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Programme d'entraînement de la cognition sociale chez l'enfant porteur d'une microdélétion 22q11.2 : étude de cas uniques

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Programme d'entraînement de la cognition sociale chez l'enfant porteur d'une microdélétion 22q11.2 : étude de cas uniques

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Résumé

Les troubles du neurodéveloppement correspondent à une perturbation du développement des compétences cognitives attendues lors du développement psychomoteur et affectif de l'enfant. Ces troubles sont souvent associés à un déficit de la cognition sociale qui entraîne un retrait social, des troubles du comportement et des difficultés d'adaptation. Ces troubles ne sont pas sensibles aux traitements médicamenteux et sont donc particulièrement invalidants. La remédiation cognitive est une thérapie rééducative agissant sur les troubles cognitifs. Cette technique recrute les compétences de la personne pour l'aider à développer ses propres stratégies alternatives afin de contourner ses difficultés cognitives. Ce soin est particulièrement développé en psychiatrie d'adulte. Son utilisation chez l'enfant demeure plus limitée. Cette thèse doctorale vise à développer et à évaluer l'efficacité d'un nouveau programme d'entraînement de la cognition sociale, basé sur les principes de la remédiation cognitive et utilisant du matériel informatique, des activités théâtrales et un eye tracker. Ce programme, appelé RC-KID, est conçu pour les enfants âgés de 5 à 11 ans. Cette thèse comprend deux publications. Le premier article présente une revue de la littérature des troubles de la cognition sociale chez les populations porteuses d'un trouble neurodéveloppemental associé à une anomalie génétique identifiée rare. Les résultats de cette revue nous ont permis de développer le programme RC-KID avec l'objectif de cibler plus spécifiquement les mécanismes déficitaires qui sous-tendent un trouble de la cognition sociale (e.g. trouble de l'exploration des visages expressifs). Nous présentons ensuite plus en détails le programme RC-KID. Dans le deuxième article, nous présentons une étude pilotes basée sur la méthodologie du cas unique évaluant l'impact du programme sur les troubles de la cognition sociale de trois enfants porteurs d'une microdélétion 22q11.2. Un fonctionnement social perturbé est une caractéristique majeure des enfants porteurs de ce syndrome. La reconnaissance des expressions faciales est perturbée et cette déficience peut être liée à une observation atypique des visages. Après la prise en charge, nous avons constaté une amélioration significative des compétences des enfants en matière de reconnaissance des expressions faciales et de compréhension des émotions. Le programme RC-KID est un nouveau programme prometteur visant à réduire les troubles de la cognition sociale chez les enfants atteints d'une microdélétion 22q11.2. Il pourrait également être adapté à d'autres troubles du neurodéveloppement présentant les mêmes déficits.

Mots clés : cognition sociale, entraînement de la cognition sociale, microdélétion 22q11.2, RC-KID

Abstract

Rare neurodevelopmental disorders often present social cognitive deficits that may underlie difficulties in social interactions and increase the risk of psychosis or autism spectrum disorders. Notably, these syndromes increase the difficulties in social interactions and present a high risk to develop psychosis or autism spectrum disorders. The doctoral research, presented here, aim to develop and assess the efficacy of a new individualized social cognitive training program using computerized material, theater activities and online eye-tracking feedback. This program (RC-KID program) is designed for children aged between 5 to 11 years old. This doctoral thesis includes two publications. In the first article, we provide an overview of social cognitive abilities in rare neurodevelopmental disorders associated with psychiatric symptoms and shed some light on the specific mechanisms that may underlie these skills in each clinical presentation. Then we present the RC-KID program. In the second article, we present three single-case studies, using a multiple baseline and ABA design with children with 22q11.2 deletion syndrome. Poor social skills and functioning are a major characteristic of children with 22q11.2 deletion syndrome and are partly linked with social cognitive impairments. Patients have difficulties in recognizing facial emotions and this impairment may be related to an atypical observation of faces. After the treatment phase, we found a significant improvement of children's skills in affect recognition and emotion understanding. The RC-KID program is a new promising social cognitive training for reducing social cognitive impairment in children with 22q11.2DS, and could also be adapted to other neurodevelopmental disorders presenting the same deficits.

Keywords: social cognition, emotion processing, social cognitive training, 22q11.2 deletion syndrome, RC-KID.

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Chapitre 1

Introduction

Interagir, comprendre les signes sociaux d'autrui, ses intentions, ses désirs, ses émotions sont des capacités cognitives que nous utilisons sans cesse au quotidien. Ainsi un trouble de la cognition sociale, elle-même définie par l'ensemble des processus qui permettent de bien comprendre les autres et d'interagir avec eux, peut vite représenter un obstacle à des relations sociales harmonieuses.

La compréhension des troubles de la cognition sociale constitue un enjeu important dans la prise en charge des troubles neurodéveloppementaux d'origine génétique. Un déficit de la cognition sociale altère sévèrement la qualité de vie et se révèle souvent associé à des difficultés d'adaptation et à des symptômes psychiatriques, tels que la dépression et l'anxiété. De même, les troubles du spectre autistique (TSA) et la schizophrénie sont une expression phénotypique classique (Crespi et al., 2008).

L'objectif de cette thèse était de développer et tester la validité d'un programme d'entraînement de la cognition sociale chez l'enfant porteur d'un trouble neurodéveloppemental. Cette thèse est soumise sous forme d'articles.

Le premier article présente une revue de la littérature des troubles de la cognition sociale chez les populations porteuses d'un trouble neurodéveloppemental d'origine génétique associé à un risque de développement de symptômes psychotiques ou autistiques (Crespi et al 2008). Nous avons principalement ciblé, lors de cette revue, les études effectuées dans la microdélétion 22q11.2 mais également dans le syndrome d'Angelman, le syndrome du X Fragile, le syndrome de Klinefelter, le syndrome de Prader-Willi, le syndrome de Rett, le syndrome de Smith-Magenis, le syndrome de Turner et le syndrome de Williams. Cette contribution a permis de mettre en évidence que dans cette population un trouble de la cognition sociale n'est pas seulement lié au QI mais aussi à une variété de mécanismes cognitifs déficitaires spécifiques aux syndromes. Nous proposons un programme d'entraînement de la cognition sociale ciblant ces principaux mécanismes.

Dans le domaine de la reconnaissance des expressions faciales, de nombreux programmes informatisés ciblant les expressions faciales ont été développés et testés avec des enfants atteints d'un trouble du spectre autistique : Emotion Trainer (Silver&Oakes 2001) , Frankfurter Test und Training des Erkennens von fazialem Affekt (FEFA) (Bölte, et al., 2002) , Mind Reading (Baron-Cohen et al.,2004), The secret agent society (Beaumont &Sofronoff 2008), the Transporters (Golan et al., 2009), let's face it (Tanaka et al., 2010) , Lifeisgame (Fernandes,et al., 2010), Asc-inclusion (Schuller et al.,2013) , Vis-à-Vis. (Glaser et al.,2012).

Concernant la microdélétion 22q11.2, seul le programme Vis-à-Vis (Glaser et al., 2012), ciblant la cognitions sociale, a été développé en français et testé avec des enfants porteurs d'une microdélétion 22q11.2 (Karagöz-Üzel, et al., 2018). L'ensemble de ces programmes ont une durée comprise entre 4 et 12 semaines et certains ont permis une amélioration significative de la reconnaissance des expressions faciales (Bolte et al., 2002; Golan et al., 2009; Karagöz-Üzel, et al., 2018; Serret et al., 2014; Rice et al, 2015).

Cependant, comme le souligne le premier article, un trouble de l'interprétation des expressions faciales dans les populations porteuses d'un trouble neurodéveloppemental d'origine génétique implique des processus tels qu'une exploration du visage efficiente, un traitement des informations dynamiques, l'intégration d'informations de sources multimodales (e.g. prosodie, expression faciale, contexte de la situation, énoncé verbal), le mimétisme. Or la plupart de ces programmes proposent seulement des stimuli statiques (dessins et photos) qui ne visent pas l'intégration d'informations de sources multimodales. De plus, en dépit de l'importance du focus sur zones saillantes pour une reconnaissance efficiente, aucun ne permet de travailler sur l'exploration des visages.

Afin de proposer une réponse à ces constats, nous avons développé un nouveau programme individualisé, utilisant un eye tracker comme outil thérapeutique. Notre programme se distingue de ces logiciels en portant un intérêt plus spécifique aux comportements d'interactions et d'adaptation sociale, visant à limiter la présence de trouble du comportement chez des enfants présentant un trouble de la cognition sociale. Il propose dans cette optique des jeux de mise en situation, inspirés des jeux d'expressions théâtrale comme l'improvisation théâtrale et le théâtre forum. Enfin il se distingue également dans la mise en place de stratégies propres à la remédiation cognitive (définie comme une technique qui recrute les compétences cognitives de la personne pour contourner ses difficultés), telles que la présence systématique d'un thérapeute, la personnalisation du programme en fonction

du profil de l'enfant, un cadre structuré, et l'accent porté au transfert des compétences à la vie quotidienne.

Le second article présente les résultats préliminaires d'une étude pilote d'évaluation du programme RC-KID auprès de trois enfants porteurs d'une microdélétion 22q11.2. Chez les enfants porteurs de ce syndrome, la problématique de la compréhension et la gestion des émotions est fréquente et handicapante.

Ce syndrome neurocomportemental d'origine génétique est le syndrome microdélétionnel le plus fréquent de la population générale, dont la prévalence est de 1/2000 à 1/6000 (Shprintzen, 2008). Les manifestations cliniques sont très variables d'un individu à un autre : plus de 180 manifestations ont été décrites, aucune n'étant pathognomonique. Associé à un large phénotype physique (e.g., cardiopathie, dysmorphie faciale, altérations cérébrales), le syndrome est également caractérisé par un phénotype psychiatrique incluant notamment une forte incidence de symptômes positifs (délires, hallucinations, agitation psychotiques) et négatifs (appauvrissement psychomoteur, émoussement affectif). Il est par exemple noté que près de 80% des enfants ou adolescents atteints d'une microdélétion 22q11.2 présentent au moins un symptôme négatif d'intensité modérée à sévère (Schneider et al., 2012).

La cognition sociale est une composante essentielle des dysfonctionnements cognitifs et au développement des symptômes psychotiques observés chez les adultes souffrant de microdélétion 22q11.2 (Debbané et al., 2006; Jalbrzikowski et al., 2012). Sa forte incidence sur les interactions entretenues avec autrui constitue sans nul doute l'une des causes principales du retrait social, des troubles du comportement et des difficultés d'adaptation dont peuvent souffrir les enfants porteurs de ce syndrome. Le programme RC-KID a été développé pour répondre aux besoins de ces enfants.

Une discussion générale sera proposée en dernière partie de cette thèse, avant de conclure par une ouverture sur des nouvelles pistes de recherche et d'intervention dans cette population.

Chapitre 2

Overview of Social Cognitive Dysfunctions in Rare Developmental Syndromes With Psychiatric Phenotype

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Abstract

Rare neurodevelopmental syndromes often present social cognitive deficits that may underlie difficulties in social interactions and increase the risk of psychosis or autism spectrum disorders. However, little is known regarding the specificities of social cognitive impairment across syndromes while it remains a major challenge for the care. Our review provides an overview of social cognitive dysfunctions in rare diseases associated with psychiatric symptoms (with a prevalence estimated between 1 in 1,200 and 1 in 25,000 live births: 22q11.2 deletion syndrome, Angelman syndrome, Fragile X syndrome, Klinefelter syndrome, Prader–Willi syndrome, Rett syndrome, Smith–Magenis syndrome, Turner syndrome, and Williams syndrome) and shed some light on the specific mechanisms that may underlie these skills in each clinical presentation. We first detail the different processes included in the generic expression “social cognition” before summarizing the genotype, psychiatric phenotype, and non-social cognitive profile in each syndrome. Then, we offer a systematic review of the social cognitive abilities and the disturbed mechanisms they are likely associated with. We followed the PRISMA process, including the definition of the relevant search terms, the selection of studies based on clear inclusion, and exclusion criteria and the quality appraisal of papers. We finally provide insights that may have considerable influence on the development of adapted therapeutic interventions such as social cognitive training (SCT) therapies specifically designed to target the psychiatric phenotype. The results of this review suggest that social cognition impairments share some similarities across syndromes. We propose that social cognitive impairments are strongly involved in behavioral symptoms regardless of the overall cognitive level measured by intelligence quotient. Better understanding the mechanisms underlying impaired social cognition may lead to adapt therapeutic interventions. The studies targeting social cognition processes offer new thoughts about the development of specific cognitive training programs, as they highlight the importance of connecting neurocognitive and SCT techniques.

Keywords: social cognition, facial emotion recognition, theory of mind, systematic review, genetics, neurodevelopmental disorders

Introduction

Neurodevelopmental syndromes are genetic abnormalities frequently associated with behavioral and/or psychiatric phenotypes. Notably, these syndromes increase the difficulties in social interactions and present a high risk to develop psychosis or autism spectrum disorders (ASDs) (1–3). While social difficulties are generally associated with several comorbidities of genetic conditions, such as intellectual impairments, facial dysmorphism, speech problems, and psychotic symptoms, the high prevalence of social cognitive disorders recently received a growing interest. The aim here is thus to provide an overview of social cognitive abilities in developmental syndromes associated with psychiatric symptoms and shed some light on the specific mechanisms that may underlie these skills in each clinical presentation.

We focus on syndromes with a psychiatric phenotype (psychosis and/or ASD) and a prevalence estimated between 1 in 1,200 and 1 in 25,000 live births: 22q11.2 deletion syndrome (22q11.2DS) (4–6), Angelman syndrome (AS), Fragile X syndrome (FXS) (7), Klinefelter syndrome (KS), Prader–Willi syndrome (PWS) (8, 9), Rett syndrome (RS), Smith–Magenis syndrome (SMS) (10), Turner syndrome (TS), and Williams syndrome (WS) (11). We first detail the different processes included in the generic expression “social cognition” before summarizing the genotype, psychiatric phenotype, and non-social cognitive profile in each syndrome. Then, we offer a systematic review of the social cognitive abilities and the disturbed mechanisms they are likely associated with. We finally provide insights that may have considerable influence on the development of adapted therapeutic interventions such as social cognitive training (SCT) therapies specifically designed to target the psychiatric phenotype.

Social Cognition

Social cognition is defined as the ability to understand, perceive, and interpret information about other people and ourselves in a social context. This includes abilities such as emotion recognition, theory of mind (ToM), attributional style, and social perception and knowledge (Figure 1). Broadly speaking, social cognition includes a wide range of processes that allow people to rapidly, effortlessly, and flexibly perceive and interpret rapidly changing

social information, and respond appropriately to social stimuli. Besides, this ability gives meaning to the actions of others. More specifically, social cognition is an “umbrella concept” that includes many heterogeneous cognitive dimensions, such as emotional information processing, social perception and knowledge, ToM, and attributional bias (12).

Figure 1:| Organizational decision chart of social cognitive training in rare neurodevelopmental syndromes with psychiatric phenotype

Emotional Information Processing

Emotional information about others is conveyed by complex signals such as prosody and emotional expressions from the face or the body (13). Regarding emotional expressions, Ekman (14) described six basic emotions (happiness, sadness, fear, disgust, anger, and surprise) that can be easily discriminated from one another depending on different facial patterns (14, 15). Such categorical perception requires the processing of fine face changes and specific observation strategies.

Theory of Mind

An individual has a ToM if he imputes mental states to himself and others. A system of inferences of this kind is properly viewed as a theory because such states are not directly observable, and the system can be used to make predictions about the behavior of others (16–18). This theory comprises two dimensions: cognitive ToM (beliefs, intentions, etc.) and affective ToM (emotional state, knowledge of emotion, etc.) (19, 20). The ToM is subtended by first- and second-order representations. The first-order representation is defined as the ability to understand another person’s mental state. The second-order representation is the ability to understand what one person thinks about another person’s thoughts. These levels are both supported by the primary ability to understand how and why an individual does something (e.g., understanding motor action and eye direction) (16).

Attributional Style

Attribution refers to the way people explain their own and other people’s behaviors (21), but individuals are not objective perceivers and sometimes attribution does not properly match reality. Some individuals suffer from attribution bias, i.e., they systematically over- and

under-use the available information, which leads to a misinterpretation of the world they live in.

Social Perception and Knowledge

Social perception refers to the understanding of social roles and rules that typically appear in social situations. Social knowledge is the awareness of the behavior expected in different social contexts and interactions (12). This knowledge consists of social experience, education, and ritualized practices that are not necessarily explicitly communicated. These processes are the basis of an accurate analysis of another person's intentions, desires, or emotional states; more generally, it is linked to ToM.

Selected neurodevelopmental syndromes

The Table 1 presents a summary of the main medical, psychiatric, and social characteristics of the neurodevelopmental syndromes cited in this review.

Table 1

Summary presentation of the main medical and social characteristics of the neurodevelopmental syndromes cited in this review

Materials and Methods

This systematic review follows the process developed by the PRISMA statement, including the definition of the relevant search terms, the selection of studies based on clear inclusions and exclusion criteria, and the quality appraisal of papers.

Search Strategy

A search of the literature was conducted using the electronic database PubMed and Google Scholar, covering the period between first January 1990 and December 2016 and focusing on articles published in English. Broad search terms were used, including “social cognition,” “theory of mind,” “mind reading,” “mentalizing,” “mentalising,” “emotion

recognition,” “emotion perception,” “emotion processing,” “affect recognition,” “affect perception,” “affect processing,” “social knowledge,” “attributional style,” “facial emotion,” “auditory emotion,” “gaze processing,” “body posture,” “social cues” in combination with the diagnostic terms “22q11.2 deletion syndrome” (22q11.2DS), “Angelman syndrome,” “Fragile X syndrome” (FXS), “Klinefelter syndrome” (KS), “Prader-Willi syndrome” (PWS), Rett syndrome” (RS), “Smith-Magenis syndrome” (SMS), “Turner syndrome” (TS) and “Williams syndrome” (WS). Reference lists of the retrieved articles were also manually searched for relevant publications. All articles investigating the perception and/or recognition of affective stimuli (facial expression, prosody, and body language), ToM, social knowledge and attributional style in patients with rare neurodevelopmental syndromes were evaluated. Only studies that involved a behavioral task were included. We excluded from our evaluation the studies that only included neuroimaging data, the studies with non-humans and the reviews, and studies that did not directly assess social cognition such as studies using only a questionnaire assessing social behavior.

A total of 256 articles were initially identified as potential papers for inclusion. After a comprehensive reading by the first author (Aurore Morel), 136 articles were excluded from the analysis (e.g., studies not focused on behavior or duplicates). A total of 120 papers met the inclusion criteria and were eligible for quality appraisal (40 duplicates).

All titles and abstracts of the identified studies were independently assessed by two authors (Elodie Peyroux and Caroline Demily) for inclusion in or exclusion from the systematic review. Papers were excluded when inclusion criteria were not met (disagreements were resolved by discussion).

Data Analysis

We extracted relevant data from the 132 studies. A meta-analysis of the studies was not feasible given the variations among study designs, social cognitive assessments used, and populations.

A thematic analysis was performed to qualitatively synthesize the data, aiming at identifying specific syndrome patterns. Data were presented in a narrative form. The analytic process was carried on through discussion between the authors (Aurore Morel, Arnaud Leleu, Elodie Peyroux, Emilie Favre, Nicolas Franck, and Caroline Demily).

Patients

We proposed a review analysis, reporting the number of subjects included, the nature of the control population, the statistical method used, and the results obtained for all current published studies (Tables 2–5).

Table 2:

Fourteen studies examining social cognition in 22q11.2 deletion syndrome (22q11.2DS)

Table 3:

Studies examining social cognition in Fragile X syndrome (FXS).

Table 4:

Studies examining social cognition in Turner syndrome (TS).

Table 5:

Studies examining social cognition in Williams syndrome (WS)

Results

The large majority of studies assessed either emotion recognition or ToM whereas fewer studies documented attributional style and social knowledge. Moreover, in some area of social cognition, very few studies or no study at all were available for some syndromes, especially AS, RS, and SMS.

Emotional Information Processing

Recognition of Facial Emotion

Basic emotions defined by Ekman (14), namely joy, sadness, anger, fear, and surprise, are the first emotions recognized in faces by children with typical development (117). No obvious deficits in basic emotion perception were reported in females with FXS (37, 79, 81, 84). However, males with FXS looked significantly longer at disgusted faces compared to

neutral faces (75), with more difficulties to recognize sadness and fear (83). The same pattern of results was revealed in children with ASD. By contrast, individuals with RS spend less time than controls exploring key facial features (eye, nose, and mouth) for all emotions (118) and have difficulties to recognize emotional expressions (happiness, fear, and sadness) in general. These results may be due to increased attentional or informative value of negative over neutral (and positive) expressions (75).

People with 22q11.2DS have difficulties to discriminate facial emotions when they are moderately expressed (66), which can explain major deficits in social interactions, especially during childhood. Moreover, they have more difficulties to perceive negative emotions such as anger, fear, and sadness and to label emotions (64, 69, 71) while happiness, sadness, and surprise recognition seems efficient (59, 67, 68). A recent study using the CANTAB ERT test (morphed images with fast cover up times to avoid ceiling effects) showed that 22q11.2DS patients are significantly less accurate in detecting sadness and happiness (71). The same results are observed in males with FXS (73, 74, 78, 80, 83, 119).

Patients with WS showed emotion recognition levels similar to controls with the same mental age or individuals with developmental disabilities (99–101, 104, 106, 107, 110, 114). They are more accurate in perceiving happiness, sadness, anger, and surprise (107) but perform more poorly on auditory stimuli for all emotions except for happiness, which seems relatively surprising considering the classical hyperacusis associated with the syndrome (103). Abnormalities in auditory processing in WS seem to be restricted to the perception of negative affective vocalizations, such as scream or gasp (96). However, children with WS had no difficulty to recognize vocal emotions compared to controls (94, 95). Emotional information can be transmitted via both visual (e.g., facial expressions and gestures) and auditory (e.g., affective prosody) channels. In social interactions, both channels are competing and require the integration of relevant multisensory emotional information. When identifying facial affects, patients with WS are as accurate as controls in both congruent and incongruent conditions. But they are less efficient when identifying non-social affects (97). These results confirmed that emotionally evocative music facilitates the ability of patients with WS to recognize emotional faces. They spend more time staring at the salient features of the face—particularly the eyes (106, 108). Interestingly, the ability to discriminate and match faces with emotions was assessed in children with WS syndrome compared to PWS syndrome, or a non-specific intellectual deficiency. The three matched groups performed at a similar level (115)

without significant correlation between chronological age (CA) and performance on face perception tasks (107). Overall, neurocognitive deficits do not seem to be the only explanation of expression recognition impairments across syndromes, as illustrated in TS (88).

Adults with WS demonstrated a normal level of performance in the identification of emotions in unimodal conditions with face stimuli alone and in congruent face-voice multisensory contexts. However, they are less accurate to identify emotions in unimodal conditions with vocal emotions alone and even worse in multisensory incongruent stimuli conditions (95, 98). This difference seems to be highly specific and central to understand the hypersociability of WS (Table 1). Patients with WS may be specifically attracted by facial information, decreasing their attention to vocal information. Interestingly, when adults with WS are asked to identify complex mental states (such as worry, disinterest, etc.) from the whole dynamic face, their performance is similar to controls matched on CA (57). However, they have difficulties with “relief” and “distrust,” which may be related to hypersociability.

The deficit is more pronounced in PWS and WS, with difficulties to recognize all basic emotions (8, 99, 101). A global emotion identification impairment was documented in 22q11.2DS, FXS, PWS, and WS but the recognition of happiness seems preserved in these syndromes (101). Regarding the recognition of complex emotions, patients with PWS are less efficient than intelligence quotient (IQ)-matched individuals with WS. This result is consistent with the distinct behavioral symptoms associated to these syndromes (complex psychological disorder with maladaptive behaviors vs. frequent hypersociability).

During a task assessing the recognition of anger, fear, disgust, or sadness, individuals with KS were less accurate in recognizing angry faces, unlike other facial expressions (120). Children and women with TS show a specific impairment for the recognition of fearful and angry faces, both when the stimulus is a whole face or the upper face only (85–89, 91, 92). More specifically, in TS, fear recognition is significantly weaker compared to other emotions, including anger (88), with difficulties to correctly identify affect tones (91). In a study using dynamic facial expressions of different emotional intensities, patients with TS, 22q11.2DS and controls did not show any deficit in recognizing fear (62, 90). But patients with 22q11.2 are slower to recognize emotions (62) with a normal level of emotion recognition in auditory stimuli (70). By contrast, dynamic stimuli in WS do not change the accuracy of emotion recognition (114).

During an emotion recognition task using photographs, patients with 22q11.2 (59) spent less time than controls observing the eye region, as observed in FXS and ASD. They spent more time looking at the mouth (63, 68), which may explain why they have less difficulty to recognize happiness, surprise and, to a lesser extent, disgust. This result is correlated with the high prevalence of ASD in 22q11.2DS and FXS. By contrast, women with TS stare longer at the mouth, but only when looking at fearful faces. This result suggests a possible mechanism for selective fear deficit (89) across syndromes. Facial emotion recognition impairment may be related to an atypical observation of faces (121). Fewer fixations on the eyes region are related to difficulties to recognize specific emotions. This deficit is a core symptom in ASD controls who stare longer at the mouth for joy, fear, and disgust; at the eye for sadness; and at the eye and nose for anger (122).

ToM in Developmental Syndromes With Psychiatric Phenotype

Ability to Infer False-Belief in Others

An important mechanism of ToM is the ability to understand that other people's beliefs or representations about the world may differ from reality.

Children with 22q11.2 did not show major difficulties in ToM tasks (60). When it comes to PWS and WS, children had difficulties attributing mental states and understanding first-order beliefs (98, 116, 123). These results were confirmed in a non-verbal picture-sequencing task, but with a preservation of the understanding of intention, social script knowledge, and physical cause-and-effect reasoning (105). These results suggest that language abilities do not influence performance on ToM in WS (116), considering the heterogeneity of the process in the syndrome (105).

Patients with FXS are less accurate in ToM tasks (76, 77) and perform at a similar level than individuals with Down syndrome (DS) (73, 74) or ASD (77), with a limited impact of autistic symptoms (124). Altogether, these findings suggest that a ToM disorder in FXS may not result solely from the high comorbidity of ASD (77).

Children with WS, PWS, or a non-specific intellectual deficiency, perform at a similar level in standard ToM tasks (115, 125). However, children with PWS had specific difficulties to attribute second-order beliefs (123, 126).

Interestingly, 22q11.2DS seems specifically associated with a poor performance on false-belief tasks (60, 61), this deficit being highly correlated with psychotic symptoms

Ability to Infer Mental States in Others

Children with 22q11.2 seem to have difficulties to link contextual and social relevant cues when the scene is visually complex (61) or based on circumstances (61). This deficit may be related to attentional and visuospatial disorders and requires families and therapists to clearly verbalize emotions during social interactions. Moreover, the comprehension of misunderstanding, persuasion, pretending, sarcasm, and white lie seems impaired in 22q11.2DS (25, 60, 71). These findings suggest that a cognitive ToM disorder causes a delay rather than a deficit (60). From this perspective, impairments in the spontaneous attribution of seducing, mocking, playing with one another, getting frightened, or elated mental states to abstract visual stimuli were reported in 22q11.2DS (65), suggesting that gaze direction is also a weakness in the syndrome (60).

As expected, patients with WS were proficient during a verbal task (111, 126) but their performance decreased when the ToM task was presented on a visual medium (111) with difficulties inferring mental states from visual cues, especially for negative intentions (93) and gaze direction (109). These results suggest that they may present a positive bias in the interpretation of social cues. An impaired social-perceptual ability may play a role in increased approachability and a deficit in the processing of basic social cues may have possible repercussions on ToM. The ability to observe and recognize other people's actions contributes to understand goals and intentions (127) and may help people with WS improve their recognition of action process (113). Indeed, in the presence of context cues, children with WS were as accurate as controls (112, 113).

Overall, patients with 22q11.2DS, FXS, or WS had difficulties determining whether someone is looking at them or elsewhere (60, 82, 102, 128) but individuals with PWS seem to yield scores within the normal range (129). When patients with FXS were asked to judge the direction of eye gazes (direct or averted), they performed at the same level than patients with similar general cognitive abilities and autism symptoms (72), and patients with a developmental delay (82). Complex emotion recognition requires knowledge and analysis of interpersonal relationships, unlike basic emotion recognition. Thus, further research on the

potential dissociation between the recognition of complex mental states and basic emotions, and the influence of the nature of the stimuli (static or dynamic) is needed.

Discussion

Interventions and Perspectives

This systematic review shows that social cognition deficits are present in neurodevelopmental disorders at different levels and remain strongly correlated with psychiatric phenotype. Emotion recognition and ToM skills impairments seem to be a core deficit in rare developmental syndromes, otherwise associated with psychosis and ASD. Although more research needs to be done to assess social cognition phenotypes in these syndromes, it is crucial to develop and evaluate appropriate therapeutic interventions. In this section, we briefly discuss therapeutic approaches and present future keys to improve social deficits in that indication

In daily life, facial expressions are typically embedded in a rich context with many distractors (e.g., noises and visual stimuli) and social information from multiple sensory channels (e.g., prosody, gestures, and change in facial expression). Therefore, social interactions necessitate fast and efficient cognitive skills. They include the ability to identify visual and spatial relationships in emotion recognition, to integrate and manipulate such perceptions, to select relevant information, to inhibit irrelevant stimuli and alternate between several sensitive channels. Emotion recognition is also a complex process involving visual attention (130), visuospatial abilities (130), working memory (131), divided attention and executive functions (132). As a consequence, improvement of these functions may have a positive impact on social cognition and behavior. Visuospatial and visuoperceptual skills play a key role in everyday life. Visual information and complex visual stimuli are analyzed with a complete unawareness of the visuoperceptual process or the complexities of the stimuli involved. This process becomes conscious in a context of learning. Repetition and familiarity enable a more spontaneous approach and turn the conscious and effortful process into an automatic one. If this ability is impaired, many types of deficits can occur, ranking from a failure to process the basic elements of a visual stimulus (i.e., colors, lines, and orientation) to more complex and integrative features, such as object identification, faces, or familiar scenes.

These deficits can include social cognition defects, especially in the area of facial emotion recognition, acquired slowly during childhood and reach adult levels in late adolescence (133).

Currently, two programs, named “Cognitus & Moi” (Cognitus & Me) and “Vis-à-Vis” have considered the link between neuropsychological functions and social cognition (facial emotion recognition). “Cognitus & Moi” is a cognitive remediation program with SCT, designed for 5- to 13-year-old children with developmental disorders. The program is specifically focused on attentional, visuospatial functions and emotion recognition (134). It involves a variety of exercises in a paper and/or pencil (n = 30) or a computerized format (n = 29) and a strategy coaching approach. “Vis-à-Vis” is a computerized training program based on a trial-and-error approach. It can be performed at home with parents and targets social cognition difficulties and working memory (135).

The ability to explore face efficiently develops during childhood. The eyes, nose, and mouth are the preferred attentional targets in facial exploration (121). These facial features play an important role in perception and recognition of emotion. However, the visual exploration developed by individuals with neurodevelopmental syndrome is mainly different, with a lack of eye contact according to a specific pattern previously observed in ASD. Individuals with neurodevelopmental syndrome may benefit from educational solutions targeting this impairment. In that regard, an important point is that dynamic information facilitates the perception of facial expressions (136, 137). Individuals with autism appear to benefit from slow dynamic information when categorizing emotional expressions (138). Considering the possibility of overlap between children with neurogenetic disorders and children with typical ASD (139), the question of a similar benefit in rare diseases should also be addressed in the future. More generally, the beneficial effect of motion may play a role in therapeutic intervention.

Some current treatment plans which are based on phenotype rather than etiology may be adapted for individual with neurodevelopmental syndrome.

For example, considering the well-established association between 22q11.2DS and schizophrenia, SCT, a program based on the cognitive enhancement therapy developed for individuals with schizophrenia (140) may be of interest in 22q11.2DS. This program targets general and high-level social skills such as the ability to practice calming techniques, to

identify the main idea in a conversation, to determine expected behaviors in different situations (social perception and social knowledge), or to clearly express one's own thoughts (ToM) (140).

It is necessary to define strengths and weaknesses of each participant and the exact nature of deficits. Indeed this review highlights the implication of different cognitive processes involved in social interaction deficits, which appear to have different effects across syndromes (Tables 6 and 7). Here, we show that social cognition impairments are not uniquely caused by syndrome comorbidities such as IQ. Understanding the differences in the social cognitive abilities may become a distinctive clinical tool to develop special trainings. In several cases, the severe cognitive impairment associated with rare diseases necessitates individual adaptation of therapeutic interventions. Individual may present severe limitations in their ability to communicate through speech and gestures. Single case reports have demonstrated that patients can develop communicative skills and social cognition, particularly affective and cognitive ToM with appropriate interventions. For example, communication by composing words on an alphabetic table may be improved by training communicative skills in RS (141). With a training focused on emotion, discrimination of facial emotion (joy, sadness, and anger) may be improved in RS (142). Moreover, although patients do not develop functional verbal skills, the eye-tracking technology has increased the possibilities to understand patients (143) and facilitated the access to augmentative and alternative communication (144–146).

Face recognition and ToM have an important role in social problem solving (14, 147, 148). These capacities allow to understand and interpret other's emotion (149). In the social interaction, recognition of expressions leads to adapt behavior (150, 151).

Table 6:

Emotion processing among rare neurodevelopmental syndrome

Table 7:

Theory of mind among rare neurodevelopmental syndrome

Limitations

This systematic review highlights some limits. Some rare syndromes received only little interest, particularly AS, KS, RS, and SMS. The lack of results regarding some areas of social cognition in these syndromes must be interpreted with caution, as the number of published studies is limited. Furthermore, very few studies have directly compared patients considering anxiety levels. Moreover, psychiatric diagnosis has not been considered and very few studies have proposed to establish a link between social cognition and behavior in rare neurodevelopmental syndromes. In fact, the psychiatric phenotype has not yet been extensively studied. Many data are available for facial emotion recognition and ToM, but a lack of research in social perception/ knowledge and attributional style has been highlighted. Thus, it remains unclear whether individuals with a rare developmental syndrome show similar impairments in these areas. Moreover, impairments may be specific to tasks and emotions, rather than all social cognitive processes. The use of relatively consistent methodology across study designs would help compare these impairments.

Summary and Conclusion

To sum up, some social trainings, such as the use of the eyetracking technology in RS or the focus on visuospatial functions in 22q11.2DS, are created among the specific profile of individuals with a neurodevelopmental syndrome. Understanding the differences in the social cognitive abilities of people with rare neurodevelopmental disorders may lead to a more personalized medicine. This review suggests that cognitive remediation therapy and SCT may be a viable way to improve the social and functional outcomes, although many questions on its effectiveness still need to be answered.

The studies targeting social cognition processes offer new thoughts about the development of specific cognitive training programs, as they highlight the importance of connecting neurocognitive and social cognitive training techniques. They point out that individuals with social cognitive impairments may need more help in terms of social interactions. They provide keys for caregivers, who may better adjust their communication with explicit social cues by mentioning what they are thinking or feeling and why. Understanding and adjusting attitudes to individuals with social cognition impairments are required to prevent frustration and maladaptive behaviors.

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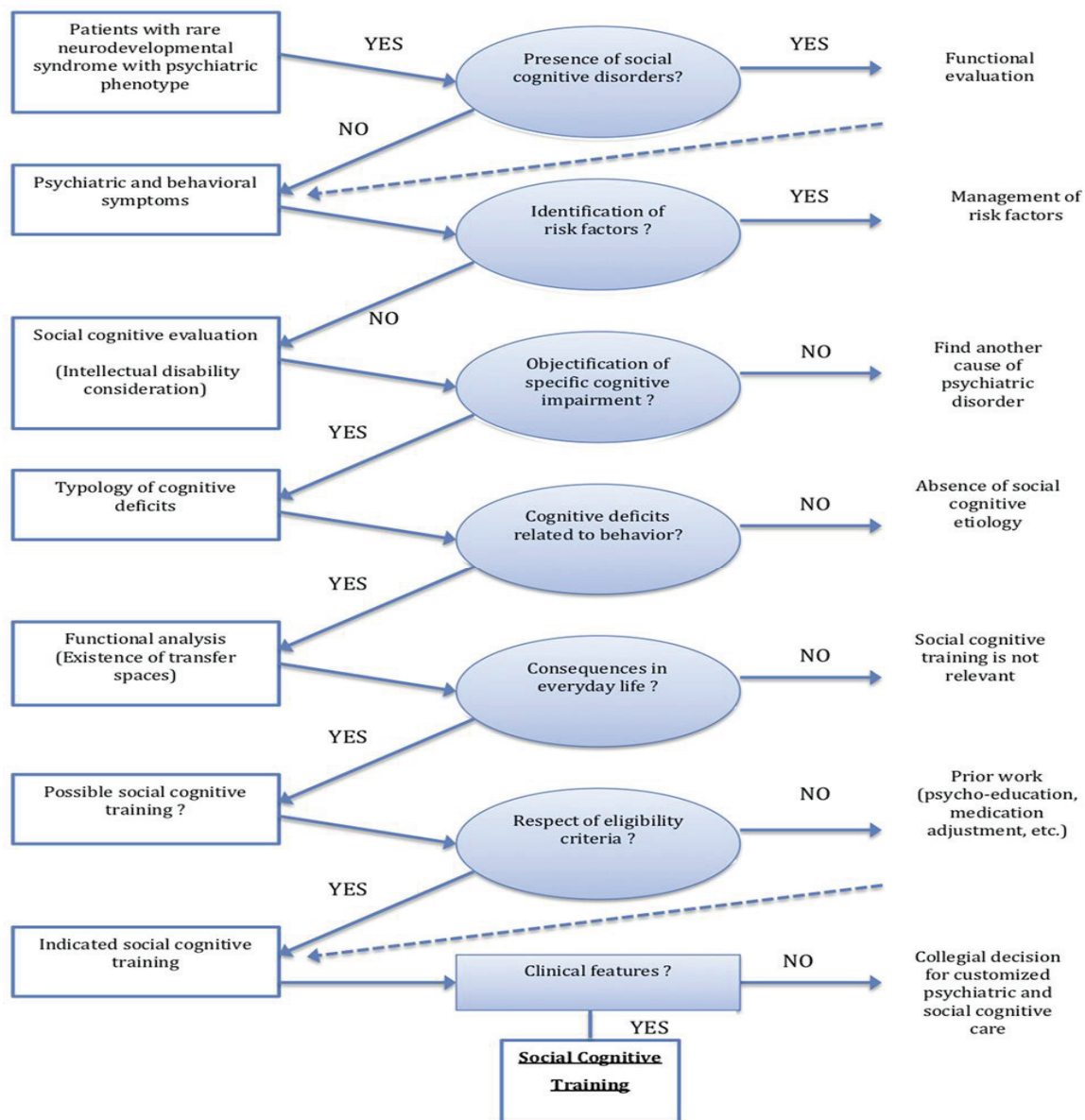


Figure 1 | Organizational decision chart of social cognitive training in rare neurodevelopmental syndromes with psychiatric phenotype.

Table 1 | Summary presentation of the main medical and social characteristics of the neurodevelopmental syndromes cited in this review

Syndrome	Chromosome	Prevalence	Medical characteristics	Main characteristics of social behavior
22q11.2 DS	22q11.2	1 in 2,000–4,000 births (22, 23)	Characteristic facial dysmorphism, mainly congenital heart disease, velopharyngeal insufficiency, cleft palate, neuromuscular problems, hypoparathyroidism, and thymic hypoplasia	Withdrawal [but normal social motivation and adaptive behavior according to Ref. (24)] Difficulties to maintain relationships High risk of development of psychotic disorders (25, 26)
Angelman syndrome	15q11q13	1 in 10,000–12,000 births (27, 28)	Microcephaly, epilepsy, feeding problems	High levels of social approach behavior toward familiar (e.g., their mothers) and unfamiliar adults, strong enthusiasm for adult attention (29, 30) Autistic behaviors such as balance and movement problems, manual stereotypy such as hand-flapping (31), absence of eye contact, fascination for certain objects, and intolerance to change (32) Frequent laughter can be caused by a minimal stimulus and is often inappropriate
Fragile X syndrome	X	1 in 1,500 births	Characteristic facial dysmorphism. Macroorchidism, hyperextensible metacarpophalangeal joints, curvature of the spine (scoliosis), seizures (epilepsy), heart murmurs	Withdrawal, anxious Autistic behaviors including avoidance of eye contact (34, 35), sensory hypersensitivity, stereotypical behavior, hand flapping, echolalia, and language delay (36, 37)
Klinefelter syndrome	X aneuploidy	1 in 667 births	Tall stature with disproportionately long legs and arms. Hypogonadism, gynecomastia, infertility. Comorbid symptoms such as taurodontism, osteopenia, breast cancer, thyroid dysfunction, and chronic autoimmune disease	High social anxiety levels and reduced social assertiveness (39). But level of social motivation is not impaired (40) Men with a prenatal diagnosis may present with fewer social difficulties, which may be due to an increased prenatal support to the family (40)
Prader-Willi syndrome	15q11-q13	1 in 15,000 births	Characteristic facial dysmorphism. Neonatal hypotonia and feeding difficulties. Hyperphagia, obsession with food, hypogonadism	Maladaptive behaviors such as outbursts, self-mutilation, impulsivity, ritualistic behaviors, repetitive conversation topics, and difficulties with routine change
Retardation syndrome	X	1 in 10,000 births	Partial or complete loss of hand skills, apraxia, spasticity, scoliosis, abnormal breathing patterns, and seizures	Atypical socio-communicative pattern that develops prior to the period of regression: the use of body movements, gestures, eye gazes, vocalization, and production of words depending on the context (expressing discomfort or happiness, making choices, requesting objects, performing activities, focusing attention, and socializing) (43–45)
Smith-Magenis syndrome	17p11.2	1 in 25,000 births	Characteristic facial dysmorphism. Brachycephaly, midface hypoplasia, prognathism, hoarse voice, infantile hypotonia, chronic otitis, sleep disorders	Strong desire for social interaction, good eye contact (47, 48) Maladaptive behaviors such as self-injury (including wrist biting, skin picking and head banging), temper tantrums, body rocking, contrasting with challenging behavior, hyperactivity, insert their hand in their mouth or objects into body orifices, sometimes with public masturbation Stereotypical behaviors including repetitive questions, routine, and the tendency to bring about recurring subjects
Turner syndrome	Complete or partial absence of one X chromosome	1 in 2,000 live births	Short stature, ovarian failure, sex hormone deficiencies, webbed neck, cardiac malformation, abnormal pubertal development, and amenorrhea with infertility	Shyness, social anxiety, low self-esteem (social acceptance, romantic relationships, etc.), social withdrawal, emotionally less mature than controls (50, 51) [but normal social motivation according to Ref. (52, 53)] Good social knowledge but difficulties to put it into practice in real life, probably due to social anxiety (54)
Williams syndrome	7q11.23	1 in 7,500 births	Characteristic facial features. Cardiovascular disease, hyperopia, strabismus, feeding difficulties, hypercalcemia, joint hypermobility	Difficulties making friends, maladaptive behaviors, non-social anxiety, and difficulties in social reciprocity similar to individuals with Autism spectrum disorder (56) Heterogeneous social skills (57, 58)

Table 2 | Fourteen studies examining social cognition in 22q11.2 deletion syndrome (22q11.2DS).

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Comparison group	Social cognit bn domain (task)	Data analyses	Main results
(59)	17	17.2	72.5 (12.7)	Typically developing (TD)	Exploring face	ANOVA	Participants with 22q11.2 spent less time observing the eye and mouth region than controls (p = 0.009)
(60)	50	11.00 (6–16)	65.80 (9.32) [40–94]	TD	Ability to infer first-order false beliefs (the Sally task) and on the Sally–Annie task. Ability to infer second-order false beliefs (Cognitive theory of mind (ToM) (strange stories))	Fisher's exact test Pearson correlation	Children with 22q11.2 did not show difference on the Smarties task (p = 0.52) and on the Sally–Annie task (p = 0.15). Only younger children with 22q11.2 showed poorer performance on second-order false belief tasks and strange stories task (p < 0.02)
(61)	24	16.75 (12–21)	75.88 (14.93) [56–115]	TD	Ability to infer second-order false beliefs Affect ToM	ANOVA	Children with 22q11.2DS had difficulty with false belief tasks based on circumstances (p = 0.001)
(62)	35	18.2 (9–33)	69.5 (11.3)	TD	Identify facial expressions of dynamic facial expression (labeling task)	MANCOVA	Individuals with 22q11.2 and controls with typical development and the same age showed similar performance (p = 0.81). But participants with 22q11.2 were slower to recognize emotion faces (p < 0.01)
(63)	26	12.36 (8–15)	74.19 (11.99)	"Idiopathic" developmental delay (DD) + TD	Exploring face	MANOVA	Participants with 22q11.2DS spent more time looking at the mouth (p = 0.002)
(64)	21	14.86 (8–32)	–	Profound + schizophrenia family member + low risk	Identify facial expressions (labeling task)	Regression analysis	Individuals with 22q11.2DS had difficulty with labeling emotion faces (p < 0.0001)
(65)	63	13.7 (6–25)	80.5 (13.7)	22q11.2DS + TD	Ability to spontaneously at-tibute mental state (social-at-tibute bn task)	ANOVA	In comparison to controls, individuals with 22q11.2DS showed significant impairments in the ability to explain purposeful behavior (intent bnality) (p < 0.001) and to describe accurately the events going on in the scene (appropriateness) (p < 0.01)
(65)	31	15.9	–	Healthy control	Cognitive ToM (TASIT task)	T-test	22q11.2DS participants exhibited impaired performance on task of ToM (p < 0.001) and in recognition of lies (p < 0.001) and sarcasms (p < 0.001)
(66)	15	14.67 (9–19)	–	TD	Percept bn of facial expression (picture-to-picture matching task with morphed face stimuli)	ANOVA	In comparison with control, individuals with 22q11.2DS had more difficulty perceiving anger (p < 0.001), fear (p = 0.049) and sadness (p = 0.028) but not disgust (p = 0.21) and happiness (p = 0.11). They had difficulty to discriminate these facial emotions when they were moderately expressed, as frequently observed in daily life
(67)	17	17.44 (12–21)	72.11 (12.99)	TD	Identify facial expressions (labeling task)	ANOVA	The 22q11.2DS group had significantly more problems correctly identifying the emotion faces (p = 0.0005), disgust (p = 0.002), fear (p = 0.001) and neutral (p = 0.009). They performed similarly to controls on facial emotion faces such as happy, surprise and sad (p > 0.05)
(68)	20	16.75 (8–21)	73.75 (13.63) [56–98]	Autism spectrum disorder (ASD) + TD	Identify facial expressions (labeling task) Exploring face	ANOVA	Participants with 22q11.2DS spent more time looking at the mouth region than controls (p = 0.002). The effect of group or interaction was not significant for the amount of time spent examining eye region
(69)	49	11	66.33 (8.6)	TD	Identify facial expressions (labeling task)	Mann–Whitney U tests	Individuals with 22q11.2DS had difficulty with labeling emotion faces (p < 0.001) in comparison with the TD group
(70)	60	10.5	–	TD	Vocal emotion recognition in situ (multi-variant semantic message (paralanguage test))	Chi-square	No significant differences were found in the emotion percept bn and processing by paralanguage subset between the two groups
(71)	29	15.7	79.52 [35–113]	TD	Identify facial expressions (labeling task with morphed image) Cognitive ToM (strange stories)	Wilcoxon rank-sum tests	Individuals with 22q11.2DS were significantly less accurate in detecting the anger (p = 4.44 × 10 ⁻⁷), fear (p = 8.0 × 10 ⁻⁴), disgust (p = 6.77 × 10 ⁻⁹), sadness (p = 5.95 × 10 ⁻⁷), happiness (p = 5.0 × 10 ⁻⁴), sarcasm (p = 1.16 × 10 ⁻⁶), and sincere (p = 6.0 × 10 ⁻⁴) but not for the surprise (p = 0.3)

Table 3 | Studies examining social cognition in Fragile X syndrome (FXS).

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Mental age (MA), verbal mental age (VMA), and non verbal mental age (NVMA) (SD) [range]	Comparison group	Social cognit bn domain (task)	Data analysis	Main results
(72)	30	20.93 (16.05–25.33)	67.78 (20.73) [40–119]	–	Comparison group (idiopathic developmental delay, intellectual disability, or learning disability)	Processing of egocentric gaze	ANOVA	Individual with FXS performed at the same level than patients with similar general cognitive abilities and autism symptoms (p = 0.53)
(73)	28	11.2 (7–15)	–	VMA 6.91 (1.75) [4.1–10.9]	Down syndrome (DS)	Ability to infer first-order false beliefs (Sally–Ann task and the appearance–reality task)	Chi-square test	Children with FXS and individuals with DS performed at a similar level during the Sally–Ann task (p = 0.77) and the appearance–reality task (p = 0.91)
(74)	22	47.91 (18–69)	105.18 (10.5)	–	Typically developing (TD) (from FXS families) + TD (from general population)	Identify facial expressions (labeling task) Identify facial expressions of complex emotions (RMET)	ANOVA	In comparison with TD group, individuals with FXS were less proficient in discriminating basic emotion (p = 0.02) and complex emotion (p = 0.008)
(75)	13	19.70 (6.60–34.19)	–	–	Autism spectrum disorder (ASD)	Spontaneous perception of facial expression (oddball paradigms in conjunction with a measure of preferential looking)	t-test	Individuals with FXS or autism looked significantly longer at disgusted faces compared to neutral faces (FXS: p = 0.001; ASD: p = 0.001)
(76)	8	12.5 (10.25–14.16)	45.3 (3.2) [40–49]	VMA 6.58 (1.66) [4.83–9.50]	Intellectual disability of unknown etiology	Ability to infer first-order false beliefs (the Smarties task)	Chi-square test	Individuals with FXS were less accurate in the Smarties task (p < 0.05)
(77)	15	13.66	–	VMA: 6.11 (2.0) NVMA: 6.0 (1.3)	FXS-A + intellectual disability group	Ability to infer first-order false beliefs (Sally–Ann task)	ANOVA	Individuals with FXS or FXS-A were less accurate in the Sally–Ann task than the Intellectual Disability group (p = 0.009)
(78)	10	16.4 (9.7–24.0)	91 (16.2) [75–124]	–	TD	Identify facial expressions (labeling task)	t-test	Individuals with FXS were less proficient in discriminating neutral faces (p = 0.048), sadness (p = 0.070) and scrambled face (p = 0.016) than TD group
(79)	19	30.47 (18–40)	92.2 (15.3)	–	Obligate carrier + TD	Perception of facial expression (picture-to-picture matching task)	ANCOVA	Fragile X women do not demonstrate a deficit in emotion perception
(80)	16	24.8 (12.1–56.1)	64 (13.7) [51–96]	MA 8.4 (3.8) [6.0–21.1]	Typically developing matched on mental age (TDMA) + typically developing matched on chronological age (TDCA)	Identify facial expressions (labeling task)	ANOVA	FXS group performing significantly worse than both TDCA (p = 0.013) and TDMA (p = 0.044) group in their ability to recognize anger. They were also significantly worse at recognizing neutral expressions compared to TDMA group (p = 0.032)
(81)	15	41.80 (17–66)	36.60 (7.74)	–	Control	Identify facial expressions (labeling task)	ANOVA	No significant differences were found in the emotion perception and processing by paralinguistic subtleties between the two groups
(37) (first study)	14	10.34	–	VMA 5.72 (0.93) [3.9–6.9]	DS + TDMA	Perception of facial expression (picture-to-picture matching task)	ANOVA	No group difference in the ability to recognize emotion from facial expression (p = 0.110)
(37) (second study)	18	8.16 (4–14)	–	–	DS + intellectual disability of unknown etiology	Perception of facial expression (picture-to-picture matching task)	Fisher exact test	No group difference in the ability to recognize emotion from facial expression
(82)	13	15.5	61.0 (14.8)	–	Developmental delay (DD) + TDCA	Processing of egocentric gaze	MANOVA	Significant differences in task accuracy were revealed between the TD group and other groups (p = 0.02, and p = 0.03 vs. DD; p = 0.001 vs. FXS) but not between the DD and FXS groups (p = 0.99 for all)
(83)	12	20.6 (12.1–38.1)	64 (14.7) [52–96]	MA 9.0 (4.2) [6.1–21.1]	TDMA + TDCA	Identify facial expressions (labeling task)	ANOVA	FXS group performing significantly more poorly than both control groups when recognizing disgusted (TDMA p < 0.001; TDCA p = 0.001) and neutral (TDMA: p = 0.035; TDCA: p = 0.015) facial expressions. TDCA group was significantly better at recognizing fearful facial expression compared to the FXS (p = 0.001) and (younger) TDMA (p = 0.001) groups
(84)	15	11.75	–	MA 4.08 (1.08)	DS + non-specific intellectual disability + TD	Perception of facial expression (picture-to-picture matching task)	ANOVA	No obvious deficit in basic emotion perception was reported in FXS group

Table 4 | Studies examining social cognition in Turner syndrome (TS)

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Mental age (MA), verbal mental age (VMA), and non verbal mental age (NVMA) [SD] [range]	Comparison group	Social cogniti on domain (task)	Data analysis	Main results
(85)	26	30.58	–	–	Typically developing (TD)	Identifi cati on of stati c facial expressions (labeling task) Ability to spontaneously attribute mental state (social-at tributi on task)	T-test ANOVA	TS women are less accurate in recogniti on of fear (p < 0.05) and sadness (p = 0.052) than TD group TS women being less accurate in describing the animati ons than TD women (p = 0.05)
(86)	51	25.1 (15–44)	–	–	Parti al X chromosome deleti on + TD	Identifi cati on of stati c facial expressions (labeling task)	MANOVA	Children and women with TS showed a specifi c impairme nt for the recogniti on of fearful (p < 0.0001) and angry faces (p < 0.006)
(87)	14	10.1 (6.92–12.92)	90.43 (12.74)	–	TD	Identifi cati on of stati c facial expressions (labeling task) Af fecti ve theory of mind (NEPSY-II)	ANOVA	Girls with TS were signifi cantly less accurate in the classifi cati on of fearful faces compared with TD controls (p = 0.007), however, did not dif fer in accuracy for the other emoti ons (happy: p = 0.073, neutral: p = 0.106, scrambled: p = 0.179)
(88)	23	24.6 (18–36)	–	–	TD	Identifi cati on of stati c facial expressions (labeling task)	ANOVA	Fear and anger were signifi cantly less well recognized by women with TS than controls: for fear (p < 0.01); for anger (p < 0.01)
(89)	18	32.6 (18–63)	104.8 (16.3)	–	TD	Identifi cati on of stati c facial expressions (labeling task)	MANOVA	The TS group were signifi cantly impaired in recognizing fear relative to control females, p < 0.013. None of the other emoti ons showed signifi cant dif ference between the two groups
(90)	40	25.44 (19–33)	90.68 (9.30) [75–106]	–	Noonan syndrome + TD	Identifi cati on of dynamic facial expression (labeling task)	ANOVA	The mixed between-within subjects ANOVA revealed no signifi cant ef fect of Group, indicati ng that the three groups did not signifi cantly dif fer in accuracy of emoti on percepti on
(91)	71	27 (17–50)	96 (9)	–	TD	Identifi cati on of stati c facial expressions (labeling task)	ANOVA	In comparison with TD group, women with TS showed a specifi c impairme nt for the recogniti on of fear (p = 0.001) and angry (p = 0.001) faces
(92)	94	31.2	98 (10)	–	Women with premature ovarian failure + TD	Identifi cati on of stati c facial expressions (labeling task)	ANCOVA	The TS group had dif ficulty to recognize “anger” (p = 0.005), but no “happy,” “sad,” “fear,” “surprise,” and “disgust”

Table 5 | Studies examining social cognition in Williams syndrome (WS)

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Mental age (MA), verbal mental age (VMA), and non verbal mental age (NVMA) (SD) [range]	Comparison group	Social cognit on domain (task)	Data analysis	Main results
(93)	27	17.41 (5.33–43.66)	47 (19) [18–84]	MA 5.75 (1.1) [3.78–8.66]	Typically developing matched on mental age (TDMA) + typically developing matched on chronological age (TDCA)	Cognitive theory of mind (ToM)	ANOVA	Individuals with WS at tributed less negative intentions than TDMA and TDCA groups ($p < 0.001$)
(57)	19	21.5 (7.16–38.83)	–	–	TDCA + TDVA	Identif tation of complex emot ions (RMET)	T-test ANOVA, Tukey post hoc tests	Adults with WS perform at similar level than TDCA group when identifying whether the actors are “deciding” ($p = 0.553$), “not sure” ($p = 0.279$), or “worried” ($p = 0.553$). They were less accurate at identifying “do not trust” in comparison to TDCA group ($p = 0.001$) and TDVA group ($p = 0.008$), “disapproving” in comparison with TDCA group ($p < 0.001$), “relieved” in comparison to TDCA group ($p = 0.013$)
(94)	24	32.36 (15.4–56.9)	65 (7.10) [50–80]	–	Typically developing (TD)	Vocal emot ion recognit ion in multisensory emot ional informat ion (paralanguage test)	T-test	Between-group differences in performance with the emotionally congruent multisensory (visual and vocal) did not reach the adjusted significance level ($p = 0.07$). But the TD group outperforming the WS group with the emotionally incongruent audiovisual stimuli ($p < 0.001$) and the unimodal auditory stimuli ($p < 0.001$)
(95)	12	11.4y (9.6–13.9)	–	–	Autism spectrum disorder (ASD) + TD	Vocal emot ion recognit ion in stimuli without semantic message (paralanguage test)	ANCOVA	No between-group differences were found ($p > 0.065$)
(96)	8	27.8y (18–42)	–	–	DD + TD	Vocal emot ion recognit ion in stimuli without semantic message (paralanguage test)	ANOVA T-test	The TD group outperforming the WS group ($p = 0.004$). The interaction effect was due to the WS group exhibiting lower recognition accuracy for negative stimuli ($p = 0.001$), while no between-group differences were in evidence for the processing of the positive stimuli ($p = 0.73$)
(97)	21	24.0 (12–40)	–	–	DD + TD	Identif tation of static facial expressions (emot ion is associated with congruent or non congruent emot ional music) Vocal emot ion recognit ion in multisensory emot ional informat ion (paralanguage test)	ANOVA	Emotionally evocative and congruent music facilitated the ability of participants with WS, DD, or TD to process emotionally facial expressions ($p = 0.03$)
(98)	57	9.24 (6.00–12.74)	72.93 (15.17) [40–97]	–	–	Ability to infer first-order false beliefs	–	WS patients had difficulties to understand false beliefs

Table 5 (continued)

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Mental age (MA), verbal mental age (VMA), and non verbal mental age (NVMA) (SD) [range]	Comparison group	Social cognit on domain (task)	Data analysis	Main results
(99)	12	8.10 (6.1–15.3)	–	VMA 5.8 (1.11) [3.4–9.3]	AUT (autism group) + TDVMA	Identifcat on of statcfacial expressions (labeling task)	ANOVA	Individuals with WS showed emot on recognit on levels similar to controls with the same mental age or individuals with developmental disabilities
(100)	25	9.5 (6–15)	54.7 (8.95)	–	–	Identifcat on of statcfacial expressions (labeling task)	–	Individuals with WS recognized facial affect at an appropriate developmental level
(101)	20	12.25 (5.6–23.58)	–	MA 5.58 (0.75) [4.25–6.83]	DS + TDCA + TDMA	Identifcat on of statcfacial expressions (labeling task)	ANOVA (pair-wise comparisons with Bonferroni correction)	In emot on recognit on task, no signifcant differences were found between participants with WS and TDMA group but participants with WS performed signifcantly lower than TDCA group ($p < 0.001$), the DS group performed signifcantly lower than the WS ($p \leq 0.001$)
(102)	11	30.6	66.4 (11.5)	–	TD	Processing of egocentric gaze	T-test	No difference in accuracy when WS and TD groups were compared ($p < 0.05$). However, WS participants were slower than controls ($p < 0.0001$) in determining the gaze direction
(103)	47	19.49 (12.1–32.4)	69.08 (12.2) [51–100]	–	Learning disability + TD	Identifcat on of statcfacial expressions (labeling task) Vocal emot on recognit on in stimuli with semantic message (paralanguage test)	ANCOVA	In labeling task and paralanguage test, WS group was signifcantly less accurate in recognit on of sadness, anger and fear ($p < 0.0001$) than TD group. No difference is revealed between WS and learning disability groups
(104)	20	16.13 (5.33–43.67)	–	–	DS + TDCA + TDMA	Identifcat on of statcfacial expressions (labeling task)	ANOVA	Individuals with WS showed emot on recognit on levels similar to TDMA group ($p > 0.1$). WS groups outperformed the DS group ($p < 0.05$). And TDCA group outperformed WS group ($p < 0.01$)
(105)	31	17.02 (5.33–43.67)	–	MA 5.65 (1.31) [3.58–9.33]	TDCA + TDMA	Ability to infer false beliefs (non-verbal picture-sequencing task)	ANOVA	The WS group performed signifcantly below the TDMA group on the false belief stories ($p < 0.01$). These groups performed similarly on all other story types (understanding of pretense and intent). TDCA group performed signifcantly better than the WS group and TDMA group on all story type ($p < 0.01$)
(106)	16	25.14 (11.42–50.58)	61 (15) [38–84]	–	TDMA	Identifcat on of statcfacial expressions (labeling task) Exploring face	ANOVA	Individuals with WS showed emot on recognit on levels similar to TDMA group: no signifcant main effect for group was revealed ($p > 0.1$) The WS group spent signifcantly more time looking at the eyes than TD controls ($p < 0.05$) but the groups spent a similar amount of time looking at the nose ($p > 0.1$) and the mouth ($p = 0.1$)

Table 5 | (continued)

Reference	N	Mean age in years (range)	Full scale intelligence quotient (SD) [range]	Mental age (MA), verbal mental age (VMA), and non verbal mental age (NVMA) (SD) [range]	Comparison group	Social cogniti on domain (task)	Data analysis	Main results
(107)	15	10.41 (6.0–15.83)	–	VMA7:2 (20)	ASD + TDVMA match with WS + TDNV match with WS + VMA match with ASD + TDNV match with ASD	Percepti on of facial expression (picture-to-picture matching task)	T-test	Parti cipants with WS were more accurate when percei ving happiness, sadness, anger, and surprise relative to TDVMA (p < 0.05) and TDNV (p < 0.01) group, who did not dif fer
(108)	14	15.16 (8.75–28.0)	–	–	ASD + TDNV matched individually with WS + TDNV matched individually with ASD	Exploring face	T-test	Individuals with WS f kated faces for longer than parti cipants who were developing typically (p < 0.001)
(109)	15	13.50 (8.66–28.0)	–	–	ASD + TDNV matched individually with WS + TDNV matched individually with ASD	Processing of allocentric gaze	T-test	In comparison with TDNV, parti cipants with WS had dif fult ies to interpret eye-gaze directi on (p < 0.05)
(110)	29	14.7 (7–27)	57.8 (12.3) [40–93]	MA 8.3 (2.9) [4–17]	TDMA + TDCA	Identifi cati on of stati c facial expressions (labeling task)	ANOVA	No such group dif ferences were found for photographs of real faces (WS vs. TDMA, p > 0.05; WS vs. TDCA, p > 0.05)
(111)	19	14.4 (7–26)	57.5 (11.0)	MA 8.3 (3.5) VMA 9.3 (3.5) PMA 7.9 (2.7)	TD	Cogniti ve ToM (strange stories)	ANOVA (turkey test)	WS group were signifi cantly less accurate on the visual than on the verbal modality (p < 0.001)
(112)	19	13.7 (5.1–30.0)	63.3 (12.33)	MA 6.5 (1.9) [4.1–11.2]	TDMA + TDCA	Processing of motor acti on	ANOVA	The WS and TDMA groups dif fered from performance of the TDCA group (p = 0.015 and p = 0.025, respectively). Most interesti ngly both the WS and the TDMA groups were signifi cantly aided by the presence of contextual cues (p < 0.001), while the presence of contextual cueing brought no variati on in performance within the TDCA group (p = 0.063)
(113)	16	12.58 (5.08–22.66)	64.9 (13.50) [44–87]	MA 6.5 (1.33) [4.1–11.2]	ASD + TDMA + TDCA	Processing of motor acti on	ANOVA	In the presence of context cues, children with WS were as accurate as children with the same chronological age and children with the same mental age in determining why others perform specifi c motor acti ons. Amount of errors made by all groups did not dif fer
(114)	29	19.1 (13.1–32.1)	68.1 (12.8) [45–94]	–	Learning/intellectual disability + TDCA	Identifi cati on of dynamic facial expression (labeling task)	ANOVA	Parti cipants with WS were less accurate than controls with TDCA (p < 0.001). But they were as accurate as parti cipants with intellectual disabilities (p = 0.87)
(115)	21	7.16 (4.5–8.58)	68 (12) [43–93]	VMA 4.91 (1.33) [3.1–8.2]	Prader-Willi syndrome (PWS) + NMR	Percepti on of facial expression (picture-to-picture matching task) Ability to infer f rst-order false beliefs (similar to the Sally-Ann task) Af fecti ve ToM (explanati on of acti on task)	Chi-square test	On the false belief questi on, more of the MRU and PWS children passed than did the WMS children (p < 0.06). The three groups performed at a similar level in picture-to-picture matching test and the explanati on of acti on task
(116)	30	9.91 (5.00–17.08)	–	–	TD	Ability to infer f rst-order false beliefs (task similar to the Sally-Ann task but presented in video and without narrati ve)	Fisher's exact test	More parti cipants in the WS group failed the false belief questi on in contrast to the TD group (p = 0.001)

Table 6 | Emotion processing among rare neurodevelopmental syndrome.

	22q11.2DS	Fragile X syndrome	Klinefelter syndrome	Prader-Willi syndrome	Ret syndrome	Turner syndrome	Williams syndrome
Basic facial emotion percept	Deficit in anger, fear, and sadness percept in comparison with typically developing matched on chronological age (TDCA) partcipants. No deficit in disgust and happiness percept	No obvious deficit in basic facial emotion percept in comparison with TDCA partcipants		Not deficit in basic facial emotion percept compared to partcipants with WS			Not deficit in happiness, sadness, anger, and surprise percept [typically developing matched on mental age (TDMA)]
Spontaneous expression of facial		Not deficit in happiness and disgust percept in comparison with typically developing (TD) partcipants			Deficit in happiness, sadness, and fear percept in comparison with TDCA partcipants		
Basic static facial emotion percept	Deficit in fear, anger, disgust happiness, and sadness percept in comparison with TDCA partcipants	Deficit in anger, sadness, and disgust percept in comparison with TDCA partcipants	Specific deficit in anger percept	Deficit in all basic emotion percept in comparison with TDCA partcipants		Specific deficit in fear and anger percept	Deficit in all basic emotion percept in comparison with TDCA partcipants; no deficit in basic facial emotion percept in comparison with TDMA partcipants
Basic dynamic facial emotion percept	Not deficit in basic dynamic facial emotion percept in comparison with TDCA partcipants					Not deficit in fear percept	Deficit in all basic emotion percept in comparison with TDCA partcipants
Complex facial emotion percept	Deficit in complex facial emotion percept (TD)	Deficit in complex facial emotion percept (TD)		Deficit in complex facial emotion percept (WS)			Deficit in static complex facial emotion percept but no deficit in dynamic facial emotion percept ("deciding," "not sure," and "worried") in comparison with TDCA partcipants
Emotion percept in auditory stimuli	Not deficit in emotion percept in auditory stimuli in comparison with TDCA partcipants					Deficit in emotion percept in auditory stimuli in comparison with TDCA partcipants	Deficit in all emotion percept in comparison with TDCA partcipants except happiness in comparison with TDCA partcipants

Table 7 | Theory of mind among rare neurodevelopmental syndrome.

	22q11.2DS	Fragile X	Prader-Willi	Turner	Williams
Ability to infer first-order false-belief	Deficit in first-order false-belief inferring in comparison with typically developing matched on chronological age (TDCA) participants	No deficit in first-order false-belief inferring compared to participant with DS or non-specific mental retardation	Deficit in first-order false-belief inferring in comparison with TDCA participants but no deficit compared to participants with WS or non-specific mental retardation		Deficit in first-order false-belief inferring in comparison with TDCA participants, but no deficit compared to participants with Prader-Willi syndrome (PWS) or non-specific mental retardation
Ability to infer second-order false beliefs	Deficit in second-order false-belief inferring (for only younger participants) in comparison with TDCA participants	Deficit in second-order false-belief inferring in comparison with TDCA participants but no deficit compared to participants with WS or non-specific mental retardation			Deficit in second-order false-belief inferring in comparison with TDCA but no deficit compared to participants with PWS or non-specific mental retardation
Affective theory of mind (ToM)	Deficit in affective ToM in comparison with TDCA participants	No deficit in ToM affective compared to participants with WS or non-specific mental retardation		Deficit in affective ToM in comparison with TDCA participants	No deficit in affective ToM compared to participant with PWS or Nonspecific mental retardation
Cognitive ToM	Deficit for only younger participants in cognitive ToM in comparison with TDCA participants	Deficit in cognitive ToM in comparison with TDCA participants			Not deficit for a verbal task [typically developing (TD)] but deficit with a visual task (TD)
Ability to spontaneously state at tribute mental state	Spontaneously at tribute mental state disability in comparison with TDCA participants			Spontaneously at tribute mental state disability in comparison with TDCA participants	Spontaneously at tribute mental state disability (not comparison group)

Chapitre 3

Entraînement de la cognition sociale : le programme

RC-KID

RC-KID est un programme visant à travailler 1) la reconnaissance de 5 émotions de bases (la joie, la tristesse, la colère, la peur, le dégoût), 2) les comportements adaptés lors d'une situation sociale (compétences émotionnelles). Ce programme s'adresse aux enfants, âgés entre 5 et 11 ans, quels que soient leur niveau de fonctionnement et leurs compétences intellectuelles. Il est personnalisable et ajustable en fonction du profil de l'enfant. Il se décline donc après une évaluation neuropsychologique, fonctionnelle et comportementale complète. Cela permet de déterminer les troubles présents, leur sévérité et leur impact dans la vie quotidienne et d'adapter les prises en charge aux forces et faiblesses de l'enfant. Ce chapitre, dans une présentation générale du programme, reprend succinctement les définitions de la cognition sociale et des compétences émotionnelles, puis présente de manière générale le programme (axes d'intervention, le matériel, l'organisation d'une séance). Il présente ensuite les différents exercices qui composent l'intervention. Enfin la dernière partie de ce chapitre s'attardera sur les principes thérapeutiques du programme RC-KID, basés sur la remédiation cognitive.

Présentation générale

Définitions : la cognition sociale et les compétences émotionnelles

La cognition sociale est définie comme l'ensemble des processus qui permettent aux individus de percevoir, d'interpréter rapidement, sans effort et de manière flexible, les informations sociales en constant changement et ainsi d'y répondre de manière appropriée. Plus spécifiquement, la cognition sociale comprend le traitement des informations émotionnelles (la reconnaissance des expressions faciales, la prosodie, les postures ou les

gestes), la perception et les connaissances sociales, la Théorie de l'Esprit et le style d'attribution (Green et al 2005).

La reconnaissance des expressions faciales est sous-tendue par des mécanismes cognitifs tels que l'exploration efficiente d'un visage et le mimétisme. Durant l'enfance nous développons notre capacité à explorer le visage, à extraire et intégrer les informations des mouvements faciaux de manière efficiente (Gosselin, 2005). Chaque visage possède la même configuration (les yeux sont en haut, le nez au milieu, la bouche en bas) mais la distance entre chaque partie du visage ainsi que leur « forme » se modifient selon les expressions. De la sorte, pour une reconnaissance efficiente nous focalisons notre attention sur les parties des visages les plus informatives, en favorisant la zone des yeux (Hernandez et al., 2009), nous extrayons chaque modification locale et la distance entre chaque partie que nous intégrons dans une représentation globale du visage. Au regard de la théorie des neurones miroirs (Rizzolatti, Fabbri-Destro 2008 ; Iacobini & al 2005), le mimétisme ou notre tendance à imiter les expressions faciales que nous observons facilite notre reconnaissance des expressions (Gallese et al., 2004 ; Hatfield et al., 2009; Niedenthal, 2007). Nous activerions nos propres connaissances motrices et nos propres expériences émotionnelles pour comprendre les émotions d'autrui.

La Théorie de l'Esprit est définie comme la capacité d'un individu à inférer des états mentaux à autrui ou à lui-même. Les états affectifs ou cognitifs d'autrui ainsi que leurs causes sont déduits à partir de la prosodie, le langage gestuel, de leur connaissance supposée de la réalité, du contexte de la situation sociale. L'accès à ses propres connaissances, ses propres expériences émotionnelles et les situations sociales permet également à l'individu de comprendre, d'anticiper les réactions d'autrui.

Ainsi dès son plus jeune âge (dès 12 mois), l'enfant commence à moduler son comportement en fonction des mouvements du visage de son interlocuteur et du contexte de la situation : le froncement des sourcils, intimant à l'enfant de cesser son comportement, le sourire encourageant l'enfant (Doi ,et al., 2010; Hertenstein & Campos, 2004; Matsunaka & Hiraki, 2014; Striano & Rochat, 2000 ; Striano & Vaish, 2006). Les études ayant évalué l'ensemble de ces compétences émotionnelles chez l'enfant, dès l'âge préscolaire, (Denham et al., 2003 ; Deneault et al., 2011 ; Deneault, et Ricard, 2013; Dodge, Laird, Lochman, & Zelli, 2002; Gal-Szabo., Spinrad, Eisenberg, Sulik, 2019; Nader-Grobois et al., 2013) suggèrent qu'elles sont positivement corrélées aux capacités d'adaptation sociale.

La théorie des compétences émotionnelles permet de décrire les liens entre la capacité à reconnaître une émotion, les capacités de la Théorie de l'Esprit et la capacité de l'individu à adopter un comportement adapté. Les compétences émotionnelles sont définies comme la capacité à identifier ses émotions et celles des autres, de les exprimer d'une manière socialement acceptable, de comprendre leurs causes et conséquences, les réguler lorsqu'elles ne sont pas appropriées au contexte ou à leurs objectifs, et les utiliser pour améliorer leur vie (Mayer et Salovey 1997; Mikolajczak 2009). Ces différentes compétences ont une relation hiérarchique entre elles (Kotsou, 2008). En effet, la régulation des émotions suppose dans un premier temps de les identifier puis de les comprendre.

Dans les troubles du neurodéveloppement d'origine génétique, un déficit de la cognition sociale est souvent décrit et entraîne un retrait social, des troubles du comportement et des difficultés d'adaptation. Ces difficultés ne seraient pas seulement dues au QI mais aussi à des mécanismes déficitaires qui s'expriment différemment selon chaque syndrome (Morel et al., 2018). Un trouble de la reconnaissance des expressions faciales pourrait être lié à une exploration des visages atypique ainsi que des difficultés à interpréter les informations faciales lorsqu'elles sont dynamiques (Morel et al., 2018). Lors de l'expression d'une émotion, les individus semblent également avoir des difficultés à faire des liens entre les indices sociaux (e.g prosodie, expressions faciales) et les indices contextuels pertinents et éprouvent ainsi des difficultés à comprendre les causes des émotions (Morel et al., 2018). Enfin beaucoup moins étudié que les stratégies d'exploration visuelles ou la Théorie de l'Esprit, le phénomène de mimétisme semble également déficient dans les populations porteuses d'un trouble de schizophrénie (Varcin 2010). Or le syndrome de 22q11.2DS est associé à un haut risque de développement de troubles psychotiques à l'âge adulte (Gothelf et al., 2005). Ce point précis doit donc également être pris en compte lors de l'entraînement cognitif.

Ces difficultés ne sont pas sensibles aux traitements médicamenteux et sont donc particulièrement invalidants. La remédiation cognitive est une thérapie rééducative agissant sur les troubles cognitifs (voir ci-après la partie "principes thérapeutiques du programme RC-KID"). Cette technique recrute les compétences de la personne pour l'aider à développer ses propres stratégies alternatives afin de contourner ses difficultés cognitives. Ce soin est

particulièrement développé en psychiatrie d'adulte. Son utilisation chez l'enfant demeure plus limitée. Pour répondre aux besoins particuliers des enfants présentant ce type de difficultés nous avons développé le programme RC-KID basé sur les principes de la remédiation cognitive et utilisant du matériel informatique, des activités théâtrales et un eye tracker.

Description des axes d'interventions proposés par le programme RC-KID

Le programme RC-KID s'articule autour de trois grandes étapes qui permettent de développer la cognition sociale en lien avec les compétences émotionnelles. Chaque étape contient des processus spécifiques de la cognition sociale et/ou des compétences émotionnelles (voir figure 1). Chaque séance de l'intervention cible en particulier un de ces processus, en fonction du profil de l'enfant.

<i>Identifier (percevoir puis identifier) une émotion</i>	<i>Exprimer/Ecouter et comprendre une émotion</i>	<i>Réguler et Utiliser une émotion</i>
<ul style="list-style-type: none"> •Extraction et intégration des informations émotionnelles issues de sources multimodales •Connaissances des patterns moteurs d'une expression (e.g. mimétisme) 	<ul style="list-style-type: none"> •Compréhension des causes d'une émotion (e.g. Théorie de l'Esprit) •Conséquences de l'expression d'une émotion sur le comportement d'autrui 	<ul style="list-style-type: none"> •Réguler ses émotions •Réguler les émotions d'autrui

Figure 1 : axes d'intervention ciblant les processus de la cognition sociale en lien avec les compétences émotionnelles

Etape Identifier (percevoir puis identifier) une émotion faciale chez soi et autrui: entraînement des mécanismes sous-jacents à la reconnaissance des émotions faciales, notamment, le mimétisme, et la capacité à intégrer les informations contextuelles issues de sources multimodales (e.g. la prosodie, le langage gestuel, l'environnement social), dont la

capacité à observer de manière efficiente un visage. Il nous semble important dans un second temps de permettre à l'enfant d'exercer ces capacités avec des exercices où plusieurs fonctions cognitives sont sollicitées comme une conversation de la vie quotidienne peut l'exiger (e.g interpréter le langage non verbale de son interlocuteur tout en écoutant et retenant les informations verbales).

Etape Exprimer/Écouter et Comprendre une émotion : entraînements des habilités qui permettent d'interpréter ses émotions et celle d'autrui de manière efficiente notamment la capacité à identifier les causes et les conséquences des émotions (e.g. Théorie de l'Esprit) et les capacités à comprendre les conséquences de l'expression d'une émotion sur autrui : habilités à écouter et exprimer une émotion de la manière la plus recevable pour autrui (utilisation de la DESC et de la communication non violente ; Kotsou 2008, 2009 ; Rosenberg, 2005) .

Etape Réguler et Utiliser une émotion : entraînement des habilités à adopter un comportement adapté pour gérer une émotion notamment la capacité à trouver des stratégies pour réguler ses émotions et celle d'autrui (pour un exemple d'intervention réalisée chez l'enfant : Larson et Lochman, 2011).

Présentation générale du matériel du programme RC-KID

Le programme RC-KID a été conçu avec l'ambition de proposer aux enfants un cadre motivant et ludique. Le matériel du programme (pour une description complète voir, ci-après, la partie "description de l'intervention") comprend des tâches dites papier-crayons créées et/ou personnalisées pour chaque enfant par le thérapeute en fonction de ses besoins et de son profil neuropsychologique, des jeux informatisés basés sur les principes des « serious games » et des jeux de mises en situation sur les principes de jeux de théâtre (improvisation, le théâtre forum).

Organisation d'une séance

De manière générale, la prise en charge est composée de 12 séances d'1h, à raison d'une séance par semaine avec le thérapeute. Chaque séance est composée de trois parties:

(1) tâches dite papier-crayon ciblant un processus des compétences sociales,

(2) tâches informatisées axées sur le même processus,

(3) exercices de mise en situation

A la fin de chaque séance, une restitution du déroulement de la séance (fonctions cognitives ciblées, exercices réalisés, durée de l'entraînement cognitif, qualité de la concentration, de l'investissement) est effectuée aux parents.

Un cahier est délivré à chaque enfant (voir Figure 2), indiquant les activités à réaliser à la maison ou au foyer. Chaque semaine correspond à une page à remplir par l'enfant. Ces activités hebdomadaires visent au maximum le transfert de compétences (les principes thérapeutiques du programme sont détaillés dans la dernière partie de ce chapitre).



Figure 2 : Quelques pages du cahier à la maison

Description de l'intervention

Les tâches papier-crayon

Les tâches papier-crayon sont précédées par un moment informel pendant lequel le thérapeute et l'enfant échangent autour « des moments forts » de leur semaine respective ou de souvenirs de moments émotionnels forts. Ce moment permet de créer avec l'enfant un climat de confiance et lui permet également de prendre conscience de l'impact des émotions au quotidien. Les exercices papier-crayon permettent à l'enfant d'élaborer des stratégies compensatoires qu'il pourra mettre en pratique avec les exercices informatiques. La difficulté de ces exercices est progressive.

Les exercices informatiques

Le programme informatisé est construit autour d'un scénario simple dont les principes de bases sont empruntés à ceux des « serious games ». Un personnage de pirate, avançant de gauche à droite, a pour objectif de ramasser de nombreux trésors afin d'améliorer son score. Il avance fortement lorsque l'enfant donne une bonne réponse et recule légèrement lorsque l'enfant se trompe.

RC-KID propose 7 jeux informatisés regroupés en deux catégories : les jeux proposant des stimuli statiques et les jeux proposant des stimuli dynamiques. Pour chaque exercice, le thérapeute a la possibilité de choisir les émotions à travailler. Certains exercices proposent également d'activer un eye tracker (une fine barre qui est placée sous l'écran de l'ordinateur) afin de regarder avec l'enfant, s'ils le souhaitent, la carte de chaleur correspondant aux endroits de la photo observés par l'enfant.

Exercices avec stimuli statiques

“Où est-ce que je regarde ?” Le portrait d’un acteur exprimant une émotion apparaît en grand écran. Puis il est demandé à l’enfant d’identifier l’expression faciale présentée. Avec l’eye tracker, le thérapeute, peut aider l’enfant à ajuster son regard pour l’observation d’un visage.

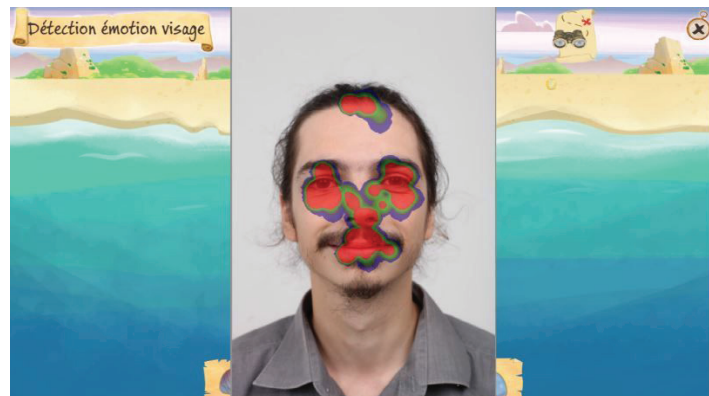


Figure 3: Capture de l'exercice "où est-ce que je regarde ?" pendant l'affichage de la carte de chaleur obtenue à l'aide de l'eye tracker

“Galerie des portraits”. Plusieurs photos d’acteurs exprimant une émotion sont présentées côte à côte. Il est demandé à l’enfant de trouver parmi ces portraits celui qui exprime la même émotion que le caillou en cartoon. Cet exercice permet de comparer les formes des différents éléments du visage (sourcils, bouche, yeux, nez) qui se modifient en fonction des expressions faciales. Il permet notamment de travailler sur les expressions faciales qui sont confondues par l’enfant.

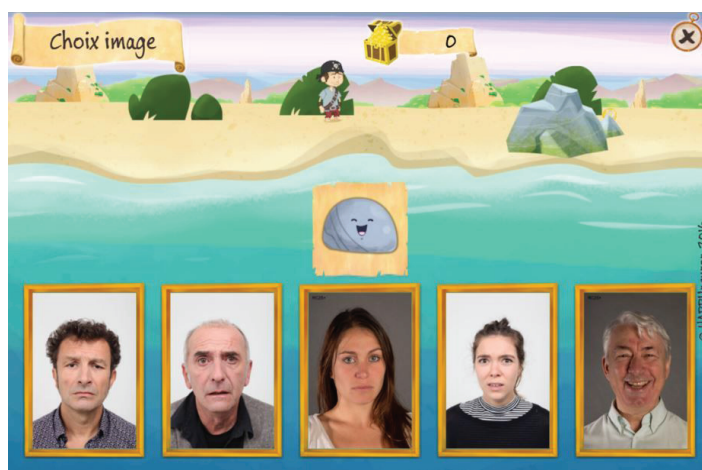


Figure 4: Capture d'écran de l'exercice "galerie des portraits"

“L’album des émotions”. Une photographie représentant une scène sociale dans laquelle les personnages expriment une émotion est présentée en grand écran. L’enfant est invité à identifier l’émotion ressentie par le personnage principal. Dans cet exercice, le thérapeute peut également activer un eye tracker. Ces scènes offrent l’opportunité d’analyser avec l’enfant une scène d’interaction sociale : comprendre les intentions, les désirs, les pensées du personnage principal en émettant des arguments en relation avec le contexte (Théorie de l’Esprit). Les situations sociales sont déconstruites en microstructures (qui, où, quand, quoi) pour que l’enfant prenne en compte leurs contextes (Peyroux & Franck, 2014a, 2014b).



Figure 5: Capture d'écran de l'exercice "album des émotions"

Exercices avec stimuli dynamiques

“Les grimaces et moi”. Un portrait est présenté à l’enfant. Avec l’aide du thérapeute, il est encouragé à imiter l’expression faciale exprimée par l’acteur. Le visage de l’enfant apparaît sur l’écran grâce à une web cam. Cet exercice offre l’opportunité de travailler sur l’expérience concrète du pattern moteur d’une émotion.

“Au ralenti”. Dans une courte vidéo (15s), un acteur exprime lentement une émotion, avec des onomatopées mais sans dialogue. L’intensité de l’émotion exprimée augmente. Durant la vidéo, le thérapeute et l’enfant explorent la dimension dynamique des expressions faciales. La possibilité de mettre en pause la vidéo ou de la redémarrer permet de focaliser son attention sur les mouvements de chaque région d’intérêt (le nez, les yeux, la bouche).



Figure 6: Capture d'écran de l'exercice "au ralenti"

“Petites histoires”. Dans une courte vidéo (15s), un acteur raconte une courte histoire. Il est demandé à l’enfant d’identifier l’émotion exprimée par l’acteur et de répondre à une question concernant l’histoire. Dans les paramètres de cet exercice, le thérapeute peut choisir différents mode de jeu : avec ou sans question. Cet exercice est une double tâche. Il cible la capacité à alterner entre deux canaux de communication (verbal et non verbal).

“En piste”. Élise et Florian sont deux personnages amusants et enfantins. L’enfant est invité à regarder une courte vidéo (scène initiale). Dans cette vidéo, les deux personnages interagissent et vont éprouver une émotion en relation avec la situation qu’ils vivent. Deux ou trois vidéos sont ensuite présentées à l’enfant dans lesquelles Florian et Élise vont exprimer leurs émotions de manière socialement acceptable ou non. Il est demandé à l’enfant de choisir la vidéo “qui est la plus agréable” pour les deux personnages.



Figure 7: Capture d'écran de l'exercice "en piste"

Les exercices de mise en situation

Ces exercices situationnels ont été inspirés par la méthode SAS (Bulgarelli, et al., 2013 ; Rossini et al., 2013). Les bases théoriques de SAS sont la théorie de la «simulation incarnée» et le système des neurones miroirs (Gallese et al 2004). Le thérapeute joue avec la marionnette une situation sociale inspirée de la vie de l'enfant. L'enfant est invité à réécrire la scène afin d'aider le personnage à trouver une solution alternative. Cette méthode a été proposée aux enfants ayant un trouble du spectre autistique (Rossini et al., 2013).

Durant le programme RC-KID, nous proposons des jeux de mises en situation, inspirés du théâtre forum. A partir d'une situation rapportée par l'enfant et/ou ses parents, un canevas/scénario est élaboré. Par exemple, dans le cadre d'un travail sur l'expression de ses émotions, une saynète peut cibler la difficulté d'un enfant à contrôler sa frustration. A partir d'une histoire vécue par l'enfant, elle met en scène l'histoire d'un garçon Léo et de sa grande sœur, Léa, qui mettent leurs chaussures pour sortir jouer dehors. Léa a rapidement mis ses chaussures et veut aider Léo. Léa lui demande de se dépêcher tout en lui apportant son

manteau. Léo ressent un énervement car "ce n'est plus un bébé". Il crie après Léa et jette ses chaussures, son sac. La saynète est jouée avec l'enfant ou des marionnettes selon l'aisance du participant. Selon les principes du théâtre forum, chaque scène est suivie d'une discussion avec le thérapeute afin d'amener l'enfant à réfléchir sur la situation. L'enfant peut choisir de modifier le scénario afin d'explorer avec le thérapeute de nouvelles façon de réagir.

Au fil de la prise en charge, lorsque l'enfant est à l'aise dans les jeux de théâtre nous lui proposons de jouer une scène improvisée. Comme pour une interaction sociale du quotidien, l'improvisation théâtrale, sous couvert de personnage, demande au comédien d'être à l'écoute de son partenaire, de le regarder, l'imiter, exprimer des émotions et de réagir à ces propositions verbales ou non verbales (Tournier, 2003).

L'ensemble de ces activités théâtrales sont l'occasion pour l'enfant de poser un regard sur ses propres attitudes, de prendre conscience de ses comportements et le verbaliser. Elles permettent à l'enfant dans un cadre ludique d'apprendre à exprimer ses émotions, à se revaloriser et à s'affirmer de manière positive.

Afin de proposer à l'enfant un cadre ludique et protégé, pour chaque jeu de mises en situation, nous nous attardons à créer un cadre clair et sécurisant avec des règles précises (Tisseron 2010). Au cours d'une activité théâtrale, le cadre est défini par les différents espaces : la scène et l'espace « public ». L'espace de la scène permet de définir le lieu où l'on joue à faire semblant. L'espace public est le lieu où le thérapeute et l'enfant échangent sur ce qui a été produit, ceci permettant à chacun d'échanger et de s'affirmer. L'enfant étant considéré comme acteur, valoriser son avis, lui demander de parler de son ressenti et d'intervenir sur la scène, lui donne des responsabilités. Les deux espaces ont donc deux rôles différents. Cette notion d'espace instaure un climat de confiance, de sécurité et de clarté entre ce qui est considéré comme du jeu et la réalité.

Les tâches à domicile

La séance d'entraînement cognitif avec le thérapeute se termine par une proposition d'une tâche à domicile. Les tâches sont adaptées aux besoins de l'enfant, tiennent compte de sa réalité quotidienne et sont toujours présentées sous forme de jeux à réaliser en famille (e.g. Créer un jeu de Memory avec les photos de la famille exprimant des émotions ; regarder une courte vidéo et analyser les émotions et les intentions des personnages ; trouver des stratégies pour réguler ses émotions; analyser une interaction sociale de la vie quotidienne et chercher

différents type d'interprétation). Nous avons également proposer de jouer à un jeu de carte que nous avons créé: ces cartes, renouvelées régulièrement, permettaient soit de travailler sur les inférences, l'empathie/comportement prosociaux (Marine mange seule à la cantine. Elle a l'air triste. Que pourrais-tu faire ?), l'expérience émotionnelle (Raconte moi un moment où tu t'es senti en colère ?), les conséquences d'une émotion exprimée de manière socialement acceptable ou non, (Paul a crié très fort sur sa petite sœur car elle lui a pris son jeu *Pokémon*. Comment se sent-elle à présent ?), la gestion des émotions : (quand je suis en colère, j'ai envie de ? Choisis une solution pour que ton émotion se calme), la gestion des conflits (Martin te demande de lui donner ton goûter. Comment te sens-tu ? Que ferais-tu ?).

Les exercices à domicile sont utiles pour promouvoir le transfert de stratégies à la vie quotidienne et leur automatisation subséquente. Afin de promouvoir la motivation pendant la tâche à domicile, l'utilisation du cahier d'exercices personnalisé permet une évaluation hebdomadaire concrète du degré de réalisation de la tâche.

Principes thérapeutiques du programme RC-KID

Le programme RC-KID s'appuie sur les principes thérapeutiques de la remédiation cognitive (RC). La RC vise la restauration des processus cognitifs altérés ou la compensation des déficits. Ces deux approches sont sous-tendues par des bases théoriques différentes. Ainsi, l'approche restauratrice (d'inspiration piagétienne) passe par l'entraînement direct de fonctions potentiellement altérées, alors que l'approche par compensation implique l'acquisition de nouvelles stratégies de traitement de l'information. Cette dernière approche semble particulièrement adaptée dans le cadre des troubles du neurodéveloppement.

Une évaluation neuropsychologique complète et détaillée est un préalable indispensable au suivi en RC (Chesnoy et al., 2013) afin de déterminer les troubles présents, leur sévérité et leurs impacts dans la vie quotidienne de l'enfant ou de l'adulte. Ensuite, la remédiation par un thérapeute est un facteur clef du succès du traitement psychologique, quelle qu'en soit la nature (Bentall 2009). L'enfant et le thérapeute vont déterminer conjointement les objectifs de la prise en charge et les réactualiser, au besoin au cours des séances (Vianin, 2013). Feuerstein (1996) décrit cette situation comme une «mediated

learning experience». Le thérapeute encourage la personne à prendre part activement à la prise en charge et va s'appuyer tout au long des séances sur :

- Le renforcement positif : Le renforcement positif est défini comme la conséquence d'un comportement qui permettra d'augmenter la fréquence d'apparition du comportement en question. Un manque de motivation a un impact négatif sur l'efficacité, le transfert et le maintien des bénéfices de la RC. Le renforcement positif permet ainsi de développer et de maintenir une dynamique de motivation.

- La verbalisation : Cette technique s'appuie sur l'idée que l'élaboration d'une solution face à un problème et l'exécution de la dite solution repose sur un langage interne (Fassoti & Spikman, 2004). Elle permet à la personne d'internaliser les étapes de la stratégie, sans l'intervention du thérapeute. L'utilisation de la stratégie est alors idéalement automatisée et généralisable. La personne est donc en mesure de développer des stratégies compensatrices en s'appuyant sur la sphère verbale.

- L'accompagnement métacognitif : L'efficacité d'un programme de RC est corrélée aux capacités d'un sujet à comprendre son propre fonctionnement pour déterminer de nouvelles stratégies. Au début du suivi, une séance de psychoéducation peut être proposée afin d'expliquer à l'enfant ses points forts et ses points faibles et leurs répercussions dans la vie quotidienne (Bussy et al., 2013). Au cours du programme de RC, le thérapeute va détailler les différents processus cognitifs impliqués (Galbiati et al., 2009) afin de donner du sens aux exercices. Les fonctions cognitives sollicitées et leurs possibles améliorations sont ainsi mises en perspective avec les bénéfices attendus dans la vie courante.

- L'organisation temporelle : Le thérapeute doit prendre en compte les capacités attentionnelles des enfants. Les feedbacks réguliers et les renforcements immédiats constituent des systèmes de récompenses qui jouent un rôle très positif dans le soin. Les séances doivent être organisées clairement, afin d'aider les personnes à faire face aux délais. Le programme de chaque session doit ainsi être présenté et la personne doit pouvoir se représenter la durée de chacun des exercices (e.g. repères visuels à l'aide d'un Time Timer).

Enfin, le but final d'un programme de RC est d'améliorer la qualité de vie de la personne, en lui permettant d'appliquer les stratégies développées pendant les séances de RC dans un contexte plus général, écologique. Le transfert à la vie quotidienne est donc

indispensable. Ensuite, pendant la prise en charge, le thérapeute et l'enfant établissent systématiquement des liens entre les compétences acquises lors des séances et les objectifs initialement définis. Pour faciliter ce travail, des activités à domicile peuvent être réalisées entre chaque séance (Vianin, 2013). Il est désormais acquis que les personnes présentant des troubles cognitifs légers utilisent d'eux-mêmes des stratégies de compensation si le type de tâche le permet (Bray et al., 1998). Malheureusement, peu de travaux portent sur cette question.

Chapitre 4

Social cognition training with eye-tracking feed-backs in 22q11.2 deletion syndrome: the RC-KID program

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Abstract

Poor social skills and functioning are a major characteristic of children with 22q11.2 deletion syndrome and are partly linked with social cognitive impairments. Patients have difficulties in recognizing facial emotions and this impairment may be related to an atypical observation of faces. Here we assess the efficacy of a new individualized social cognitive training program using computerized materials and online eye-tracking feedbacks. We conducted three single-case studies, using a multiple baseline and ABA design with children with 22q11.2 deletion syndrome. After the treatment phase, we found a significant improvement of children's skills in affect recognition and emotion understanding, thanks to the use of eye-tracking device allowing the participant to correct their visual scanpaths online during the task. This pilot study provide further significant data showing that social cognitive training based on eye-tracking feed-backs are a promising way for helping people with 22q11.2 deletion syndrome to change their visual scanpaths of face and compensate for their social cognitive impairments.

Keywords: 22q11.2 deletion syndrome, emotion processing, social cognitive training, eye-tracking, social functioning.

Introduction

22q11.2 deletion syndrome (22q11.2DS) is a rare disease leading to a wide range of manifestations including a frequent psychiatric phenotype, and notably an increased risk for developing schizophrenia (Gothelf et al., 2007). In childhood, poor social skills and functioning compared to typically developing peers are a major characteristic of children with 22q11.2DS (Woodin et al., 2001). These difficulties could be related to impairments of social cognition (SC) (Jalbrzikowski et al., 2012), which refer to mental operations that enable people to perceive and to interpret constantly changing social information (Couture et al., 2006). Social cognitive processes allow a rapid, effortless and flexible perception and interpretation of rapidly-changing social information. It includes heterogeneous cognitive dimensions such as emotional information processing, social perception and knowledge, Theory of Mind (ToM) and attributional bias (Green et al., 2008).

Individuals with 22q11.2DS exhibit impaired emotion processing. They actually have difficulties to perceive facial emotions when they are moderately expressed, as frequently observed in daily life (Leleu et al., 2016, 2019). Facial emotion labeling is also impaired (Campbell et al., 2010; Goldenberg et al., 2012; McCabe et al., 2013; 2011 2016; Vangkilde et al., 2016). A study using dynamic facial expressions showed that individuals with 22q11.2DS had similar performances than controls with typical development in terms of accuracy of responses but were significantly slower to recognize emotions (Franchini et al., 2016). Moreover, in emotion recognition tasks, people with 22q11.2DS made significantly more intrusive errors (one emotion is mistakenly perceived as another) than healthy controls (Leleu et al, 2016; Peyroux et al., in press). These results suggest that emotional categories may be less sharply defined in people with 22q11.2DS, which leads to greater confusions between emotions.

The facial emotion recognition impairment in 22q11.2DS may be related to an atypical observation of faces (Hernandez et al., 2009; Glaser et al., 2010). Indeed, preliminary studies have reported that facial features (eye, nose and mouth region) are salient for accurate emotion recognition. However, using eye tracker, previously data suggest that individuals

with 22q11.2DS display an atypical gaze exploration of face, characterized by fewer fixations on salient features, especially the eye area (Campbell et al., 2010) in favor of the mouth (McCabe et al., 2013; Zaharia et al., 2018).

Social cognitive dysfunction has been proposed by some authors as a viable predictive factor of psychosis in 22q11.2DS (Jalbrzikowski et al., 2012; Antshel et al., 2010; Weinberger et al., 2016; Badoud et al., 2017). Actually, people with 22q11.2DS and psychosis have more severe social cognitive impairments than non-psychotic patients, and these deficits seems to precede the onset of psychosis. Therefore social and communication skills enhancement appears to be a major challenge for a personalized care in this population.

Since few years, several social cognitive training programs (SCT) have been developed to improve social cognitive capacities especially in neurodevelopmental and psychiatric area. SCT acts as a complement to medication, speech therapy, motor skills and behavioral therapies. SCT have been notably developed and tested in children with autism spectrum disorders with significant positive results on both emotions, mental states recognition, and social skills (Beaumont & Sofronoff, 2008; Bolte et al., 2002; Golan et al., 2009; Serret et al., 2014; Silver & Oakes, 2001; Tanaka et al., 2010). Concerning 22q11.2DS, the “Vis-à-Vis” program (Glaser, et al, 2012) was designed in French and tested with children with 22q11.2DS (Karagöz-Üzel, et al., 2018). These SCT have durations ranging from 4 to 12 weeks and appear to significantly improve facial emotion recognition (Bolte et al., 2002; Golan et al., 2009; Karagöz-Üzel, et al., 2018; Serret et al., 2014; Rice et al, 2015).

However, the interpretation of facial movements involves visual processes (visual exploration of the face, dynamic information processing), knowledge based on individual’s experience (integration of context, emotional experience) and processes underlying emotional experience (theory of simulation and mirror neuron system). Yet most of the SCT programs only offer static stimuli (drawings or pictures). Moreover, despite the importance of focusing on salient features for emotion recognition, current SCT programs take into account neither the individual development of gaze direction strategies nor the presence of a specific genetic developmental disorder.

To overcome these findings, we developed the RC-KID program, as a new SCT using eye-tracking feedbacks in the perspective of improving visual scanning of faces and thus social skills and functioning. RC-KID was designed as an individualized SCT focusing on

main emotional processes (sadness, joy, disgust, surprise, etc.) for children and young adolescents with neurodevelopmental disorders.

Previous to the elaboration of the RC-KID program, we conducted a systematic review of the literature to enhance knowledge about social cognitive profiles in neurodevelopmental disorders (Morel et al., 2018). As a result, RC-KID targets: (1) recognition of isolated expressions (2) facial expression imitation and (3) adapted behavior during social interactions. In addition, the program is based on the concept of emotional competences (EC) developed by Mayer & Salovey 1997 & Mikolajczak 2009, including the ability in identifying, expressing, understanding, regulating and using own and others' emotions.

The first part of the RC-KID program is based on the recognition of isolated facial expressions. The program is based on an active coaching approach. The therapist encourages the participant to focus on salient feature of emotional faces with the feed-back of the eye-tracking, leading to an accurate gaze direction (Figure 1).

Figure 1:

Example of a heat map obtained with the RC-KID program

It also allows differentiating specific emotion, and notably those that are often perceived as another. The therapist helps the children to determine the particular physiognomy of each emotion and the key elements of the face (for example the frowning eyebrows for “anger”). Taking into account the dynamic aspect of emotions, RC-KID is composed of six exercises regrouped in two categories: static versus dynamic stimuli. Dynamic stimuli aim at generalizing specific trained emotion recognition skills to real-life situations.

The second part of the RC-KID program is dedicated to the understanding of social context according to emotional situations. In addition, the therapist helps the child to self-determine the impact of his/her emotions on his/her behavior. Finally, computerized exercises allow the therapist highlighting how the emotions, and notably there expression, can influence others' behavior. Finally, some exercises allow the regulation of physical sensations during emotional experience.

In order to promote participant's motivation, which is an essential element for successful training (Schunk & Zimmerman, 2007) the RC-KID program is based on an

attractive and ludic computer interface, with direct feedbacks and positive reinforcements (Figure 2). Moreover, each SCT session ends with the proposal of a home-based task in collaboration with the parents or the educational team (eg, creating a memory game with pictures of family expressing emotions; watching a short movie and analyzing the emotions and intentions of the characters; finding strategies to manage emotions; analyzing of a social interaction and searching for different interpretations). Exercises take into account the level of performance of the participant, and are related to the concrete objectives defined at the beginning of the RC-KID program.

Figure 2

Screen capture of the RC-KID program: an exercise with dynamic stimuli.

In this pilot study we present preliminary results of RC-KID program efficiency in 22q11.2DS using single cases studies.

Method

Participants

Three French speakers and clinical stable children with 22q11.2DS (one girl and two boys) aged from 6 to 11 years old were enrolled in these single cases studies. For each participant, the diagnosis of 22q11.2DS was confirmed by array-CGH and FISH. Children exhibited neither a severe neurological phenotype nor an intellectual deficiency according to DSM-V criteria, and they were not included in another SCT or cognitive remediation program. They were considered clinically stable without any psychotropic medication. The characteristics of the participants are summarized in Table 1.

Assessments

A complete and detailed behavioral, cognitive and functional assessment have been proposed to each participant prior to the SCT, thanks to the Wechsler Intelligence Scale for

Children fourth or fifth edition (WISC-IV or V; Wechsler, 2003; 2014), the Vineland Adaptive Behavior Scale, second Edition (Sparrow, Cicchetti, et Balla, 2005), the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS-PL, Kaufman, 1997) and the Aberrant Behavior Checklist (ABC, Aman 1985).

Concerning social cognition, emotion recognition was assessed thanks to:

The subtest “affect recognition” of the NEPSY-II (Korkman, M., Kirk, U., & Kemp, S. 2007) which assess the ability to match pictures of children expressing basic emotions. For the study, we selected the global raw score that is the number of correct answers.

The TREF (Gaudelus et al., 2014) allows evaluating ability to identify facial emotions. The test is composed of 54 photos of adults expressing joy, anger, sadness, fear, disgust or contempt and each emotion is represented at nine intensity levels from 20 to 100%. The TREF is designed for adults, thus we selected two raw scores for the study: the total percentage of emotions recognized and the total detection threshold that is the intensity level necessary for emotions to be recognized with certainty.

ToM abilities have been measured through:

The subtest “theory of mind” of the NEPSY-II (Korkman, M., Kirk, U., & Kemp, S. 2007). This test is composed of two tasks. In the verbal task, the participant had to answers questions about various stories or pictures that require understanding another individual’s point of view. The contextual task assesses the capacity to select a photo depicting the appropriate affect of a young girl presented in a social context. We selected two raw scores: the total score and the verbal score.

The Reading the Mind in the Eyes Test – Child version (RMET, Baron-Cohen et al., 2001) assess the ability to identify complex emotional states in 28 images of eyes, with forced choice between 4 mental-state terms for each. For the study we selected the total score of correct answers on 28.

The ToM-15 (Desgranges et al., 2012) is a false belief task designed for adults with 15 stories (8 stories of first-order false believe and 7 stories od second-order) allowing assessing cognitive dimension of ToM. This test is designed for adults, thus for the study we measure three raw scores: the total score of correct answer, the first-order score and the second-order score.

Results of the three participants are summarized in Table 1.

Table 1:

Clinical data of the three participants before the therapy and Pre-post comparison of functional and social cognitive assessment for patients A, B and C

Study design

An ABA single subject design has been used to assess the effectiveness of the RC-KID program. This design involves a comparison between experimental time periods, known as phases with: (A) a phase with three baseline sessions separated by a 1-week interval to assess the stability of measures; (B) training sessions conducted for 45 minutes per week for a total of 12 weeks; and (A) another phase with three baseline sessions at a 1-week interval to assess both the stability of measures and the evolution of performances, have been proposed. The program design is resumed in Figure 3.

Three kinds of baselines have been collected before and after the intervention:

- Targeted component - Specific Baselines (SB)
 - Emotion identification (SB1): composed by 18 photos, including 6 of children, 6 of women and 6 of men extracted from “Mind Reading” (Baron-Cohen, et al., 2004). Participant had to determine the emotion depicted. A total score on 18 is measured on each baseline.
 - Emotion comprehension (SB2): 10 short stories derived from the Test of Emotion Comprehension (Pons & Harris 2000) have been proposed. The patient answered questions about the mental states of the characters depicted in the stories and a total score on 16 is calculated.
- Untargeted component - Aspecific Baselines (AB)

It measures visual memory, a neurocognitive process that should not be affected by the intervention. Participants had to memorize from 3 to 7 abstract or realistic shapes by plate presented (extracted from Blaye & Bonthoux, 2001). A score on 24 is measured.

- Generalization - Intermediary baselines (IB)

It measure cognitive function linked with targeted processes but that are not directly concerned by the SCT. The improvement of this measure would evidence the generalization of benefits. We selected a task of entangled objects (extracted from a game created by the SBT group). Participants has to identify specific objects (like flowers, fruit, animals, geometrical figures, or amoebas) composing a more complex figure. This task assesses visual perception skills, and notably the ability to extract information from a surrounding gestalt, which seems important to accurately recognize emotional faces (Leleu, et al., 2016). A total score on 18 is calculated for each baseline session.

Figure 3:

Description of the design of the single case studies

Statistical analyses

Data from all pre-therapy and post-therapy sessions were collected. For each participant, we obtained a 2*k statistical plan, 2 being the two (pre and post) measurement phases and k being the baselines with four modalities: Emotion identification (SB1), emotion comprehension (SB2), Visual memory (AB) and Entangled objects (IB). We checked for each patient that the three measures performed for each baseline at a weekly interval prior to the therapy (pre-therapy) and after the treatment (post-therapy) were stable. This excluded the possibility that the results might be linked to natural behavioral evolution or test-retest effect.

Statistical analyses were conducted with the Q' (Michael, 2007), which is the equivalent of a non-parametric analysis of variance (ANOVA) based on proportions. The Q' allows testing the hypothesis of equal proportions and proportion differences in 2*k plan (comparison of two phases in k tests or conditions). The analysis of the difference between pre-and post-therapy scores was performed using the standardized Mellenbergh & Van den Brink Test (1998) for evaluations for which the standard deviation of the reference control population is known, and with the Q' Test (Michael, 2007) for measures for which the standard deviation of the population control is unknown.

Results

Patient A

At the end of the treatment phase, the interactions between factors (measurement phases and baselines) were significant ($Q'(3)=8.63$; $p=0.0346$). We observed significant main effects between pre- and post-therapy measures ($Q'(1)= 17.26$; $p<.0001$) and between the various baselines ($Q'(3)=13.17$; $p=0.0043$). Multiple comparisons were carried out to analyze these results.

Concerning specific baselines, significant improvements of both “emotion identification” (SB1) ($q'=4.72$; $p<.001$) and “emotion comprehension” (SB2) ($q'=3.25$; $p=0.014$) measures were highlighted. We also documented a significant enhancement of “entangled objects” (IB) score ($q'=2.88$; $p=0.040$). In accordance with our assumption, any evolution of “visual memory” (AB) score have been observed ($q'= 0.69$; $p = 0.925$) (Figure 4).

Figure 4:

Comparisons between the 2 phases (pre and post) in the 4 baselines for patient A.

Patient B

Significant interactions between factors have been observed at the end of the treatment phase ($Q'(3)=8.75$; $p=0.0328$) with significant main effects between pre- and post-therapy measures ($Q'(1)=14.53$; $p=0.0001$) and between the baselines ($Q'(3)=20.28$; $p = 0.0001$). Multiple comparisons were performed to analyze these results. Concerning specific baselines, we highlighted a significant improvement of both “emotion identification” (SB1) ($q'=3.36$, $p=0.01$) and “emotion comprehension” (SB2) ($q'=4.45$; $p<.001$) scores, “entangled objects” (IB) measure enhanced also significantly ($q'=2,93$; $p=0.035$) without evolution of “visual memory” (AB) score ($q'=0.35$ $p=0.989$) (Figure 5).

Figure 5:

Comparisons between the 2 phases (pre and post) in the 4 baselines for patient B.

Patient C

The interactions between factors at the end of the treatment were also significant for patient C ($Q'(3)=10.98$; $p = 0.0118$). We observed significant main effects between pre- and post-therapy measures ($Q'(1) = 8.22$; $p =0.0041$) and between baselines ($Q'(1) = 8.22$; $p =0.0041$). Multiple comparisons were also conducted.

For specific baselines, we observed a significant improvement of both “emotion identification” (SB1) ($q'=2.90$; $p= 0.038$) and “emotion comprehension” (SB2) ($q'=3.17$; $p=0.018$) scores. Concerning intermediary baseline, the “entangled objects” (IB) score enhanced significantly ($q'=2,93$; $p=0.035$). In accordance with our assumption, any evolution of “visual memory” (AB) score have been observed ($q'=0.70$; $p=0.920$) (Figure 6).

Figure 6:

Comparisons between the 2 phases (pre and post) in the 4 baselines for patient C.

Pre/post comparisons of social cognitive and functional assessments for patients A, B and C are summarized in Table 1.

Discussion

Since 22q11DS is a common genetic condition and the highest risk factor for schizophrenia among genetic disorders (1-2%), the public health impact from the psychiatric morbidity associated with this syndrome is significant. This makes it imperative to develop effective cognitive and behavioral interventions. Considering the high impact of social cognitive dysfunctions in psychotic processes, SCT is a key to enhancing the future prognosis and functional outcomes in patients with 22q11.2DS.

A large body of research has investigated the recognition of emotions from facial expression and reported that 22q11DS individuals exhibit difficulties in discriminating or identifying facial emotional signals. Impaired detection of facial emotions and abnormal visual exploration of expressive faces have also been described, leading to elaborate customized remediation care plans. The RC-KID program was constructed taking into

account these main principles. We decided to develop a new SCT program specifically dedicated to children and adolescents with neurodevelopmental disorders (named RC-KID) by using eye-tracking feedback to improve face-related visual scanning skills.

Here, we show that the RC-KID program resulted in significantly and specifically improved social cognitive functioning. The three cases presented here highlighted improvement in children's skills in targeted processes, i.e., emotion recognition and understanding. These improvements were emphasized through specific baselines for each participant. The results also show improvements in an intermediate baseline that involves the ability to extract information from a surrounding gestalt, a process that seems important to accurately recognize emotion in faces. Finally, no changes were observed in the baseline that did not involve any of the trained processes. Overall, these results suggested that the RC-KID had an impact on all processes that are necessary for identifying and understanding emotions.

The comparison of social cognitive assessments from before and after the therapy showed mixed results. In fact, patient A improved his performance in emotion labeling as measured by the TREF, but the scores in the NEPSY-Affect recognition task did not reveal any change. Patient A also had significantly improved ToM abilities as measured by the NEPSY-ToM task and by the ToM-15 test, but scores on the RMET, which measure affective ToM, did not change. Regarding patient B, no change in the social cognitive measures was found at the end of the program despite a significant enhancement of baseline performance measuring emotional processes. Patient C had a positive trend with the NEPSY-Affect recognition score, but the TREF score remained unchanged. ToM abilities were significantly enhanced in patient C, as shown through the NEPSY-ToM score. We also noted a significant improvement in the second-order score on the ToM-15. The variability in the improvement according to these assessments can be explained by the baseline level of each participant. In fact, we observed that the lower the performance was before the training, the more significant the improvement was after the therapy. Moreover, our data indicated that the RC-KID program was feasible and associated with a significant level of compliance and satisfaction.

Few previous papers have described the impact of SCT on emotion recognition in children with 22q11.2DS. To our knowledge, RC-KID is the first program that includes regular and timely feed-back. In this respect, our tool design was truly original. Our data are consistent with those obtained with the Vis-à-Vis program (VAV) (Glaser et al., 2012). The VAV program is an SCT of four 20-minute weekly sessions for 12 weeks completed with an

adult and is composed of three modules: focus on the eyes, emotion recognition and understanding, and working memory. A study evaluating the impact of VAV program in children and adolescents with 22q11.2DS compared to both a population of patients with autism spectrum disorders and a population of children with developmental delay in an fMRI task consisting of faces and tools showed a change in activation after treatment (Karagöz-Üzel, et al., 2018). In fact, whereas the 22q11.2DS group showed atypical activation to faces compared to controls before the VAV program, their performances resembled those of controls in the bilateral superior temporal gyrus, insula, bilateral precentral gyrus, right lingual gyrus and right middle frontal cortex after the treatment and three months later. The increased BOLD signal in the right fusiform gyrus in children with 22q11.2DS was linked with improvement in VAV tasks. Unfortunately, no pre/post data concerning social cognition and functioning was assessed in this pilot study.

In the present work, we might actually consider that our specific and significant results on social cognitive functions were linked to the use of an eye-tracking device, which is a novel intervention relative to previous programs. As previously described, several studies using eyetracking technology reported alterations in visual scanpaths during face and emotion processing in individuals with 22q11.2DS compared to controls (Hernandez et al., 2009; Glaser et al., 2010). When looking at faces, children and adolescents with 22q11.2DS spend less time on the eyes region and more time on the mouth compared to controls and developmentally delayed patients (Campbell et al., 2010; McCabe et al., 2013; Zaharia et al., 2018). According to Glaser et al. (2010), the time spent on the eyes may contribute to face processing difficulties and interact with anxiety levels to exacerbate socioemotional dysfunction

Moreover, as suggested by Zaharia et al. (2018), eye-tracking is a promising tool to gather valuable information during face processing, such as the temporal and spatial attention allocated to particular aspects of the stimulus. This pilot study showed that this technology can also be used during SCT to guide the patient to focus on the salient features of faces, allowing better recognition and discrimination of emotions. Considering that people with 22q11.2DS show a bias toward the mouth region during the first two fixations on faces, have longer fixations and spend more time looking at less relevant regions (Zaharia et al., 2018), the use of an eye-tracking device during the SCT allows the participant to correct their visual scanpaths because of the real-time feedback during the task. A limitation of this work is that

we did not analyze the participants' visual scanpaths across the faces before and after the SCT. It would be interesting to assess the impact of the RC-KID program on scanpath patterns and then assess functional activations throughout the brain in regions related to face processing.

Concerning the transfer of the benefits of the program to social functioning, the three patients and their family reported subjective impacts on daily life. However, these subjective impacts were only partly confirmed by the scales assessing adaptive behavior (Vineland II) and aberrant behavior (ABC). Actually, we did not observe any change in these scores in patients A and B. Only a significant improvement of the subscore “excessive speech” on the ABC scale was highlighted in patient C. Patient C is the participant who had the higher scores on this scale before the training. We could thus assume that the RC-KID program had a greater impact on participants with more severe behavioral disorders, but this assumption remains to be verified. Moreover, the assessed measures may have been too different from the aspects of daily life practiced during the RC-KID program. In fact, other measures such as observations in daily life could be adapted to better reflect the patients’ achievements in social functioning than the questionnaires used in our single-case studies.

In conclusion, the RC-KID program is a new promising SCT for reducing social cognitive impairment in children with 22q11.2DS and could also be adapted to other neurodevelopmental disorders presenting the same deficits. A randomized controlled trial needs to be conducted to establish the validity of the RC-KID program in a larger sample of children with 22q11.2DS.

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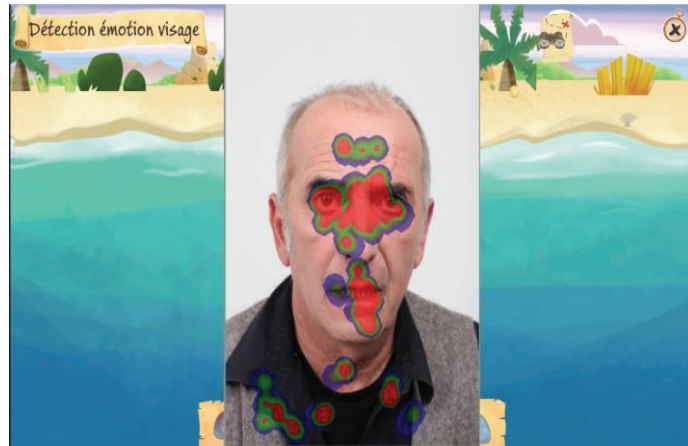


Figure 1: Example of a heat map obtained with the RC-KID program.



Figure 2: Screen capture of the RC-KID program: an exercise with dynamic stimuli.

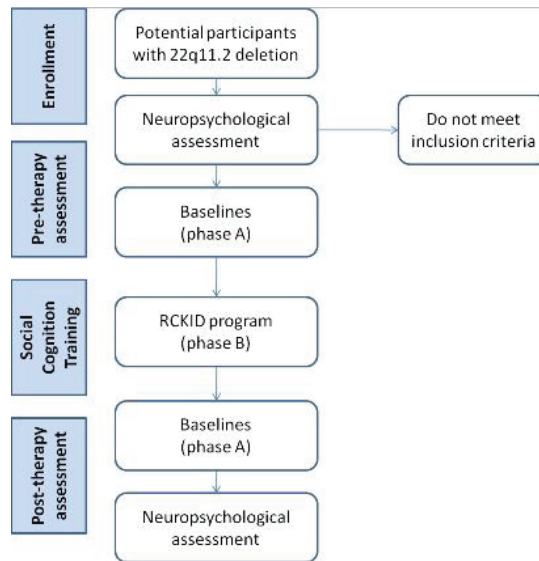


Figure 3: Description of the design of the single case studies

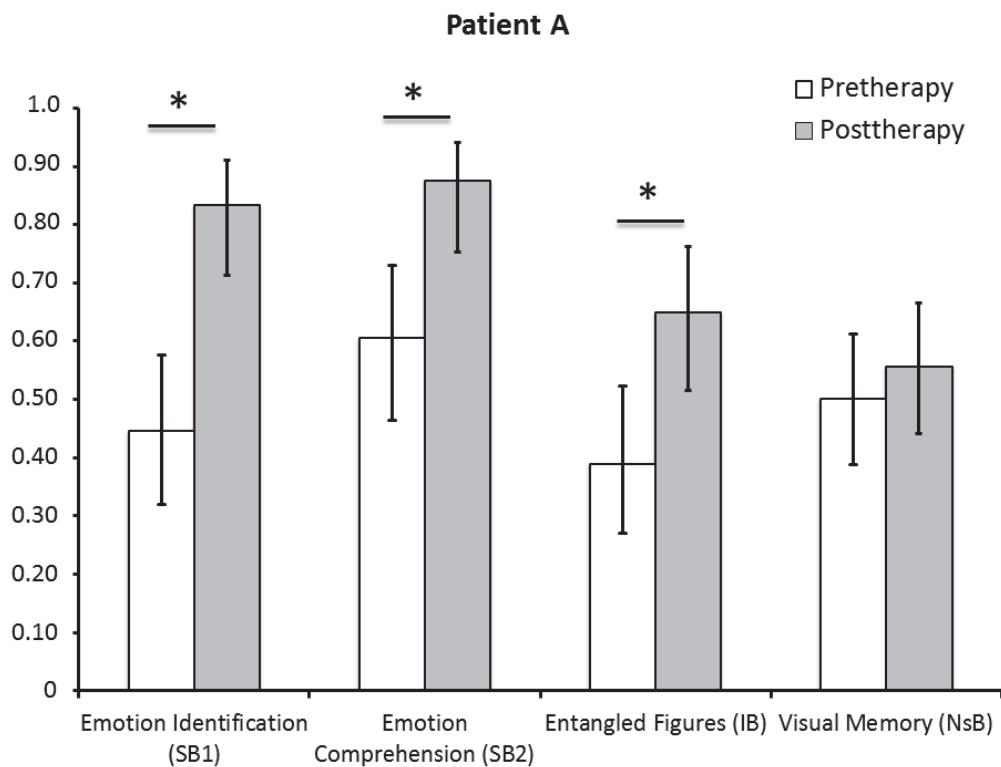


Figure 4: Comparisons between the 2 phases (pre and post) in the 4 baselines for patient A

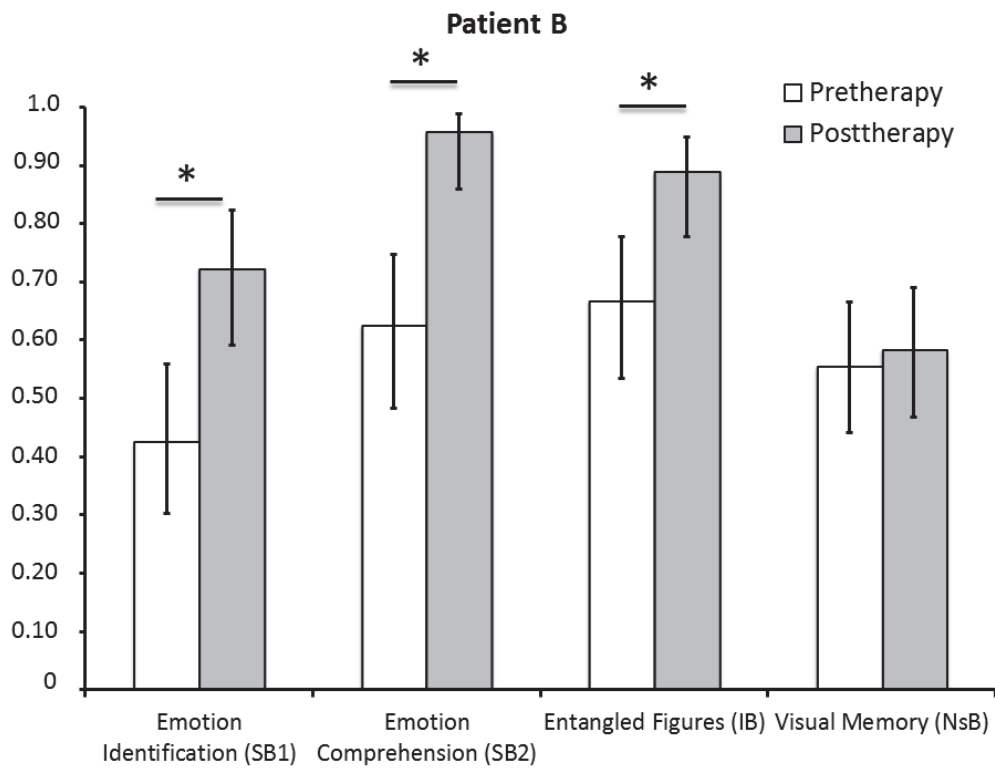


Figure 5: Comparisons between the 2 phases (pre and post) in the 4 baselines for patient B.

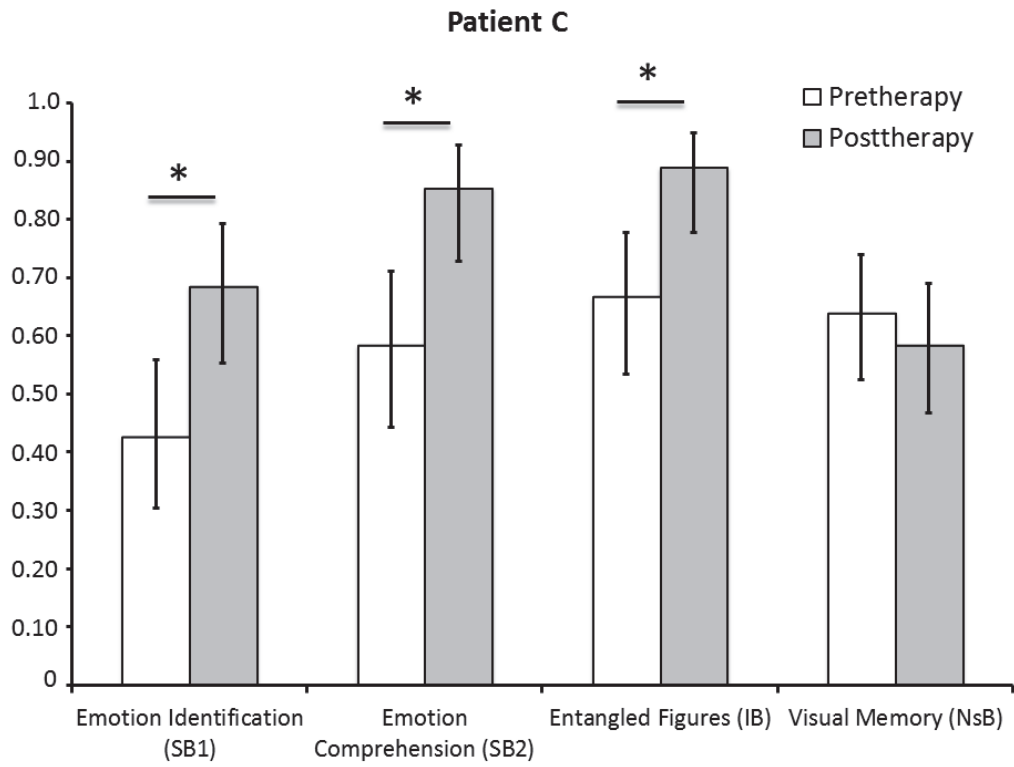


Figure 6: Comparisons between the 2 phases (pre and post) in the 4 baselines for patient C.

Table 1. Clinical data of the three participants before the therapy and Pre-post comparison of functional and social cognitive assessment for patients A, B and C

	Patient A				Patient B				Patient C				
Gender	Female				Male				Male				
Age	6y, 11m				9y, 9m				10y, 6m				
Clinical phenotype	<ul style="list-style-type: none"> Hearing loss Velar deficiency Reduced motor skills 				<ul style="list-style-type: none"> Hearing loss Reduced motor skills 				<ul style="list-style-type: none"> Immune deficiency Anomaly of the aortic arch Reduced motor skills 				
Psychiatric phenotype	<ul style="list-style-type: none"> Anxiety disorder Social dysfunction 				<ul style="list-style-type: none"> Oppositional disorder Social dysfunction Difficulties to maintain relationships 				<ul style="list-style-type: none"> Attentional disorder Oppositional disorder Anxiety disorders Social dysfunction 				
Current therapies	<ul style="list-style-type: none"> Speech therapy 				<ul style="list-style-type: none"> Speech therapy Psychomotricity 				<ul style="list-style-type: none"> Speech therapy Psychomotricity 				
IQ	Index (WISC-IV)		Composite score		Index (WISC-IV)		Composite score		Index (WISC-V)		Composite score		
	Verbal comprehension		81		Verbal comprehension		81		Verbal comprehension		84		
	Perceptual reasoning		99		Perceptual reasoning		107		Visuospatial		92		
	Working memory		94		Working memory		73		Fluid reasoning		76		
Processing speed		106		Processing speed		88		Working memory		97			
Adaptive Behavior Scale – Vineland II	Raw score pretherapy	Raw score posttherapy	Z _{pre-post}	p	Raw score pretherapy	Raw score posttherapy	Z _{pre-post}	p	Raw score pretherapy	Raw score posttherapy	Z _{pre-post}	p	
	Receptive	36	36	0	.5	34	34	0	.5	33	33	0	.5
	Expressive	90	90	0	.5	93	94	-.15	.56	99	99	0	.5
	Written	29	29	0	.5	36	36	0	.5	37	38	-.16	.56
	Personal	58	65	-1,2	.88	70	70	0	.5	70	70	0	.5
	Domestic	9	9	0	.5	19	21	-.16	.56	8	8	0	.5
	Community	48	47	.07	.53	35	35	0	.5	52	52	0	.5
	Interpersonal relationships	58	58	0	.5	47	52	-.44	.67	58	58	0	.5
	Play and leasures time	49	49	0	.5	47	48	-.18	.57	49	49	0	.5
Coping skills	45	45	0	.5	27	30	-.29	.61	25	25	0	.5	
Aberrant Behavior Checklist-ABC	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	
	Irritability (/45)	2	3	.12	.73	19	15	.54	.46	33	24	2,83	.09
	Social withdrawal (/48)	0	0	0	1	9	13	.66	.41	17	11	1,29	.26
	Stereotypy (/21)	0	0	0	1	3	0	1,88	.17	8	5	.76	.38
	Hyperactivity (/48)	1	1	0	1	17	15	.13	.71	39	31	2,41	.12
	Excessive speeh (/12)	0	0	0	1	3	0	2,42	.12	11	4	8,74	.00 **
TREF	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	
Total raw score (DS)	13/54 (-6.87)	40/54 (-0.28)	22,54	<.00****	29/54 (-2.96)	30/54 (-2.72)	.03	.87	31/54 (-2.47)	30/54 (-2.72)	.03	.87	
NEPSY-Affect recognition	Pretherapy	Posttherapy	Z _{pre-post}	p	Pretherapy	Posttherapy	Z _{pre-post}	p	Pretherapy	Posttherapy	Z _{pre-post}	p	
Raw score	18	26	-1.10	.14	27	27	0	.5	21	28	-1,52	.06	
Standard score	9	12			11	10			7	11			
NEPSY-ToM	Pretherapy	Posttherapy	Z _{pre-post}	p	Pretherapy	Posttherapy	Z _{pre-post}	p	Pretherapy	Posttherapy	Z _{pre-post}	p	
Total raw score	13	22	-1.90	.03*	18	22	-.97	.17	15	20	-1,66	.05*	
Standard score	6	51-75			2-5	26-50			<2	6-10			
Verbal score	11	17			14	17			13	15			
Standard score	26-50	51-75			2-5	26-50			<2	6-10			
RMET	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	
Raw score (DS)	7 (-0.98)	14 (0.27)	2,86	.09	10 (-1.72)	15 (-0.66)	1,36	.24	7 (-2.36)	11 (-3.83)	.97	.32	
TOM-15	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	Pretherapy	Posttherapy	Q'	p	
Total score	7/15	13/15	4.69	.03*	13/15	12/15	.17	.67	5/15	10/15	2,95	.09	
First-order score	4/8	7/8	2.49	.11	8/8	6/8	1,64	.20	5/8	6/8	.26	.61	
Second-order score	3/7	6/7	2.85	.09	3/7	6/7	.36	.55	0/7	4/7	5,95	.01*	

WISC: Wechsler Intelligence Scale for Children ; TREF: Test de Reconnaissance des Emotions Faciales ; NEPSY: A Developmental NeuroPsychological Assessment ; RMET: Reading the Mind in the Eyes Test.
 * = p<.05; ** = p<.01; *** = p<.001; **** = p<.0001

Chapitre 5

Discussion

Cette thèse de doctorat avait pour objectif le développement d'un programme d'entraînement de la cognition sociale chez l'enfant, le programme RC-KID. La thèse est composée de deux publications. Le première est une revue de la littérature des troubles de la cognition sociale chez les populations porteuses d'un trouble neurodéveloppemental d'origine génétique et met en lumière les mécanismes déficitaires qui sous-tendent ces habilités dans chaque syndrome. Le second article est une étude pilote évaluant l'efficacité du programme RC-KID (développé à partir des résultats du premier article) chez l'enfant porteur d'une microdélétion 22q11.2. Ce chapitre présente une synthèse des résultats obtenus pour chaque publication et expose leur répercussion clinique. Il résume ensuite les limites de la thèse et propose des pistes d'amélioration du programme RC-KID pour les futures recherches dans le domaine.

Cognition sociale dans les troubles neurocomportementaux d'origine génétique de l'enfant : revue de la littérature .

Résumé des principaux résultats

Un déficit en cognition sociale est un élément prédictif de la qualité de vie des patients porteurs d'un trouble neurodéveloppemental associé à une anomalie génétique et contribue certainement à un retrait social, à des symptômes psychiatriques et à des difficultés d'adaptation. Chaque syndrome cité dans cet article présente un profil de la cognition sociale qui lui est propre notamment concernant la reconnaissance des expressions faciales et la Théorie de l'Esprit (voir chapitre 2).

Les modèles de traitement des visages (Bruce & Young, 1986 ; Haxby & Gobbini, 2011 ; Palermo, O'Connor, Davis, Iron and McKone ; 2013) suggèrent l'existence de deux étapes dans la reconnaissance de l'émotion : la perception et l'identification. La perception est la capacité à analyser la configuration des muscles faciaux comme leur orientation et leurs mouvements. L'identification implique dans un premier temps la perception d'une expression faciale puis dans un second temps les processus impliquant la connaissance des émotions afin d'associer un pattern moteur à une émotion puis à un label (Palermo et al., 2013 ; Wilhelm, Hildebrandt, Manske, Schacht and Sommer, 2014).

La perception des émotions semble perturbée dans la microdélétion 22q11.2, le syndrome de Prader-Willi (PWS) et le syndrome de Williams Beuren (WS) mais préservée dans le syndrome du X fragile (FXS). La capacité à identifier une émotion est déficitaire dans le 22q11.2DS, le FXS, le syndrome de Klinefelter (KS), le PWS, le syndrome de Turner (TS) et le WS. Cependant, ce trouble de la reconnaissance des expressions faciales s'exprime différemment selon les syndromes. En effet, un déficit global est identifié dans le 22q11.2DS, le FXS, le PWS et le WS, alors qu'un déficit spécifique (touchant une ou deux émotions) est rapporté dans le KS et le TS. Dans ces deux syndromes, ces résultats suggèrent que le déficit ne serait pas seulement dû à un trouble du développement mais serait spécifique au syndrome.

La nature des stimuli (statiques vs dynamiques) joue également un rôle dans la reconnaissance d'une expression faciale. Dans le 22q11.2DS et le TS, le déficit de la reconnaissance de la peur s'amointrit lorsqu'une expression faciale est dynamique (Franchini et al., 2016; Roelofs, et al., 2015). Toutefois, les individus porteurs d'un 22q11.2DS ont besoin de plus de temps que les participants témoins pour identifier une émotion (Franchini et al., 2016).

Un trouble de la reconnaissance des émotions faciales peut être lié à une observation atypique des visages (Hernandez et al, 2009). La région des yeux avec les régions du nez et de la bouche sont les zones du visage les plus informatives (Baron-Cohen et al., 1997; Hernandez et al, 2009). Une observation moindre de ces régions pourrait être en lien avec des difficultés à reconnaître les expressions faciales (Djukic et al., 2014).

L'observation de la zone de la bouche est atypique dans le 22q11.2DS, le syndrome de Rett et le TS (Djukic et al., 2014; Glaser et al., 2010; Mazzola, et al., 2013) et pourrait être en lien, dans le TS, avec un déficit sélectif pour la reconnaissance de la peur. L'observation de la

zone des yeux est également atypique dans le 22q11.2DS, le FXS et le KS (Campbell et al., 2010; Crawford et al., 2015 ; Dalton, Holsen, Abbeduto and Davidson, 2008; Djukic et al., 2014; Van't Wout et al., 2009). Les personnes avec WS ont tendance à observer les visages plus longtemps que les participants avec un développement typique (Riby and Hancock, 2009).

La Théorie de l'Esprit est également perturbée dans le 22q11.2DS, le FXS, le PWS, le TS et le WS. Cependant ce déficit s'exprime différemment selon chaque syndrome. Dans le 22q11.2, ce trouble serait lié à un retard d'acquisition de la Théorie de l'Esprit plutôt qu'à un déficit (Campbell, et al., 2011). Dans le PWS le déficit de la Théorie de l'Esprit serait plus prononcé pour les états mentaux résultant des situations sociales, tels que la jalousie, l'envie, l'admiration et l'appréciation (Koenig et al, 2004). Ceci suggère que le trouble de la cognition sociale est plus prononcé dans le domaine émotionnel et ne serait pas seulement dû au QI. Dans le WS, ce trouble serait également déficitaire en comparaison au PWS (Tager-Flusberg et al., 2000), ce qui suggère que ce trouble de la cognition sociale n'est pas seulement dû au QI et/ou aux habilités verbales.

Dans l'ensemble des études citées précédemment, il est explicitement demandé aux participants d'interpréter les indices sociaux (visages expressifs, contextes). The «social-attribution task » permet d'évaluer l'habileté à attribuer spontanément des états mentaux (Heider & Simmel 1944). Des difficultés dans l'attribution spontanée d'états mentaux est reporté dans le 22q11.2DS et le WS (Ho et al 2012; Van der Fluit, Gaffrey and Klein-Tasman ; 2012). Or les situations du quotidien nécessitent d'interpréter les réactions d'autrui spontanément.

Enfin beaucoup moins étudié que les stratégies d'exploration visuelles ou la Théorie de l'Esprit, le phénomène de mimétisme semble également déficient dans les populations porteuses d'un trouble de schizophrénie (Varcin 2010). Or le syndrome de 22q11.2DS est associé à un haut risque de développement de troubles psychotiques à l'âge adulte (Gothelf et al., 2005). Ce point précis doit donc également être pris en compte lors de l'entraînement cognitif.

Ainsi, les résultats de cette revue suggèrent qu'un trouble de la cognition sociale ne serait pas seulement lié au QI. Cependant, ils révèlent également que la littérature comporte peu d'études dans certains domaines de la cognition sociale comme le style d'attribution et la

perception sociale. Certains syndromes, notamment le syndrome d'Angelman et le syndrome de Smith-Magenis, sont particulièrement peu étudiés. Les études portant sur les aspects de la cognition sociale ont également des limites : petites cohortes, manque d'études longitudinales et impact sélectif des troubles visuo-spatiaux.

La compréhension des troubles de la cognition sociale et plus particulièrement des mécanismes déficitaires qui sous tendent ces troubles constitue un enjeu majeur dans la prise en charge des troubles neurocomportementaux d'origine génétique. En réponse à ce constat, nous souhaitons proposer un programme d'entraînement de la cognition sociale (le programme RC-KID) qui cible plus spécifiquement ces mécanismes déficitaires (e.g. un trouble de l'exploration des visages, traitement des informations dynamiques, capacité à comprendre la cause des émotions en se basant sur les indices contextuels et sociaux; voir chapitre 3). L'objectif final de ce programme est de réduire l'impact cognitifs des déficits dans la vie quotidienne.

Évaluation du programme RC-KID

Le programme RC-KID est destiné aux enfants porteurs d'un trouble de la cognition sociale. Ce programme est d'une durée de 12 séances d'1h par semaine. Chaque séance est individuelle, personnalisée et construite autour d'exercices de type papier-crayons, des exercices informatisés et des jeux de mise en situation. Le programme informatisé propose des outils concrets pour travailler sur les processus de la cognition sociale. Les jeux de mises en situation, basés sur des activités théâtrales, sont utilisés comme support dans l'enseignement et la mise en pratique de la cognition sociale et des compétences émotionnelles. Ce programme implique la famille de l'enfant dans la prise en charge à l'aide des rencontres fréquentes ainsi que des jeux et des tâches à domicile pour généraliser les apprentissages. Nous souhaitons ainsi favoriser le transfert de ces connaissances à leur vie quotidienne.

Le programme RC-KID s'affranchit d'une logique protocolaire en terme de contenu et ce notamment sur le contenu des exercices papier-crayon et les jeux de mise en situation. En effet, le programme est individualisé et même si la structure reste la même pour chaque enfant (temps informel, exercice papier-crayon, jeux informatisés, mise en situation, rencontre avec

les parents), il évolue en fonction de l'enfant et des situations qu'il a rencontrées. Le temps informel du début de chaque séance et le temps de rencontre avec les parents de l'enfant sont donc très importants pour déterminer l'axe de la séance et notamment l'axe des jeux d'expression théâtrale basés sur l'expérience des enfants.

Le programme RC-KID a été proposé aux enfants porteurs d'une microdélétion 22q11.2. Mais il a été conçu de telle façon qu'il peut être facilement adapté par les thérapeutes, pour aider d'autres enfants présentant des troubles similaires.

Une étude pilote nous a permis de rencontrer trois enfants, le patient A, le patient B et le patient C, présentant des similarités dans leur profils (difficultés dans la reconnaissance des expressions faciales, trouble des capacités de la Théorie de l'Esprit, difficultés à comprendre et réguler ses émotions) mais également des différences et notamment sur leur comportement social (voir chapitre 4).

L'objectif principal de cette étude pilote constituée de trois études de cas uniques était d'évaluer l'impact du programme RC-KID sur les troubles de la cognition sociale chez trois enfants porteurs d'une microdélétion 22q11.2. Les trois études de cas uniques ont mis en évidence l'amélioration des processus ciblés, à savoir la reconnaissance des expressions faciales, la compréhension des émotions et les capacités de la Théorie de l'Esprit.

Résumé des principaux résultats

Impact de RC-KID sur les processus de la cognition sociale

Le programme RC-KID a considérablement et spécifiquement amélioré les compétences sociales des trois enfants. L'étude pilote a mis en évidence une amélioration des compétences des trois enfants dans des processus ciblés, c'est-à-dire une incidence sur la reconnaissance et la compréhension des émotions (e.g la cause d'une émotion, le ressenti). Ces améliorations ont été soulignées au moyen de lignes de base spécifiques pour chaque participant. La comparaison des évaluations sociales cognitives proposées avant et après la thérapie a donné des résultats plus contrastés. Le patient A a amélioré ses performances mesurées par le TREF dans la labellisation des émotions (exprimées à forte mais aussi faible intensité), mais les scores de la tâche de perception des émotions obtenus avec la NEPSY-Affect sont restés stables. Le patient A a également amélioré de manière significative les

capacités de Théorie de l'Esprit mesurées par la tâche NEPSY-ToM et par le test ToM-15; mais les scores obtenus avec le RMET qui mesurent la ToM affective, sont restés stables. En ce qui concerne le patient B, l'évolution de ses performances aux évaluations de la cognition sociale ne sont pas significatives. Toutefois concernant la Théorie de l'Esprit, ses scores sont maintenant dans la norme attendue pour un garçon de son âge. Le patient C a montré une tendance positive concernant le score de reconnaissance de la NEPSY-Affect mais le score obtenu au TREF est resté stable à la fin du programme. Les capacités de la Théorie de l'Esprit se sont considérablement améliorées chez le patient C, comme le montre le score de la NEPSY-ToM. Nous avons également noté une amélioration significative du score de second ordre obtenu au ToM-15.

Contrairement aux lignes de bases, les tests NEPSY-Affect et NEPSY-ToM (Korkman et al., 2007), font intervenir d'autres processus neurocognitifs tels que la mémoire de travail et les fonctions exécutives (Bachelier, Roger-Kosiorowski, Roch, 2019). Ces résultats suggéreraient ainsi l'importance, en entraînement cognitif, de permettre à l'enfant d'exercer ses compétences de reconnaissance des expressions faciales et de la Théorie de l'Esprit dans un milieu écologique qui demande, en général, à l'individu de mobiliser plusieurs fonctions cognitives à la fois. Par exemple, dans une conversation, en général, nous exprimons nos émotions en parlant ou en effectuant d'autres gestes de la vie quotidienne et notre interlocuteur doit se concentrer sur notre langage non verbal tout en retenant les informations verbales. Enfin les objectifs d'intervention étaient différents selon les enfants, bien que chaque axe fut abordé : pour le patient A nous nous sommes principalement concentrés sur l'axe d'intervention "identifier une émotion" alors que pour les patients B et C nous nous sommes principalement concentrés sur l'axe d'intervention "exprimer/écouter et comprendre une émotion".

Transfert des connaissances à la vie quotidienne

Nous avons à cœur de proposer à ces enfants dont le nombre de prise en charge est important et dont le sentiment «d'être différent» est pesant, des séances qui soient amusantes, ludiques et de ce fait motivantes. En accord avec la littérature, nous constatons l'effet bénéfique des jeux de mises en situation sur l'implication des enfants dans leur prise en charge. L'intégration des marionnettes et des jeux d'expression théâtrale semblent en effet impacter positivement la motivation des enfants et le transfert des connaissances à la vie quotidienne (Chevrier, 2008 ; Fagot, Salle-Collemiche, Poinso et Naudin, 2014 ; Langry

2011 ; Nader-Grobois et al., 2016 ; Richoz et Rolle, 2015). Le travail sur le corps (e.g. imitations, postures, ton de la voix) semble aider les enfants à parler de leurs difficultés (Fagot et al., 2014). Inventer des histoires, personnaliser les décors sont autant de situations sociales (e.g. collaboration, demander de l'aide, respect d'autrui) qui permettent à l'enfant d'exercer ses capacités à interagir de manière efficiente avec autrui (Nader-Grobois et al., 2016).

En ce qui concerne le transfert des impacts de la thérapie à la vie quotidienne, les parents des trois enfants ont rapporté des améliorations subjectives sur le fonctionnement social de leur enfant, liées aux stratégies développées en séance (suivant les principes de la remédiation cognitive) : amélioration de la capacité à reconnaître spontanément une émotion et de mettre des mots sur les causes de ses émotions, apparition de nouvelles capacités d'expression et de régulation de ses émotions (e.g. s'excuser et revenir sur une situation source de conflit) et de comportements empathiques (e.g. réconforter un proche, lui proposer son aide s'il semble en avoir besoin). Cependant, ces impacts subjectifs n'ont été que partiellement confirmés par les échelles d'évaluation du comportement adaptatif (Vineland II) et du comportement aberrant (ABC). En fait, nous n'avons observé aucune évolution de ces scores chez les patients A et B (le patient A ayant un comportement adapté selon cette échelle). Seule une amélioration significative du sous-score «discours excessif» de l'échelle ABC a été mise en évidence chez le patient C. Ce dernier est le participant qui avait le score le plus élevé sur cette échelle avant l'intervention. On peut donc supposer que le programme RC-KID semble avoir plus d'impact sur les participants présentant des troubles importants du comportement, mais cette hypothèse reste à vérifier. De plus, les mesures proposées ont peut-être été trop différentes des aspects de la vie quotidienne pratiqués pendant le programme RC-KID. En réalité, d'autres mesures, telles que les observations dans la vie quotidienne, pourraient être plus adaptées que les questionnaires utilisés dans cette étude pilote pour refléter les réalisations des patients en matière de fonctionnement social.

Limites du programme RC-KID

Aujourd'hui, nous avons peu de recul sur le maintien des bénéfices apportés par les programmes d'entraînement de la cognition sociale à long terme et ce, d'autant plus chez les enfants porteurs d'une microdélétion 22q11.2. D'autre part, la durée d'un programme d'entraînement de la cognition sociale est une notion importante. Pourtant, il n'y a pas à notre

connaissance de données dans la littérature portant sur la durée qui pourrait être optimale pour les enfants porteurs d'une microdélétion 22q11.2. Des bénéfices ont été cependant montrés avec un entraînement d'1h par semaine pendant 12 semaines (Glaser et al., 2012, Karagöz-Üzel et al., 2018). Toutefois, durant notre étude nous avons pu observer la limite du matériel informatique du programme RC-KID (nombre de vidéos, de photographies) : au-delà, d'une douzaine de séances, il est fort probable qu'il devienne redondant.

Par ailleurs, il est difficile d'évaluer l'impact sur l'évaluation post-thérapie des processus de la cognition sociale de différents facteurs que nous ne pouvons pas contrôler comme l'implication des parents des enfants dans la prise en charge ainsi que les difficultés familiales qu'ont pu traverser les enfants (i.e. divorce des parents et déménagement pour le patient B et le patient C).

De plus, les tests d'évaluation que nous avons utilisés présentent quelques limites. En effet, il existe peu de tests standardisés et normés en français évaluant la cognition sociale chez les enfants et encore moins concernant les compétences émotionnelles. Nous avons donc dû utiliser des tests de perception des expressions faciales et de la Théorie de l'Esprit (notamment la Nepsy) qui font intervenir d'autres processus neurocognitifs tels que la mémoire de travail et les fonctions exécutives (Bachelier, Roger-Kosiorowski, Roch, 2019).

Nous avons également utilisé le TREF, test de labellisation, qui n'est pas standardisé pour les enfants, bien que ces résultats restent intéressants pour la pratique clinique. Enfin, il aurait été intéressant d'effectuer une troisième évaluation post-test six mois à un an après l'intervention afin d'évaluer si les bénéfices de la prise en charge ont perduré à travers le temps.

Pistes d'améliorations du programme RC-KID

L'outil informatique basé sur les principes du serious game fut très motivant pour les enfants. Nous pensons qu'il serait donc intéressant de développer cet aspect des exercices informatiques. Ainsi pour que cette attractivité perdure avec la même intensité tout au long de l'entraînement cognitif, nous pensons qu'il serait intéressant de proposer aux enfants un serious game qui évolue dans le temps (e.g. possibilité de personnaliser le décor ou son personnage en gagnant des accessoires, comme un nouveau chapeau, de nouvelles bottes).

Ces études de cas nous permettent d'ouvrir de nouvelles perspectives concernant la problématique de transfert des connaissances, développées en séance d'entraînement cognitif,

vers la vie quotidienne de l'enfant. Les séances avaient pour objectif final d'aider chaque enfant à développer ses connaissances et à faire des liens entre les apprentissages acquis lors de l'entraînement et son quotidien.

Dans le cadre du programme RC-KID nous avons globalement proposé à l'enfant de travailler sur les trois niveaux d'acquisition d'une compétence (Tardif, 2006) : accroître les savoirs théoriques (e.g. lors de la tâche papier-crayon, apprendre à identifier les traits spécifiques de chaque expression faciale), transformer ses connaissances en savoir-faire grâce aux exercices informatiques, mobiliser ses connaissances lors de jeux de mise en situation. Néanmoins, dans le cadre d'une prise en charge, il est difficile de proposer des situations où l'enfant doit spontanément utiliser ses connaissances sans qu'il soit influencé par le fait d'être dans un cadre spécifique et le fait d'être observé par son thérapeute. C'est pourquoi en dehors des séances d'entraînement cognitif nous invitons les enfants et leurs parents à mettre en pratique leurs connaissances afin de développer leurs savoir-faire et leurs habiletés.

Bien que les séances individuelles ont eu un impact sur le quotidien de l'enfant, RC-KID semble avoir apporté à l'enfant des connaissances théoriques (reconnaissance et compréhension des émotions) qui ne sont pas encore complètement transformées en connaissances pratiques (comportement adapté au cours d'une interaction sociale émotionnelle). Par ailleurs, nous n'avons pas pu proposer aux enfants un travail en profondeur sur leur capacité à exercer leur compétences de reconnaissance des expressions faciales et de la Théorie de l'Esprit dans un milieu écologique proche qui demande, en général, à l'individu de mobiliser plusieurs fonctions cognitives à la fois. Il serait intéressant d'évaluer si un nombre de séances plus élevé pourrait influencer ces constats.

Nous proposons pour une future étude, des séances de groupe en complément des séances individuelles. Ces séances permettraient aux enfants de se rencontrer dans un cadre sécurisant, de vivre des expériences sociales communes et de partager avec des enfants ayant des problématiques similaires. D'autre part, ces séances pourraient être un espace de transfert des connaissances à la vie quotidienne.

Enfin, nous aimerions travailler sur la possibilité de proposer aux parents de participer à un groupe d'échange sur les compétences émotionnelles de leurs enfants. De nombreux auteurs suggèrent ainsi des programmes de formation parentale ciblant les pratiques éducatives pour développer la cognition sociale et les compétences émotionnelles (Barkley,

2006 ; Daffe et Nader-Grosbois, 2009, Denham, Mitchell-Copeland, Strandberg, Auerbach, Blair, 1997, Nader-Grosbois, 2012, Eisenberg, Fabes et Murphy, 1996, Fabes et al., 1994, Twachtman-Cullen 2000).

Les programmes à destination des parents permettent d'offrir un soutien social, un espace convivial où l'on peut dédramatiser les difficultés éprouvées au quotidien. En effet, lors de nos rencontres régulières, les parents ont souvent été source d'idées à partager pour améliorer la qualité de vie de leur enfant et de leur famille.

En conclusion les résultats des études préliminaires de cette thèse tendent à supporter l'idée qu'un programme d'entraînement de la cognition sociale constitue une stratégie d'intervention pouvant s'avérer efficace pour certains enfants porteur d'un trouble neurodéveloppemental.

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