of these acoustic descriptors significantly differ between baby boys and girls, including fundamental frequency (perceived as pitch), perturbation and noise parameters, roughness, or cry duration. Critically, given that our study focused on short cries, we cannot completely rule out that acoustic features describing dynamic variation in these parameters over larger temporal scales may be related to sex. Nevertheless, our results suggest that idiosyncratic variations related to the individual identity of the baby are much more prominent markers of differences between babies than are possible sexed features.

**Cries change with age but retain an individual signature.** Our results highlight changes in infant cry acoustics with age. For instance, we found that babies' cries become more tonal from 0.5 to 3.5 months of age as acoustic entropy decreases and harmonicity increases with age for all three causes of crying. This result corroborates previous research showing a significant decrease in the noisy components of cries across the first 3 months of life<sup>64</sup>. This trend may be due to the maturation of the vocal folds<sup>65</sup> and/or to changes in the neurophysiology of crying as the infant's brain matures (see<sup>5</sup> for review). Another explanation for age-related changes may be that individual infants learn to cry in ways that most effectively arouse the attention of (and thus elicit aid from) their own parents or caregivers. Indeed, infants older than 2.5 months of age cry more predictably in response to external events that they have already encountered, compared to newborns whose cries appear more endogenously controlled<sup>66</sup>. Human infants rapidly increase their repertoire of complex vocal crying during the first 3 months of life<sup>67</sup> and subsequent months<sup>68</sup>. The possibility of learning is also supported by neuro-

psychological maturation with an increased understanding of the environment and thus, possibly, of nonverbal behaviors that most effectively attract caregivers<sup>2,69</sup>.

In our study, we did not record as many crying babies at 3.5 months as at younger ages, as babies typically cry less frequently at older ages<sup>1</sup>. This may have weakened the classification power of the classifiers, and it cannot thus be excluded that at 3.5 months—and a fortiori at later developmental stages – babies' cries may become more informative about their causes. Manual corroboration of the specific acoustic results obtained here would be necessary in order to be confident that they align with underlying phonatory behaviors and physiologies. In future, it will also be important to study the developmental trajectory of crying over a broader age range and using more sensitive acoustic descriptives, including pitch contours and measures of temporal dynamics within bouts of crying.

Remarkably, we show that the drift observed in the acoustic characteristics of baby cries with age is individually predictable. Infant cries bear a very well-defined individual signature, allowing efficient identification of the baby by caregivers, across cry contexts. In two previous studies, our team showed that this individual cry signature and the possibility of its identification by caregivers are already present at birth<sup>39</sup> and at 2.5 months of age<sup>40</sup>. In particular, we previously showed that the ability to identify a baby by their cry is independent of the sex of the listener, as well as their parental status. Both women and men are able to identify a crying baby after a short exposure to its cries, but people with previous experience with babies perform better. Here, we show that this static information carried by the baby's cry predictably drifts over time. This predictability in the evolution of the individual acoustic signature may provide caregivers with a reliable adjustment of their ability to identify the baby throughout the baby's growth, especially in early ontogeny, as observed in other animals in which parental recognition of offspring is critical, such as seals and various bird species<sup>70,71</sup> (see<sup>3</sup> for a review). Human caregivers may seldom need to identify their baby through his or her cries alone. Nevertheless, they must constantly assess the baby's physiological state. The presence of a unique, predictably drifting vocal signature in a baby's cries may therefore provide caregivers with a stable reference point. Any deviation from this predictable trajectory of one or more of the acoustic features defining this signature could signal the onset of a possible problem deserving special attention. It can be hypothesized that the individual signature present in the baby cry has been selected in our ancestors for this purpose. Although they lived in small groups, where the probability of confusing one baby with another was probably small, they were able to assess the baby's condition by knowing the stable characteristics of their cries.



**Cries carry no specific contextual information.** Finally, our results support the hypothesis that the human baby cry is a graded signal of distress rather than a signal that codes for specific causes of crying<sup>33</sup>. Past studies testing this hypothesis focused on a small number of infants and a small number of acoustic parameters, recorded at one point in time and typically evoked using a trigger<sup>72–76</sup>. Here we employed an innovative methodology by recording 24 infants in real-life contexts over several months using a supervised automated method for cry segmentation, analysis, and classification. We retained only cries with sufficient signal quality and for which a parental report was given. This conservative approach led to the exclusion of some cries, for instance, excessive crying due to colic<sup>77</sup>. Thus, we focus on the three most commonly reported cry contexts: hunger, isolation, and discomfort, together representing 75% of the cries identified by parents. Only 0.2% of cries were labeled as pain cries, too few to examine their acoustic structure and perception. Without separating by age or baby identity, we found only very modest acoustic variation by cry cause. Notably, we did not find context-specific differences in any of the acoustic features considered, including fundamental frequency (pitch). Our study thus provides evidence that in the absence of other information (e.g., visual cues or contextual information such as time lapse between feeding events) and with the probable exception of pain, which we did not consider here, it is almost impossible to identify the cause of crying from individual cries alone.

Accordingly, our playback experiments provide evidence that naïve human listeners have major difficulties discriminating between babies' cries according to their ostensible causes, even following brief explicit training, and that the parental status of participants does not predict their ability to identify cry causes. It is noteworthy, however, that women performed slightly better than men did in our explicit training recognition task. One possible explanation could be that nonparent women in our sample had more experience with infants than did nonparent men, as women are often more involved from a young age in family tasks and cooperation in caring for infants<sup>78</sup>. Indeed, nonparent women in the explicit training experiment did indeed report more prior experience than did nonparent men. However, this imbalanced involvement of females and males in infant care is by no means a rule in the human species<sup>78,79</sup>, and previous work has demonstrated that fathers, when they spend comparable time with their children, are as successful as mothers at recognizing their infant's cries<sup>40</sup>. It should also be noted that, although our psychoacoustic experiments did not reveal a significant ability of adult listeners to identify the cause of a cry, factors such as the age of the baby (the experiments were conducted with cries from babies aged 1.5 months only) or the duration of the listeners' training could impact this ability. It is therefore possible that highly trained listeners, with cries from older babies, could perform better.

**Limitations.** The present study has its limitations. As one cannot simply ask a preverbal baby why he or she is crying, we labeled the ostensible cause of each cry based on parental responses and behaviors that stopped the cry, and did not include rare and more extreme cry causes such as pain, wherein pain cries can be characterized by severe deviations from typical cry acoustic profiles<sup>6,36</sup> (see also<sup>80</sup> for an analysis of pathological sounds emitted by babies). By using a parental questionnaire, we obviously took the risk that parents might have a biased assessment of their babies' cries. However, the fact that there was a 75% correspondence between the parents' assessments and what actually stopped the cry suggests that this assessment was fairly valid. We also took the precaution of considering the action that

stopped the cry rather than the parental assessment if the two did not match, which did not change our pattern of results.

In order to obtain high-quality cries for acoustic analysis and perception experiments, our results are based on brief individual cries extracted from longer cry sequences. While this ensured that our cry stimuli were devoid of noise and allowed for robust acoustic measurements, it is possible that focusing on long cry sequences may have produced different results. For example, we cannot exclude the possibilities that the number and duration of pauses in cry sequences lasting several seconds or minutes may be informative features or that information about cry cause may be encoded in the temporal, prosodic, or melodic structure of cry bouts, rather than in the spectrotemporal features of individual cries.

While our perception experiments corroborate earlier work showing that discriminating the cries of a given infant improves following brief familiarization<sup>81</sup>, the ability to recognize an infant's cry among others depends mainly on the time spent with the child<sup>39</sup>. Cry recognition is thus likely to improve substantially with more extensive exposure and possibly also with exposure to longer cry bouts. We also highlight the fact that identification of cry context is typically multi-modal for parents, depending on visual, auditory, and olfactory cues as well as contextual cues (e.g., time of day or since feeding) that together may help parents to identify the cause of crying and resolve it in real-life contexts. Finally, as noted, the use of short cries may limit information about dynamic cry structure and temporal parameters, cues that parents may use to decide on caregiving interventions<sup>11</sup>. It would thus be worthwhile to conduct perception experiments using longer cry sequences to test the full extent to which human listeners can effectively decode contextual information from babies' cries. Moreover, by including cries from babies of various ages in listening experiments and varying listeners' time of exposure to those cries, researchers can test whether baby age and training intensity predict how well human listeners can decode cry cause by babies' cries.

## Conclusion

In conclusion, the present study suggests that the human infant did not evolve a universal discrete repertoire of cries to communicate the causes of its cries. Instead, each baby's cry encodes an individual signature that changes predictably with age and probably expresses general distress in a graded manner. While stable indexical signals to identity, sex, and age in the voice can be adaptive, for example, for parent-offspring recognition, one ultimate question remains: why haven't babies developed a universal discrete system for encoding contextual information in their cries? A first element of response is that a system using discrete signals to code for categories of information is not very flexible. Conversely, a strategy such as the one developed by human babies allows them to adapt their communication both to the causes of their cries (which can be diverse) and to the responses of their caregivers. This flexibility may contribute to the construction of individualized cry strategies such as the ones some of the babies in our sample may have developed. The condition for this system to be effective is obviously that the caregivers are familiar with the baby. This flexible coding seems rooted in our evolutionary tree as great ape infants seem to have developed a similar strategy<sup>82,83</sup>. The absence of discrete cry categories is thus reminiscent of what is observed in the vocal repertoires of other primate species. For example, bonobos show a graded structure of vocalizations with an individual vocal signature<sup>84</sup>. Unlike other so-called referential vocalizations, these graded acoustic signals do not allow for the designation of environmental elements or very precise contexts. This vocal flexibility is, therefore, characteristic of human infant



cries and reflects an evolutionary equilibrium of a dynamic communication system where both the sender and the receiver of the information must constantly adjust to the context as well as to their mutual interactions<sup>85</sup>.

### Data availability

The raw data and source data supporting this article have been uploaded to the Open Science Framework (OSF) at <https://osf.io/ru7na/> (<https://doi.org/10.17605/OSF.IO/RU7NA>).

### Code availability

All R codes supporting this article have been uploaded to the Open Science Framework (OSF) at <https://osf.io/ru7na/> (<https://doi.org/10.17605/OSF.IO/RU7NA>).

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## Author contributions

M.L.B., A.A., and K.P. have contributed equally to all aspects of this manuscript (data collection, sound analysis, statistical analysis, formatting of the database, writing of the manuscript). S.C. did the playback experiments. C.C. was involved in all aspects of the manuscript and was responsible for formatting the database. L.P. took part in the sound analysis. F.L. was involved in acquiring the recordings and analyzing the data. C.F. contributed to the playback experiments and data interpretation. H.P., N.M., and D.R. jointly supervised this work.

## Competing interests

The authors report no competing interests.

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# Annex II: Parenthood modulates the brain connectome engaged when listening to baby cries

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## **Abstract**

The baby's cry is a prodigiously evocative signal. It activates a set of connected brain networks driving caregiver behaviors crucial to the infant's survival. These networks are more activated in people with parenting experience, particularly mothers. This suggests that experienced people are better able to grasp the level of distress encoded in the cries' acoustic features. However, the precise impact of parental experience and sex on the brain connectome activated by babies' cries is unknown. Here we show that this connectome is more specialized in parents, and that this specialization manifests differently in fathers and mothers. We found that, when the cry contained vocal roughness (an acoustic marker of distress), non-parents show higher connectivity in the empathy network, while parents show higher connectivity in the mentalizing and emotion regulation networks. While most mothers demonstrate higher global connectivity than most fathers, it is in parents with the highest emotional empathy, regardless of sex, that vocal roughness most actively recruits the parental vigilance network. These findings suggest that the brain remodeling induced by parenting depends more on individual factors such as the level of emotional empathy than on sex. We anticipate that our study will be a starting point for an in-depth understanding of the effect of parental experience on the ability to decode information carried by infant cries. In this perspective, the use of acoustic resynthesis, which allows the fine control of signal characteristics as we have done here, is a powerful tool paving the way for systematic and in-depth investigations.

**Key words:** baby cry, brain network, fMRI, pain, parenting.

## **Significance statement**

When listening to a baby cry, various brain regions work together to apprehend the amount of distress expressed and implement a response to the infant's solicitations. Here we analyzed this brain connectivity in men and women, parents and non-parents, by playing them cries expressing different levels of pain. We found that parenting experience results in a specialization of cry-induced brain activity, with greater connectivity within and between networks involved in cognitive evaluation, emotional regulation, and vigilance. While the brain connectivity engaged by infant cries differs in some respects between fathers and mothers, our results highlight significant individual variability linked to each person's level of emotional empathy and therefore independent of sex.

## Introduction

Crying is the primary signalling strategy available to the human baby for eliciting parental care (1). It is typically triggered by pain, discomfort, hunger or separation from parents or other caregivers (2). Cries consist of sequences of complex acoustic signals produced by vibration of the vocal folds -the *source*- and filtered by the vocal tract -the *filter*- (3, 4). The frequency of vocal folds vibration determines the fundamental frequency  $f_0$  (and its harmonic overtones) of the cry, which is responsible for its perceived pitch. The sound is then modified during the passage through the upper airways: the frequencies corresponding to the resonances of the vocal tract are enhanced, leading to the formation of broadband components called formants (5). Cries often present nonlinear phenomena responsible for vocal 'roughness': biphonation, subharmonics, deterministic chaos, and vibrato-like frequency modulation (6). Some of the information carried by cries is static and relates to individual characteristics of the emitter -sex, age, size- while some can be dynamic and related to their current emotional and physiological states -immediate needs (7). Both the sound source and the filter can contribute to the encoding of static and dynamic acoustic cues (4). While the existence of discrete types of cries associated with different contexts (e.g., pain cries, hunger cries, etc) is often assumed (8-12), cries are in fact better described as *graded* signals whose spectral and temporal acoustic characteristics vary along a continuum according to the degree of discomfort or pain experienced by the baby (5, 13-16). Thus, pain calls are characterized by higher and more variable pitch, higher amplitude, and prevalence of acoustic roughness (6, 17, 18). The baby cry is therefore a signal that conveys relevant information through non-linguistic acoustic traits (2). These acoustic traits inform parents and other caregivers of the baby's current level of need, and the amount of care they will provide primarily depends on this information (19). Intra-individual variations in cry acoustics are used by listeners to understand the baby's emotional and physiological state and to measure the degree of urgency (20), e.g., longer, louder, and higher-pitched cries elicit greater attention toward the baby (8, 13-15, 19, 21-26).

The cry thus represents an effective signal used by the baby to tailor the response of parents or other caregivers (27, 28). How is this signal integrated and processed by the nervous system of these listeners, and how does their brain shape their behavioral response? It is now clear that how the brain processes a baby cry is not a purely sequential process but involves complex interactions between different neural networks. In their review, Witteman et al (2019) detail current knowledge based on a meta-analysis of previous studies and highlight the involvement of at least four main neural circuits, whose functions are articulated from the auditory

perception of cry to the implementation of the parental response. Here is a brief summary of the main points (see also Nummenmaa et al. 2023 (29) and Hoegholt et al. 2023 (30)). Firstly, the analysis of cries by the brain mobilizes the auditory circuit in the temporal lobe. The anteroposterior axis of the superior temporal sulcus is involved in the auditory processing (core and belt primary auditory cortex A1 -Heschl's Gyrus - and parabelt -Superior Temporal Gyrus-STG) and semantic processing (Anterior and middle Temporal Gyrus aSTG) of the sound signal to identify it as cry and assess the level of encoded discomfort or distress (31). This bilateral set of auditory regions identifies the auditory information conveyed by the cry. Specifically, the STG may play a role in the processing of the acoustic properties of the cry, such as its pitch and timbre, and may support auditory processing of emotional prosody (32). Meanwhile, the arrival of auditory information conveyed by the cry engages another set of regions comprising the Inferior Frontal Gyrus IFG, and the medial superior frontal gyrus (comprising the dorsolateral prefrontal cortex DLPFC) (31, 33). These regions enable the integration of auditory information with motor programs managing the parental response. A third neural circuit involves the subcortical-paralimbic system through the amygdala (34) and the thalamocingulate pathway (dorsal anterior thalamus and posterior cingulate cortex PCC) which plays an important role in the listener's ability to focus attention on the crying baby and to regulate emotions (35). This circuit is thought to act as a multisensory integration hub, functioning as a “neural alarm signal” (36, 37). Fourth, the fronto-insular regions are also strongly activated by the perception of baby cries. Specifically, the dorsal anterior insula, the mid cingulate cortex MCC and the temporo-parietal junction TPJ may contribute to the processing of emotional information, be involved in empathy induced by cries, and play a role in their interpretation and salience in the environment(36, 38). The DLPFC and the ventro-medial prefrontal cortex vmPFC should also be involved in assessing the emotional relevance of the cry and mentalizing (39). Finally, the basal ganglia, in particular the right caudate nucleus and the left putamen, and the supplementary motor area (SMA) are involved in the initiation and planning of the parental motor response, according to the valence and vigilance attached to the cries (33, 40-42) (see Figure 1B).

Although we have a fairly good knowledge of the brain areas involved when listening to baby cries, we know less about how the activity of these brain networks is modulated by the characteristics of the listener (parenthood, sex), and we have virtually no idea how this activity is modulated by the acoustic features of the cry (expressing different degrees of discomfort or pain). A thorough understanding of how the brain processes the information conveyed by

babies' cries therefore requires answering two key questions: Are the neural networks involved in the analysis of cries and the elaboration of a behavioral response to the baby's needs activated differently in parents and non-parents, and in men and women? And how do these different categories of people see their brains mobilized according to the degree of discomfort or pain expressed by the baby's cry? Previous studies have shown that after the birth of a baby, the parents' brain structure undergoes dynamic functional changes which appear to be involved in the development of parental care behaviors (43-48). Certain parts of the brain are thus more activated by baby cries in parents than in non-parents, in particular the amygdala, the insula, the right caudate nucleus and the SMA, making the parental brain more likely to plan a behavioral response adapted to the emotional level of the cry (49-54). It should be noted, however, that most studies of the brain's response to baby cries have been carried out on women. The fact that the brain correlates of the changes induced by parenthood were first described as the 'maternal brain' underlines this methodological bias (27, 43, 55-58). Yet, studies have now shown that men's brain also undergoes changes as a result of parenthood, and the brain regions activated by baby cries appear to be roughly similar to those identified in mothers, with three key cerebral aspects relating to mentalization, embodied simulation and emotion regulation processes (see (59) for a review and (54, 60)). Some studies have also suggested the possibility of differential brain activations between mothers and fathers, with the latter showing preferential activation of social-cognitive networks and less activation of limbic regions than in mothers (61-63). However, the data are still fragmentary and the differences in activation induced by baby cries between the brains of mothers and fathers have not been fully established - which in any case would say nothing about their origin, whether genetically rooted or acquired through experience during pre-parental life (59, 63, 64). In a previous study, we thus showed that both parents distinguish between pain cries emitted by their own baby (recorded during a vaccination session) and discomfort cries recorded during a bath (6). We have also recently shown that previous experience with babies is a key factor for identifying pain encoded in a cry and that this effect is independent of sex (65).

We have even less information about the impact of the degree of discomfort or pain expressed by a cry on brain activation. It is known that the acoustic structure of cries makes them aversive, encourages listeners to pay attention to them (66, 67), and induces high levels of arousal and potential alterations in cognitive control (17). Cries are graded signals, the acoustic characteristics of which vary according to the intensity of the stress felt by the baby (16). Pain cries are characterized by a higher and more variable pitch, a higher amplitude and acoustic

roughness due to non-linear phenomena such as acoustic chaos and sub-harmonics (6, 18, 19). Roughness is a common acoustic feature in animal alarm and distress signals, inducing haemodynamic changes in the amygdala (68) and synchronization in the large-scale brain networks involved in aversion processing (69). Our knowledge of the cerebral correlates of the acoustic characteristics of cries remains however rudimentary. For instance, while Li et al. (2018) (60) found no correlation between cry roughness with brain response to cries, their study only tested fathers listening to a single cry from their own baby and the cry of an unfamiliar baby. To our knowledge, there has not yet been a study systematically exploring the impact of the acoustic features of cries on brain activation by having subjects listen to a range of baby cries showing different levels of roughness.

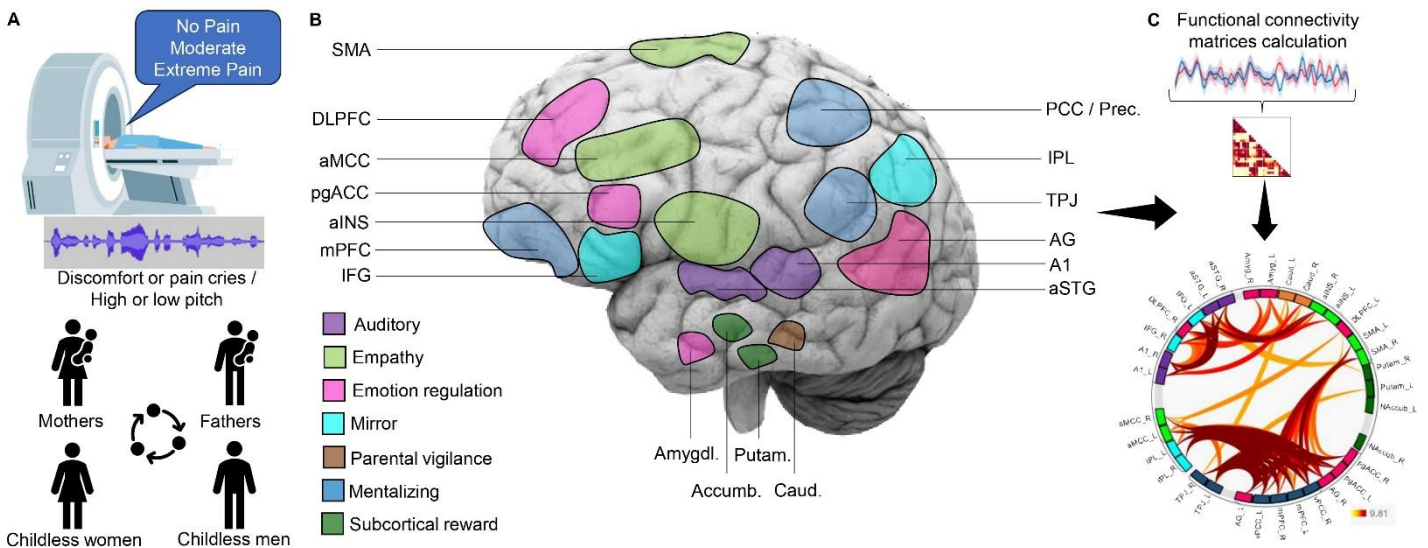
In the present study, we explore the brain connectome engaged when listening to baby cries and determine the effect of parenthood, sex and emotional empathy on the organization and activity of this connectome. We played cries recorded from different babies to a large sample of adult men and women, parents and non-parents (80 persons), and identified how the baby cry connectome activates in response to baby cries expressing different levels of discomfort and pain (Figure 1A). We tested the hypothesis that parental experience results in increased specialization of the brain connectome mobilized when listening to babies' cries. We also predicted that the connectome is similar between fathers and mothers, but that certain networks such as the parental vigilance network are more activated in mothers. We then predicted that non-parents' brains respond less specifically than parents' brains to cries expressing different levels of pain. Furthermore, we predicted that the brain response to cries with the most acoustic roughness - a marker of pain level - is more specific in adults with stronger emotional empathy, regardless of their sex. Overall, our results provide the first general framework of cerebral functional connectivity in response to baby cries and the information they carry, and highlight the importance of parental experience, sex, and inter-individual variability of emotional empathy in the brain response to these critical sound signals.

## **Results**

### **The baby cry connectome**

We first conducted a whole brain analysis in fMRI to establish a neural connectome across all adults – i.e., 20 mothers, 20 fathers and 40 childless adult men and women – when listening to baby cries (Figure 1). We tested these adults with cries from 20 babies aged around 2 months

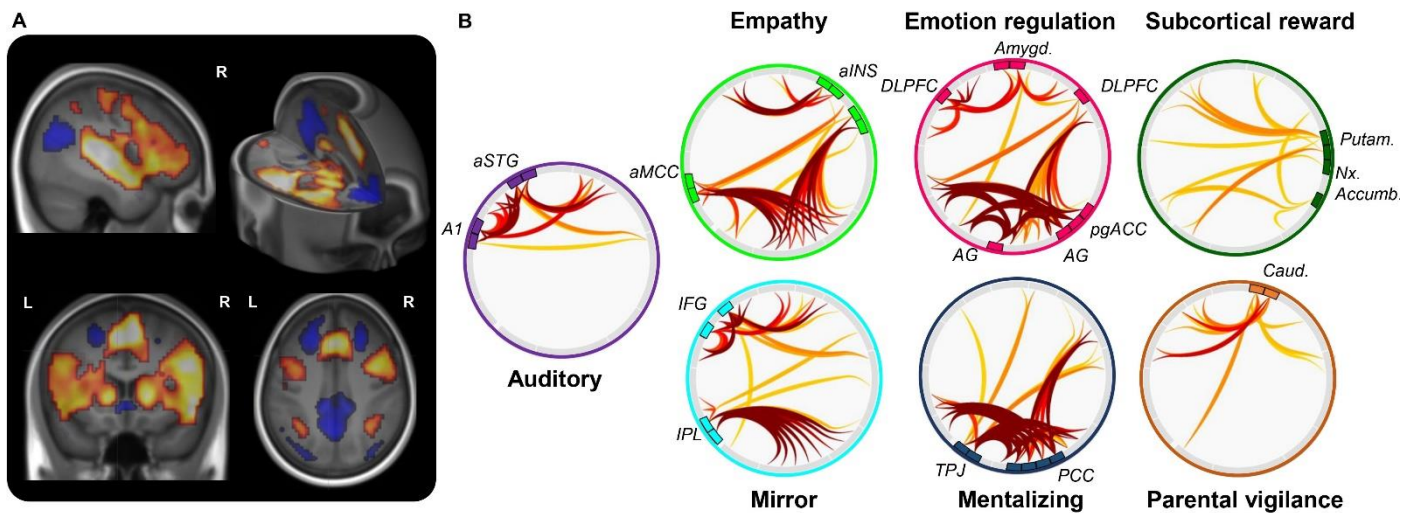




**Figure 1. Overview of the experimental procedures and brain connectome related to cries decoding.** (A) While in the MRI scanner, participants listened to 80 discomfort and pain cries with two pitch levels, delivered in a randomized order (20 stimuli per condition). After hearing a stimulus, they had few seconds to rate the level of pain expressed by the cry (1 = cry expressing no pain, 2 = moderate pain, 3 = expressing extreme pain). 20 mothers, 20 fathers and 40 childless adults were included. (B) The adult brain connectome of baby’s cry perception, set of brain regions (17 bilateral areas) considered here to be involved in processing sound distress signal from babies see S1 Material and Methods and Table S1). They are organized in 7 networks named auditory, empathy, emotion regulation, mirror, parental vigilance, mentalizing and subcortical reward networks. (C) Computing functional connectivity between this set of regions of interest allow us to construct individual and sub-group average connectivity matrices, and to calculate the number of links between and within the 7 networks of interest.

AG : Angular Gyrus; aINS: anterior insula ; aMCC : anterior Mid Cingulate Cortex ; amygd.: amygdala ; Caud. : caudate nucleus ; DLPFC / dmPFC: dorso lateral / medial prefrontal cortex ; Hipp.: hippocampus ; IFG: inferior frontal gyrus; IPL : Inferior Parietal Lobule; Nx. Accumb. : nucleus accumbens ; PCC : Posterior Cingulate Cortex ; pgACC : perigenual Anterior Cingulate Cortex; Putam.: putamen ; SFC: superior frontal gyrus ; SMA : Supplementary Motor Area; TPJ : Temporo-Parietal Junction; L, left; R, right.

(10 boys and 10 girls), each recorded under two conditions, during a bath (“discomfort cries”) and during a vaccination session (“pain cries”). This large number of recorded babies ensured a wide diversity of acoustic markers of discomfort and pain encoded in cries. To discern the effect of cry roughness – a reliable marker of pain level – from that of pitch – an acoustic characteristic essentially idiosyncratic to each baby (70)-, we had participants listen to two variants of each of the 20 discomfort cries (Discomfort360: variant 1 with pitch set at 360 Hz; Discomfort500: variant 2 with pitch set at 500 Hz; Figure 1A) and two variants of each of the 20 pain cries (Pain360 and Pain500). Each of the 80 adults was thus tested with all 80 stimuli



**Figure.2. Brain activations and functional networks associated with listening to baby's cries in adults.** (A) Whole-brain analysis revealed distributed brain regions activated and deactivated (voxel level  $p$ -FWE corr)  $< 0.01$  in response to distress cries (average of painful and non-pain cries in the 80 participants). (B) This included a strong functional connectivity between these regions in 7 sub-networks involved in auditory processing, empathy and mirror processes, mentalizing, emotion regulation, subcortical reward and parental vigilance (network level  $p$ -FDR corrected  $< 0.05$ ; statistics based on mass/intensity network; see Table S1).

AG : Angular Gyrus; aINS: anterior insula ; aMCC : anterior Mid Cingulate Cortex ; amygd.: amygdala ; Caud. : caudate nucleus ; DLPFC / dmPFC: dorso lateral / medial prefrontal cortex ; Hipp.: hippocampus ; IFG: inferior frontal gyrus; IPL : Inferior Parietal Lobule; Nx. Accumb. : nucleus accumbens ; PCC : Posterior Cingulate Cortex ; pgACC : perigenual Anterior Cingulate Cortex; Putam.: putamen ; SFC: superior frontal gyrus ; SMA : Supplementary Motor Area; TPJ : Temporo-Parietal Junction; L, left; R, right.

(duration of a stimulus = 6 seconds). To our knowledge, our study is the first to explore the brain activation induced by listening to baby cries with such a wide range of stimuli and in such a large number of subjects, non-parents and parents, men and women (see *Methods*).

As shown in Figure 2, listening to cries is associated with changes in activity and higher functional connectivity within several brain networks ( $t(79) > 6.19$ ; Supplementary Methods; Tables S1 and S2). This cerebral connectome of infant cries listening involves: 1) *the auditory network*, marked by strong functional connectivity between the primary auditory cortex (A1) and the anterior superior temporal gyrus (aSTG); 2) *the empathy network*: anterior insula (ant INS), anterior mid cingulate cortex (aMCC), supplementary motor area (SMA); 3) *the mirror network* (cognitive evaluation): inferior frontal gyrus (IFG) and inferior parietal lobule (supramarginal rostro-dorsal (IPL)); 4) *the emotion regulation network*: amygdala (Amyg),

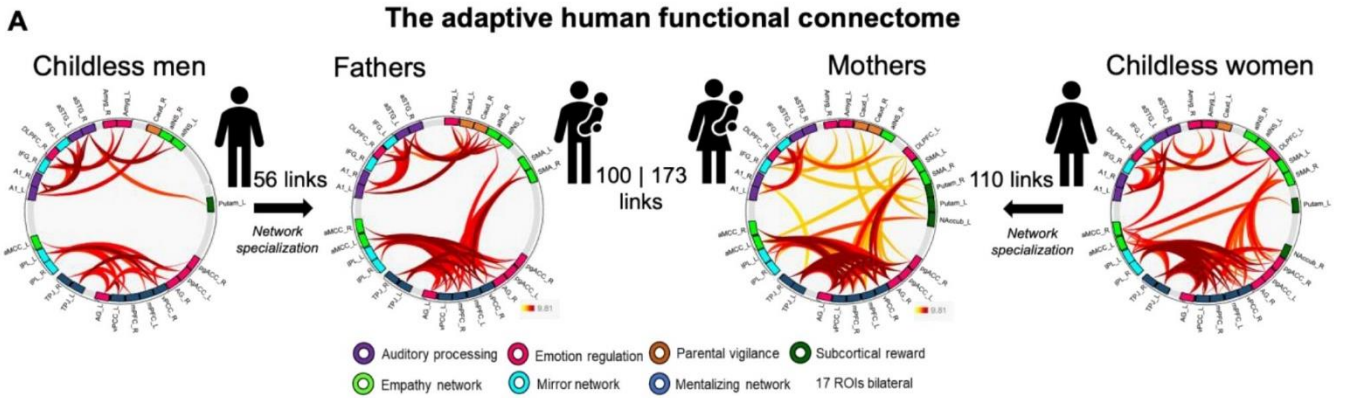
dorsolateral prefrontal cortex (dlPFC), the angular gyrus (AG), and the pregenual anterior cingulate cortex (pgACC); 5) *the mentalizing network*: temporo-parietal junction (TPJ: supramarginal ventro-caudal), medial prefrontal cortex (mPFC), precuneus and posterior cingulate cortex (Prec/PCC); 6) *the subcortical reward network*: putamen (Putam) and accumbens nucleus (Nx. Accumb.); and 7) *the parental vigilance network*: caudate nucleus (Caud.).

### **Parenthood brings changes in brain functional connectivity.**

Functional connectivity between regions of the brain connectome involved when listening to cries is influenced by parenthood and the sex of the listeners. As shown in Figure 3A the overall connectivity of these regions is higher in parents than in non-parents ( $t_{(78)} = 2.48$ ;  $P = 0.01$ ), and in women than in men ( $t_{(78)} = 5.34$ ;  $P < 0.001$ ). Among all the categories of people tested, it was men without children who showed a particularly low density of connections recruited by listening to cries (men without children: 56 connections, fathers: 100; women without children: 110, mothers: 173; significant links at the corrected  $p$ -FDR  $< 0.05$  connection threshold). These different densities of connectivity support the hypothesis that the brain connectome activated by a baby's cry is more specialized in parents than in childless adults, and that this specialization manifests differently in fathers and mothers.

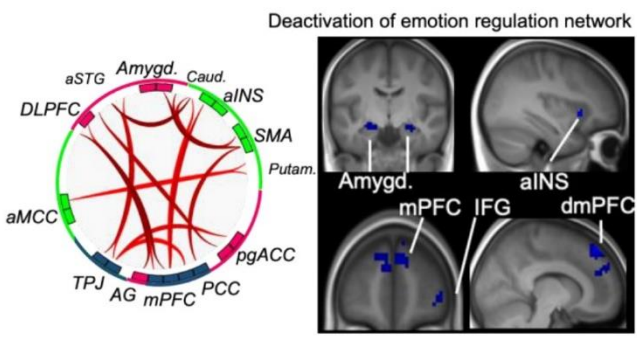
As illustrated in Figure 3B (left panel), fathers' brains show stronger functional connectivity between emotion regulation, mentalizing and empathy networks than the brains of childless men ( $t(38) > 3.03$ ;  $p$ -FDR-corr  $< 0.03$ ). This more pronounced connectivity was accompanied by lower activity in the dorsal and medial prefrontal cortex, amygdala, anterior insula and right inferior frontal gyrus ( $t(38) > 4.94$ ;  $p$ -FDR-corr  $< 0.034$ ; Figure 3B right panel). Remarkably, listening to cries mobilized the amygdala nuclei less in fathers than in other adults (Figure 3C; Right Amygdala, unpaired Cohen's  $d$  between fathers and men = 1.95 [95.0%CI 1.4, 2.44],  $p = 0.01$ ; between fathers and mothers = 1.29 [95.0%CI 0.789, 1.74],  $p < 0.001$ ; between fathers and women = 1.52 [95.0%CI 0.957, 2.02],  $p = 0.01$ ; Left Amygdala, unpaired Cohen's  $d$  between fathers and men = 1.51 [95.0%CI 0.969, 2.01],  $p = 0.01$ ; between fathers and mothers = 0.959 [95.0%CI 0.404, 1.48],  $p = 0.005$ ; between fathers and women = 1.53 [95.0%CI 0.915, 2.11],  $p = 0.01$ ). Some specific functions that are influenced by the amygdala include the processing of biologically significant stimuli, the recognition of emotions, and the evaluation of their salience (71). The attenuated activity in fathers' amygdala compared to other



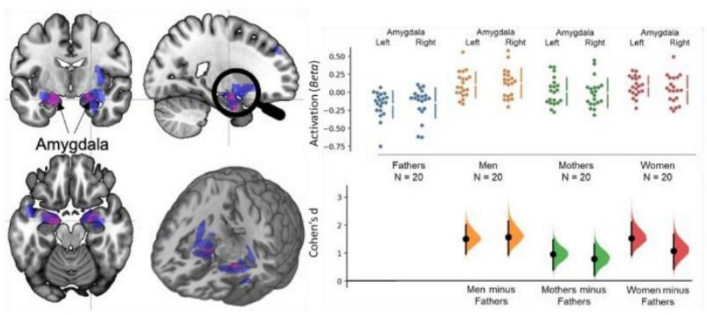


### Group comparisons

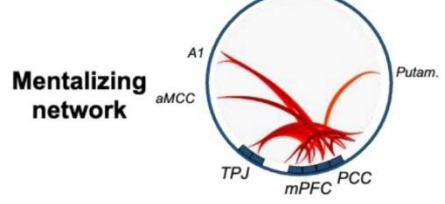
#### B Fathers > childless men



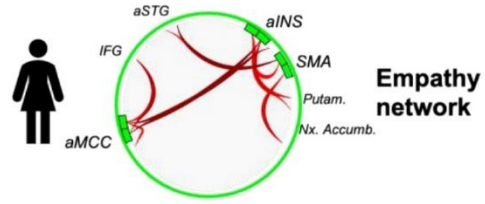
#### C Fathers vs. others – Amygdala activity



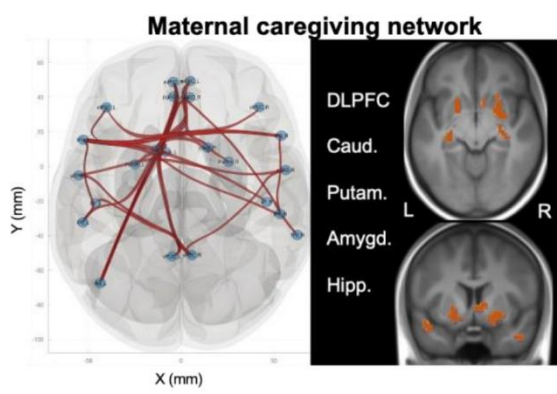
#### D Mothers > childless women



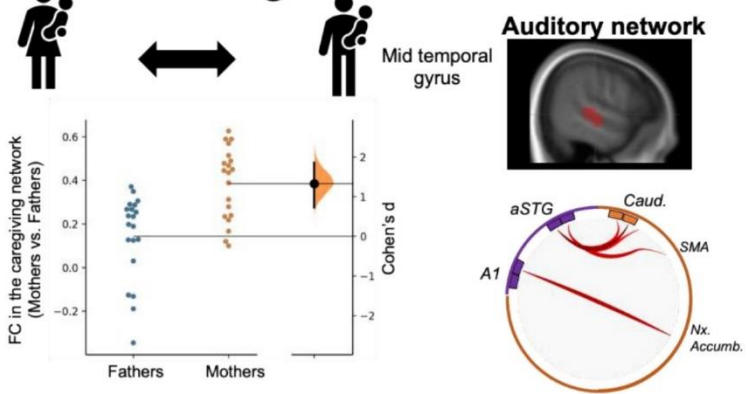
#### E Childless women > Mothers



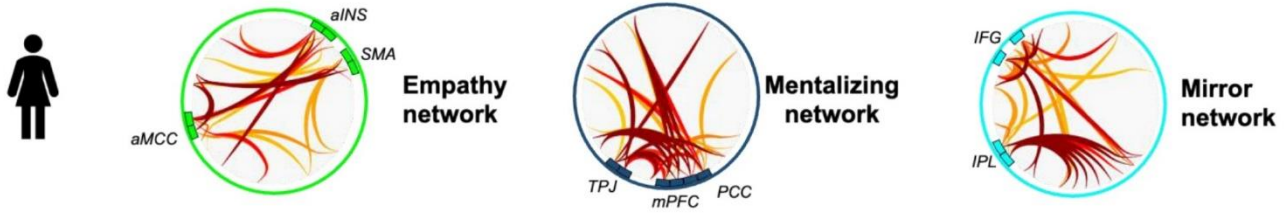
#### F Mothers > Fathers



#### G Fathers > Mothers



#### H Childless women > Childless men



**Figure 3. Specialization of the brain connectome activated by baby cries as a function of parenting experience and listener sex.** (A) The functional connectomes differ between the four groups of subjects. Those of parents of both sexes show specialization with a higher number of significant connections (links) compared with childless adults (average network connectivity; fisher's z-transformation of Pearson's correlation). (B) Left: Fathers' brains show stronger functional connectivity between emotion regulation, mentalization and empathy networks than the brains of childless men ( $t_{(38)} > 3.03$ ;  $p\text{-FDR-corr} < 0.03$ ). (C) Right: This more pronounced connectivity was accompanied by lower activity in the dorsal and medial prefrontal cortex, amygdala, anterior insula and right inferior frontal gyrus ( $t_{(38)} > 4.94$ ;  $p\text{-FDR-corr} < 0.034$ ). Fathers' brain shows lower activity in the amygdala compared with mothers and non-parents. (D) Left: mothers show significantly higher functional connectivity than childless women in the mentalizing network ( $t_{(38)} > 1.96$ ;  $p\text{-FDR-corr} < 0.02$ ). (E) Right: connectivity is conversely lower in the empathy network ( $t_{(38)} > 2.18$ ;  $p\text{-FDR-corr} < 0.04$ ). (F) Mothers' brain has higher activity and functional connectivity in the subcortical reward network (notably the putamen, amygdala, and hippocampus) compared with fathers. (G) Upper: Fathers show higher activity than mothers in the auditory association cortex (middle temporal gyrus;  $t_{(38)} = 4.87$ ;  $p\text{-FDR-corr} < 0.03$ ), and stronger functional connectivity between the auditory network and the parental vigilance network (i.e. caudate nucleus; Lower panel;  $t_{(38)} > 3.46$ ;  $p < 0.002$ ). (H) Childless women show higher global functional connectivity than childless men, particularly in the empathy, mirroring and mentalization networks ( $t_{(38)} > 1.87$ ;  $p\text{-FDR-corr} < 0.034$ ).

Statistical maps are thresholded at FWE-corrected cluster-based threshold of  $P < 0.05$  after a voxel threshold at  $P < 0.001$ .

participants suggest that fathers could find cries less aversive or be less vigilant, as a possible consequence of habituation phenomena associated with childcare experience.

Mothers and childless women did not differ in their overall BOLD activity, i.e. the amplitude of brain activations/deactivation associated with listening to cries were not significantly different. However, we found significant differences regarding connectivity, i.e. the temporal synchronicity between regions of the brain connectome. Thus, mothers showed significantly higher functional connectivity than childless women in the mentalizing network (Figure 3D;  $t_{(38)} > 1.96$ ;  $p\text{-FDR-corr} < 0.02$ ), while connectivity was conversely lower in the empathy network (Figure 3E;  $t_{(38)} > 2.18$ ;  $p\text{-FDR-corr} < 0.04$ ). Mentalization and empathy are two processes involved in theory of mind that allow us to understand other humans through the representation of their mental states and moods respectively (72). By showing that mothers engage the mentalizing brain network more and empathy network less than childless women, our results suggest that maternal experience results in a more active mobilization of cognitive capacities when listening to babies' cry.

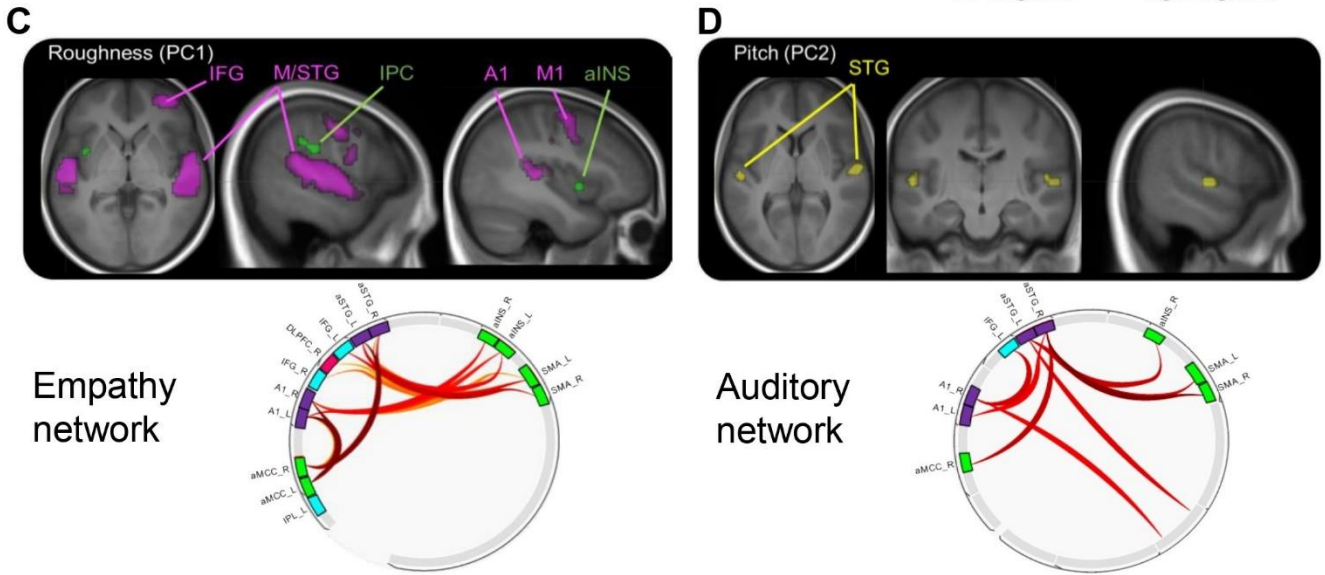
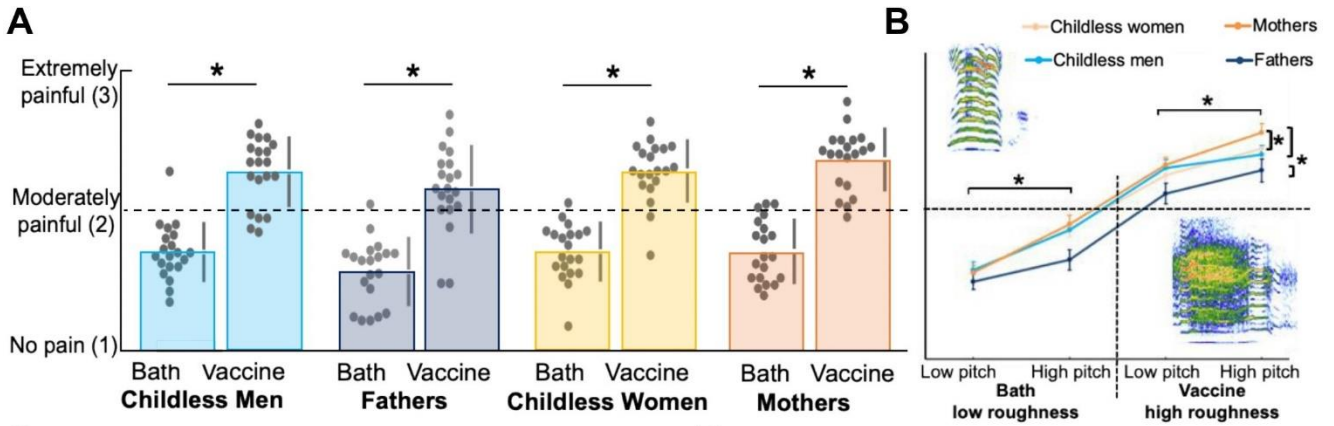
If becoming a parent is accompanied by significant changes in the functional connectivity of the brain network engaged by listening to a baby's cries, the parent's sex is also a factor modulating this connectivity. Mothers showed significantly higher activity and more pronounced functional connectivity than fathers in the dorsolateral prefrontal cortex and in a set of subcortical regions including the amygdala, putamen, hippocampus and caudate nucleus (Figure 3F;  $t(38) > 4.62$  ;  $p\text{-FDR-corr} < 0.02$ ). These regions correspond to the maternal care network encompassing the “emotion regulation”, “the subcortical reward” and “the parental vigilance” subnetworks, as reported in the literature (27, 43, 55-58). Functional connectivity between this set of regions and the subcortical reward network was also stronger in the mothers ( $t(38) > 2.01$  ;  $P < 0.027$ ).

Fathers show higher activity than mothers in the auditory association cortex (mid temporal gyrus; Figure 3G upper panel;  $t(38) = 4.87$  ;  $p\text{-FDR-corr} < 0.03$ ), and stronger functional connectivity between the auditory network and the parental vigilance network (i.e. caudate nucleus; Figure 3G lower panel;  $t(38) > 3.46$  ;  $p < 0.002$ ). Results support that mothers have greater activity in subcortical-paralimbic structures supporting mammalian caregiving in the brain connectome, whereas fathers had higher recruitment of auditory brain regions, connected to the caudate nucleus (parental vigilance network). This may reflect distinct neural circuits between fathers and mothers for baby's cries perception.

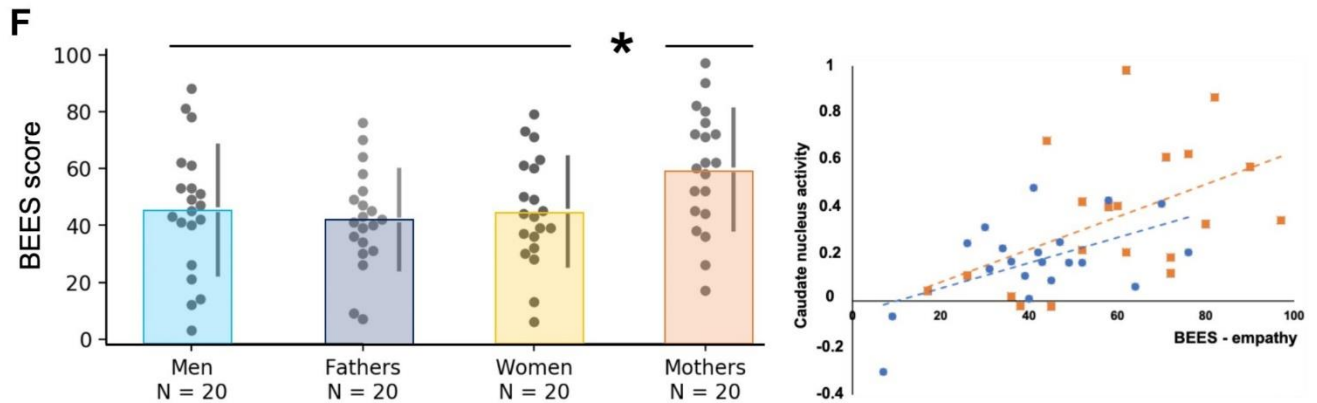
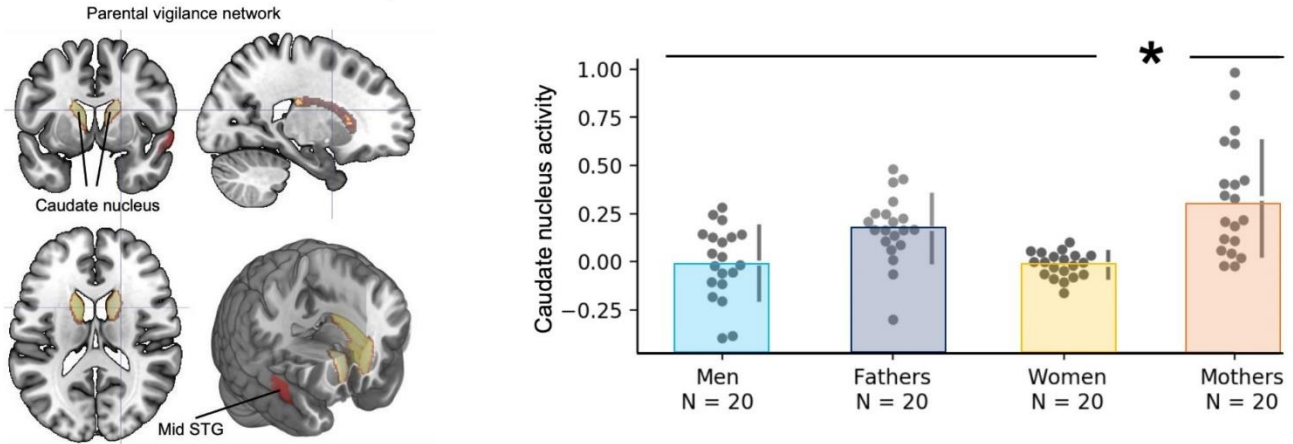
Contrary to what we found in parents, we did not identify any influence of sex on the brain activity of men and women without children. However, childless women show higher global functional connectivity than childless men, particularly in the empathy, mirror and mentalizing networks (Figure 3H;  $t(38) > 1.87$  ;  $p\text{-FDR-corr} < 0.034$ ).

### **Cry roughness reflects the baby's level of pain**

Participants were asked to classify each cry they heard according to the following pain scale: 1 = cry expressing no pain, 2 = cry expressing moderate pain, 3 = cry expressing extreme pain (see Methods). As shown in Figure 4A, pain assessment profiles are very similar between participant categories - although the variability within each category is noteworthy - and strongly depend on the recording context: cries recorded during a bath are predominantly classified as expressing little pain, whereas cries recorded during a vaccination session are perceived as expressing strong pain (GLM model, dependent variable = pain perceived by listener, fixed factors = recording context, cry pitch, listener sex, listener parenthood, random factor: baby identity, subject identity;  $F_{(1,4714)}=1166.47$ ,  $p < 0.0001$ ).



**E Pain cries discrimination in parents**



**Fig. 4. Effect of cry roughness and pitch on brain activity and connectivity as a function of parenting experience, sex and emotional empathy.** (A) All participants rated cries recorded during a bath as expressing little pain, whereas cries recorded during a vaccination session were perceived as expressing strong pain. (B) Discomfort cries show a well-defined harmonic structure while pain cries include nonlinear acoustic phenomena (“vocal roughness”). Adult listeners rate cries with more vocal roughness as expressing more pain. The interaction between roughness and cry pitch is significant, showing that the influence of roughness on the perception of pain expressed by the cry is all the more sensitive the lower the pitch of the cry. Overall, fathers underrate pain compared to other categories of listeners. Conversely, mothers tend to overrate it, especially for the roughest and highest pitched cries. (C) Lower panel: The presence of vocal roughness recruits the empathy brain network. (D) Right panel: The cry average pitch, a poor marker of pain, recruits mainly the auditory network. (E) Left: In parents, acoustic roughness induced greater activity in the middle temporal gyrus (A5) and caudate nucleus in mothers than in fathers ( $t_{(38)} > 4.29$ ;  $p\text{-FDR-corr} < 0.036$ ). Right: The caudate nucleus, an essential component of the parental vigilance network, was significantly more activated by cries with high acoustic roughness in mothers and some fathers than in non-parents. (F) Participants' emotional empathy (BEES score) is higher in mothers, and in some fathers compared to non-parents. (F) Caudate nucleus activity is significantly correlated with the level of emotional empathy of both fathers and mothers (respectively:  $r^2=0.25$ ;  $Q=2.45$ ,  $p = 0.025$ , and  $r^2=0.29$ ;  $Q=2.69$ ,  $p = 0.015$ ).

This difference in pain level differentiating bath cries from vaccine cries is mainly explained by the difference in roughness between the two categories of cries (Figure 4B) and appears independent of cry pitch since it is present for both pitch levels set in our stimuli (360 and 500 Hz). We further clarified the importance of cry roughness by directly testing the effect of this acoustic characteristic on the participants' evaluation of the cries. In a previous study, we quantified the level of roughness of the cries used here in the form of a PC1 index (derived from a principal component analysis) that integrates non-linear acoustic phenomena such as biphonation, subharmonics, deterministic chaos and vibratory frequency modulation (see (6) and Table S3). A higher roughness PC1 index is associated with greater estimated pain, regardless of participant category (GLM model: dependent variable = pain perceived by listener, fixed factors = cry roughness, cry pitch, random factors = recording context, listener sex, listener parenthood, baby identity,  $F_{(1,5289)}=913.0$ ,  $p < 0.0001$ ). Note that the interaction between roughness and cry pitch was also significant ( $F_{(1,11510)}=64.36$ ,  $p < 0.0001$ ), showing that the influence of roughness on the perception of pain expressed by the cry is all the more sensitive the lower the pitch of the cry (Figure 4B, Table S4, Supplementary Results, and Figure S2). Within each recording context, the highest-pitched cries are perceived as expressing more pain by the listeners (Figure 4B;  $F_{(1,4706)}=135.52$ ,  $p < 0.0001$ ; Table S4). Although the different



categories of participants show similar pain assessment profiles (Figure 4A), fathers underestimate the pain expressed in cries compared to the other participants (mean  $\pm$  SD =  $1.8 \pm 0.04$ ;  $F_{(1,4714)}=6.17$ ,  $p = 0.013$ ). Mothers, on the other hand, appear particularly sensitive to the pain expressed in cries with a high degree of roughness (vaccine cries in mothers: mean  $\pm$  SD =  $2.4 \pm 0.04$ ;  $F_{(1,79)}=3.24$ ,  $p = 0.027$ ). Finally, women, with or without children, rated the highest pitched cries as expressing the highest level of pain, irrespective of roughness (high-pitched cries: mean  $\pm$  SD =  $2.15 \pm 0.03$ ; low-pitched cries: mean  $\pm$  SD =  $1.89 \pm 0.03$ ;  $F_{(1,4706)}=7.03$ ,  $p = 0.008$ ;  $T_{(1,37)}= 4.48$   $p = 0.01$ )).

### **Roughness-induced brain activation and functional connectivity are modulated by parental experience and sex**

The acoustic characteristics of the cries impact participants' brain activity: listening to cries expressing pain (high level of roughness) recruits the empathy network to a greater extent, whereas listening to cries marking simple discomfort merely activates the auditory regions. Acoustic roughness thus accompanies an increase in functional connectivity in the empathy network (Figure 4C;  $t(79) = 3.04$  ;  $p$ -FDR-corr < 0;003; see Methods for details of statistical analysis of brain correlates). Cries marked by higher acoustic roughness induce greater brain activity in the bilateral anterior insula and inferior parietal cortex ( $t(79) > 5.77$ ;  $p$ -FDR-corr <0.001), while their listening accompanies a decrease in the activity of the bilateral auditory association cortex (M/STG, A5), premotor areas (M1) and dorsolateral and inferior right frontal cortex (DLPFC, IFC; ( $t(79) > 5.45$  ;  $p$ -FDR-corr < 0.01; Table S5). The pitch of the cry is essentially correlated with the activity of a restricted group of the STG comprising the primary auditory area (A1: peak of maximum activity), and the lingual gyrus ( $t(79) > 4.01$  ;  $p$ -FDR-corr < 0.02), and associated with changes in functional connectivity within the auditory network (Figure 4D;  $t(79) = 2.97$  ;  $p$ -FDR-corr < 0.04; Table S5).

These differential recruitments of brain regions according to the roughness of the cry (and therefore the level of pain expressed by the cry) are modulated by the parenthood and sex of the participants. In non-parents (men and women), the connectivity of the empathy network mobilized when hearing a cry is higher than in parents ( $t(79) = 4.58$  ;  $p$ -FDR-corr < 0.02). In the parents' brains, on the other hand, functional connectivity is higher in the mentalizing and emotion regulation networks ( $t(79) = 2.08$  ;  $p$ -FDR-corr < 0.045).

In parents, acoustic roughness induced greater activity in the mid temporal gyrus (A5) and caudate nucleus (an essential component of the parental vigilance network) in mothers than in fathers ( $t_{(38)} > 4.29$ ;  $p$ -FDR-corr  $< 0.036$ ; Figure 4E; left panel). Mothers also showed higher functional connectivity than fathers between the auditory network, the emotion regulation network and the parental vigilance network ( $t_{(38)} = 2.08$ ;  $p$ -FDR-corr  $< 0.045$ ). Furthermore, the caudate nucleus was significantly more activated by cries with high acoustic roughness in mothers and some fathers than in non-parents (unpaired Cohen's  $d = 0.64$  95.0% CI [0.0631, 1.19],  $p = 0.046$ ; Figure 4E; right panel; Table S5).

We measured participants' emotional empathy and identified wide individual variations (Figure S3 and Table S6; empathy measured by a BEES "Balanced Emotional Empathy Scale" score, see Methods). While mothers expressed the most empathy on average (permutation tests; effect size = 14.7 [95.0%CI 2.55, 26.2];  $p < 0.03$ , Table S6), the distributions within each category of participants (parents and non-parents, men and women) were largely overlapping (Figure 4F right panel). As shown in Figure 4F (left panel), caudate nucleus activity is significantly correlated with the level of emotional empathy of both fathers and mothers (respectively:  $r^2=0.25$ ;  $Q=2.45$ ,  $P < 0.025$ , and  $r^2=0.29$ ;  $Q=2.69$ ,  $P < 0.015$ ). This result highlights that inter-individual variability in emotional empathy better explains inter-individual variations in parental vigilance network activity than parent sex. We found no effect of sex on brain activity and functional connectivity when listening to cries in non-parents.

## **Discussion**

The brain mechanism to integrate the cry of a baby involved a set of neural networks interacting functionally together within a connectome, the resulting perception in caregivers allow them to provide an adapted behavioral response to the situation (29). These networks have been thoroughly described in adults with parenting experience, particularly in mothers, showing adaptations of specific functions in the maternal and paternal brain responses to infant cries.

However, we know less about how the activity and connectivity of these brain networks are modulated by the characteristics of the listener (parenthood, sex, and empathy) and the information carried in cries (acoustic features). Cries are graded signals, the acoustic characteristics of which vary according to the intensity of the stress felt by the baby (16), and therefore pain cries are characterized by higher acoustic roughness than simple distress cries, due to the increment of non-linear phenomena. In a previous study, we illustrated that exposure

through parenting shapes the auditory and cognitive abilities involved in decoding the pain information conveyed by the level of roughness in babies' cries.

Here we examined the brain connectome (activity and functional connectivity) in men and women, parents, and non-parents, by playing them a range of baby cries expressing different levels of roughness (from stress to pain situations). To understand in-depth the effect of parental experience on the ability to decode information carried by infant cries, we also used acoustic resynthesis to finely control the cries characteristics.

The current study is, to our knowledge, the first to chart an overall model of brain functional connectome specialization with parenting experiences in women and men in response to different levels of baby distress vocalizations.

First, our results describe a global brain network when listening to cries that was consistent across adults (parents and non-parents) and involved cortical regions implicated in auditory processing, empathy, vigilance, cognitive evaluation, emotional / motivational regulation, and subcortical structures supporting mammalian caregiving (Figure 1 & 2). Compared with the mammalian maternal care circuit, one important difference in the human caregiving brain connectome is the large connectivity of the subcortical structures (hypothalamic-midbrain-limbic-paralimbic-cortical circuits) to multiple insula-cingulate and fronto-temporo-parietal networks, which are integrated into the human care connectome along the subcortical areas described in animal models (46,63). Such interconnectivity allows the integration of high-order (later-evolving) cognitive structures implicated in empathy, emotion regulation, embodiment and socio-affective processes enabling adults to create a conscious representation of the baby's state from listening to his/her vocalizations.

The response pattern changed fundamentally with parental experience, with an extensive enhancement of functional connections within the crying-induced connectome in parents. Such findings are consistent with the hypothesis that the parental brain evolve from a substrate that exist in all adults and will be dynamically adapted through experience of baby caring. Human parenting brings neurophysiological changes that are shaped through responsive caregiving and commitment to children's well-being. Increased brain activity has been illustrated in several regions including the insular cortex, inferior frontal gyrus involved in empathy and subcortical regions (e.g., caudate nucleus) involved in parental vigilance. In the same vein, studies have pointed to increased brain plasticity in humans, which provides an opportunity for reorganization of the parent's brain (46). Repeated interactions with their child and the

attachment relationship may have adaptively reinforced the number of functional connections in our parents' brain connectome, which could be linked to the daily processing of their babies' cues, enabling a better reallocation of resources towards babies' signals, and the development of parental care. These different densities of connectivity show that the brain connectome activated by a baby's cry is more specialized in parents than in childless adults, but this specialization manifests differently in fathers and mothers.

Second, we found sex differences in the brain connectome, mothers exhibited higher activity and connectivity in a set of subcortical-limbic regions involved in parental care than most fathers, and previously identified as the maternal care system (27, 44, 55-58). Engagement of this circuitry, encompassing the emotion regulation, the subcortical reward, and the parental vigilance networks, is supposed to promote positive maternal behavior (55). Oxytocin, which is involved in attachment processes, is released in mothers during childbirth and the following interaction with the baby increases its production (37). It has been demonstrated that these hormonal secretions participate to modulate the activity and connectivity state of the maternal brain network (45, 62, 73). This reorganization (or specific neural wiring) in the maternal brain is involved in the mothers' motivation and vigilance, in parallel to suppressing aversion to infant cues (46, 56). Consistently, in our study, it may reflect the stronger sensibility of mothers to the distress vocalizations of unknown babies, associated with a high rating of pain expressed in cries with a high degree of roughness.

The paternal brain connectome had also a specific functional organization, characterized by a lower engagement of the amygdala nuclei and empathic/mirror areas (e.g., anterior insula and inferior frontal gyrus) in response to cries than other adults. These structures play a key role in the processing of biologically significant stimuli and the evaluation of their importance in the environment (74). The amygdala is a central node of the mammalian parenting network, is reciprocally connected to mesolimbic reward-motivation network and empathy network and is considered the core regions of the 'emotional brain' (63, 75). Previous studies comparing mothers' and fathers' fMRI responses also illustrated a greater amygdala activation in mothers and greater cortical activation in fathers (63). Sex differences in the connectome functional organization support the distinct pathway hypothesis between mothers and fathers.

Moreover, fathers have the same capacity to recognize their newborn from their cries (7, 76), they also distinguish the cries' distress level, but underestimate (underate) the pain expressed in them. The attenuated activity in the paternal brain connectome and low assessment of pain

vocalizations may suggest that some fathers find cries less aversive or alarming, as a possible consequence of habituation phenomena associated with childcare experience. This assumption is consistent with previous imaging studies, which showed that older fathers have an attenuated neural response to their infant's cry and find them less aversive (60). This effect is extended here to distress cries of unknown babies, and in the context of our experiment, it may constitute a valid strategy to avoid the unpleasantness associated with empathic over-arousal in response to repetitive listening to cries (60). Therefore, a specific brain network organization may be involved in facilitating fathers' sensitivity and responses to baby cries (59).

Our study highlights that parenthood has differential effects on men and women brains, including two potential distinct systems in the parental connectome: a specific maternal system involving emotion regulation, motivational networks, and subcortical structures sensitive to pain evoked in the vocalizations, and a paternal system operating via a downregulation of salience-detection networks (including the amygdala nuclei and empathic areas) to regulate emotional contagion, and an increased synchrony of brain high-order cortical networks involved in cognitive empathy to identify the cries' valence.

Third, we also observed that the degree of pain expressed in a baby's cry resulted in variations in brain activity and connectivity depending on parenting experience.

All participants were able to distinguish pain cries from distress cries. It was previously illustrated in parents (6, 17), but this capacity seems to be conserved even in childless adults with no experience with baby's care. A plethora of neuroimaging studies have illustrated the brain correlates of empathy for pain (see (77-79)), showing that it involves a core network of bilateral anterior insular cortex and medial/anterior cingulate cortex, which overlap directly with experienced pain. To our knowledge, very few indirect studies or no studies have investigated the brain activity and connectivity evoked by empathy for pain baby cries.

In the present study, listening to cries expressing pain recruits the empathy network (bilateral anterior insula and inferior parietal cortex) to a greater extent (according to the increase level of roughness), whereas listening to cries marking simple discomfort (low level of roughness) merely activates the auditory regions. Identification of pain in the cries require cognitive associative brain structures involved in empathy for pain, whereas distress vocalizations with no pain valence. It may represent a gradual system to enter the brain connectome, where primary auditory areas are enough to identify simple distress vocalizations with no pain valence,

but identification of pain in the cries require cognitive-associative brain structures (empathy networks) involved in empathy for pain (for finer valence-detection). This shift from low level sensory processing to high level cognitive processing is also found to brain activity dissociating alarm screams compared non-alarm screams (80) or high-distress cries compared to low-distress cries (81). In addition, neither pain identification nor roughness processing in babies cries have shown involvement of brain regions associated with aversion like other rough acoustic signals (69).

Finally, activity and connectivity of the parental vigilance network, including the caudate nucleus, was associated with the difference of pain cries discrimination between fathers and mothers. However, there were a large inter-individual variability in these brain changes, mainly explained by psychological factors such as the participants' emotional empathy. Activity in the caudate nucleus, a main node the parental vigilance network, correlated with the level of emotional empathy of both fathers and mothers. Caudate nucleus is part of cortico-striatal motor loops (with the SMA) and plays a key role in the planning and initiation of the parental response. As expected, this circuit is highly heterogenous from one parent to another independently of sex.

## **Conclusions**

To our knowledge, there has not yet been a study systematically exploring the impact of the acoustic features of cries on brain activation by having subjects listen to a range of baby cries showing different levels of roughness. These findings help to disentangle the brain connectome involved in perception of distress baby cries as well as its malleability with parenthood experiences. They suggest that parenthood-induced remodeling of brain connectivity may facilitate an appropriate response to the diversity of information conveyed by a baby's cry. While this remodeling is expressed on average differently in mothers and fathers, it is highly variable and depends more on individual factors such as the level of emotional empathy than on sex.

## **Methods**

### **Participants**

The study included data from 80 participants: 40 parents (20 fathers; mean age  $\pm$  SD =  $32.8 \pm 2.3$ , [30-38] and 20 mothers; mean age  $\pm$  SD =  $30.7 \pm 2.6$ , [37-26]) and 40 age- and sex-matched non-parents (20 childless men; mean age  $\pm$  SD =  $28.9 \pm 3.7$ , [35-21] and 20 childless women; mean age  $\pm$  SD =  $28.2 \pm 5.1$ , [40-20]). All participants were in good health and reported no history of psychiatric, neurological, hearing disorders, depression(73) or anxiety(74). All participants took the Balanced Emotional Empathy Scale (BEES) and the interpersonal reactivity index (IRI) (75) to assess their basal level of emotional empathy(76). Participants were recruited using poster boards and in collaboration with the pediatrics department of Saint-Etienne hospital, particularly for parents. Parents had a baby aged between 28 days to 2 years at the time of the experiment. For non-parents, we checked that they were not in contact with a baby on a regular basis (midwives, pediatricians, nannies, person with baby-sitting experience or in contact with a baby in their close circle were excluded). All participants gave written informed consent to the study approved by the local ethics committee (February 2018 – Comité d’Ethique du CHU de Saint-Etienne, Institutional Review Board: 2017-A01180-53; ClinicalTrials.gov Identifier: NCT03190486). They received €80 for their participation.

### **Recording and acoustic analysis of babies’ cries**

We included 20 full-term babies (10 girls and 10 boys aged of  $60 \pm 3.2$  days on the day of vaccination). Pain cries were recorded during a routine vaccination session performed at the paediatrician doctor's office, without oral glucose administration or pharmacologic analgesia. Vaccination consisted of 0.5 ml of 13-valent pneumococcal conjugate vaccine (PCV13, Prevenar 13®; Pfizer Ltd, Sandwich, Kent, United Kingdom(77)), and is known to induce pain(78). Mild discomfort cries were recorded during bathing, undressing or dressing by parents at the baby’s home (number of days between recording of pain and bath cries =  $6.9 \pm 3$  days).

Babies were recorded with a microphone (Sennheiser MD42), placed about 30 cm from the baby and connected to a portable digital recorder (Zoom H4n, sample frequency = 48 kHz, uncompressed .wav files). To prepare the stimuli used in the present study, we selected for each baby a single discomfort cry (bath cry) from the set of cries recorded during bathing, and the first cry emitted in response to the vaccine injection (vaccine cry). Each selected cry lasted 6 seconds.

## Acoustic analysis of cries

We described the acoustic structure of the cries using the following 23 acoustic parameters (Praat software(79)): *duration*, *%voiced* (the percentage of the signal that is characterized by a detectable pitch), *meanF0*, *maxF0*, *minF0*, *rangeF0*, *startF0* and *endF0* (respectively, the mean, maximum and minimum, range, start and end F0 calculated over the duration of the signal) and *F0CV* (coefficient of variation of F0 over the duration of the signal, i.e. the standard deviation of the frequency contour divided by the mean of the frequency contour). Inflection points were counted (as each change in the sign of the derivative the fundamental frequency contour) after two smoothing procedure: one with a relatively broad bandwidth ('Smooth ...' command in Praat, bandwidth = 25) to suppress short-term frequency fluctuations, while preserving minor intonation events (such as bleat-like frequency modulation), and a second with a narrow bandwidth (bandwidth = 2) to characterize strong F0 modulation (major intonation events). Both bandwidth parameters were chosen empirically as they provided adequate smoothing to characterize the two levels of intonation variation. The number of inflection points was divided by the total duration of the voiced segments in each recording, resulting in two distinct indexes of F0 variation (*inflex25* and *inflex2*). We also characterized the variability of the cries' intensity by calculating *intCV*, the coefficient of variation of the intensity contour estimated using the 'To intensity y' command in Praat. We quantified the periodic quality of the cries by estimating their harmonicity (*harm*, degree of acoustic periodicity, measured as the ratio of harmonics to noise in the signal and expressed in dB), an index of jitter (*jitter*, small fluctuation in periodicity measured as the average of 'local', 'rap' and 'ppq5' measures in Praat) and an index of shimmer (*shimmer*, small variation in amplitude between consecutive periods, measured as the average of 'local', 'apq5' and 'apq11' parameters in Praat). A final procedure characterized the spectral envelope of the cry by applying a cepstral smoothing procedure (bandwidth: 900 Hz) to each crying sequence, followed by the extraction of the first four spectral prominences (*SP1*, *SP2*, *SP3* and *SP4*) of the resulting smoothed spectrum. Finally, nonlinear phenomena were characterized by conducting a visual inspection of narrowband spectrograms. We measured: the percentage of time with biphonation (*BP*), the percentage of time with periodic, vibrato-like frequency modulation (*FM*), the percentage of time with subharmonics (*SH*) and the percentage of time with deterministic chaos (*DC*).

To reduce this set of acoustic variables to a smaller number of uncorrelated factors, a principal component analysis (PCA) was performed on all 23 acoustic variables extracted from the cries. The first component had an eigenvalue > 3 and explained 23% of the variance. Variable



loadings indicate that PC1 can be interpreted as an index of cry *roughness*: cries with higher PC1 values are less voiced, have a more variable  $F_0$ , are less harmonic, have higher level of *jitter* and *shimmer* and more occurrences of deterministic chaos. In a previous paper, we showed that the composite factor "*roughness*" (characterizing the level of aperiodicity of the cries), varied according to the levels of distress experienced by the baby(6). This variable PC1 can therefore be used to assess levels of distress in babies' cries(6, 80). The full methodological procedure to the Principal Component Analysis is detailed here(6). PC1 (roughness) score was used in the present study to reflect the level of pain encoded in the cries.

### **fMRI experimental procedure**

Participants (n = 80) underwent magnetic resonance imaging in a 3T MR system (Prisma Siemens, Erlangen, Germany, EU) with a 64-channel head/neck coil. The procedure began with a high-resolution T1-weighted anatomical scan with 3D fast gradient-echo (MP-RAGE; TR = 2000 ms; TE = 2.19 ms, flip angle 8°, 192 sagittal slices, FOV = 240 mm, voxel size =  $0.9 \times 0.9 \times 0.9$  mm, matrix  $256 \times 256$ ). This was followed by an fMRI protocol during which participants listened to baby cries. Changes in blood oxygen level dependent (BOLD) T2\*-weighted MR signal were measured using an interleaved gradient echo-planar imaging (EPI) sequence (TR = 2200 ms, TE = 30 ms, voxel size =  $3.0 \times 3.0 \times 3.0$  mm, flip angle 90°, slices/volume 40) in four functional sessions of 9 min 43 s each.

As illustrated in Figure S1, each participant listened to a series of 80 cries distributed over 4 consecutive playback sessions. In each of the 4 sessions, the 20 cries were evenly distributed between the 4 categories: bath cries with pitch set at 360 Hz, bath cries with pitch set at 500 Hz, vaccine cries with pitch set at 360 Hz, vaccine cries with pitch set at 500 Hz). The 20 cries were played in a random order.

Each cry lasted 6 seconds and was repeated once, for a total sound stimulus duration of 12 seconds. The cries were played through high-quality headphones (MR compatible earphones S14, Sensimetrics Corporation, MA, USA), with a pseudo-randomized inter-stimulus interval of between 8 and 20 seconds, to avoid anticipatory effects. Immediately after hearing a stimulus, the participant was given 3 seconds to rate the level of pain expressed by the cry on the following scale: 1 = cry expressing no pain, 2 = cry expressing moderate pain, 3 = cry expressing extreme pain. The participant indicated their rating using two buttons (model Lumina LU400-PAIR; Cedrus Corporation, USA), which respectively decreased and increased

a visually displayed score. A computer running E-Prime 2.0 software (Psychology Software Tools, Inc.) ensured synchronization between the acquisition of the participant's rating and the start of the next sound stimulus.

All instructions were given to the participant before the start of the experiment and recalled between each of the 4 playback sessions. The anatomical scan period served as the habituation phase, during which the participant was trained in the use of the rating buttons. The volume of the headphones was adjusted to ensure optimal listening.

At the end of the fMRI protocol, each participant was interviewed in a brief debriefing conversation to confirm that all the cries had been heard. If this was not the case, the data acquired for this participant was not taken into account (did not occur in the present study).

### **Analysis of fMRI data**

Image processing and analysis were carried out using Statistical Parametric Mapping software (SPM12, Wellcome Trust Centre for Neuroimaging, UK). The first two scans of each playback session were systematically removed, then the images were slice-time corrected, spatially realigned, co-registered with the MNI152 brain using nonlinear warping, segmented using masks derived from the anatomical scan and smoothed with a 6-mm FWHM Gaussian kernel. We then applied a high-pass temporal filter with a cutoff of 128 s to suppress intrinsic scanner-related signal drift. Image quality check and noise correction enhancement were carried out using ArtRepair software(81), at various stages of the analysis.

### **Parametric modulation analysis**

Analysis of the brain activity and connectivity involved when listening to baby cries was carried out considering all stimulation conditions (painful and non-painful stimuli), and thresholded at corrected  $p < 0.01$  (family error, FWE voxel level).

We performed first-level individual analyses with a within-subject general linear model (GLM). We constructed the design matrix incorporating the 4 playback sessions. Each session included two regressors of interest: the cry stimuli (12s) and the rating phase (3s). The four cry conditions (bath 360 or 500 and vaccine 360 or 500) were also incorporated into the model.

To model the variability of the neural response to the acoustic features of the cry, we added two parametric modulators to the cry regressor in the GLM: the roughness of the cry (PC1 value)

and the pitch (360 or 500 Hz). Roughness (range [-3.39 – 7.14]) modulated the regressor with a positive weight when the level of distress carried by the cry was high (vaccine condition) and a negative weight when it was low (non-painful bath condition). This approach made it possible to identify brain functional areas according to the level of roughness of the cry or its pitch.

The regressors were convolved with the canonical hemodynamic response function (HRF) and its time-derivative. Non-brain volumes (i.e., cerebrospinal fluid and white matter) and 6 motion parameters were regressed out, leaving only the grey matter. The map of voxel-wise parameter estimates (beta values) for each regressor was obtained at the single-subject level.

We performed second-level group effect analyses considering all participants ( $n = 80$ ) to highlight the brain network associated with regressors and modulators (relative to baseline; threshold at  $p < 0.01$  voxel-corrected FWE), assess the impact of the latter on brain activity, and measure the effect of listener sex and parental status on brain activity associated with cry perception and the pain level rating task. BOLD contrasts between groups were computed with two-sample  $t$  tests between the main groups ( $n = 40$ ; parents *versus* non-parents and men *versus* women). Sex differences were also estimated separately in the parents (mothers *versus* fathers) and nonparents (childless women *versus* childless men). Differences in neuronal activation due to parental status were assessed separately for women (mothers *versus* childless women) and for men (fathers *versus* childless men). The resulting SPM  $z$  maps were thresholded at  $p < 0.001$  according to the Gaussian field theory, and clusters that survived the FWE correction for multiple comparisons  $p < 0.05$  were reported. In addition, we applied an inclusive mask of grey matter (C1- average group). Anatomical regions were labeled using Hammersmith(82, 83) and Human Connectome Project(84) atlases (HCP MMP 1.0).

### **Functional connectivity analysis**

By measuring the synchronization of the BOLD signal between brain regions, the connectivity analysis aimed to highlight the functional relationships between the brain areas activated by hearing baby cries. We performed this analysis using open-source functions from the CONN toolbox (under Matlab/SPM-based; [www.nitrc.org/projects/conn](http://www.nitrc.org/projects/conn), RRID:SCR\_009550)(85). This approach enables fine temporal preprocessing of task-related fMRI data and formal characterization of the organization of the brain's functional connectome at the level of the listener and the considered group (males, females, parents and non-parents).

The individual functional connectivity matrix was formed from the 34 cortical and subcortical nodes of the parental brain network(45) (see Supplementary Methods and Table S1 for a detailed description of the regions of interest) and significantly activated by infant cries (Table S2). Design matrices, defining task events (i.e., cry and rating phases), were imported from SPM for each subject and functional session.

We applied the CONN denoising pipeline and performed component-based noise correction (CompCor) to reduce voxel specific noise. Potential confounds from white matter and cerebrospinal fluid (based on masks produced from T1-weighted tissue segmentation for each subject) were added as covariates in CONN. The effects of head motion detected during spatial pre-processing (6 motion parameters estimated per volume) were used as covariates to further reduce noise. These steps increase the sensitivity of FC results(85). We also implemented bandpass filtering to further eliminate physiological noise and to limit the BOLD between 0.01 and 0.08 Hz.

To investigate the effect of cry roughness and cry pitch, we used a generalized psychophysiological interactions (PPI) approach (first-level analysis; bivariate option), which reveals whether functional connectivity between two nodes changed as a function of any of these acoustic factors. Covariates for cry roughness and cry pitch (mean-centered parametric modulators convolved with HRF) were extracted from individual SPM files and imported into CONN. We averaged the raw time-series data were averaged and then extracted on voxels in the 34 selected regions of interest (ROI- to-ROI functional correlation). Correlation matrices were computed individually by estimating the Pearson correlations between the time course of each pair of nodes (34 x34) from the preprocessed BOLD signal related to the cry regressor, *roughness* and *pitch* parametric modulators. These matrices were then fed into a second(group)-level random-effect analysis. Correlation values were converted to Z-scores with Fischer-transformed r values for subsequent statistical analysis (i.e., second-level analyses, including post-hoc analyses).

We assessed significant functional connections associated with cry listening, roughness and pitch changes for all participants and as a function of sex and parenthood factors using Network based statistics(86) (cluster threshold  $p < 0.05$  network-level  $p$ -FDR corrected, NBS mass/intensity; connection threshold:  $p < 0.001$  p-uncorrected). We finally constructed an average Z-correlation matrix for each group by averaging the connectivity matrix of participants to represent the FC structure associated with men and women, parents and non-parents.

### **Statistical analysis of pain ratings by participants**

We first assessed the impact on the pain rating (dependent variable) by participants of the following parameters: recording context (bath or vaccine), cry pitch (360 or 500 Hz), listener sex (male or female), and listener parenthood (parent or non-parent). These four parameters were included as fixed factors in a GLM model, while the participant's identity and identity of the recorded babies was included as a random factor (see Table S4 – GLM 1).

We built another GLM model to assess the impact on pain assessment of the acoustic roughness of cries and their pitch. In this second model, pain rating by participants was still the dependent variable, while cry roughness (PC1 scores) and cry pitch (360 and 500 Hz) were set as fixed factors. Context (bathing or vaccine), listener sex (male or female), listener parenthood (parent or non-parent) and baby identity were included as random factors (see Table S4 – GLM 2).

**Data availability.** The data that support the findings of this study are available upon reasonable request from the corresponding author Dr. C.F. The data are not publicly available due to third party restriction and patient privacy issues of the institution.

**Code availability.** Code for functional connectivity is available at [www.nitrc.org/projects/conn](http://www.nitrc.org/projects/conn), RRID:SCR\_009550

**Author contributions.** C.F, N.M, D.R, R.P conceptualized the study. C.F acquired the data and created the figures. C.F and I.F analyzed the data. C.F, S.C, N.M, D.R, R.P wrote the original draft and contributed to the interpretation of the data, to the editing and revising of the paper.

**Competing interests.** The authors declare no competing interests.

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## **Supplementary Methods**

The brain basis of human adults to perceive distress signal from infant involved large and interconnected brain functional networks, integrating conserved subcortical structures supporting mammalian caregiving with later-evolving high-order cognitive brain networks involved in the social functions of parenting<sup>1</sup>.

The set of brain regions (named the adult brain connectome of baby's cry perception) that we considered in our study include 7 sub-networks with 34 regions of interest significantly activated by our task (i.e., listening to baby's cries) and anatomically defined according to previous literature.

1) The auditory network comprises primary auditory cortex - Heschl (A1) and the superior temporal gyrus (aSTG), and is involved in integrating and processing auditory signals, a first level of cries integration<sup>2,3</sup>.

2) The empathy network includes the anterior insula (aINS)<sup>4,5</sup>, anterior mid cingulate cortex (aMCC)<sup>6</sup>, and the supplementary motor area (SMA), for understanding and resonating with others' affective and physical state, including pain<sup>4,7-10</sup>. Therefore, it helps an individual to respond to infant pain and distress by representing it in themselves, and also afford perceptual-motor coupling in the adult's brain via the mirror neuron system (SMA)<sup>11</sup>.

3) The mentalizing network comprises frontoparietal and temporal regions, including the temporo-parietal junction (TPJ)<sup>12</sup>, posterior cingulate cortex (vPCC / precuneus)<sup>8</sup>, and the medial prefrontal cortex (mPFC)<sup>2,5</sup>, and subserves cognitive functions to understand non-verbal signals and infer infant intentions and feelings as well as perspective-taking<sup>1,9,13</sup>.

4) The mirror network includes pre-sensorimotor regions, inferior parietal lobule (IPL)<sup>2,5,11</sup>, and inferior frontal gyrus (IFG), and is involved in embodied stimulation of infant action, and action understanding<sup>11,14,15</sup>.

5) The emotion regulation network is engaged in multitasking, arousal and emotion inhibition/regulation, and action selection (executive control), and includes the dorsolateral prefrontal cortex (DLPFC)<sup>16</sup>, angular gyrus (AG)<sup>17,18</sup>, perigenual anterior cingulate cortex (pgACC)<sup>6,19</sup>, and subcortical structures such as the amygdala (Amygd.)<sup>20</sup>, connected to cingulo-insular empathy network and limbic reward regions<sup>21</sup>. Amygdala play a key role in pain perception and is considered as a central hub of the 'emotional brain'<sup>22-24</sup>. This network enables top-down control over attentional, emotional, and cognitive processes<sup>1,25</sup>.

6) The subcortical reward and/or motivation network includes the putamen and nucleus accumbens, dopaminergic structures of the mesolimbic pathway supporting motivational

behavior (positive reinforcement), the incentive value of infants and the reward from relief of self and others' pain<sup>26</sup>.

7) The parental vigilance network<sup>1</sup> is centered on the caudate nucleus belonging to the mammalian parenting network and found to be activated by infant cue in mothers, and it is expected to promote positive parental behaviors<sup>27</sup>.

The anatomical coordinates of these regions are provided in supplementary Table 2 (below), they were determined in previous literature investigating these functions and brain atlases (i.e., Human Connectome Project atlas<sup>2</sup> and Hammers brain parcellation atlas<sup>28,29</sup>).

**Table S1.** Brain regions of interest (ROIs or nodes) considered for functional connectivity analysis (N = 17 x 2). MNI coordinates were defined using previous literature (see supplementary methods 1), and ROI were created using Human Connectome Project and Hammers brain parcellation atlas.

Networks	ROI name	MNI coordinates (x, y, z) center of mass		Index area name (Atlas: HCP, and Hammers)	Atlas' volume (cc)	
		Right	Left		Right	Left
<b>Auditory</b>	A1 (Heschl)	46 -21 8	-46 -21 6	A1/MBelt/LBelt	1.7	2.7
	aSTG	57 -1 -10	-57 -5 -8	antSTG_9	3.6	3.8
<b>Empathy</b>	aINS	40 13 -7	-38 13 -6	AAIC/AVI/MI	5.4	5.0
	SMA	18 -3 66	-14 -5 63	6ma/6mp	5.8	5.4
	aMCC	7 14 36	-6 16 33	a24pr/33pr/p32pr	2.6	2.6
<b>Mentalizing</b>	TPJ	63 -39 33	-60 -46 35	SMvc/PSL/PF/40c	2.7	3.2
	PCC (/Prec)	6 -51 33	-5 -52 32	v23ab/7m/31apv	4.3	5.3
	mPFC	-4 49 -14	5 51 -15	10r/10v (HCP)	5.0	5.0
<b>Mirror</b>	IPL	54 -28 45	-53 -33 42	SMrd/PFt/PF/40rd	1.5	2.0
	IFG	54 18 12	-53 16 12	44	2.8	2.6
<b>Emotion regulation</b>	DLPFC	43 35 28	-41 36 28	46/p9-46v	5.3	4.5
	AG	47 -64 32	-43 -68 31	PGi/PGs	6.8	6.4
	Amygd.	23 -4 -21	-23 -5 -20	n30/r95	1.7	1.9
	pgACC	4 40 0	-4 41 -1	a24	1.6	1.5
<b>Subcortical reward</b>	Putam.	26 3 0	-25 1 0	39-38	6.1	6.3
	Accumb. Nx	-25 1 0	-8 8 -9	37-36	0.4	0.5
<b>Parental vigilance</b>	Caud. Nx	14 10 9	-13 9 9	35-34	5.4	5.5

*A1: primary auditory cortex; aSTG: anterior superior temporal gyrus; aINS: anterior insula; SMA: supplementary motor area; aMCC: anterior mid cingulate cortex; TPJ: temporo-parietal junction (supramarginal ventro-caudal); PCC: posterior cingulate cortex; mPFC: medial prefrontal cortex; IPL: Inferior parietal lobe (supramarginal rostro-dorsal); IFG: inferior frontal gyrus; DLPFC: dorso lateral prefrontal cortex; AG: angular gyrus; Amygd.: amygdala; pgACC: perigenual anterior cingulate cortex; Putam.: putamen; Accumb. Nx: accumbens nucleus; Caud. Nx: caudate nucleus.*

## Supplementary Results

**Table S2:** Main clusters and cortical peak activations for the 'audio cry' regressor independently of the pain conditions (i.e., all audio stimuli).

Group level: Voxel level  $p$  (FWE corr)  $< 0.01$ ;

Group comparisons: FWE-corrected cluster-based  $p < 0.05$  after voxel threshold at  $p < 0.001$ .

[Regressor] cluster size	Side	Peaks localization Macro-anatomical Hammers's atlas (HCP regions or Morel areas)	Peak coordinates MNI(x , y, z)	Z score
<b>[all cries]</b> 3470	L	<b>Activations</b> Early auditory areas, middle part (MBelt) Primary auditory cortex (A1) Para and lateral auditory parts (PBelt, LBelt) <i>(cluster extends on the superior temporal gyrus, inferior frontal cortex and frontal opercula)</i>	-42 -19 3 -39 -31 14 -54 -31 11	25.10 22.03 17.63
5031	R	Primary auditory cortex (A1) Early auditory areas, middle part (MBelt) Para and lateral auditory parts (PBelt, LBelt) <i>(cluster extends on the superior temporal gyrus, inferior frontal cortex and frontal opercula)</i>	40 -23 12 50 -16 6 54 -14 5	19.42 19.22 19.08
1020	L/R	Mid Cingulate Cortex including supplementary motor areas (SCEF) Medial Prefrontal Cortex (8BM)	6 5 62 6 17 51 -6 14 50	16.89 16.62 19.08
65	L/R	Superior Parietal Cortex (3a, LIPd, AIP)	36 -52 44 -36 -52 41	8.23 7.92
2665	R	<b>Deactivations</b> Inferior parietal cortex and Precuneus (PGp, Pf, 7m, 31pd, POS2)	47 -76 29	15.95
1645	R	Anterior cingulate cortex (a24, p24, p32, 10r)	6 38 -4	14.84
896/319	L/R	Peri-hippocampal areas (PHA)	-30 -37 -13	13.99
57	L	Superior parietal cortex (PF)	-61 -32 35	10.41
189	R	Dorso-lateral prefrontal cortex (8Ad)	27 32 47	9.76
39	R	Temporo-Parieto-Occipital Junction and angular gyrus (Pf, PGs)	54 -25 29	6.65
<b>[all cries]</b>		<b>Parenthood: Fathers &lt; childless men</b>		
68	R	Dorso medial prefrontal cortex (8BL)	12 41 53	5.46
67	R	Medial prefrontal cortex (9m)	4 48 23	4.23
56	R	Superior premotor subdivisions (6d)	39 11 56	4.18
35	L	Amygdala	-21 -10 -16	4.32
53	R	Amygdala	27 -7 -16	4.15
36	R	Inferior frontal cortex (p47r)	42 50 2	4.00
31	L	Medial prefrontal cortex (9m)	-6 56 26	3.89
26	R	Anterior insula (MI)	38 15 2	4.32

79	R	<b><u>Sex differences:</u></b> Fathers > Mothers Auditory association cortex (A5)	66 -25 -1	4.87
		<b>Mothers &gt; Fathers</b>		
38	R	Striatum (caudate nucleus)	5 12 -3	5.51
63	L	Dorsolateral prefrontal cortex (9a, 9-46d, 46)	-27 44 26	5.13
39	L	Hippocampus	-30 -25 -7	5.04
31	L	Inferior frontal region (45)	-51 32 -4	4.81
173	R	Amygdala and putamen	23 -7 -19	4.78
28	R	Hippocampus	36 -28 -11	4.78
14	R	Superior frontal gyrus (9m)	9 56 32	4.77
82	L	Amygdala and putamen	-20 -5 -18	4.62

**Table S3:** Level of roughness of the cries used in the present study. Roughness values are reported in the form of a PC1 index (derived from a principal component analysis) that integrates non-linear acoustic phenomena such as biphonation, subharmonics, deterministic chaos and vibratory frequency modulation.

Baby ID	Sex	Bath / Vaccine	Pitch	F0CV	harm	PC1
0	Male	B	360	0,18	16,31	-1,73
0	Male	V	360	0,13	9,72	0,11
0	Male	B	500	0,18	16,31	-1,73
0	Male	V	500	0,13	9,72	0,11
1	Female	B	360	0,15	21,13	-2,70
1	Female	V	360	0,17	20,06	-1,47
1	Female	B	500	0,15	21,13	-2,70
1	Female	V	500	0,17	20,06	-1,47
2	Male	B	360	0,13	13,45	-1,96
2	Male	V	360	0,26	14,35	0,10
2	Male	B	500	0,13	13,45	-1,96
2	Male	V	500	0,26	14,35	0,10
3	Male	B	360	0,10	17,16	-1,67
3	Male	V	360	0,31	9,11	4,42
3	Male	B	500	0,10	17,16	-1,67
3	Male	V	500	0,31	9,11	4,42
5	Female	B	360	0,19	14,55	0,24
5	Female	V	360	0,37	8,70	5,03
5	Female	B	500	0,19	14,55	0,24
5	Female	V	500	0,37	8,70	5,03
6	Female	B	360	0,22	8,61	1,21
6	Female	V	360	0,19	5,62	3,78
6	Female	B	500	0,22	8,61	1,21
6	Female	V	500	0,19	5,62	3,78
8	Male	B	360	0,07	15,66	-2,67
8	Male	V	360	0,17	22,81	-0,91
8	Male	B	500	0,07	15,66	-2,67
8	Male	V	500	0,17	22,81	-0,91
9	Female	B	360	0,14	19,87	-1,36
9	Female	V	360	0,07	18,27	-2,67
9	Female	B	500	0,14	19,87	-1,36
9	Female	V	500	0,07	18,27	-2,67
10	Female	B	360	0,05	17,43	-2,18
10	Female	V	360	0,09	11,99	-1,26
10	Female	B	500	0,05	17,43	-2,18
10	Female	V	500	0,09	11,99	-1,26
11	Male	B	360	0,14	15,54	-1,31
11	Male	V	360	0,12	16,26	-0,15
11	Male	B	500	0,14	15,54	-1,31
11	Male	V	500	0,12	16,26	-0,15
12	Male	B	360	0,10	20,39	-3,39
12	Male	V	360	0,20	17,29	-0,59
12	Male	B	500	0,10	20,39	-3,39
12	Male	V	500	0,20	17,29	-0,59
13	Male	B	360	0,13	21,69	-2,12
13	Male	V	360	0,33	13,35	3,66

13	Male	B	500	0,13	21,69	-2,12
13	Male	V	500	0,33	13,35	3,66
14	Female	B	360	0,17	14,08	-1,20
14	Female	V	360	0,22	17,48	-1,10
14	Female	B	500	0,17	14,08	-1,20
14	Female	V	500	0,22	17,48	-1,10
16	Male	B	360	0,20	18,51	-2,22
16	Male	V	360	0,15	22,77	-1,34
16	Male	B	500	0,20	18,51	-2,22
16	Male	V	500	0,15	22,77	-1,34
23	Female	B	360	0,31	19,09	-0,35
23	Female	V	360	0,26	4,34	4,22
23	Female	B	500	0,31	19,09	-0,35
23	Female	V	500	0,26	4,34	4,22
25	Female	B	360	0,16	21,46	-1,85
25	Female	V	360	0,36	4,87	3,66
25	Female	B	500	0,16	21,46	-1,85
25	Female	V	500	0,36	4,87	3,66
26	Female	B	360	0,16	9,77	0,75
26	Female	V	360	0,33	2,38	7,14
26	Female	B	500	0,16	9,77	0,75
26	Female	V	500	0,33	2,38	7,14
31	Male	B	360	0,12	12,05	-0,11
31	Male	V	360	0,27	7,87	2,82
31	Male	B	500	0,12	12,05	-0,11
31	Male	V	500	0,27	7,87	2,82
32	Male	V	360	0,14	15,22	-0,24
32	Male	B	360	0,07	18,72	-2,50
32	Male	V	500	0,14	15,22	-0,24
32	Male	B	500	0,07	18,72	-2,50
33	Male	B	360	0,09	16,22	-0,86
33	Male	V	360	0,21	15,26	2,76
33	Male	B	500	0,09	16,22	-0,86
33	Male	V	500	0,21	15,26	2,76



**Table S4: Mixed Model analysis.** The GLM models used in data analysis, respectively;

**GLM 1:** dependent variable = pain perceived by listener, fixed factors = recording context, cry pitch, listener sex, listener parenthood, random factor: baby identity, subject identity.

**Type III Tests of Fixed Effects<sup>a</sup>**

Source	Numerator df	Denominator df	F	Sig.
Intercept	1	76.413	9710.181	.000
Sujetsexe	1	76.413	6.390	.014
Parentality	1	76.413	1.249	.267
crycontext	1	4714.187	1166.477	.000
pitch	1	4706.587	135.519	.000
Sujetsexe * Parentality	1	76.413	9.640	.003
Sujetsexe * crycontext	1	4714.187	.411	.522
Sujetsexe * pitch	1	4706.587	7.025	.008
Parentality * crycontext	1	4714.187	1.047	.306
Parentality * pitch	1	4706.587	.000	.994
crycontext * pitch	1	4696.349	8.430	.004
Sujetsexe * Parentality * crycontext	1	4714.187	6.172	.013
Sujetsexe * Parentality * pitch	1	4706.587	1.352	.245
Sujetsexe * crycontext * pitch	1	4696.349	.787	.375
Parentality * crycontext * pitch	1	4696.349	1.889	.169
Sujetsexe * Parentality * crycontext * pitch	1	4696.349	1.234	.267

a. Dependent Variable: rating.

**GLM 2:** dependent variable = pain perceived by listener (rating), fixed factors = cry roughness (PC1), cry pitch, random factors = recording context, listener sex, listener parenthood, baby identity.

**Type III Tests of Fixed Effects<sup>a</sup>**

Source	Numerator df	Denominator df	F	Sig.
Intercept	1	244.957	11141.546	.000
pitch	1	11529.022	266.883	.000
PC1	1	5289.161	913.009	.000
pitch * PC1	1	11510.967	64.364	.000

a. Dependent Variable: rating.

### Supplementary results - Cry roughness reflects the baby's level of pain

There was a significant effect of the cry recording condition on all participants' pain ratings ( $F_{(1,4714)}=1166.47, p < 0.0001$ ): pain ratings were lower for bath cries (mean  $\pm$  SD=  $1.67 \pm 0.02$ ) than for the vaccination cry (mean =  $2.26 \pm 0.02$ ). The effect of cry's pitch was also significant ( $F_{(1,4706)}=135.52, p < 0.0001$ ), and pain ratings were higher for cries fixed at 500hz than for cries at 360hz. The effect of pitch level on pain rating was stronger for bath cries, reflected in an interaction between pitch and cry's condition ( $F_{(1,4696)}=8.43, p = 0.004$ ).

Neither the listener's identity ( $F_{(1,76)}=1.25, p = 0.27$ ) nor the interactions between listener's identity and condition ( $F_{(1,4714)}=1.05, p = 0.31$ ) or between listener's identity and pitch ( $F_{(1,4706)}=inf, p = 0.99$ ), had a significant effect on cry classification related-to the evoked pain. However, we found a significant effect of listener's sex ( $F_{(1,76)}=6.39, p = 0.01$ ), and importantly a significant interaction between listener's sex and identity ( $F_{(1,76)}=9.64, p = 0.003$ ): fathers had lower pain ratings (mean  $\pm$  SD=  $1.83 \pm 0.04$ ) than other participants (mean  $\pm$  SD: Mothers =  $2.06 \pm 0.04$ ; Males =  $2.0 \pm 0.04$ ; Females =  $1.98 \pm 0.04$ ) in bath high pitch, and vaccine conditions; whereas mothers showed higher pain ratings to vaccine condition compared to childless females, the significant listener's identity\*sex\*condition interaction ( $F_{(1,4714)}=6.17, p = 0.01$ ) reflected this hyper-sensibility of mothers to painful situation. There was also a significant interaction between listener's sex and cry's pitch ( $F_{(1,4706)}=7.03, p = 0.008$ ) on pain rating, showing that females in both identities (i.e., parents and non-parents) were more influenced by an increase of pitch (360 vs. 500) than males.

No sex-differences or parental effects were found in the brain responses dissociating the pitch levels.

**Table S5:** Main clusters and cortical peak activations for cry regressors associated with acoustic features of crying: the roughness (reflecting the pain spectrum; composite score (PC1) reflecting the cry's harmonic and intonation) and the pitch (two levels).

Group level: Voxel level  $p$  (FWE corr)  $< 0.05$ ;

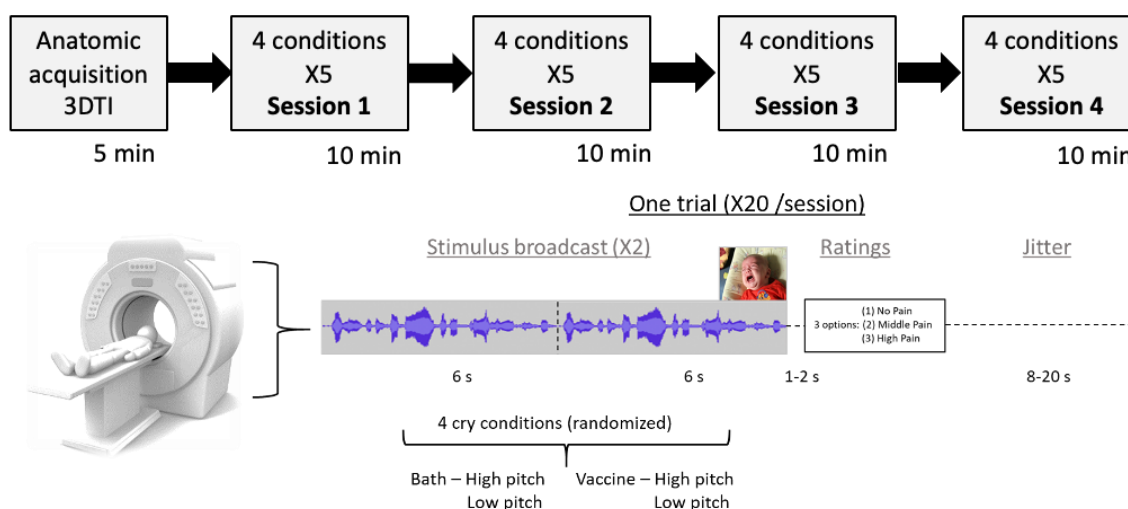
Group comparisons: FWE-corrected cluster-based  $p < 0.05$  after voxel threshold at  $p < 0.001$ .

[Regressor] cluster size	Side	Peaks localization Macro-anatomical Hammers's atlas (HCP regions or Morel areas)	Peak coordinates MNI(x, y, z)	Z score
<b>PC1 negative values</b>				
<b>[Rough- ness]</b> 265	L	Auditory association cortex (A1-5, STSdp)	-60 -21 2	7.26
374	R	Auditory association cortex and para auditory parts (A1-5, STSdp, PBelt)	57 -10 2	7.18
60/50	L/R	Sensorimotor and premotor areas (3b, FEF)	-51 -16 53 / 54 -12 43	6.61/ 6.27
49	R	Dorsolateral and inferior prefrontal cortex (a9-46v, 8c IFSa)	33 56 11	5.45
<b>PC1 positive values</b>				
43	L/R	Inferior parietal cortex (PFop, PF)	-60 -25 26	5.96
16	L/R	Anterior insula (MI)	-39 5 -4	5.77
<b>360 Hz vs 500 Hz variations</b>				
<b>[Pitch]</b> 57	L	Auditory association cortex (A1, MBelt)	-51 -22 11 -51 5 -25	4.63
54	R	Auditory association cortex (A1, PBelt)	51 -19 8	4.13
34	L/R	Lingual Gyrus (V4)	-21 -67 -4	4.01
<b>Sex differences in parents</b>				
<b>[Rough- ness]</b> 25	R	Auditory association cortex (A5)	58 -16 -3	4.29

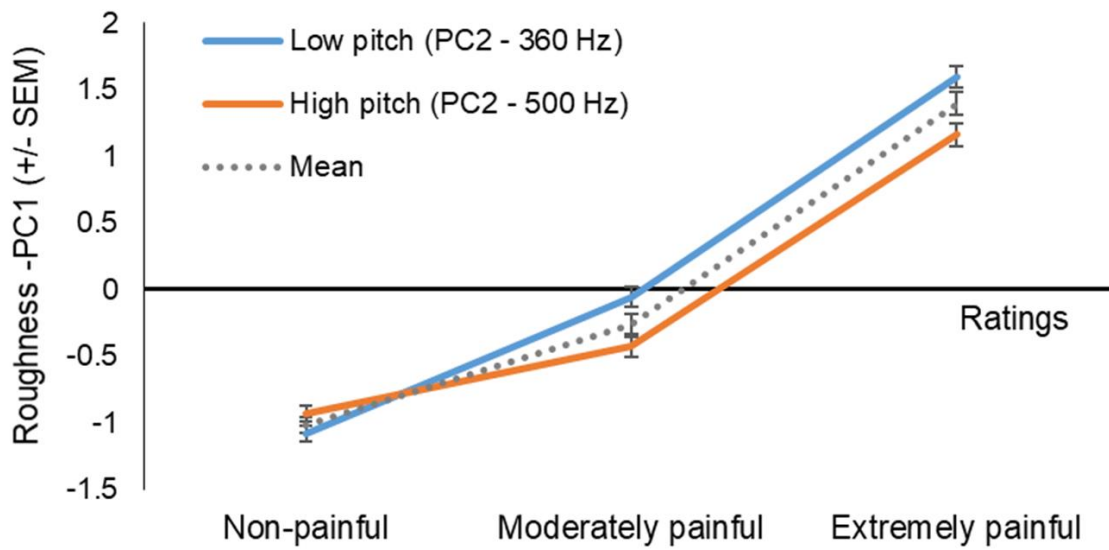
**Table S6:** Psychometric information of the parent and non-parent groups. Mean ( $\pm$ SD) Balanced Emotional Empathy Scale (BEES): measure the emotional aspect of empathy

Groups	Men	Fathers	Women	Mothers
Age	28.9 $\pm$ 3.7	32.8 $\pm$ 2.3	28.2 $\pm$ 5.1	30.7 $\pm$ 2.6
BEES	45.3 $\pm$ 23.7	42 $\pm$ 17.5	45.1 $\pm$ 19.6	<b>59.3 <math>\pm</math> 20.5*</b>
IRI				
Cognitive empathy	2.5 $\pm$ 0.4	2.2 $\pm$ 0.5	2.6 $\pm$ 0.6	2.5 $\pm$ 0.6
Emotional empathy	2.3 $\pm$ 0.4	<b>2.0 <math>\pm</math> 0.4</b>	2.3 $\pm$ 0.4	<b>2.4 <math>\pm</math> 0.5*</b>
IRI subscales				
<i>Empathic Concern</i>	3.0 $\pm$ 0.6	2.7 $\pm$ 0.5	2.9 $\pm$ 0.5	2.9 $\pm$ 0.5
<i>Perspective taking</i>	2.7 $\pm$ 0.4	2.4 $\pm$ 0.6	2.7 $\pm$ 0.5	2.4 $\pm$ 0.6
<i>Fantasy Scale</i>	2.4 $\pm$ 0.7	2.1 $\pm$ 0.7	2.6 $\pm$ 0.7	2.5 $\pm$ 0.6
<i>Personal Distress</i>	1.5 $\pm$ 0.5	<b>1.3 <math>\pm</math> 0.6</b>	1.7 $\pm$ 0.5	<b>1.9 <math>\pm</math> 0.6*</b>

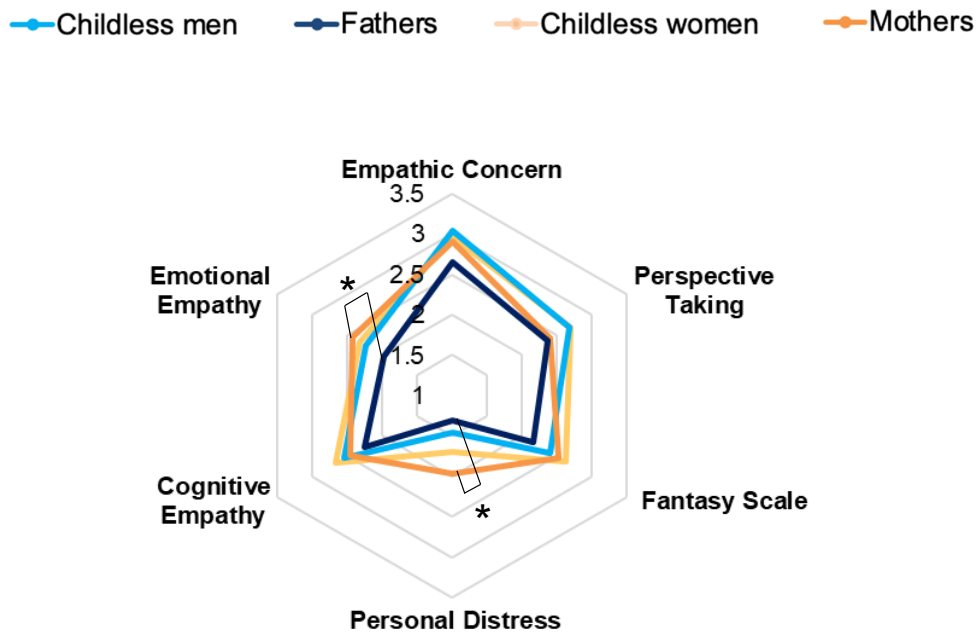
**Figure S1: Experimental design – general overview.** Each participant listened to a series of 80 cries distributed over 4 consecutive playback sessions. In each of the 4 sessions, the 20 cries were evenly distributed between the 4 categories: bath cries with pitch set at 360 Hz, bath cries with pitch set at 500 Hz, vaccine cries with pitch set at 360 Hz, vaccine cries with pitch set at 500 Hz). The 20 cries were played in a random order.



**Figure S2.** Crying scores according to the roughness scores (PC1) in the two pitch levels (360 Hz: blue and 500 Hz: orange). The grey dotted line represents the mean.



**Figure S3.** Empathy scores measured using the interpersonal reactivity index (IRI). The results confirm those obtained with the BEES questionnaire.



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