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# Study of associative learning with a sensory preconditioning task using an eye-tracking system with different conditioning variables and testing the role of verbal strategies

Charlotte Renaux

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Study of associative learning with a sensory preconditioning task using an eye-tracking system with different conditioning variables and testing the role of verbal strategies.

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# Résumé

Ce projet de thèse visait à étudier un phénomène particulier du conditionnement d'ordre supérieur par l'utilisation du paradigme du pré-conditionnement sensoriel (PCS, Brogden, 1939). Dans une première phase, deux stimuli conditionnés (SCs) ont été associés l'un à l'autre un certain nombre de fois (Phase 1, SC2-SC1), avant que l'un (SC1) soit associé à un stimulus inconditionné (SI) provoquant ainsi une réponse conditionnée (RC) de l'organisme (Phase 2 : SC1-SI). On parle de SPC lorsque le stimulus conditionné SC2, qui n'avait jamais été associé directement au stimulus inconditionné, provoque cette même réponse conditionnée.

Les résultats disparates de la littérature scientifique ont démontré maintes fois ce phénomène chez différentes espèces animales. Un des objectifs de cette thèse a été de répliquer une même tâche à travers différents groupes expérimentaux en utilisant la réponse oculaire comme mesure, via un système d'eye-tracking, évitant ainsi l'utilisation de consignes écrites ou verbales. Combiné à un ordinateur conventionnel, nous avons ainsi recueilli les temps de fixations visuelles de chaque participant. Lors de ces expérimentations, les participants étaient libres de tout mouvement et devaient regarder l'écran de l'ordinateur afin de réaliser la tâche. Notre paradigme a été de présenter simultanément dans une première phase deux SCs (SC2-SC1 et SC4-SC3) un certain nombre de fois, avant d'associer SC4 et SC2 respectivement à un SI aversif ou appétitif. Lors de cette phase, les participants devaient apprendre à anticiper l'apparition de SI+ (c.à.d. le SI appétitif correspondant à un court extrait vidéo) en présence de SC1 et à anticiper l'apparition de SI- (c.à.d. un son aversif) en présence de SC3. Un critère d'acquisition était requis afin de passer au test final, au cours duquel les participants étaient testés sur leur capacité à répondre à SC2 et SC4 conformément à la nature du SI qui a suivi le SC auquel ils étaient associés.

Ainsi, ce travail a fait l'objet de deux parties de recherches. La première partie étudiait la réponse de SPC selon certains paramètres environnementaux (contiguïté des stimuli conditionnés et nombre de présentations de ces stimuli) afin de créer une procédure expérimentale permettant l'observation de ce type de réponse sans utilisation d'instructions. Le second axe s'intéressait à l'évolution de cette réponse à travers les âges en soutenant l'hypothèse que la présence de comportements verbaux n'était pas nécessaire pour l'observation de la réponse conditionnée. Afin de tester cette hypothèse, nous avons choisi des personnes présentant des compétences verbales limitées (c.à.d. enfants avec troubles autistiques

non verbaux et personnes âgées avec démences séniles) et des participants n'ayant pas encore accès au langage (c.à.d. bébés entre 4 et 9 mois).

## **Partie 1**

Notre première étude comparait les effets de la contiguïté spatiale sur la réponse conditionnée. Pour cela, la distance entre deux SCs a été manipulée en laissant soit un espace entre les deux stimuli présentés (condition A), soit en les rapprochant de manière à ce qu'aucun intervalle spatial entre les deux stimuli ne soit visible (condition B). Au test, nos résultats ont clairement indiqué un taux de fixation visuelle anticipatoire plus élevé sur la zone du SI+ lorsque SC2 apparaissait en condition B plutôt qu'en condition A. Ce travail montrant l'avantage d'une contiguïté sur la réponse conditionnée a été présenté oralement à l'ABAI Denver 2017 et a fait l'objet d'une publication dans *Behavioural Processes*.

Les deux expériences suivantes visaient à étudier le rôle du nombre de présentations des appariements de SCs en phase 1 sur la réponse conditionnée en phase test, chez le sujet adulte jeune et chez le sénior. Nous avons ainsi varié le nombre de présentations des couples de stimuli en les présentant 10 fois (condition *ad10 pairings* et *se10 pairings*) ou 20 fois (condition *ad20 pairings* et *se20 pairings*). Les résultats ont montré un taux d'erreurs d'apprentissage plus conséquent lorsque les stimuli avaient été présentés plus souvent (conditions *ad20 pairings* et *se20 pairings*). Chez l'adulte comme chez le sénior, un nombre élevé de répétitions des stimuli semble détériorer la performance du participant. Ce travail a été présenté lors d'une communication orale à l'ABAI Paris 2018. Les résultats mis en exergue dans cet axe ont permis la réalisation d'une tâche expérimentale spécifique afin d'observer au mieux les réponses conditionnées attendues, sans utiliser d'instructions. Cette tâche a ensuite été répliquée à travers les groupes expérimentaux présentés dans la Partie 2.

## **Partie 2**

Dans cet axe, un premier aspect développemental a été exploré en utilisant une tâche de PCS chez des participants n'ayant pas encore accès au langage ; des bébés âgés entre 4 et 9 mois. L'objectif ici était de tester ce type d'apprentissage réputé comme faisant appel à des compétences relatives au langage. L'expérience a ainsi été réalisée chez le bébé âgé de 4 à 9 mois sans trouble développemental. Les bébés étaient placés dans une chaise adaptée à leur taille et leur permettant de fixer les stimuli sur l'écran de l'ordinateur. Nous avons observé un taux de fixation visuelle élevée sur la zone où apparaissait le SI+ lorsque SC1 et SC2 étaient présentés. À l'inverse, les bébés évitaient l'émission du son aversif SI- lorsque SC3 et SC4 apparaissaient. Ici, nous avons donc observé une réponse de PCS chez des individus dépourvus

de stratégies verbales et à un stade développemental précoce. Ces travaux remettent en question les prérequis à l'établissement de compétences complexes faisant appel à la mémoire. Cette étude a été présentée à l'ABAI San Diego 2018.

Une deuxième étude concernait le conditionnement d'ordre supérieur chez les enfants avec troubles autistiques. Chez l'humain, ce conditionnement est généralement expliqué par l'utilisation de stratégies verbales (Jara et al., 2006). Cependant, les enfants avec troubles autistiques présentent des défauts de stratégies verbales, notamment par un dysfonctionnement des comportements verbaux dans le répertoire comportemental de l'individu. A notre connaissance, aucune expérience n'avait testé le pré-conditionnement sensoriel chez les enfants avec troubles autistiques, malgré l'existence de nombreux programmes expérimentaux se focalisant sur l'apprentissage de comportements verbaux. Nous avons donc testé deux groupes d'enfants diagnostiqués comme ayant des troubles autistiques : des enfants verbaux et des enfants non verbaux, tous pris en charge par des services de type ABA. Nous avons observé indifféremment des taux élevés de fixations visuelles pour la zone du SI+ lorsque le SC2 était présenté à un enfant non verbal ou verbal. Ces résultats ont soutenu notre hypothèse que le comportement verbal n'est pas nécessaire à l'établissement du conditionnement d'ordre supérieur. Cette étude fait l'objet d'une soumission à un journal scientifique et a également été présentée à l'ABAI Miami 2018.

Enfin, une dernière étude s'est focalisée sur la réponse conditionnée chez le senior médicalisé en service EHPAD et souffrant de démence sénile. L'objectif était d'étudier l'absence de comportements verbaux chez des individus âgés dont les capacités mnésiques étaient impactées. Un groupe de personnes âgées avec démence sénile a été ainsi comparé à un groupe contrôle de personnes âgées ne présentant pas de démence. Nous avons observé, ici, un meilleur évitement du SI- chez la personne âgée avec démence sénile, en comparaison de la personne âgée non démente. Cela suggère donc un meilleur apprentissage de l'évitement d'un stimulus aversif chez des personnes âgées démentes et hospitalisées en EHPAD. Ces résultats font l'objet d'une soumission en journal scientifique et ont aussi été présentés à SQAB Denver 2017.

**Mots clés :** apprentissage associatif, PCS, poursuite visuelle, contiguïté spatiale, répétition, développement, comportement verbal.

# Préambule

Depuis les travaux de Pavlov (1927), de nombreux chercheurs se sont focalisés sur l'établissement de conditionnements d'ordres supérieurs. Entre autres, Brodgen (1939, 1942 & 1947) a étudié le paradigme de pré-conditionnement sensoriel (PCS) chez plusieurs espèces animales. Ses travaux ont souligné la difficulté d'observer un tel phénomène d'apprentissage associatif, quelle que soit l'espèce animale testée. En 1942, Brodgen réplique chez l'homme une procédure expérimentale permettant d'observer du PCS chez le chien. Dans cette étude, Brodgen (1942) souligne qu'aucune réponse de PCS n'a été observée chez l'humain en comparaison aux travaux effectués chez l'espèce canine. Quelques années plus tard, Brodgen (1947) ajoute des instructions écrites à sa tâche expérimentale destinée à tester le PCS chez l'homme. Par cet intermédiaire, Brodgen (1947) observe de meilleurs taux de PCS chez l'homme après avoir posé des questions explicites en test concernant les associations possibles entre les différents stimuli présentés. Ainsi, Brodgen (1942, 1947) souligna l'importance de l'utilisation d'instructions dans les tâches expérimentales étudiant le PCS.

Dès lors, les rares études étudiant ce type d'apprentissage associatif chez l'humain ont utilisé des instructions écrites dans leurs paradigmes expérimentaux (cf. Jara et al., 2006, & Craddock et al., 2014, pour exemples). La question principale de cette thèse était de déterminer pourquoi l'observation de PCS était impossible chez l'humain sans utilisation d'instructions. En effet, l'hypothèse prédominante concernant l'établissement du PCS chez l'humain repose essentiellement sur la formation de stratégies verbales favorisées par l'insertion d'instructions expérimentales. Or, de nombreux chercheurs ont observé chez d'autres espèces animales des taux élevés de PCS sans utiliser la moindre instruction. En effet, ce type d'apprentissage a été observé chez les pigeons (cf. Reid et al., 1952), les poissons (cf. Hall et al., 1995), ainsi que chez les abeilles (Müller et al., 2000). Notre premier objectif de recherche consistait donc à observer l'établissement d'un tel apprentissage associatif chez l'homme dans une tâche n'utilisant pas d'instructions et ainsi similaire aux paradigmes expérimentaux utilisés dans d'autres espèces animales. Le second objectif consistait à observer l'évolution de cette réponse conditionnée à travers différents âges car la plupart des études focalisées sur le PCS ont été uniquement testées de jeunes adultes. Enfin, le dernier objectif consistait à émettre l'hypothèse que l'utilisation de stratégies verbales n'était pas nécessaire à l'observation de PCS chez l'humain. Nous avons observé cette réponse conditionnée chez le bébé, l'enfant non vocal avec des troubles autistiques, ainsi que chez la personne âgée avec ou sans démence sénile. Ces

différentes populations aux stades développementaux divers comportent toutes des défauts concernant l'élaboration de stratégies verbales.

Ce travail de recherche se découpe en deux parties distinctes :

- La première partie décrit la procédure utilisée pour observer le PCS chez l'humain sans utilisation d'instructions.
- La deuxième partie est focalisée sur l'étude de cette réponse à travers différents stades développementaux avec défaut de stratégies verbales.

# Foreword

Since Pavlov's seminal work (1927), many researchers have focused on the establishment of higher order conditioning. Brodgen (1939, 1942, & 1947) studied conditioning within the sensory preconditioning paradigm (SPC) in several different animal species. His work highlighted that learning could occur without being evident to an observer. Moreover, it challenged Thorndike's (1931) Theory of Reinforcement which posited that learning required the delivery of a biologically significant outcome such as food or electric shock. In both of these respects, it served as the Pavlovian analogue of Tolman's (1930) demonstration of « latent learning » in rats allowed to explore mazes devoid of reinforcement at the time of exploration. In 1942, Brodgen replicated in humans the procedure that he had previously used to demonstrate SPC in dogs. In this study, Brodgen (1942) observed that no sensory preconditioning response in humans in contrast to the SPC responses he had previously observed in the canine species. A few years later, Brodgen (1947) added written instructions into his experimental task to assess SPC in humans. With the instructions, Brodgen observed an appreciable degree of SPC in humans after he asked participants explicit questions at test concerning the possible associations between the different conditioned stimuli (CS) presented. Thus, Brodgen (1942, 1947) emphasized the need for using verbal instructions in order to observe SPC in humans.

Therefore, the few subsequent reports of SPC in humans used written instructions in their experimental paradigms (see Jara et al., 2006, & Craddock et al., 2014, for examples). The main problematic was to determine whether the observation of SPC was truly impossible in humans without the use of instructions. In fact, the predominant hypothesis concerning the establishment of SPC in humans rests essentially on the formation of verbal strategies promoted by the presentation of experimental instructions. However, many researchers have observed high rates of SPC in other animal species without using any instructions. For example, SPC had been observed in pigeons (see Reid et al., 1952), fishes (Hall et al., 1995), and bees (Müller et al., 2000). ). Thus, the first primary research goal was to seek SPC in humans using a non-instructional task, similar to experimental paradigms used with other animal species. A second objective was to assess potential differences in SPC across different developmental ages because most of the studies tested SPC only in young adults. A final goal was to assess whether SPC could be observed in humans without their using verbal strategies. In order to answer this last question, we tested for SPC in babies, and non vocal children with autistic disorders, as

well as in the elderly with or without severe senile dementia. Lack of verbal strategies had been demonstrated in those populations.

Thus, this research was divided into two parts:

- A first part in which a procedure to observe SPC in humans without using instructions was developed.
- A second part in which SPC was studied across different developmental stages with lacks of verbal strategies.

## PART 1 :

Elaboration of a SPC procedure without using any instructions in humans.

## CHAPTER 1 : INTRODUCTION

Chapter 1 introduces (1) the history of SPC, (2) some studies concerning visual attention measured by eye-tracking system, (3) then anticipatory and avoidance responses in Pavlovian conditioning.

### 1. History of SPC

SPC is a type of higher-order conditioning because that type of learning is more complex than simple dyadic conditioning with CS → US. According to Miltenberger's definition (2011), higher order conditioning is observed when a neutral stimulus (NS) is paired with a conditioned stimulus (CS), thus becoming itself a CS eliciting a conditioned response (CR). Since the beginning of the 20th century, this kind of learning had been the subject of many studies in several animal species, especially in humans for its relationship to conditioned emotional responses.

#### 1.1. Conditioned emotional responses with Watson and Rayner's work (1920) :

The first historically important study concerning this type of conditioning was Watson and Rayner's work (1920), focused on the conditioned emotional responses (CER) in young humans. It should be noted here that this experimentation could no longer take place today because of the ethical and deontological issues it would rise. In that study, the child tested was the famous 11-month-old Little Albert, a nurse's son who was accustomed to the hospital environment. Before the initial experiment, the child had been determined to be "robust and stable" (Watson & Rayner, 1920), and that there was no fear observed as a result of presentation of rodents in the laboratory. Initially, the researchers struck a metal bar (US) with a hammer, causing the child to cry (UR). Then, a rat (NS) was introduced into the experiment. When Albert touched the rat, the experimenter hit the metal bar with the hammer causing Albert to cry. After several blocks of presentations, the presence of the rat (CS) alone elicited Albert's tears and cries (CR). A few months later, Watson and Rayner placed again Albert in front of a rat, a rabbit, a dog, a fur coat and cotton wool. After each presentation of the rat, a negative emotional response was observed. The same conditioned fear was observed when the rabbit and the fur coat were individually presented to the child, while no negative emotional reaction appeared in the presence of the dog or the cotton wool. Watson and Rayner concluded that most fears conditioned in humans could be established and maintained in the long term by this type of learning. Studies of conditioned fear in species other than rats have raised many questions

concerning Watson and Rayner's work (1920). Harris (1979) reported some errors in the scientific literature concerning Watson and Rayner's experimentation. For example, many studies referred to a conditioned fear of white items in the Watson and Rayner (1920) experiment, which was not presently the case (for example, see Helms & Turner, 1976). Although it is possible that such conditioned fears could have arisen from an overgeneralization of stimuli (Carr, 1925), it is difficult to be certain about it because of the lack of appropriate control conditions. Nevertheless, the report of Watson and Rayner demonstrated that conditioned fear initially neutral stimulus was possible as a result of pairings with unconditioned stimuli.

### 1.2. First experiments of first order and second order conditioning with Pavlov (1927) :

At the same time, Pavlov (1927) published in his renowned book *Conditioned Reflexes* the principles of Pavlovian conditioning by studying salivary responses in dogs. One of the most famous examples of first order conditioning concerns the sound of a metronome associated with food, eliciting alone the salivary response in the dog. Initially, the presence of food (US) caused the unconditioned response of salivation (UR). Then, a neutral sound (NS) from a metronome was presented before food delivery on successive trials. At tests, Pavlov (1927) observed the same conditioned salivary response (CR) to the mere presentation of the metronome (CS). Pavlov's demonstration led to the view that a biologically significant outcome was necessary for conditioning to occur, despite the fact that conclusion currently going beyond the evidence. Specifically, to become a CS, Pavlov suggested that stimulus had to be a more important "biological determinant" than the US with which it was being paired. This implied that an effective outcome in conditioning had to be a "biological determinant" (i.e., an US capable of eliciting an UR).

In the framework of the experimental preparation described previously, Pavlov (1927) associated various NSs with the sound of the conditioned metronome (CS), causing these previously neutral stimuli to now elicit the same CR of salivation as the metronome. For example, a light (NS) paired with the conditioned metronome over several trials came to elicit conditioned salivation in the dog. Pavlov described this learning as second order conditioning (i.e., the lowest level of higher order conditioning). Then, another neutral stimulus such as the odor was paired with light several times, and came to elicit the same salivation response (i.e., third order conditioning). Pavlov observed a diminution of the saliva amount with each higher successively higher order of conditioning. Indeed, the saliva recovered in the cup after each test was less and less abundant after second order conditioning compared to first order conditioning.

These results were observed up to fifth order conditioning by other researchers such as Finch and Culler (1935) using thoracic shocks as negative unconditioned stimuli in the canine species, the unconditioned response here being the avoidance of shocks.

### 1.3. SPC, emerged and developed through species :

Later, Brogden (1939) focused on another type of second order conditioning in dogs. Brogden noted the relative difficulty in obtaining second order conditioning in canines. Initially NS (ringing bell, air blast, light and brief noise) were paired with food 200 times each. Subsequently, out of ten tested dogs, only four dogs could be conditioned on several levels of higher order conditioning. Therefore, Brogden (1939) emphasized the difficulty to observe second order conditioning (i.e., CS1-US followed by CS2-CS1). Toward better understanding why this sort of second order conditioning was difficult, Brogden introduced SPC. In SPC, in a first phase, two stimuli (CS1 and CS2) are presented a number of times together without the presentation of an US (i.e., the preconditioning phase). In a second phase, CS1 is paired with the US, thereby causing CS1 to elicit a CR. At tests, the same CR is elicited by CS2 as CS1, albeit weaker, despite CS2 never having been paired with the US (Figure 1).

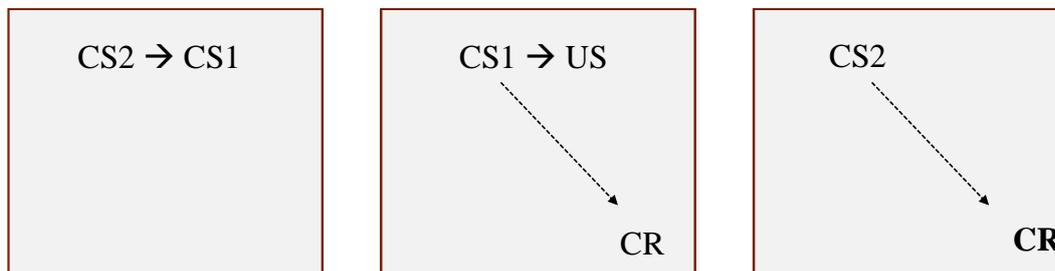


Figure 1. Representation of SPC from *Principles of Learning and Behavior*, Figure 4.5 page 99 (Domjan, 2014)

Since the introduction of SPC by Brogden (1939), the data concerning the observation of this type of second order conditioned response are disparate from one species to another and as a function of certain variations of experimental parameters that we will develop in the next paragraph (see Table 1). For example, Prewitt (1967) observed SPC in rats by simultaneous pairings of a brief sound with a flash of light, followed by one of these stimuli being associated with an electric shock (US) with the result that the other stimulus came to elicit a negative emotional conditioned response (CER). Compared with control groups for which the stimuli were presented either separately or sequentially, Prewitt (1967) observed a higher CER-frequency in rats that experienced CSs presented simultaneously in the first phase. Although other studies demonstrated SPC in pigeons (Reid, 1952), bees (Müller, Gerber, Hellstern, Hammer, & Menzel, 2000), and fishes (Hall & Suboski, 1995), Brogden (1942, 1947) reported

difficulty in observing this type of learning in humans without the use of instructions in the experimental tasks. We will elaborate on Brogden's research in Axis 2.

As a consequence of Brogden's (1942, 1947) reports, many researchers subsequently used instructions in SPC experimental paradigms with human subjects. For example, we previously used instructions when we used reaction times to assess SPC in humans (Craddock, Renaux, Lefèvre, Nelson, & Molet, 2014). In a first phase, different stimulus pairs were presented interspersed (e.g., pairing different primary colors with different letters of the alphabet (Phase 1: CS2 - CS1). Then, one of these stimuli was associated with the appearance of a picture (Phase 2 : CS1 - US+). In a control condition, CS3 was associated with the non-appearance of the picture. At tests, subjects were asked to click on the "Yes" icon when he thought that the stimulus presented would be followed by the picture. If participants thought that the stimulus was not going to be followed by the picture, they had to press the "No" icon. Written instructions appeared on the computer screen and were standardized for all participants. The response rate for "Yes" when the stimulus appeared on the screen and the reaction times for the participant's response (i.e., the appearance of the CS1, CS2 or CS3 stimulus) were recorded. Results showed a higher conditioned response rate for "Yes" when CS1 was presented on the screen, as well as a lower rate when CS2 appeared. We observed similar results for reaction times: participants answered "Yes" more quickly when CS1 was presented compared to CS2. Although conditioned response rates were higher after CS1 than CS2. But critically, the response rate for CS2 was significantly higher than the response rate recorded for CS3 presentation. Thus, this experiment demonstrated SPC (relative to control conditions lacking either the Phase 1 or Phase 2 pairings) using written instructions at tests in humans. The specific form of the instructions here were « Do you think the picture will appear ? » after CS presentation at test. However, the use of instructions assume certain levels of subjective understanding that could be specific to each participant. That is why we wanted to determine whether we could create a successful SPC procedure for humans without using any instructions.

The diversity of conditioned and unconditioned stimuli within several animal species shows us the universal character of SPC (Table 1). Our research was concerned with the establishment of SPC in humans. For this purpose, one of our objectives was to develop an experimental task similar to other tasks used in animals, where verbal and/or written instruction could be avoided through the use of an eye tracking system.

<i>Species</i>	<i>Authors</i>	<i>CS in Phase 1</i>	<i>US in Phase 2</i>	<i>Use of instructions ?</i>	<i>SPC observed ?</i>
Rat	Berridge & Schulkin (1989)	Gustatory	US+ et US- : aversive and appetitive food	No	Yes
Rat	Lavin (1976)	Olfactory	US- : aversive food	No	Yes
Rat and rabbit	Pfautz, Donegan, & Wagner (1978).	Sound and visual	US- : shock	No	Yes
Rat	Rizley & Rescorla (1972)	Sound and visual	US- : shock	No	Yes
Rat	Ward-Robinson & Hall (1996)	Sound and visual	US- : shock	No	Yes
Rat	Ward-Robinson & Hall (1998)	Olfactory	US- : aversive odor	No	Yes
Bee	Müller, Gerber, Hellstern, Hammer, & Menzel (2000)	Gustatory	US+ : sucrose solution	No	Yes
Fish	Hall & Suboski (1995)	Olfactory and visual	US- : aversive solution	No	Yes
Human	Brogden (1942)	Sound and visual	US+ : pression on a lever	No	No
Human	Brogden (1947)	Sound and visual	US+ : pression on a lever	No	No
Human	Chernikoff & Brogden (1949)	Sound and visual	US+ : pression on a lever	Yes	Yes
Human	Craddock & al. (2014)	Visual	US+ : pression on « Yes »	Yes	Yes

Table 1. Sensory preconditioning in various species with or without using instructions.

## **2. Visual attention and eye-tracking**

Throughout this research, we used eye tracking systems, relying on the phenomenon of visual attention as measured by eye gaze and fixation times.

### **2.1. Visual attention as a measure of attention :**

Visual attention is a phenomenon that has been studied for over a hundred years. Its study was initially limited to the observation of eye movements and subsequently become more complex thanks to the development of modern engineering to measure and record foveal direction. In 1925, Von Helmholtz considered visual attention as an indispensable part of visual perception. More precisely, Von Helmholtz was interested in displacements of eye movements with respect to specific spatial areas, thus suggesting that those movements were indicative of attention. Subsequently, James (1981) suggested that visual attention may reflect the intent and willingness to look at a specific item by the individual. Yarbus (1967) was one of the first to study ocular pursuits by presenting a scenic image to participants, who were subsequently asked questions about the scene. For each question, participants' eye movements were recorded and the direction of their gaze varied according to the relevant information needed to answer the question asked to participants. These results are illustrated below in Figure 2. A picture located at the top left was the scene that participants had to observe and illustrated an excerpt from the daily life of a social group. For recording 1, participants were asked to view this scene freely. A large number of ocular pursuits throughout the picture area were then recorded. For recording 2, the participants had to estimate the socio-economic level of the characters. Yarbus (1967) found more eye fixations on the contextual cues during recording 2, with participants looking in part at the pictures on the wall of the image and tableware on the table in the image. For recording 3, the instruction was to estimate the age of the characters. Results showed that participants mainly looked at the characters' faces before giving their estimates. Subsequently, the participants had to guess what the people in the image were doing before the arrival of the visitor (recording 4), remember their clothes (recording 5), the location of the characters and objects (recording 6) and estimate the time of the last visit of the guest (recording 7).

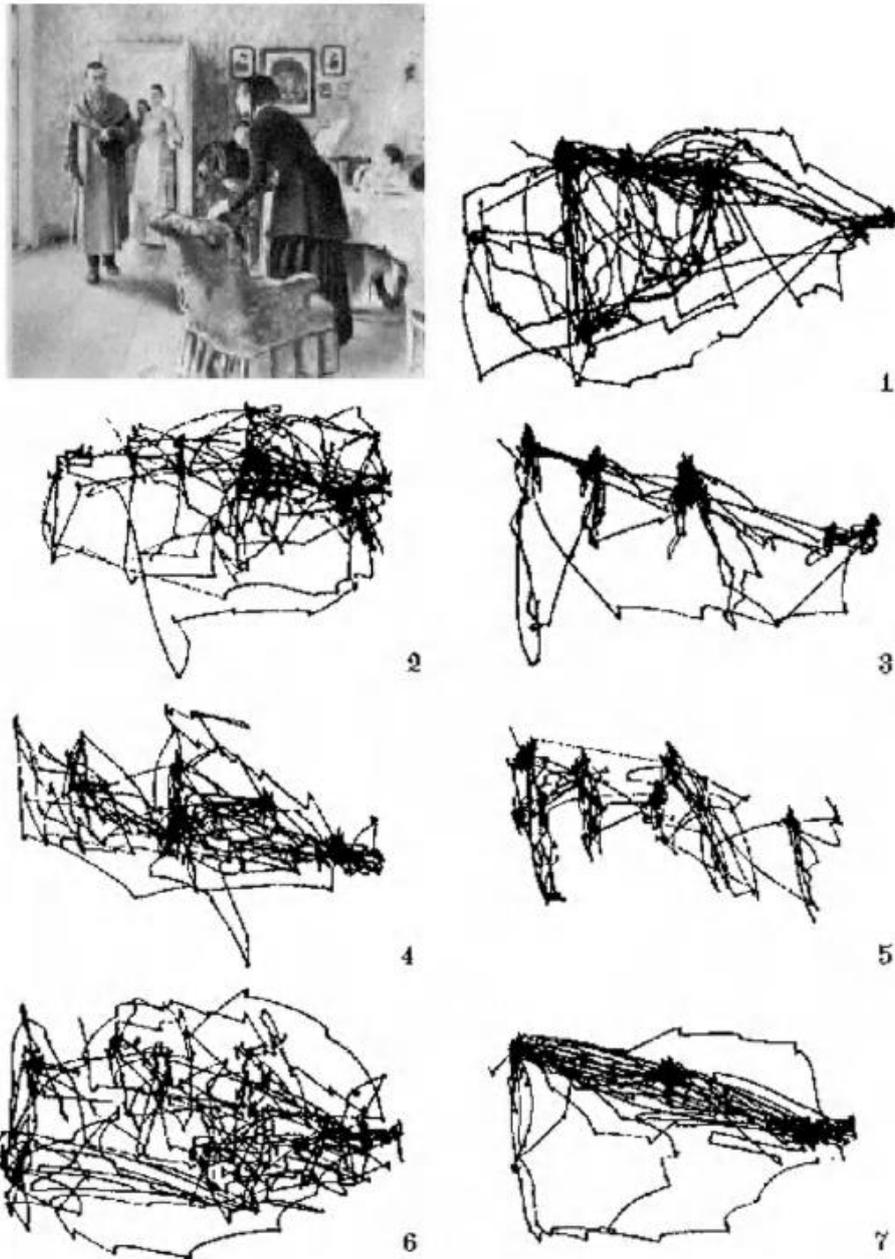


Figure 2. Yarus's experiment (1967).

Since Yarus's work (1967), many theories had been proposed with respect to visual attention. These are summarized in a short book by Gregory (2000). Among these theories, Posner et al. (1980) suggested an attentional mechanism in which visual attention would function as a "spotlight" in front of a cinema scene (from the original term "spotlight"). These authors differentiated two features of visual attention: orientation and detection. Orientation is a focal point of attention on which the subject focuses, whereas detection depends on the sensitivity to the target stimulus relative to the context in which it is situated. If we go back to the work of Yarus (1967), the focus of orientation is indicated by areas with large numbers of visual

fixations; detection corresponds to the movements of these fixations in the form of the singular features within areas as recorded in Figure 2.

## 2.2. Uses of visual attention in paradigms :

Nowadays, studies of visual attention are predicated on the assumption that visual attention objectively reflects the attention that an individual directs to a given visual stimulus (Duchowski, 2007). For example, Kruschke, Kappenman, and Hetrick (2005) tested some Pavlovian phenomena such as blocking using an eye-tracking system to test an attentional hypothesis. This preparation allowed the researchers to objectively argue that the blocking phenomenon results from diminished visual fixation on the added (i.e., blocked) stimulus. In addition, many researchers such as Kaakinen, Hyönä and Keenan (2002) have reported higher visual fixation times on relevant stimuli than irrelevant stimuli in experimental tasks. For example, participants view more precursor stimuli for "biologically critical" events than stimuli that are not followed by any event.

Within psychological research, visual attention is often used in the study of facial expressions which can be tracked and partially recognized thanks to the continuing improvement of computer systems (Black & Yacoob, 1995). For example, Fuchs (1967) used an eye-tracking system in monkeys to observe and study monkey's eye movements during emotional states. Monkeys are often studied with respect to facial expressions because of their similarities with humans. In his study, Fuchs examined several possible measures such as velocity's eye movements, the number of ocular saccades, and the latency eye movement from one stimulus presentation to the targeted zone. In this way, many researchers use eye-tracking systems for therapeutic as well as experimental purposes for the many benefits provided by these systems. Indeed, visual attention can be a near universal measure for humans within the visual domain because the ocular response in humans develops in uterine life and is maintained globally stable throughout life. Gredebäck, Johnson and Hofsten (2009) consider this measure to be relevant for the baby and toddler, in that it allows experimenters to avoid the use of written instructions that would not be understood by subjects. Isaacowitz, Wadlinger, Goren, and Wilson (2006) used eye tracking for older adults for similar reasons in a learning task. In adults, eye-tracking is often used for commercial purposes and allows experimenters to objectively observe product preferences via specific eye fixations of participants (Wedel & Pieters, 2008). Recently, eye-tracking systems have also been used to study learning about the use of new media products, and how to facilitate this learning by inserting applications and other tools relevant to the individual (Van Gog & Scheiter, 2010). Moreover, attentional models of some behavioral

disorders such as depression (Kellough, Beevers, Ellis, & Wells, 2008), affective disorders found in bipolar or schizophrenic patients (Iacono, Peloquin, Lumry, Valentine, & Tuason, 1982, Armstrong and Olatunji, 2012), and patients with neuromuscular disorders (Wachtman, VanSwearingen, & Manders, 2001) assume that deficient attention underlines some of the symptoms and can be assessed with eye-tracking systems.

In our study, ocular fixation response time was the common measure to all of our experimental populations from the baby to the elderly. This measure has proved useful for testing learning in people with developmental disorders like in the autism spectrum and senile dementia because ocular fixations do not require the acquisition of social and verbal skills. For example, a non-verbal child with severe autistic disorder could not have answered questions from the examiner. The same is true for a 6-month-old baby and for a non-verbal elderly person with senile dementia. Using an eye-tracking system, Klin et al. (2002) demonstrated different visual fixation patterns in autistic children compared to typical children. All participants were placed in front of a computer screen and had to look at the movies presented. Autistic children could be seen to have social deficits because of a lack of gaze on the relevant stimuli in order to engage in efficient communication. Indeed, typical children (controls) look at the experimenter’s eyes during social interaction, while autistic children used to look at the experimenter’s mouth or clothes during social interaction. By using eye tracking systems, Klin et al. demonstrated differences in visual fixation during social and nonsocial stimulus presentations. For example, the experimenter’s eyes were more fixated by typical children compared to autistic children during social interaction. Controversially the experimenter’s body zones were more fixated by autistic children compared to typical children (see Figure 3).

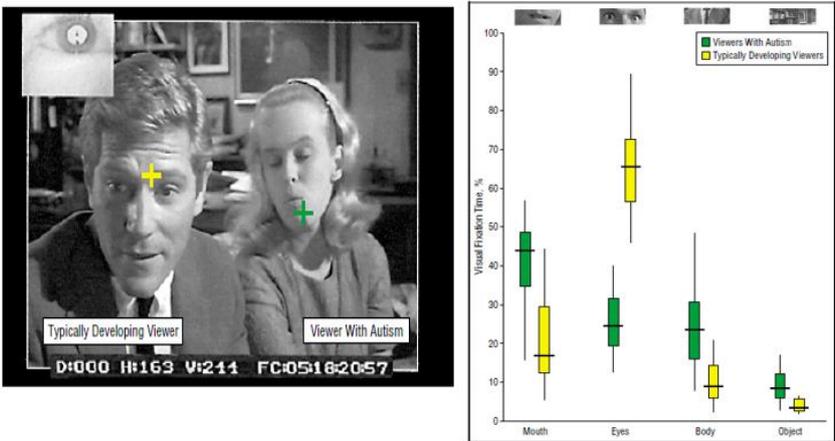


Figure 3. Representative still frame used of coding of visual fixation patterns across groups and box plots comparisons of visual fixation time on the mouth, eyes, body, and objects regions for autistic children and typically developing viewers, from Klin and al. (2002) experiment.

Using eye fixation as a response allowed us to study higher order conditioning learning in atypical populations. Since the use of instructions was considered necessary for the observation of SPC in humans (Chernikoff & Brogden, 1949), no study to date has highlighted this sort of learning in subjects with verbal deficiencies. In addition, ocular fixation allowed us to avoid any costly behavioral response such as fine motor skills (e.g., pushing a button) or global motor skills (e.g., raising a hand to indicate the presence of a stimulus ). Depending on the experimental groups, some individuals would not have been able to emit this type of behavior. For example, a 6-month-old baby could not press a button as quickly as an adult, which would have induced many experimental biases.

Thus, we were able to place each participant in front of the same behavioral task, free of any movement other than the eyes, with the only requirement being that they look at the screen of the computer. Thanks to eye tracking systems and eye gaze as a measure, we had the opportunity to create an experimental task closer to that used with other species, that is, devoid of any instructions.

### **3. Anticipatory and avoidance responses in Pavlovian conditioning :**

In our study, participants had to anticipate the appearance of an US+ and to avoid the emission of an US-.

#### **3.1. Adaptative nature of anticipatory and avoidance responses :**

Pavlov (1927) referred to anticipation and avoidance responses in observations reported in his book *Conditioned Reflexes*. Pavlov observed that the conditioned salivatory response could be elicited even before food was delivered to the dog. Thus, Pavlov spoke about a possible adaptive nature of the conditioned reflex; the presence of a stimulus present in the environment could prepare the organism for the reception of food. Presumably, salivation present in the mouth of the animal immediately before receiving food would allow better ingestion and digestion. Even if Pavlov had not clearly defined these observations as anticipatory behavior, his work showed that there was no incompatibility between Pavlovian conditioning and the establishment of anticipatory responses.

Vast numbers of Pavlovian conditioning studies had been conducted since Pavlov's (1927) seminal work. Today, anticipatory and avoidance behaviors have been reported in many animal species. Hollis (1989) investigated the anticipation response in sexual behavior in blue gourami fish and showed that both males and females learned to anticipate the behavior of their mating

partners in order to reproduce more efficiently. Anticipatory behaviors are established when environmental stimuli are frequently accompanied by biologically important events for the individual (Hollis, 1989). Stormark, Hugdahl, and Posner (1999) also noted that the reaction times of anticipated responses are faster compared to reaction times of unanticipated responses. In their experiment, Stormark et al. paired a previously neutral stimulus with an aversive sound (US-), measuring the electrodermal responses of individuals in the presence of the US-. When the stimulus previously paired with the aversive sound was presented, Stormark et al. observed a shorter reaction time of the electrodermal response to the US- compared to a stimulus never associated with the US-.

Domjan (2005) listed the diversity of anticipatory behaviors in various areas such as eating, sexual, addictive, escape, and emotional reactions. Because our experimental task focused on the anticipation of a US+ and the avoidance of a US-, we will illustrate below these two phenomena in order to discuss about their adaptive value.

### 3.2. Focus on anticipatory responses :

With regard to the anticipation of an US+ event, or a CR to a CS previously paired with the US+, Cusato and Domjan (1998) illustrated anticipatory responses based on earlier observations of Schwartz and Schwartz (1949) research with Japanese quail. In their preparation, when a male quail saw a quail in his natural environment, he saw only one part of the other bird's body, namely the neck and head of the other individual. By approaching these visual stimuli (head and neck), the male could differentiate whether the individual was a male or a female in order to have the opportunity to copulate with a female. Cusato and Domjan replicated this natural sequence in the laboratory, presenting to male quails pictures of heads and necks of different specimens. They observed that male quails did not emit the behavior of copulating when exposed to pictures of the heads and necks of females. Subsequently, Cusato and Domjan (1998) physically presented a female quail (US+) with which the male copulated, following the presentation of the previously neutral pictures. Thereafter, the mere presentation of pictures elicited anticipatory copulatory behaviors in the male subject, that would then attempt to copulate with the presented artificial head and neck. In another experiment, Cusato and Domjan paired another neutral stimulus with the CS pictures and observed anticipatory copulation responses in males at the mere presentation of the initially neutral stimulus. Thus, in that study, the authors demonstrated anticipatory responses using a second order conditioning procedures.

### 3.3. Focus on avoidance responses :

Regarding avoidance responses, it would be informative to first present an example of unconditioned fear. Ohman and Mineka (2001, 2003) focused on negative emotional reactions in humans and monkeys after presenting a snake illustration (US-). In the natural environment, conditioned fears are caused by the appearance of precursor stimuli of an aversive event. Such precursors are easily observable with respect to predator-prey interactions. Ohman and Mineka recorded the electrodermal responses of humans and monkeys following snake illustration (US-) presentations compared to NS. Their results showed a higher electrodermal response when US- was presented to the individual. Here, Ohman and Mineka (2001, 2003) highlighted the phylogenetic character of this reflex, the simple hissing of a snake (US-) causing unconditioned fear (UR) in many mammals - this type of reflex being necessary for the survival of an individual over many prior generations. Cook, Hodes, and Lang (1986) confirmed these results in humans comparing the hissing of a snake with the sound of a firearm. Cook et al. observed electrodermal responses and higher heart rates in humans after the hissing of a snake compared to the sound of the firearm. However, the evolutionary nature of unconditioned stimuli should be noted, considering that the results of this experiment may differ today given recent societal events including the massive use of firearms. Thus, these studies illustrated the notion of avoidance: with the presentation of an US-, avoidance behavior will be emitted by the individual to escape to the potentially dangerous stimulus in the interests of survival.

An avoidance response is generally defined as a behavior that prevents contact with an aversive stimulus (Catania, 1992). Researchers used to study it within the avoidance paradigm in which an initially neutral stimulus is a precursor to an aversive stimulus. In our experiments, we used the same paradigm in which a visual stimulus CS3 was associated with an US- aversive sound. Similarly, Myers, Cohn, and Clark (2005) studied avoidance responses to an aversive stimulus in mice that were placed in an experimental box consisting of two parts separated by a corridor. In their experiment, an initially neutral stimulus (i.e., a light) was followed by an air jet (i.e., US-), these stimuli pairs being randomly presented in each part of the experimental box. Researchers noticed that the mouse escaped from the jet of air as soon as it was emitted in one part of the box, by taking refuge in the other part. After several NS-US- pairings, Myers and al. observed that the mouse avoided the aversive stimulus as soon as the light (CS) was presented in the box. Thus, the initially neutral stimulus became precursor to the occurrence of an aversive event that the mouse could avoid at the onset of the conditioned stimulus.

These different examples demonstrate the adaptive function of anticipation and avoidance behaviors. Indeed, anticipation could be considered as necessary for the survival and reproduction of the individual (Cusato & Domjan, 1998) and avoidance presumably prolongs this survival by minimizing proximity with potentially dangerous stimuli (Myers, Cohn, & Clark, 2005). This point of view is supported by many researchers such as Domjan (2005) or more recently Jozefowicz (2014): anticipatory behaviors favor and maximize contact with appetitive events and, conversely, avoid contact with aversive and harmful stimuli.

Therefore, we adapted the concepts of anticipatory and avoidance behaviors for our experimental task. Those type of behaviors have not previously been frequently studied in higher-order conditioning. One of our objectives was to observe these anticipatory behaviors as a function of manipulated environmental variables.

## CHAPTER 2 : CREATION OF A SPC PROCEDURE

### 1. Sensory preconditioning paradigm :

We studied associative learning using a sensory preconditioning task. Associative learning is assumed to have occurred when as a consequence of a cue-outcome pairing treatment, the presentation of one stimulus elicits behavior related to the other stimulus (Godefroid, 2001). This type of learning has been studied since Aristotle, who proposed three principles for the establishment of associations : contiguity, similarity, and contrast (cited by Warren, 1921). Of these, the contiguity principle had been widely studied over the last century (see Chapter 3), and states that if two events repeatedly occur together in time and space, they will become associated. The similar and contrast principle states that two stimuli will become associated if they share similarities in some respects (e.g., both are round and green) or have some contrasting characteristics (e.g., one short stimulus versus one tall stimulus). Those principles are still examined today, and there is still no widely held consensus that defining mechanisms of associative learning.

In our study, we used several CSs as CS1 and CS2 in order to observe an SPC phenomenon. Specifically, a US+ (i.e., an entertaining movie clip as positively reinforcing unconditioned stimulus) was presented after CS1 appearance in Phase 2. As a control condition, we used two other CSs identified here as CS3 and CS4, with CS3 being paired with a US- (i.e., an aversive sound as negatively reinforcing unconditioned stimulus) in Phase 2. See Figure 4 :

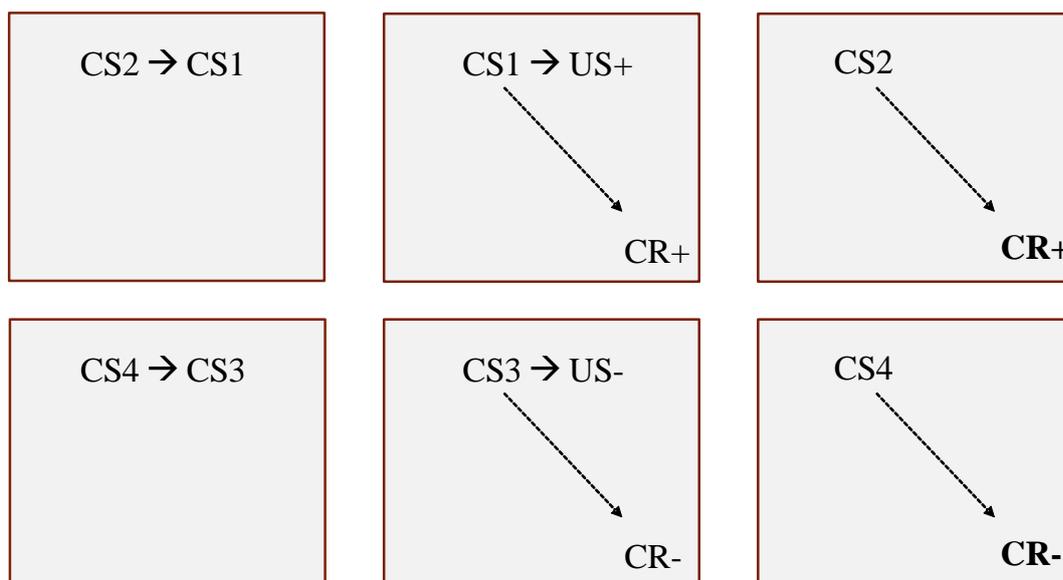


Figure 4. Representation of SPC configuration used in our experimental task using both US+ and US- in Phase 2.

The use of control conditions in SPC in some studies has focused on the higher order conditioning aspects (see Craddock et al., 2014). Using CS3 and CS4 in a control condition confirmed a better discrimination of conditioned responses after CS2 and CS1 presentations with CS1 paired with a US+, compared to other CS4 and CS3 presentations with CS3 paired with a US-. Thanks to the control conditions used, SPC observed upon CS2 presentation on test trials could not be viewed as a spurious or pseudoconditioned response because participants had to emit different conditioned responses according to specific CSs to pass the experimental task for SPC. Thus, participants had to anticipate the appearance of US+ and to avoid the emission of US- in Phase 2. We recorded conditioned responses after CS2 and CS4 presentations at tests.

## **2. Choice of CSs, US+ and US- :**

Conditioned and unconditioned stimuli used in SPC experiments with impaired humans have to be both easily discriminable and not painful. Indeed, experiments with other species can use electric shock as US- (e.g., Pfautz et al., 1978 ; Rizley & Rescorla, 1972 ; Ward-Robinson et al., 1996) or aversive odors (Hall & Suboski, 1995 ; Ward-Robinson et al., 1998). Primary needs can be exploited with the use of appetitive food as US+ (e.g., Müller et al., 2000). Conditioned stimuli used as CS1, CS2, CS3 and CS4 are sometimes auditory and visual (Brogden, 1939 ; Rizley & Rescorla, 1972 ; Ward-Robinson et al., 1998), olfactory (Lavin, 1976 ; Ward-Robinson, 1998) or gustatory (Berridge & Schulkin, 1989 ; Müller et al., 2000). Because of evident ethical considerations, we could not use shock as a US- or food as US+ in humans. Thus, the conditioned and unconditioned stimuli we used in our experiment were similar to other CSs used in conditioning studies focused on humans.

### 2.1 Choice of CSs :

Concerning the choice of the stimuli used as CS1, CS2, CS3 and CS4, we had to identify stimuli that would be discriminable by all participants (from babies to impaired elderly). In prior second order conditioning studies, we had used letters and numbers as conditioned stimuli (see in Figure 5 some stimuli from Craddock, Wasserman, Polack, Kosinski, Renaux, & Miller, 2017 ; Nelson, Craddock, Molet & Renaux, 2017) :

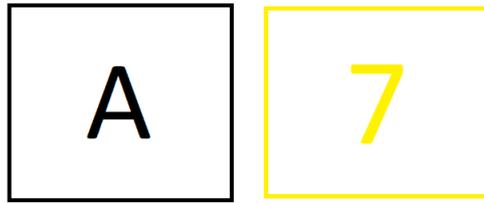


Figure 5. Representations of CSs used in Craddock and al. (2017) and Neslon and al. (2017) experiments.

We observed higher order conditioning with both letters and numbers as CSs. However, because we wanted to tested participants with verbal deficiencies, using letters and numbers seemed inappropriate. Primary colors and shapes are discriminable from the first months of human life and across the life span (Smith et al., 1992). Thus, we selected 6 cm x 6 cm colored geometric squares as we had previously used in one study with normal adults (see Figure 6 from Craddock, Renaux, Lefèvre, Nelson, & Molet, 2014) :



Figure 6. Representations of CSs used in Craddock and al. (2014) experiment.

In Chapter 3, we created CSs based on stimuli used in a SPC procedure published in 2014. We added geometric shapes within the colored squares in order to add a further discriminative element to each CS. In summary, each CS1, CS2, CS3 and CS4 was a distinct shape and color. See Figure 7 :

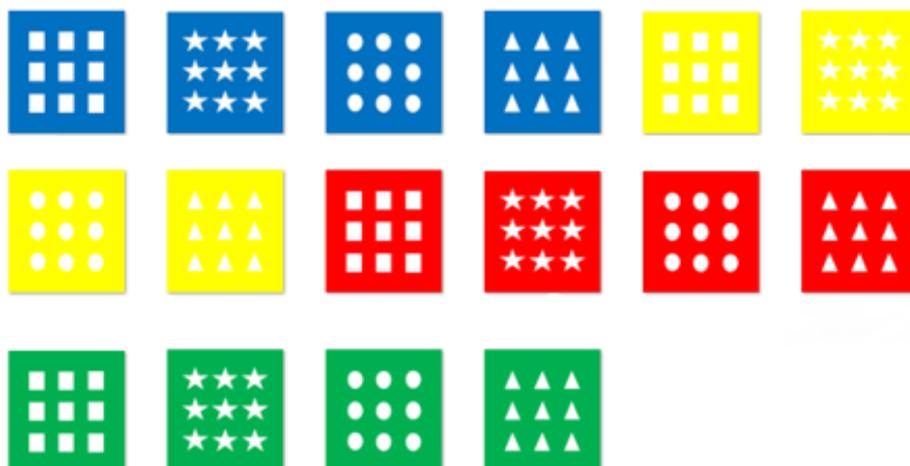


Figure 7 : Representations of CSs used in Chapter 3.

We observed higher-order conditioning after CSs presentations in Part 1 as described in Chapter 3. Nonetheless, a concern about experiments with elderly subjects arose with respect to the size of shapes within the CSs. Because each characteristic of the CS had to be discriminable by the elderly, we created 6 cm x 6 cm simpler and more visible stimuli (see Figure 8) which were used in all chapters except Chapter 3. For each participant, one CS was chosen among those previous stimuli and was defined as CS1 ; and it was always the same CS1 for each participant. CS2, CS3 and CS4 were defined by the same way.

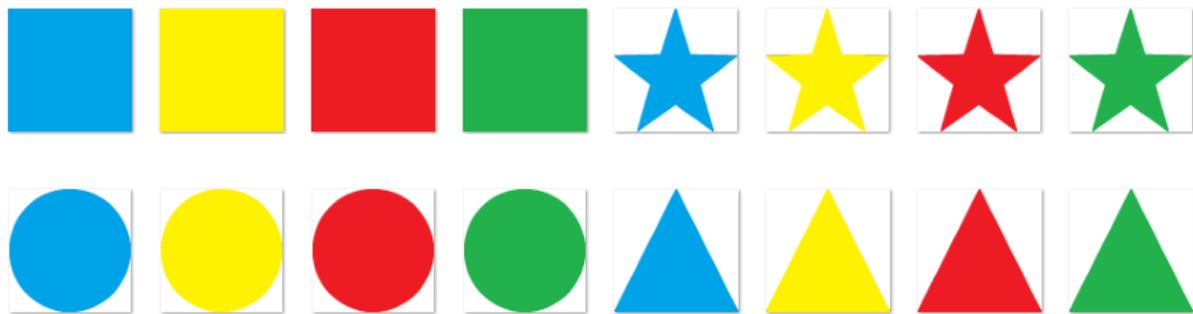


Figure 8 : Representations of CSs used of all participants in Chapter 4 - 5 as CS1, CS2, CS3 and CS4.

Additionally, the paired conditioned stimuli were presented simultaneously as CS2-CS1 and CS4-CS3 dyads. We used simultaneous pairings instead of sequential pairings because some studies found higher rates of higher order conditioning using simultaneous pairings rather than sequential (see Barnet et al., 1991 ; Rescorla, 1980 ; Rescorla, 1982).

### 2.2 Choice of US+ and US- :

Sensory preconditioning paradigms tested in humans often used points or virtual money as US+ (see Craddock, Wasserman, Polack, Kosinski, Renaux, & Miller, 2017 ; Nelson, Craddock, Molet, & Renaux, 2017) and sometimes still pictures (Craddock, Renaux, Lefèvre, Nelson, & Molet, 2014). Other studies focused on conditioning used video clips as efficient US+ thanks to the availability of bimodal sensory inputs (e.g., Courtney et al., 2010 ; Tong et al., 2007). Thus, we created short entertaining film clips from well-known cartoon movies as US+s with a duration of 2s – the same duration of other stimulus presentations in our experiment. The 2s presentation of the US+s appeared in a 13 cm x 8 cm rectangle in a corner of the computer screen, as seen in Figure 9 :

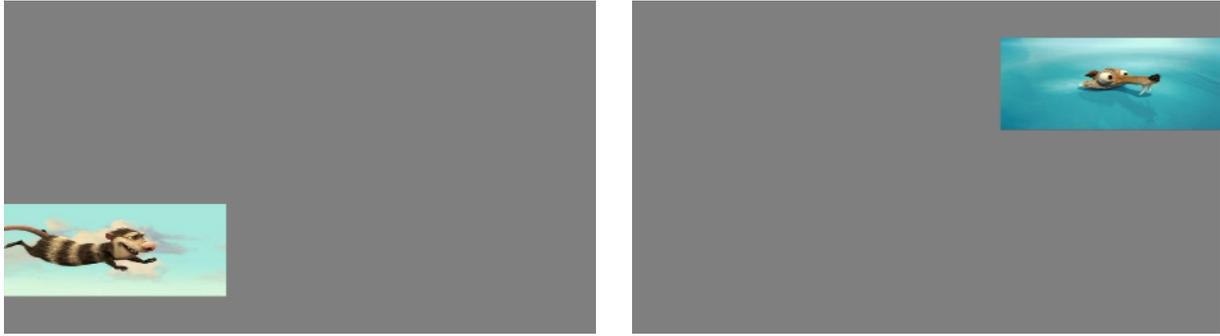


Figure 9 : Representations of 13 cm x 8 cm US+ appearing in one corner of the computer screen.

To our knowledge, no study in humans concerned with SPC ever used an US- in tasks. I had previously examined Pavlovian conditioning using aversive sounds in human participants. An important study informing my choice of US- was Water et al.'s (2009) research which focused on childhood anxiety. In that study, Waters et al. tested acquisition and extinction of conditioned responses in 17 anxious children, using geometric shapes as US+s and loud sound as US-s. Waters et al. recorded subjective verbal responses concerning the CSs and skin conductance responses in anxious children compared to non-anxious control children. In that study, the loud sound proved to serve as an efficient US- because the rate of conditioned responses was high after its presentation and was maintained over trials in both groups. Thus, in the present research we used a similar 100 dB loud sound as a US- with a duration of 2s – the same duration as the US+s and other stimuli. The 2s presentation of US- was emitted by the computer as the US+.

### 2.3 Choice of the background on the computer screen :

Finally, we had to consider the background of the computer screen. Indeed, eye tracking systems require specific light conditions between white light and penumbra, in order to track the pupils of participants. A white background during experimental tasks is tiring for participants who are placed in front of the computer screen for several minutes, while black backgrounds contrast too little with colors of CSs. Thus, we used a gray background as was used in other experiments (Craddock et al., 2014, for example).

### **3. Time choices according temporal contiguity**

In Pavlovian conditioning, high rates of conditioning are seen to be facilitated by their temporal duration being short as well as the temporal relationships between the onsets of the two events (Pavlov, 1927). For example, a close proximity in time between two events is necessary for the establishment of first- and higher-order conditioning. However, the role of temporal contiguity was little considered in the traditional theories of associative learning (e.g., Pearce & Hall,

1981 ; Rescorla & Wagner, 1972). According to those models, animals do not learn the temporal relationships between two events in Pavlovian conditioning preparations.

### 3.4. Temporal coding hypothesis :

Somewhat more recently, some authors proposed the so-called temporal coding hypothesis (Barnet et al., 1991 ; Miller et Barnet, 1993), which posited that temporal information between two events are necessary for the establishment of Pavlovian paradigms. Specifically, Barnet et al. (1991) focused on higher order conditioning and argued that higher order stimuli (i.e., CS2) were established as predictors of first order stimuli that were associated with USs. Their studies supported the view that simple contiguity between two events was sufficient for associative acquisition in first order conditioning and SPC.

Barnet et al. (1991) used an SPC procedure with rats in which sounds and lights served as CS3-CS1 and CS4-CS2, which were presented in a first phase of treatment. In a second phase, first order conditioning was implemented using forward or backward order training (i.e., CS1 → US in forward order conditioning ; US → CS2 in backward order conditioning), associating CSs with a loud sound which elicited a conditioned response consisting of suppression of drinking. CS1 and CS2 were presented for 5s whereas CS3 and CS4 10s. More specifically, Barnet et al. first presented CS4 for 5s alone before presenting CS2 for 5s. The same was done for CS3 and CS1. In the second phase, the US was a 0.5s, 0.8 mA foot shock, and was presented both before CS2 (i.e., backward order) and after CS1 (i.e., forward order). There was no gap between paired events (i.e., neither in Phase 1 nor in Phase 2). Barnet et al. observed SPC responding after both backward and forward conditioning. Notably, there was a higher conditioned response rate with backward conditioning compared to forward conditioning. Thus, the authors highlighted the important role of temporal information for encoding US-CS relationship influencing conditioned responses after higher order stimulus presentations, using short time intervals between event occurrences.

Matzel, Held, and Miller (1988) examined SPC using forward, simultaneous, and backward arrangements. In that study, duration of CSs (i.e., click and tone) and of a constant current US- (i.e., foot shock) were equally presented for 5s. SPC was observed after forward, simultaneous and backward conditioning arrangements. Thus, Matzel et al. confirmed that predictive information (i.e., forward order conditioning) was not necessary for the establishment of higher-order conditioning and that temporal relationships between events are actually encoded as part of associative learning.

### 3.5. In our experiment :

In a previous experiment of our own (Craddock et al., 2014), we used 2s duration in Phase 1 (i.e., CSs simultaneous pairings), first order conditioning in phase 2 (i.e., CS1-US) and then a test trial (i.e., CS2) in typical young adults. In that study, participants were aged between 4 months and 93 years old. In pretest, I tested with the same 2s trials on a few children and a few elderly, and observed conditioned responses. Thus, we used 2s duration trials in our SPC paradigm. In a first phase, CSs were simultaneously presented at the center of the screen for 2s immediately followed by another pairing of CSs (Phase 1 : CS2-CS1 then CS4-CS3). In the second phase, CS1 appeared at the center of the computer screen and was immediately followed by a 2s US+ ; while CS3 was immediately followed by a 2s US- if participants looked at the target zone. At the test, we presented CS2 and CS4 with 2s test trials.

## **4. Sensory Preconditioning Corpus**

In the previous chapters, we explained the basis for our choices concerning conditioned and unconditioned stimuli to be presented within specific 2s intervals. We used an eye-tracking system in conjunction with a conventional computer (Dell Model Optiplex 7010) equipped with infrared cameras that monitored eye movements (FaceLAB#5.1). At the beginning of the experiment, participants first had to sign an informed consent form (see Appendix 1) where they read in French, « The duration of the experiment is approximately 10 minutes. During this time, you will be exposed to different stimuli that appear on the computer screen. Your eye movements will be recorded with an eye-tracking system to determine your visual fixation times. This experiment is composed of 4 phases: a first calibration phase necessary for good monitoring by the eye-tracking system; a second phase in which two stimuli will appear simultaneously; a third phase in which a stimulus will appear and will be followed or not followed by another stimulus. Finally, there will be a test phase composed of stimuli already observed. ». Then we provided only one oral instruction which was « Please sit down and look at the computer screen » before the beginning of the experiment. Our SPC paradigm consisted of the three phases described below.

### 4.1 Phase 1 :

In a first phase, simultaneous CS2-CS1 and simultaneous CS4-CS3 pairings were presented at the center of the computer screen for 2s each. See Figure 10.

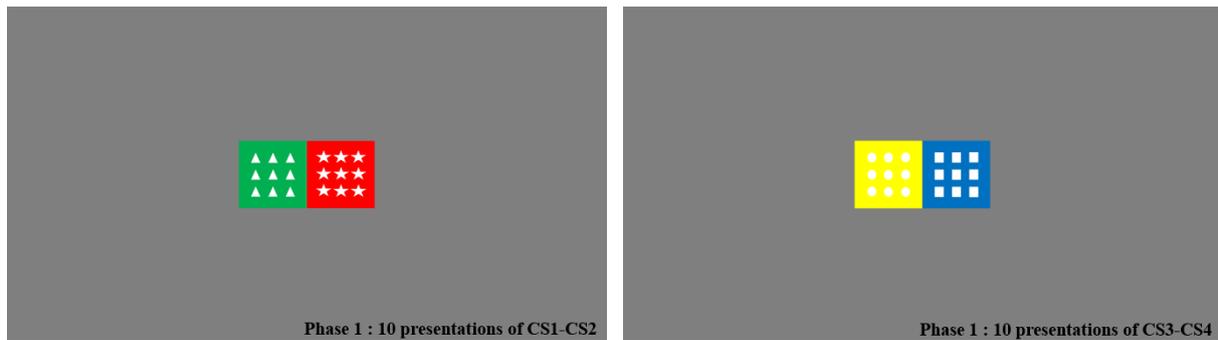


Figure 10 : Representations of simultaneous CS2-CS1 and simultaneous CS4-CS3 pairings in Phase 1.

We counterbalanced the position of CSs in pairing presentations : sometimes CS1 was presented on the left apparatus CS2-CS1 ; sometimes on the right. The same thing was done with CS4-CS3 pairings. Our goal was to avoid some irrelevant learning : participants did not have to learn the spatial localisation of one CS but had to learn color and shape CS. At the end of Phase 1, eye gaze on the CS2-CS1 and CS4-CS3 zones was recorded (i.e., times of visual fixation on each of these zones).

#### 4.2 Phase 2 :

At the beginning of the second phase, CS1 appeared at the center of the screen and was immediately followed by a fixation cross in the appropriate zone of the screen. As soon as participants looked at the cross, an US+ was delivered for 2s (see Figure 11). To avoid the use of instructions, we shaped conditioned responses with visual guidance. Specifically, we used a stimulus fading procedure described by Krantz and McClannahan (1998) in which stimuli first appeared in full lines before being presented as dots as shaping progressed (see below for further description of the shaping procedure). For each participant, US+ was always presented in the same US zone, randomly assigned between four zones and the zone that the participants' looking at produced US- was also randomly assigned to each participant and consistent within each participant.

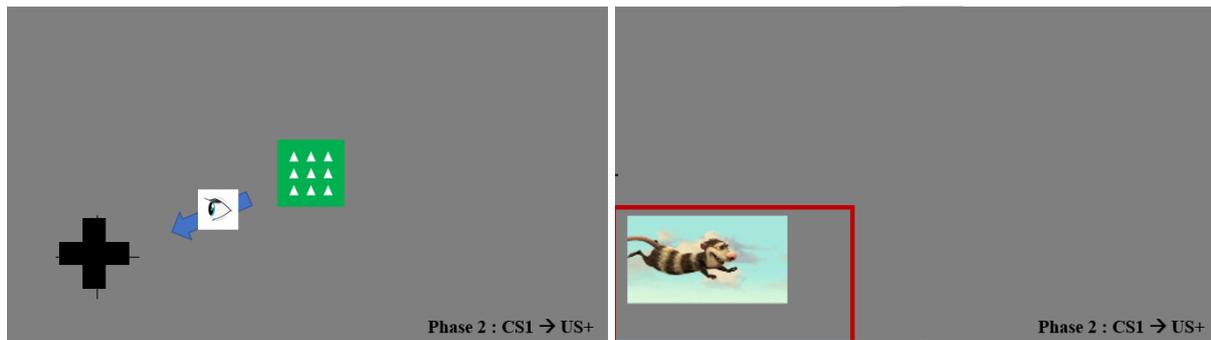


Figure 11 : Representation of CS1 → US+ in Phase 2 with visual guidance using a full-line cross. The cartoon movie was presented when participants looked on the zone indicated by the red box (which participants did not see).

Concerning CS3, its first presentation was followed by an aversive sound (i.e., US-) in order to expose participants to all contingencies. Then, CS3 appeared alone at the center of the screen and was immediately followed by a 2s US- only if participants looked at the US+ zone. If participants did not look at the US+ zone during CS3 presentations, no US- was delivered and trial terminated after 2s (see Figure 12).

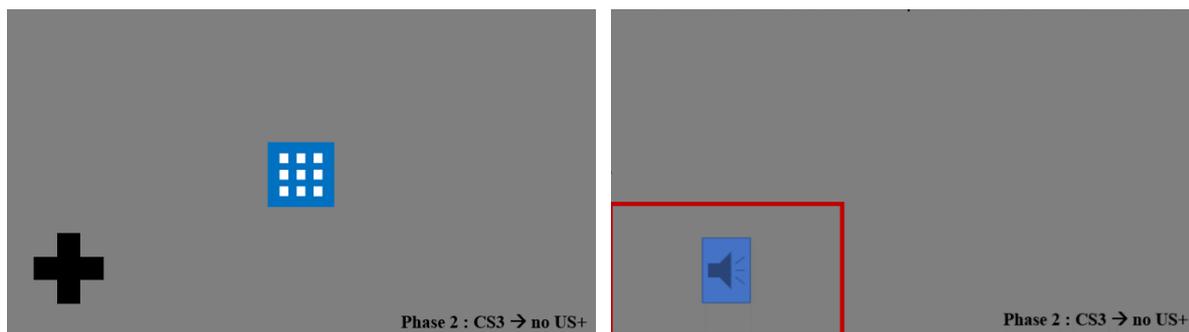


Figure 12 : Representation of CS3 → US- in Phase 2 with visual guidance using a full-line cross. The aversive sound was emitted when participants looked on the targeted zone indicated by the red box (which participants did not see).

We used an acquisition criterion to fade out the visual guidance within successive [CS1 → US+] and [CS3 → US-] trials. Specifically, after three successive anticipatory responses toward US+ upon CS1 presentations and three successive avoidance responses of US- upon CS3 presentations, the full cross became a dotted cross according to conventional behavioral fading procedures (see Krantz & McClannahan, 1998). Then, the dotted cross was completely removed following three consecutive correct anticipatory and avoidance responses. Thus, at the end of the second phase, all participants succeeded in anticipating the US+ by looking at the US+ zone after CS1 presentation ; while avoiding US- by avoiding the US+ zone after CS3 presentation. As soon as the CS1 appeared, participants looked at the US+ zone. Moreover, participants did

not look at the US+ zone when CS3 appeared to avoid the US- presentation (see Figures 13 & 14).

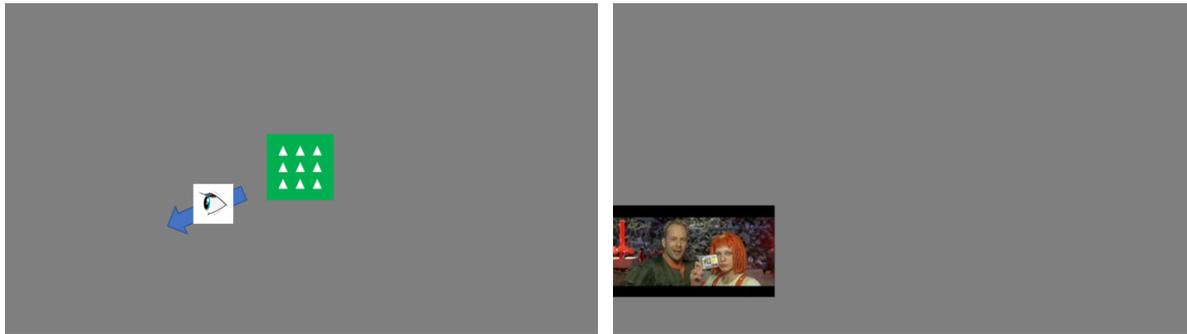


Figure 13 : Representation of CS1→ US+ in Phase 2 without visual guidance. As soon as CS1 appeared, participants typically looked at the US+ zone.

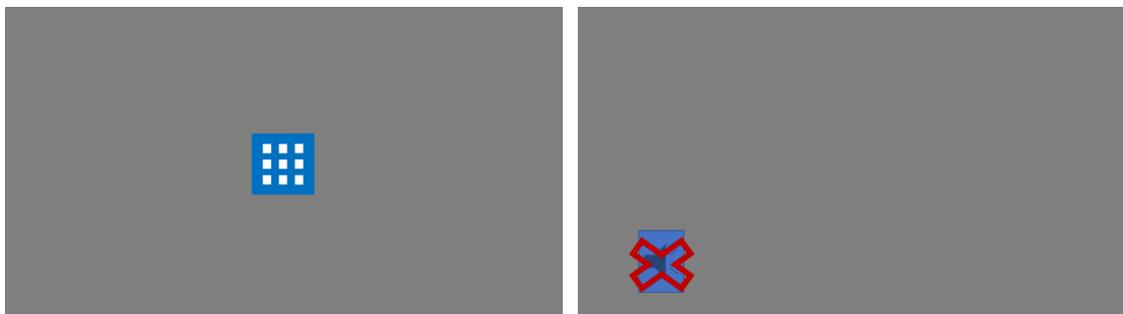


Figure 14 : Representation of CS3→ US- in Phase 2 without visual guidance. As soon as CS3 appeared, participants typically avoided US- presentation by not looking at the US+ zone.

We further constrained the SPC procedure so that participants had to look first at the CSs before looking at any zones of the screen for an outcome to occur. Thus, participants had to look first at the CS1 presented before looking at the US+ zone for the movie clip to be presented; correspondingly they had to first look at the CS3 before looking at other zones in the computer screen except the US+ zone to avoid the loud noise. If participants looked at the US+ zone directly after CS1 appearance, the eye tracker recorded a « 1 » response. If participants looked another zone before targetting the US zone after CS1 presentation, the eye tracker recorded a « 0 ». After CS3, if participants looked at any zone except the US+ zone, that trial was coded as a « 0 ». After CS3, if participants looked at any zone except the US+ zone, that trial was coded as a « 0 » for the SPC sensory preconditioning task ; additionally, we recorded eye gaze for each zone. If participants failed in Phase 2 (i.e., did not anticipate the US+ and/or did not avoid the US-), the experiment ended after 20 minutes of unsuccessful training (i.e., participants who did not reach the learning criterion were eliminated from the experiment). Thus, participants who reached our experimental task criterion were tested during the next 7-15 minutes, while

participants who failed could try during 35 minutes before being stopped and removed from our experimentation (i.e. calibration time of 15 minutes + 20 minutes in Phase 2).

#### 4.3 Test :

Following Phase 2, we tested CS2 only one time and CS4 only one time, because of quick extinction effects that have been reported following higher order stimuli presented without USs (Maztel et al., 1988). We counterbalanced across participants the test order : sometimes CS2 was tested first, sometimes CS4 was (Test : CS2 / CS4, or CS4 / CS2).

When CS2 was presented at test during a 2s trial, we recorded eye gaze on each computer zone. Because CS2 had been paired with CS1 in Phase 1, and CS1 being associated with US+ in Phase 2, we assumed that a conditioned response would be observed in the US zone after the CS2 presentation. When CS4 appeared, we expected no eye gaze on the US- zone, because CS4 was firstly paired with CS3 in Phase 1, and CS3 had been paired with the US- in Phase 2. See Figure 15.

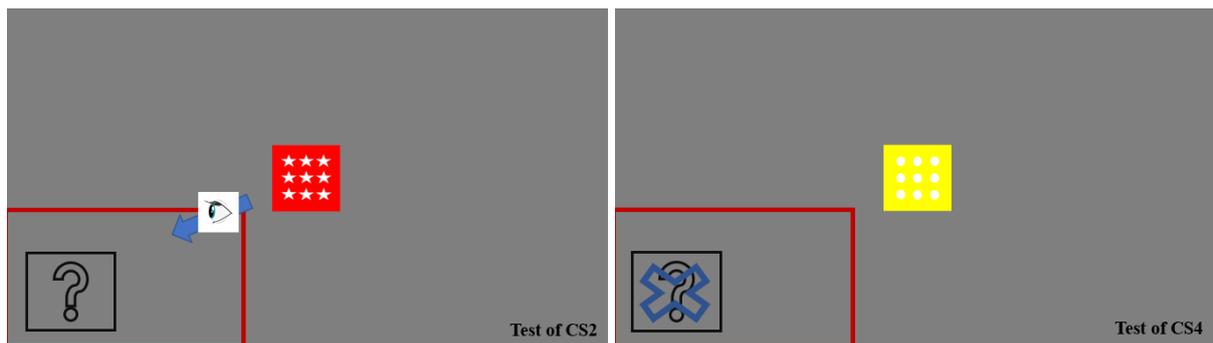


Figure 15 : Representation of CS2 and CS4 tests. The red box was not seen by participants and was only used by the computer to automatically define the targeted zone.

Our total experiment duration was approximately 7-15 minutes, depending on participants' performances in Phase 2. If participants failed in Phase 2 (i.e., do not anticipate the US+ and/or do not avoid the US-), the experiment ended after 20 minutes of incorrect responses in Phase 2. Thus, participants who quickly reached our experimental training criteria were tested within 7-15 minutes, whereas participants who failed could try for up to 35 minutes before being stopped and removed from the experiment. Concerning the location of US zone, we counterbalanced the position of each zone across participants, which was always consistent for each participant. Thus, US zone could be at the bottom left, bottom right, top left or top right (see Figure 16). The size of each zone was the size of the US+ (i.e., 13 cm x 8 cm), which means there was a center zone which was not monitored by eye-tracking system. This is an additional weakness of the experimental paradigm. When participants looked anywhere other

than at one of the four monitored zones, we did not monitor where participants were looking, including in this center zone.

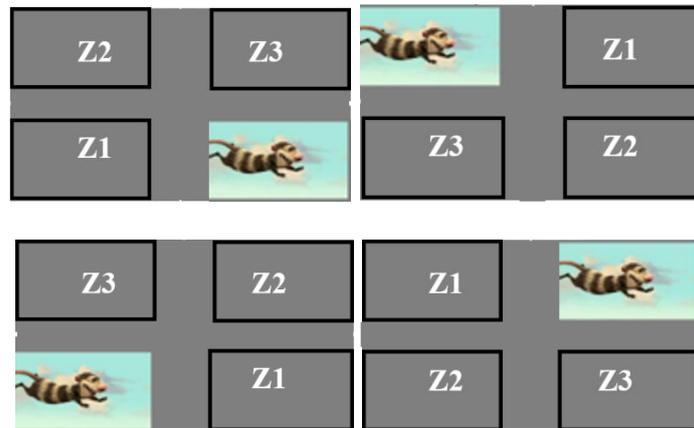


Figure 16 : Possible spatial configurations across participants. The black boxes were not seen by participants and were only considered by computer software.

#### 5. Choice of measures (i.e., dependent variable) :

Eye tracking systems record a large amount of raw data. From these data, I focused on different possible measures such as reaction times (RTs) between CSs presentations and conditioned response emissions, distance traveled by the participants' gaze, participants' pupil diameters, and finally eye gaze duration. In this part, I will introduce some possible recorded measures, and explain why I focused on eye gaze as the dependent variable across all of the experimental groups.

##### 5.1 Reaction times between CSs presentations and CR, and distance traveled by the eye's participants :

In a previous study of ours focused on SPC (Craddock et al., 2014), we used RTs of participants who had to press a button « Yes » or « No » to say whether one specific CS was a predictor of a US+. Contrary to the present experiments, that previous study did not use an eye-tracking system. In the present series, I first looked at RTs across participants groups (see Table 2).

Group	N'participants	RT mean (s)	SD	min (s)	max (s)
adults 10 pairings	20	1,038	0,54	0,1	1,98
adults 20 pairings	20	1,217	0,52	0,12	1,99
seniors 10 pairing	20	1,109	0,57	0,1	1,99
seniors 20 pairings	20	1,341	0,61	0,13	1,99
adults a spatial	20	1,09	0,51	0,11	1,98
adults b spatial	20	1,172	0,53	0,1	1,99
babies	24	1,001	0,51	0,1	1,99
typical children	20	1,174	0,53	0,11	1,99
verbal autistic children	11	1,25	0,56	0,1	1,98
non-verbal autistic children	14	1,182	0,55	0,1	1,99
typical seniors	20	1,402	0,59	0,12	1,99
seniors with dementia	20	1,388	0,54	0,11	1,99

Table 2 : Reaction time means (s), Standard Deviation, min (s) and max (s) values for each experimental group.

I noticed a huge variability in RTs within participants and also large inter-participant differences, perhaps because of the visual aspect of conditioned responses used. For example, see in tables 3 and 4 two participants' results at the end of Phase 2 and Test – RTs are written in red. « NaN » signifies that the participant did not look at the US zone after looking at the CS.

We concluded that RTs were poor measures for my experimental task because of the huge intra-participant and inter-participant variability of RTs as have also been highlighted by other studies like Kellough et al. (2008), who ultimately focused on eye gaze rather than other measures. Our inspection of the data led to the same concerns with respect to the distance traveled by participants' eyes. Moreover, the distance between CS1 and US+ was always the same because of the reinforcement corridor, where participants firstly had to look at CS1 before targeting the US+ zone that delivered the 2s US+. The same problem arose for the test of CS2.

Participant X1 :

Time elapsed	Number of trial	Phase	CS	Response	Cotation	RT (s)
103.004	21	2	3	0	1	NaN
112.760	22	2	1	1	1	0.225
119.249	23	2	3	0	1	NaN
126.644	24	2	1	1	1	0.000
135.264	25	2	3	1	0	1.603
141.748	26	2	3	0	1	NaN
149.196	27	2	1	1	1	0.121
155.691	28	2	3	0	1	NaN
163.312	29	2	1	1	1	0.804
169.813	30	2	3	0	1	NaN
Time	Trial	Phase	CS	Behavior	Point	RT
178.199	31	3	2	1	1	1.324
186.577	32	3	4	0	1	NaN

Table 3 : Example of RTs observed in Phase 2 and Test for Participant X1.

Participant X2 :

Time elapsed	Number of trials	Phase	CS	Response	Cotation	RT (s)
105.671	21	2	1	1	1	1.704
112.164	22	2	3	0	1	NaN
121.396	23	2	1	1	1	1.689
127.951	24	2	3	1	0	0.520
134.439	25	2	3	0	1	NaN
143.579	26	2	1	1	1	0.709
150.057	27	2	3	0	1	NaN
159.156	28	2	1	1	1	1.685
165.636	29	2	3	0	1	NaN
Time	Trial	Phase	CS	Behavior	Point	RT
174.044	30	3	2	1	1	0.107
182.420	31	3	4	0	1	NaN

Table 4 : Example of RTs observed in Phase 2 and Test for Participant X2.

## 5.2. Pupil diameters :

A central limitation of my eye tracking equipment is that no pupil diameters could be recorded because of technological reasons. It could have been an interesting measure as reported in several published papers for emotional aspect (e.g., Bradely et al., 2008 ; Morimoto et al., 2000).

## 5.3. Eye gaze :

Finally, I examined eye gaze as an efficient measure to test the SPC paradigm I created. Eye gaze is considering as an efficient measure in visual attention paradigms because of its universal aspect (e.g., Kellough et al., 2008 ; Morimoto et al., 2005). Eye gaze data have been used in ophthalmology, neurology, psychology, and related areas to study oculomotor characteristics and abnormalities, and their relation to cognition and mental states. The main advantage of eye gaze is that there are poor intra-participant and inter-participant variability with short duration presentations (Morimoto et al., 2005). In our experimental task, we used this kind of measure because we wanted to study the differences of associative responses across the lifespan, without any bias caused by intra-individual differences about latences of ocular reflexes (as observed with RTs). Thus, the eye tracking system accurately recorded eye gaze for each zone of the computer screen for each participant. Specifically, after 2s of CS2 and 2s of CS4 presentations, eye gaze was recorded for each zone with respect to the last 2s.

For each participant, we obtained the following data concerning the amount of gaze time spent in each zone of the computer screen (see Table 5) :

Participant 35	ZUS(s)	Z1(s)	Z2(s)	Z3(s)
CS1	85.62	0	14.38	0
CS2	46.39	15.19	5.12	33.3
CS3	0	100	0	0
CS4	0	0	65.39	34.61

37	ZUS(s)	Z1(s)	Z2(s)	Z3(s)
CS1	100	0	0	0
CS2	100	0	0	0
CS3	0	0	100	0
CS4	0	0	0	0

Table 5 : Representations of the amount of time of eye gaze data for participants numbers 35 and 37 on ZUS, Z1, Z2, and Z3, after CSs presentations.

For CS1 and CS3, we obtained the mean percent of eye gaze by using all trials in Phase 2 where CS1 and CS3 were presented without any visual guidance. For CS2 and CS4, we obtained the mean percent of eye gaze for each single trial in Test after CS2 and CS4 presentation. As explained in next chapters, mean percent of eye gaze for each single trial after CS2 and CS4 presentations were transformed in dichotomous measure.

As can be seen in Table 5, participants typically targeted one zone after a CS presentation. Participant 37 looked only US zone after CS1 presentation, the same thing for CS2 (i.e., quotation « 1 »). After CS3 presentation, we observed a high visual fixation in Z2, while participants did not look at the zones at all after CS4 presentation (i.e., quotation 0). In that case, participant looked at the center of the screen where the stimulus appeared. If participants did not look at the computer screen (which sometimes happened at the beginning of the experiment, but not after Phase 1), the experimental task was momentarily stopped until the participant looked again at the computer screen. If this happens, a « Err » message was recorded and participant was removed from our experiment.

## CHAPTER 3 :SPATIAL CONTIGUITY AND SPC

In order to create an experimental task to assess SPC in humans without using any instructions, we investigated some parameters considered to be central to the establishment of higher order conditioning in other species. Indeed, temporal and spatial contiguity are often discussed as being critical in first and higher order conditioning. That is why the role of spatial contiguity is discussed below.

### 1. Introduction :

Warren (1921) reported Aristotle's thoughts from *On memory and Reminiscence* which focused on the role of spatial and temporal contiguity in the establishment of associative learning. Based on observation, Aristotle proposed that the two closer events were physically and temporally, the better the subsequent recall of one given presentation of the other. Since then, many studies have confirmed his reflections in the temporal domain as underlined by Savastano and Miller (1998), while the role of spatial contiguity has been less studied.

#### 1.1. First order conditioning and spatial contiguity :

Wasserman, Franklin, and Hearst (1974) is one of the better known reports that focused on the role of spatial contiguity in Pavlovian conditioning. Here, the behavior of pigeons pecking a response key to obtain food was studied. In a first phase, a light was paired with the delivery of feed independent of the pigeon's behavior. Subsequently, at the mere presentation of this light, the pigeon pecked the keylight obtaining food. In parallel, another light discriminated by the pigeon was associated with key pecking not being reinforced with food. When this light appeared in the box, the pigeon did not go to the food hopper and did not get food. In a second phase, Wasserman et al. manipulated the spatial location of these lights, bringing them closer to the hopper. In an experimental condition, the lights appeared near the response key. In another condition, these lights were positioned opposite the feeder. Wasserman et al. observed that the accuracy of the discriminative behavior was higher in the condition where the CS+ keylight was close to the hopper (source of the US). Although these results are questionable because of possible cost-of-response biases in the condition that the two stimuli were distant from each other, the authors demonstrated that the spatial contiguity between these two stimuli favored emergence of the target behavior.

Cabrera and Vila (1986) found similar results in a learning task where the pigeon had to press keylight (CS) delivering food when a light (CS) appeared with a small or large located distance from the lever. In one of their experiments, two experimental conditions were tested: a first in

which the keylight was close to the hopper and a second where this light was placed at the opposite end away from it. Thus, spatial contiguity was tested with 5 possible localization (i.e. A ; B ; C ; D and E) : A condition was the closest zone to the food hopper, B was a position with a little more distance between the keylight and the hopper, until the farthest placement E where the distance between keylight and hopper was greatest. Cabrera and Vila observed that the rate of conditioned responses was higher in the condition where the light was close to the hopper, compared to the condition where the keylight appeared at its opposite extreme.

Similarly, Christie (1996) demonstrated the role of spatial contiguity in a task with a reinforcement delay. Doves were placed in a box where a light (CS) was placed from 11 cm or 74 cm from a hopper (US) which allowed access to food. In addition, the time to obtain food after the light came on ranged randomly up to 5 seconds for each dove. Mean proximity and number of approaches were recorded in both experimental conditions. Christie (1996) observed a higher number of approaches in the condition in which the light was placed close (11 cm) to the keylight, regardless of the delay in obtaining the food.

Thus, the role of spatial contiguity had been demonstrated in first order conditioning. The studies previously described highlighted the need to experimentally assess the role of spatial contiguity in higher order conditioning, specifically on the role of spatial contiguity between CS2-CS1 pairings.

### 1.2.Higher order conditioning and spatial contiguity :

Unfortunately, there are very few studies focused on the role of spatial contiguity in the establishment of higher order conditioning. One of those is the famous study of Rescorla and Cunningham (1979). In that study, Rescorla and Cunningham presented to pigeons a CS1 associated with a US in Phase 1, followed by several presentations of CS2-CS1 pairings in Phase 2. More specifically, a light (CS1) was associated with pecking a response key, thus enabling food delivery. Later, this light (CS1) was paired several times with another light (CS2) without presence of the response key. Second-order conditioning was observed when the conditioned response of pecking the key was elicited after CS2 presentation. Here, Rescorla and Cunningham manipulated the distance between the two CS2-CS1 stimuli: these stimuli were either presented separately or close together. In one condition, CS2 and CS1 were presented together in the same side of the box ; in another condition one CS was presented on one side of the box and the other CS at the opposite side. Results showed a higher conditioned response rate of pecking in the presence of CS2 alone in the condition when CS2 and CS1 had been

presented on the same side of the box, compared to the response rate observed in the condition where CS2 and CS1 were presented spatially separated. Thus, Rescorla and Cunningham highlighted the role of the spatial contiguity in the establishment of higher order conditioning using a second order conditioning procedures (not to be confused with SPC in which the two phases of training are reversed relative to second order conditioning).

There is, however, a huge difference between the tasks described previously and our experimental task. All those experiments implied a spatial contiguity between a conditioned stimulus (CS) and an unconditioned stimulus (US, i.e., a biologically significant stimulus) during the pairings presentations (Cabera & Vila, 1986, Christie, 1996, Wasserman, et al., 1974). The same is true for the second order procedure mentioned above: the US was paired with CS1 in phase 1 (Rescorla & Cunningham, 1979). Critically, West et al. (2009) argued that the success of second order conditioning depended on the US to receive greater attention compared to other stimuli used in higher order conditioning. In that study, several biological determinants were presented to humans. Precisely, participants were exposed to neutral faces (NS) compared to facial expressions of joy and anger (US). Gaze time was recorded for all faces. West et al. observed a higher gaze time on faces with facial expressions of joy and anger compared to neutral faces. In addition, the attention paid to neutral faces was higher when these initial NSs that had been paired with faces of joy and anger than when they had not been. When West et al. paired neutral faces with joy and anger faces (NS-CS), the neutral stimuli were more looked at more after being paired with CSs.

### 1.3. In our experiment :

To our knowledge, no study of SPC has ever manipulated spatial contiguity. Here we asked whether, when the two neutral stimuli (CS2 and CS1) are close to each other during Phase 1, conditioned responding to CS2 at the test would be stronger than when CS2 and CS1 were more distant from each other. The present experiment examined the role of spatial contiguity using two experimental conditions: a space between CS2 and CS1 (A) and no space between CS2 and CS1 (B). The procedure consisted of three phases: Phase 1 in which two neutral stimuli (CS2 and CS4) were each simultaneously paired with another neutral stimulus, that is, CS2-CS1 and CS4-CS3 were presented; and Phase 2 in which CS1 was sequentially paired with a US+ (potentially making it an effective CS for US+) and CS3 was paired with a US- (potentially making it an effective CS for US-). Cue offset and US onset were simultaneous in Phase 2. Then, in Phase 3 all four cues were tested independently. Critically, in Phase 1 the

two stimulus elements of each pair were separated by 100 pixels in Condition A, whereas they were immediately adjacent in Condition B. Except for the difference in inter-stimulus distance during Phase 1, exactly the same procedures were used in Conditions A and B.

## **2. Method :**

### **2.1. Participants :**

Forty French university students (27 females and 13 males; 18-30 years old) volunteered; participants were randomly assigned to one of two groups (A or B,  $n_s = 20$ ). Each participant read and signed an informed consent form prior to the experiment. The experiment had been approved by the University of Lille Institutional Review Board.

### **2.2. Apparatus :**

An eye-tracking system was used in conjunction with a conventional computer. Participants faced a computer screen (Dell Model Optiplex 7010) equipped with infrared cameras that monitored eye movements. The eye-tracking system (FaceLAB#5.1) recorded the participants' eye movements including visual fixations. There was no physical restraint of participants' heads because the system was programmed to track the participants' visual focus, even when they moved their heads. Thus, participants were only required to watch the computer screen. This system facilitated our not having to provide participants with any explicit instructions.

### **2.3. Materials :**

The CSs were four 6 cm x 6 cm colored squares (red, blue, green, and yellow), each containing different shapes (triangles, squares, rounds, or stars). For each participant, the CSs were randomly created combining a unique color and a unique shape (see Chapter 2 for examples). Thirty 2s, video cartoon clips of pleasant scenes were used as US+ and one of them, randomly selected without replacement, was presented immediately after each correct response during Phase 2. Each video included action by cartoon characters such as Kung Fu Panda, Dragons, or Kuzco. A single 100 dB, 2s, unpleasant sound was used as US- and was emitted from the computer's two speakers for each error during Phase 2.

The four colored squares were presented at the center of the computer screen. The 2s presentations of the US+ were presented in a 13 cm x 8 cm rectangle in a corner of the screen and US- (an aversive noise) was also produced by the computer. The experimental procedure was controlled by Matlab 7.0 software, which was also used to analyze the data.

#### 2.4. Procedure :

Participants were initially seated in front of a dark gray background computer screen. At the start of the experiment, four visual stimuli were randomly selected as CS1, CS2, CS3, and CS4.

Phase 1 began with a sequence of ten simultaneous pairings of CS1 with CS2 and ten simultaneous pairings of CS3 with CS4. On each Phase 1 trial (CS2-CS1 or CS4-CS3), the pair of cues were presented horizontally aligned at the center of the screen. On each trial, which cue was to the left was randomly determined. To avoid possible configuring of the two squares as a single elongated rectangle in Condition B, on each trial, the left cue 'flew' in from the left edge of the screen (bottom, center, or top, randomly selected on each trial) and the right cue 'flew' in from the right edge screen (bottom, center, or top, randomly selected on each trial). The arrival flights took 15 ms. Each cue pair then persisted at the center of the screen for 2.0 s. Each stimulus pair appeared ten times in a random order. Critically, even in the distal condition the visual angle subtended by the pair of stimuli, outer edge to the outer edge, was only 9 degrees. Thus, the cue pairs were fully within participants' visual field in both conditions A and B.

Phase 2 immediately followed Phase 1. CS1 and CS3 were individually presented in random order at the center of the screen, after entering the screen in motion as described above for Phase 1. When the US+ appeared at the termination of the 2 s CS1, it was presented in a unique specific zone of the computer screen randomly selected for each subject (top right, top left, bottom right, or bottom left), but consistent for all trials for any given participant. When CS1 appeared, a solid line black 7 cm x 7 cm cross was presented in the US+ zone. Participants had to fixate on that zone before the cue presentation was over in order to obtain the short video clip. If they failed to do so, the trial ended and a new trial with CS1 began with this sequence being repeated until the correct response was emitted. After three consecutive correct responses to CS1, the cross was faded into a dotted line cross. Participants still had to look at the US+ zone to obtain the video clips. When CS3 appeared, participants had to look away from the US+ zone; otherwise the US- (i.e., an unpleasant sound) was emitted and a new trial with CS3 began. Phase 2 ended when a participant emitted three consecutive correct responses with the dotted line cross for CS1 and three consecutive correct responses for CS3 without an intervening error. When participants reached this performance criterion, they were tested on CS2 and CS4. We used this criterion for Pavlovian conditioning to be sure that CS1 was associated with the US+ and CS3 was associated with the US-: this

first order conditioning is known to be necessary to reveal any SPC established during Phase 1 (e.g., Rescorla, 1980).

CS2 and CS4 were each separately tested once, entering in motion as described before. We used a single test trial for each cue to avoid extinction effects that would have permitted early test trials to reduce the sensitivity of subsequent test trials. The critical question was whether participants would anticipate the appearance of a movie clip when CS2 or CS4 was presented. Testing was in extinction; that is, even if participants looked at the US+ zone, no video clip was presented. To avoid possible order-of-testing effects, we controlled for whether the first test trial was a CS2 or a CS4 presentation. For 10 participants in each condition, testing began with the CS2 trial followed by the CS4 trial; for the other ten participants in each condition, the order was reversed.

The experiment used one dependent variable: eye gaze on the different zones of the computer screen which was recorded by the eye-tracking system and Matlab 7.0. During Phase 2 and testing, eye gaze to different zones was recorded from the beginning of each trial (i.e., CS onset) to its termination (i.e., time of CS termination regardless of whether a US was presented). For CS1 and CS3 presentations during Phase 2, percent of CS1 trials and percent of CS3 trials with CRs were calculated for each participant. This percentage per participant was then used to compute means eye gaze across participants within each of the two groups. The same procedure was used for CS2 and CS4 test trials except there was only one trial per CS. Thus, we used the percentage of participants responding to CS2 and CS4 instead of mean eye gaze. CS2 and CS4 were considered as targeted if visual fixation times were higher in the US zone compared to other computers' zones after CSs presentations.

### **3. Results :**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of the means of two independent groups, we obtained a recommended sample size of at least 106 participants, with at least 53 participants per group. However, despite this recommended group size, in this study we managed to recruit only 40 participants, with 20 in each group. Hence, we conducted our analysis with nonparametric statistics to our interpretations of these results.

#### 3.1. Statistical issues :

Some floor and ceiling effects were observed and variance in the results was artificially low across participants within our experimental groups. Moreover, our samples did not yield normality in the data within groups. See below the statistical nonparametric tests used in order to illuminate the results of the experimental task with  $p (<.05)$ .

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution. We used the Mann-Whitney U test in previous studies (i.e., Craddock et al., 2014 ; Renaux et al., 2017).
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.
- The **Cliff's Delta** statistic is a nonparametric effect size measure that quantifies the amount of difference between two groups of observations beyond p-value interpretation.

### 3.2. Statistical analysis :

#### 3.2.1. *Phase 1* :

Figure 16 shows visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1. There was no statistical difference in visual fixation duration between the A and B conditions (respectively,  $U = 144.00$ ,  $p = .13$  and  $U = 136.50$ ,  $p = .09$ ) nor between the two types of stimuli pairs (for condition A,  $W = -.71$ ,  $p = .48$  and for condition B,  $W = -.83$ ,  $p = .41$ ). That is, visual fixation duration was approximately the same for CS1-CS2 and CS3-CS4 presentations in both conditions: 87.45% of visual fixation for CS1-CS2 in condition A and 82.79% in condition B; 89.70% of visual fixation for CS3-CS4 in condition A and 82.51% in condition B. Note that the statistically nonsignificant tendency for more fixation time in condition A than condition B would, if anything, favor better conditioning in condition A than B. This would be contrary to the expectation that the closer spatial contiguity of cues in condition B than A would encourage stronger conditioning in condition B than A.

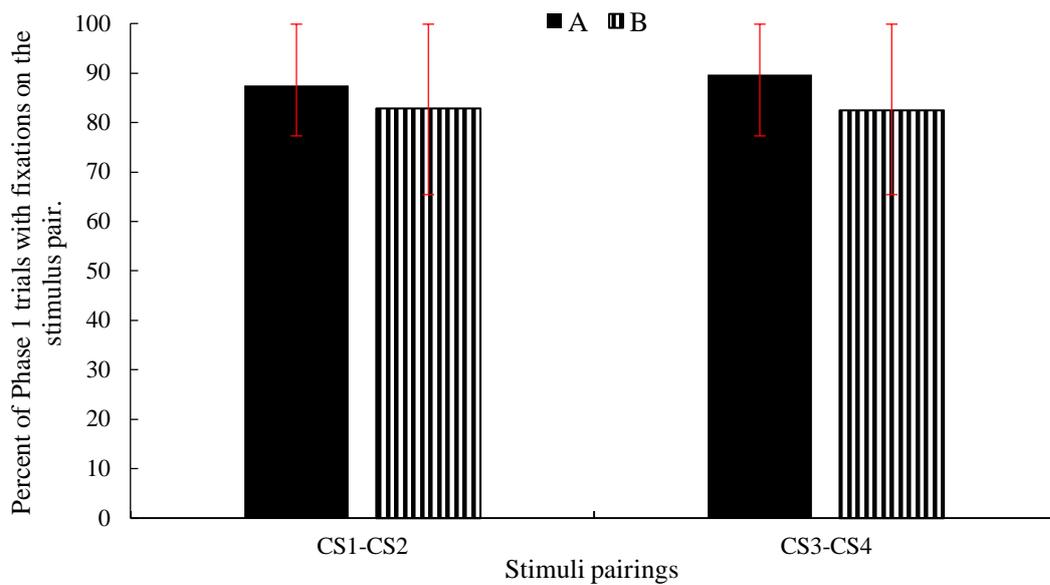


Figure 16. Mean percent of Phase 1 trial duration in which participants visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. With 2 s trials and 10 trials of each type, the maximum fixation time was 20 s for each stimulus pair. Error brackets represent SEMs.

### 3.2.2. Phase 2 :

Phase 2 first-order conditioning results are depicted in Figure 17. Not surprisingly, there was higher responding to CS1 than to CS3 both in condition A ( $W = 151, p = .005, \text{Cliff's } d = 1.0$ ) and in condition B ( $W = 166, p = .002, \text{Cliff's } d = 0.9$ ). Thus, all participants finally approached the US+ location when CS1 appeared and avoided the US- location when CS3 was presented. No interaction was observed between Condition and Cue. Consequently, it is implausible that any differences observed in SPC test performance were caused by differences other than those in Phase 2 conditioning.

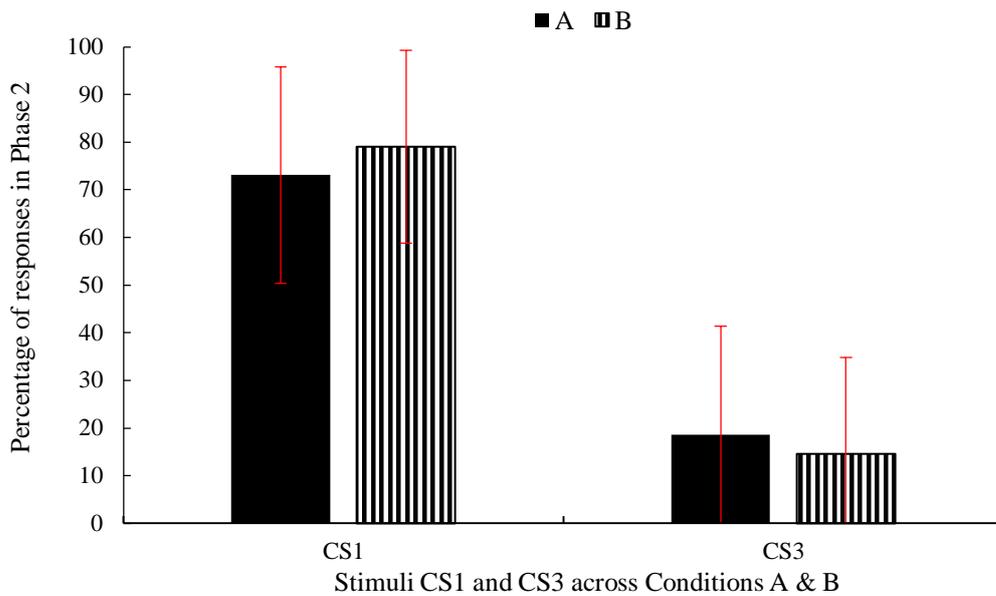


Figure 17. Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during Phase 2. Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 18 displays the number of participants exhibiting SPC responses at the test as defined by visually responding to CS2 (i.e., visual fixation to the US+ site). In Condition A, SPC was observed in only 8 of the 20 participants (i.e., 40%) compared to 16 of the 20 in Condition B (i.e., 80%), Fisher's exact test  $p = .013$ . Thus, we demonstrated that SPC is greater when the neutral stimuli in Phase 1 were presented adjacent compared to a condition when there was a distance between them. There was no difference between conditions A and B in the low percent of participants with saccades to the site of US+ in response to CS4. One cannot differentiate here between participants actively looking away from the site of US+ and no SPC to S4 having occurred. Notably, our SPC task actually consisted of two tasks, approaching the US+ location given CS2 and avoiding the US+ location given CS4. However, as avoiding the US+ location on CS4 test trials was not distinguishable from an absence of learning, only the greater responding to CS2 in condition B in contrast to condition A is indicative of increased SPC with greater spatial contiguity.

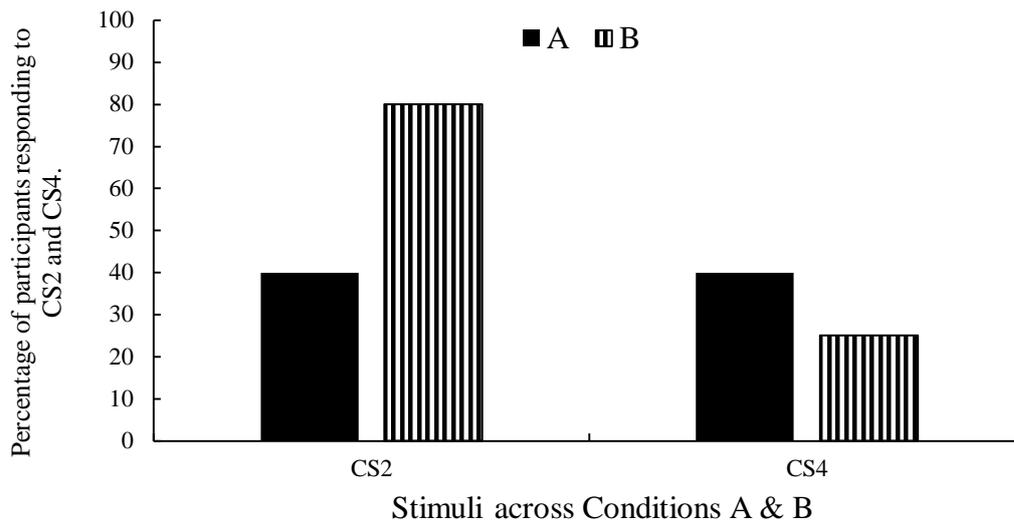


Figure 18. Percentage of participants during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of saccades to the video site during the CS4 test in conditions A and B.

#### 4. Discussion :

Our results show a greater SPC response in condition B compared to condition A, whereas there was no difference between the two conditions in first order responding to CS1 nor to CS3. The experiment demonstrated that spatial contiguity enhances the formation of associations in SPC. When neutral stimuli were adjacent (i.e., condition B), we observed greater SPC compared to a condition in which the CSs were separated (i.e., condition A). This observation replicates what previous studies found with regard to the effect of spatial contiguity on higher order conditioning when one of the stimuli had already been made biologically significant through prior conditioning (i.e., second order conditioning; Rescorla and Cunningham, 1979). Thus, the present observations lend support to the conclusion that spatial contiguity, like temporal contiguity, facilitates higher order conditioning just as it is well known to facilitate first order conditioning.

The importance of spatial contiguity to conditioning is already incorporated into numerous applications. For example, the benefits of good spatial contiguity are already used in applied behavior analysis for training individuals with developmental disabilities (Barnes, Smeets, & Leader, 1996). Here we observed higher conditioned responses to a neutral stimulus that was previously paired with another neutral stimulus when the two cues were closer together in space. As this parallels prior observations concerning the important of spatial proximity for first order conditioning, SPC's dependence on spatial contiguity seems to add weight to the

view that associative learning between neutral stimuli is driven by the same processes that govern the acquisition of associations between stimuli when one of them is biologically significant. Notably, this conclusion is contrary to that of at least some other research (e.g., Rescorla, 1981) that suggests that SPC involves different processes than first order conditioning.

One final aspect of the present data is worthy of note. Associations between two adjacent stimuli were established despite participants' being given no instructions and the associates both lacking biological significance. This suggests that SPC is a default process that occurs whenever subjects attend to presented stimuli. This preparation in conjunction with our observation of SPC could provide an opportunity to use behavioral procedures to assess basic associative learning in individuals lacking verbal abilities (e.g., dementia, infancy), as SPC responses such as ours can be obtained without using any instructions or restraints.

## CHAPTER 4 :

### NUMBER OF STIMULI PAIRINGS IN PHASE 1 OF SPC IN ADULTS

Another concern presents in the first and higher order conditioning literature in rats and pigeons is the number of stimuli pairings used in experimental tasks. Because we wanted to test the same conditioned response across ages (i.e., young adults and the elderly), we had to examine the role of the number of pairings on conditioned responding – seeking a number that would work the same for young and elderly humans.

#### 1. Introduction :

Many studies have tried to evaluate the minimum required number of CS-US pairings for first order conditioning (for review, see DeHouwer, Thomas, & Baeyens, 2001, p.856-857). For example, several studies showed that the rate of conditioned response increased monotonically with the number of stimuli pairings. Baeyens, Eelen, Crombez, and VanDerBergh (1992) observed such a phenomenon on electrodermal responses after visual stimuli presentations. In that study, stimuli were presented 2, 5, 10 or 20 times. Baeyens and al., observed a higher rate of electrodermal response after ten stimuli presentations. Then, a decrease of the response rate was observed after the tenth pairing until the end of the experiment. However, authors demonstrated a better recall of those stimuli after 20 presentations and stated that the more the stimuli were presented, the better its recall was.

Such conclusions were not shared by other researchers like Martin and Levey (1987). In addition, Stuart, Shimp, and Engle (1987) demonstrated that a single CS-US pairing could be sufficient to establish a conditioned response. In their experiment, Stuart et al., paired visual conditioned stimuli with outcomes of negative or positive valence. Conditioned responses were recorded starting with the first CS-US presentation. Here, Stuart and al. emphasized the significance of the valence of the US they used, which were human facial expressions such as happiness (US+) and anger (US-). In Pavlovian conditioning, Urcelay et al. (2012) highlighted a phenomenon called « the post-peak depression » based on previous work by Pavlov (1927). In a first experiment, four groups of rats received 5, 10, 20, or 50 pairings of a clicker followed by a footshock. At tests, all rats were tested for suppression linking. Urcelay and al. (2012) observed a decreased suppression to the CS at test after increasing the number of reinforced trials in the training context. Precisely, the conditioned response was lower after 50 pairings compared to 5, 10, and 20 pairings conditions. There were no differences in the degree

of suppression response across the 5, 10, and 20 pairings groups, which is in contrast with Baeyens's (1992) works.

### 1.1. Number of stimuli pairings in higher order conditioning studies :

Few studies focused on the role of the number of stimuli pairings in the establishment of higher-order conditioning. Prewitt (1967) was one of the first scientists to study that parameter in the establishment of SPC. In that study, 72 rats were exposed to 0, 1, 4, 16 or 64 stimulus pairings, one of those stimuli being paired with an emotional US in the second phase of the task. CSs were composed of a light and a tone, with one of those then being paired with a footshock (US-) when rats were close to a food area. Prewitt (1967) observed a higher rate of SPC after 16 stimuli pairings presented in first phase compared to other conditions. In addition, they observed that the response rate was significantly lower after 64 stimuli pairings presented in first phase as compared to the response rate after 16 pairings in the first phase. Prewitt discussed the disparity of his results as compared to those of his contemporaries.

A few years later, Yin, Barnet, and Miller (1994) studied second order conditioning. In that study, the stimuli pairings were presented 12 or 24 times in a second phase of the paradigm. Here, sounds (CSs) were presented to rats after being associated with a footshock (US-). Conditioned responding was observed at the test in the form of a decrease in the number of licks in the water dispenser when CS1 or CS2 was presented. Results showed a decrease in licking after CS1 presentation in all experimental conditions. When CS2 was presented, the conditioned decrease in licking was greater after 12 stimuli pairing presentations compared to 24 stimulus pairings in the second phase. Yin et al. concluded that the number of stimuli pairings was crucial in the observation of higher conditioning. Indeed, too many stimuli pairing presentations could be antagonistic to that kind of associative learning. Subsequently, Stout, Escobar, and Miller (2004) confirmed these results by presenting 0, 4, 20, or 100 CSs pairings to rats, one of those stimuli then being paired with a footshock (US-). Once again, Stout and al., (2004) observed a decrease of the conditioned stimulus control of behavior by the 20th stimulus pairing in second phase.

Thus, those studies underline the role of the number of stimulus pairings in the establishment of higher order conditioning when an aversive unconditioned stimulus US- was used. Here, we note that no experiment to our knowledge focused on that experimental variable using an appetitive unconditioned stimulus US+. One of my goals was to assess the impact of the number of CS-CS stimuli pairings using both a US+ and a US- in the SPC paradigm.

## 1.2. In our experiment :

The number of stimuli pairings of CS2-CS1 and CS4-CS3 was thus manipulated, presenting each stimulus pairing 10 times (condition *ad10 pairings*) or 20 times (condition *ad20 pairings*) in the first phase of the SPC task. Specifically, CS1 was simultaneously presented with CS2 several times (10 or 20 times across conditions). The same procedure was used between CS3 and CS4 presentations. In the second phase, CS1 was followed by an appetitive unconditioned stimulus US+ while CS3 was paired with an aversive unconditioned stimulus US-. In tests, visual fixation times were recorded for each participant to the different computer areas after individual presentations of CS2 and CS4. This methodology was the same for both experimental conditions, except for the number of stimuli pairings presented in the first phase of the SPC task. In condition *ad10 pairings*, stimulus pairings CS2-CS1 and CS4-CS3 were simultaneously presented 10 times with the two types of trials in random order. In condition *ad20 pairings*, stimulus pairings were presented in the same way 20 times. Our hypothesis was that we would observe a lower visual fixation rate on the US+/- zone in condition *ad20 pairings* when CS2 was presented compared to condition *ad10 pairings*. In addition, we sought to observe the same results showed by Prewitt (1967) with another SPC task, that is, the avoidance of an aversive stimulus US- (i.e., in our study, the US- was a loud sound). In our experience, such an observation would result in a low rate of visual fixation on the US+/- zone after the presentation of CS4 in condition *ad20 pairings*.

## 2. **Method** :

### 2.1. Participants :

Forty French university students (29 females and 11 males ; 19 (min) and 35 (max) years old) volunteered ; participants were randomly assigned to one of the two groups (*ad10 pairings* or *ad20 pairings*, ns = 20). Each participant read and signed an informed consent form prior to the experiment. That experiment had been approved by the University of Lille Institutional Review Board.

### 2.2. Material :

An eye-tracking system was used in conjunction with a conventional computer. Participants faced a computer screen (Dell Model Optiplex 7010) equipped with infrared cameras that monitored eye movements. The eye-tracking system (FaceLAB#5.1) recorded the participants' eye movements including visual fixations. There was no physical restraint of participants' heads because the system was programmed to track the participants' visual focus

even when they moved their heads. Thus, participants were only required to watch the computer screen. This system facilitated our avoiding giving participants any explicit instructions.

The CSs were four colored geometric shapes (red, blue, green, and yellow, see Figure 8 Chapter 2 for examples). Thirty 2 s, video cartoon clips of pleasant scenes were used as US+ and one of them, randomly selected without replacement, was presented immediately after each correct response during Phase 2. Each video included action by cartoon characters such as Kung Fu Panda, Dragons, or Kuzco. A single 100 dB, 2 s, unpleasant sound was used as US- and was emitted from the computer's two speakers for each error during Phase 2.

The four colored geometric shapes were presented on the center of the computer screen. The 2 s presentations of the US+ were presented in a 13 cm x 8 cm rectangle in a corner of the screen, and US- (an aversive noise) were both produced by the computer. The experimental procedure was controlled by Matlab 7.0 software, which was also used to analyze the data.

### 2.3. Procedure :

The following procedure is similar to the one presented in Chapter 3, except for the parameters concerning the number of stimulus pairings in Phase 1 and the shapes of the CSs.

Participants were initially seated in front of a dark gray background computer screen. At the start of the experiment, four visual stimuli were randomly selected as CS1, CS2, CS3, and CS4. Phase 1 began with a random sequence of simultaneous pairings of CS1 with CS2 and simultaneous pairings of CS3 with CS4. In condition *ad10 pairings*, stimuli pairings were presented 10 times. In condition *ad20 pairings*, stimulus pairings were presented 20 times. On each Phase 1 trial (CS2-CS1 or CS4-CS3), the pair of cues were presented contiguously, horizontally aligned at the center of the screen. On each trial, which cue was to the left was randomly determined. The stimuli 'flew' onto the screen as described in Chapter 3. Each cue pair then persisted at the center of the screen for 2s. Each stimulus pair appeared ten times in a random order.

Phase 2 immediately followed Phase 1. CS1 and CS3 were individually presented in random order at the center of the screen, after entering the screen in motion as described in Chapter 3. When the US+ appeared at the termination of CS1, it was presented in a unique specific zone of the computer screen randomly selected for each subject (top right, top left, bottom right, or bottom left), but consistent for all trials for any given participant. When CS1 appeared, a solid line black 7 cm x 7 cm cross was presented in the US+ zone. Participants had to look at that zone before the cue presentation was over in order to obtain the short video

clip. If they failed to do so, the trial ended up and a new trial with CS1 began until the correct response was emitted. After three consecutive correct responses to CS1, the cross was faded into a dotted line cross. Participants still had to look at the US+ zone to obtain the video clips. When CS3 appeared, participants had to look away from the US+ zone; otherwise the US- (i.e., an unpleasant sound) was emitted and a correction trial with CS3 began. Phase 2 ended when a participant emitted three consecutive correct responses with the dotted line cross for CS1 and three consecutive correct responses for CS3 without an intervening error. We used this criterion for Pavlovian conditioning to be sure that CS1 was associated with the US+ and CS3 was associated with the US-: this first order conditioning was necessary to reveal any SPC established during Phase 1.

CS2 and CS4 were each separately tested once, entering in motion as described before. We used a single test trial for each cue to avoid extinction effects that would have permitted early test trials to reduce the sensitivity of subsequent test trials. We investigated whether participants would anticipate the appearance of a movie clip when CS2 or CS4 was presented. Testing was conducted in extinction; that is, even if participants looked at the US+ zone, no video clip was presented. To avoid possible order-of-testing effects, we controlled for whether the first test trial was a CS2 or a CS4 presentation. For 10 participants in each condition, testing began with the CS2 trial followed by the CS4 trial; for the other ten participants in each condition, the order was reversed.

That experiment used eye gaze as dependent variable, like in Chapter 3. Eye gaze on the different zones of the computer screen was recorded by the eye-tracking system and Matlab 7.0. During Phase 2 and testing, eye gaze to the different zones was recorded from the beginning of each trial (i.e., CS onset) to its termination (i.e., time of CS termination regardless of whether a US was presented). For CS1 and CS3 presentations during Phase 2, percent of CS1 trials and percent of CS3 trials with CRs were calculated for each participant. This percentage per participant was then used to compute means eye gaze across participants within each of the two groups. The same procedure was used for CS2 and CS4 test trials except there was only one trial per CS.

### **3. Results**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis

viewed as a comparison of the means of two independent groups, we obtained a recommended sample size of at least 106 participants, with at least 53 participants per group. However, despite this recommended group size, in this study we managed to recruit only 40 participants, with 20 in each group. Hence, we conducted our analysis with nonparametric statistics to our interpretations of these results.

### 3.1. Statistical issues :

We used the same statistical tools in Chapter 3 (Renaux et al., 2017) :

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution. We used the Mann-Whitney U test in previous studies (i.e., Craddock et al., 2014 ; Renaux et al., 2017).
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.
- The **Cliff's Delta** statistic is a nonparametric effect size measure that quantifies the amount of difference between two groups of observations beyond p-value interpretation.

### 3.2. Statistical analysis :

#### *3.2.1. Phase 1 :*

Figure 19 shows visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1. There was no statistical difference between the two types of stimuli pairs ( $W = -.35$ ,  $p = .72$ ), nor between the *ad10 pairings* and *ad20 pairings* conditions (respectively,  $U = 112.00$ ,  $p = .17$  and  $U = 152.00$ ,  $p = .19$ ). That is, visual fixation duration was approximately the same for CS1-CS2 and CS3-CS4 presentations in *ad10 pairings* and *ad20 pairings*: 88.75% of visual fixation for CS1-CS2 in condition *ad10 pairings* and 62.95% in condition *ad20 pairings*; 84.30% of visual fixation for CS3-CS4 in condition *ad10 pairings* and 67.95% in condition *ad20 pairings*.

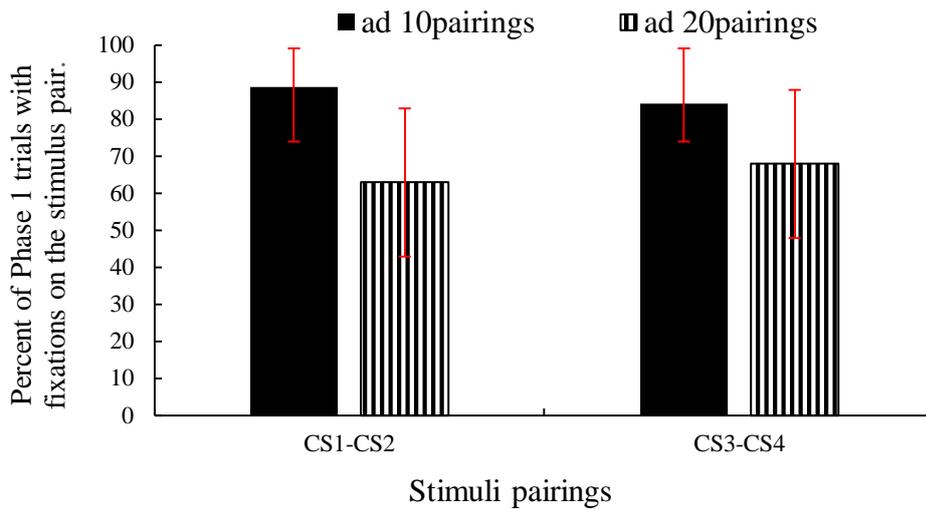


Figure 19. Mean percent of Phase 1 trial duration in which participants visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. Error brackets represent SEMs.

### 3.2.2. Phase 2 :

Phase 2 first-order conditioning results are depicted in Figure 20. There was greater responding to CS1 than to CS3 both in condition *ad10 pairings* ( $W = 157, p = .005, \text{Cliff's } d = 0.9$ ) and in condition *ad20 pairings* ( $W = 141, p = .003, \text{Cliff's } d = 0.8$ ). Thus, all participants finally looked at the US+ location when CS1 appeared and avoided the US- location when CS3 was presented. There was no interaction observed between Condition and Cue. That is, performances in Test were caused by Phase 2 conditioning.

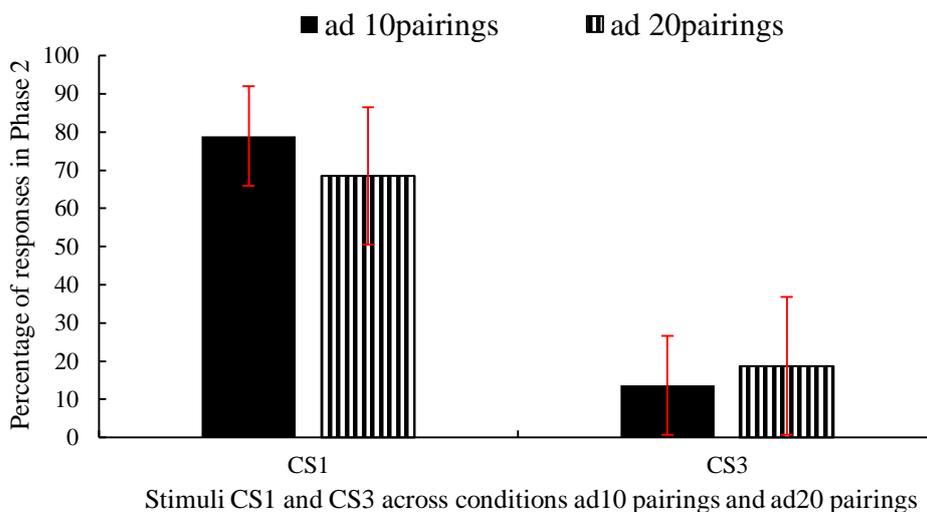


Figure 20: Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during the Phase 2. Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 21 displays the number of participants exhibiting SPC responses at test. In condition *ad10 pairings*, visual fixation after CS2 presentation was observed in 15 of the 20 participants (i.e., 75%) compared to 14 of the 20 in condition *ad20 pairings* (i.e., 70%), Fisher's exact test  $p = 1$ . We observed a difference in visual fixation after CS4 presentation. In condition *ad10 pairings*, visual fixation after CS4 presentation was observed in only 4 of the 20 participants (i.e., 20%) compared to 11 of the 20 in condition *ad20 pairings* (i.e., 55%), Fisher's exact test  $p = .048$ .

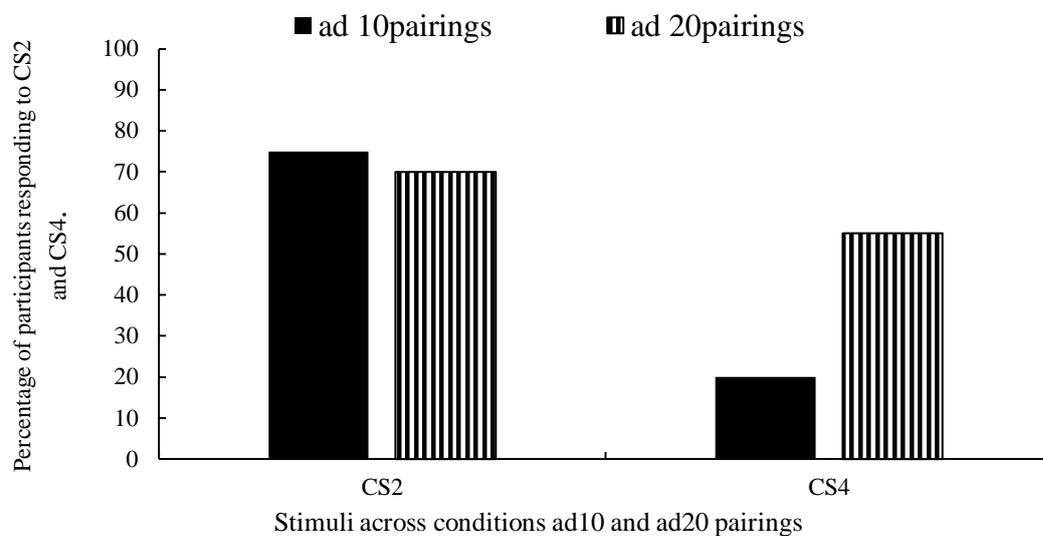


Figure 21. Percentage of participants during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of visual fixation to the video site during the CS4 test in conditions *ad10 pairings* and *ad20 pairings*.

## 5. Discussion :

Thus, we observed a better avoidance response when the neutral stimuli in Phase 1 were presented 10 times compared to a condition when stimuli were presented 20 times. There was no difference between conditions *ad10 pairings* and *ad20 pairings* concerning anticipatory phenomenon with responses to CS2.

Our results conceptually replicate the work of Prewitt (1967) who observed a higher rate of avoidance responses in rats after a moderate number of CS2-CS1 pairings when CS1 was subsequently paired with an unconditioned stimulus US- in an SPC task. Our work is also consistent with results found in other higher order conditioning procedures (Yin et al., 1994,

Stout et al., 2004) and others focusing on first order conditioning. For example, Baeyens et al. (1992) demonstrated that electrodermal response rates were maximal after 10 CS-US presentations and then decreased as the number of presentations increased to 20. Urcelay et al. (2012) also demonstrated the effect of "extended reinforced training" on the conditioned response. In that experiment, a cohort of rats was exposed to an increasing number of electric shocks (i.e., 5, 10, 20, and 50 presentations) contingent delivered after the appearance of a stimulus. Urcelay et al. (2012) observed a gradual decrease of the conditioned response rate as the number of trials increased.

Compared to the studies mentioned above, our results highlight the role of the number of stimuli pairings presented in the first phase in a higher order conditioning involving an appetitive unconditioned stimulus US+. In our experiment, we observed a higher rate of avoidance response with a lower number of stimuli pairing presentations, using US- in a SPC procedure. Here, the number of stimuli pairings seems to affect both CS-CS/US- conditioning relations, but not CS-CS/US+ conditioning relations. Therefore, we can conclude that the role of the number of stimuli pairings is critical in the establishment of associative learning, including SPC. When participants are confronted to a large number of stimuli pairings, weaker rates of conditioned response will be observed.

Explanations of the role of the number of stimuli pairings differ and are diversely discussed across the various papers reporting higher order conditioning. For example, Yin et al. (1994) and Stout et al. (2004) focused on the second order conditioning paradigm, which is related to the SPC paradigm but differs in the order of the two phases of training. In the Second-Order Conditioning procedure, these researchers explained the role of the number of stimuli pairings presented in the second phase in terms of extinction of the CS1-US association acquired in phase one. From a temporal point of view, the higher the number of CS2-CS1 presentations in the second phase, the more the CS1-US association of the first phase will be extinguished. So, few stimulus pairings presented in the second phase of Second-Order Conditioning could facilitate the observation of that kind of associative learning in the test phase. This account does not directly apply to SPC, but an analogous one might. In SPC, possibly the CS2-CS1 pairing acquired in Phase 1 is partially extinguished over many CS1-US pairings.

## CHAPTER 5 :

### ROLE OF TRIAL REPETITION FOR ELDERLY PEOPLE

In the previous chapters, we demonstrated that a limited number of stimuli pairings presented in the first phase of SPC was beneficial for its establishment (i.e., using US-). However, some geriatric studies have suggested that learning performances of elderly people differ from typical young adults. According to those studies, it was proposed that repetition had a more beneficial role in the acquisition of learning by the elderly compared to younger people. Moreover, because our next axis of research is concerned with the ontogeny of the SPC response through the human life span, it seems essential to test the effect of repetition on learning in elderly people. However, if large differences were observed between the elderly compared to younger people in basic learning, we could not use the same experimental task paradigm.

#### 1. Introduction :

##### 1.1. Beneficial role of repetition :

Some studies in geriatrics focused on the role of repetition in the elderly people with the aim of acquiring and maintaining learning at that developmental stage. For example, Law, Hawkins, and Craik (1988) compared performances of young adults with performance of seniors on a similar task of visual stimuli recall (here, different pictures). These authors observed lower performances in seniors in comparison to the younger participants. However, performances in elderly people were improved in the context where the stimuli were more often repeated. According to the study of Law et al. (1988), the effect of repetition does not appear to be as important in young adults in most experimental recall tasks. On the contrary, Swick and Knight (1997) demonstrated that repetition was beneficial in the recall of words and non-words in young adults as well as in elderly people. In that experiment, participants had to keep in mind lists of non-words (i.e., unknown words) and lists of words (i.e., existing words). The experimental task was to remember the items presented and determine whether each item was an existing word. Each word was repeated one to three times across experimental groups (i.e., young adults and elderly people). Swick et al. reported a higher recall rate in both experimental groups when the stimuli were repeated three times rather than only once. In addition, these authors found that stimulus repetitions were essential for seniors when they were asked to repeat and to discriminate an existing word from an unknown word.

Thus, different processes involved in verbal skills were highlighted by Swick and al. : repetition of stimuli seems to be necessary in elderly people for the differentiation between non-word and

word, but not for the simplest recall of the existing words. Conversely, repetition seems to have a significant effect on the young adults recalling stimuli, whereas the discrimination between non-words and words was not influenced by the stimuli repetition. In conclusion, Swick and Knight supported the beneficial role of repetition in learning about discrimination in seniors. In our behavioral task, which could be considered a discriminative task, we wanted to test the potential beneficial effect of the stimuli repetitions presented in the first phase of SPC on the conditioned response observed in tests.

### 1.2. Repetition in elderly with dementia :

Here, the role of repetition concerns neurodegenerative diseases possibly producing an impairment of memory and a general decrease in intellectual skills. Based on the hypothesis that verbal behavior may affect associative learning, one of our experimental groups was elderly people with senile dementia. We focused on the role of repetition of pairings in the establishment of SPC within this population. Camp and Shaller (1989) illustrated the effect of repetition in a representative study case in a hospital caring for elderly people with senile dementia. In their study, a 68-year-old patient had been hospitalized for several months in a retirement home specializing in cognitive impairment. This patient was hospitalized with many cognitive impairments, in addition to excessive alcohol consumption which compromised his safety outside the center. The learning task was to remember the given names and surnames of four staff members in the health center. The procedure consisted of presenting to the patient photos of the various staff members at varying time intervals of 5, 10, 20, 40, 60, 90, and 120 seconds. The patient was placed in front of an experimenter who presented pictures to him one by one according to specific intervals. For each picture presented, the patient had to declare the name of the individual corresponding to the picture. If the answer was correct, the trial was completed and the experimenter showed another picture. If the answer was incorrect, the test was repeated until the patient succeeded. The social reinforcer used in this case study was enhanced attention of the experimenter when the patient's performance was correct. In addition, Camp and Shaller followed up after six months and found that the patient's recall performance was largely correct. The beneficial effect of repetition highlighted in this case study was also found in other Alzheimer's patients with the same previously described procedure (Camp, 1989). Using a similar procedure, Ferraro, Balota, and Connor (1993) emphasized the role of repetition in typical elderly individuals and elderly people with Alzheimer's syndrome.

Nowadays, repetition is widely considered to have an important impact on the establishment of learning in elderly people, with or without senile dementia. Although its effects have been

demonstrated, frequency of repetition has not been tested in the studies presented above (e.g., Law & al., 1988). For example, Fleishman and Gabrieli (1998) reviewed studies that do not demonstrate the beneficial effect of repetition on learning in patients with Alzheimer's disease. Jacoby (1999) demonstrated the ironic effects of repetition on the performance of young adults and seniors. In this experiment, participants had to answer "yes" or "no" to words with respect to whether they had already been stated by an experimenter. The author observed that the more the stimuli were repeated, the more the number of recall errors increased in adults and seniors. Also, the number of repetitions was correlated with auto-aggressive behaviors at the end of the experiment. Therefore, Jacoby (1999) concluded that a high repetition frequency could perturb individuals learning, with negative consequences for performances.

### 1.3. In our experiment :

The goal of our experiment was to determine the effect of repetition on SPC in typical adults and seniors. Because the results had been demonstrated as disparate between young adults and seniors, we wanted to determine whether these performances would differ specifically in our SPC task. For each participant of this research, the task was only to look at the screen of the computer, which was a readily produced response by seniors who might have had difficulty if the task required using modern materials such as a tablet electronic or iPhones.

The procedure used was the same as was used with younger adults, as reported in Chapter 4. The number of CS2-CS1 and CS4-CS3 pairing presentations was again manipulated. Stimuli pairings were presented 10 times (condition *se10 pairings* – se for seniors) or 20 times (condition *se20 pairings*). CS1 was simultaneously presented with CS2 10 or 20 times depending on the condition. The same procedure was applied for CS3 with CS4. In a second phase, CS1 was followed by an unconditioned stimulus US+ while CS3 was followed by another unconditioned stimulus US-. Finally, the test phase consisted of recording the visual fixations of seniors when CS2 and CS4 were individually presented on the computer screen.

This methodology was the same for both experimental conditions (*se10 pairings* and *se20 pairings*), except for the number of stimulus pairings presented in Phase 1. In the *se10pairings* condition, the CS2-CS1 and CS4-CS3 pairings were presented simultaneously and randomly 10 times. In *se20 pairings*, stimuli pairings were presented in the same way 20 times. Our hypothesis was that the visual fixation rate would be lower on the US zone in the *se20 pairings* condition when SC2 appeared.

## **2. Method :**

### 2.1. Participants :

Forty French elderly people (27 women and 13 men, aged between 65 and 83 years old) volunteered; participants were randomly assigned to one of two groups (*se10 pairings* or *se20 pairings*,  $n_s = 20$ ). Each participant read and signed an informed consent form prior to the experiment. The experiment had been approved by the University of Lille Institutional Review Board. No diagnosis of senile dementia was declared.

### 2.2. Material :

This experiment was identical to the previous experiment, except the age of the experimental groups. Therefore, material is the same previously described (see Chapter 4).

### 2.3. Procedure :

For the reasons mentioned above, the Procedure was identical to that was described in Chapter 4.

## **3. Results :**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of the means of two independent groups, we obtained a recommended sample size of at least 106 participants, with at least 53 participants per group. However, despite this recommended group size, in this study we managed to recruit only 40 participants, with 20 in each group. Hence, we conducted our analysis with nonparametric statistics to our interpretations of these results.

### 3.1. Statistical issues :

Some floor and ceiling effects were observed and variance in the results was artificially low across participants within our experimental groups. Moreover, our samples did not yield normality in the data within groups. See below the statistical nonparametric tests used in order to illuminate the results of the experimental task with  $p (<.05)$ .

- A **Kruskal-Wallis test by ranks**, also called a one-way ANOVA on ranks, is a nonparametric method to test whether samples originate from the same distribution.

This test is often used for comparing more than two independent samples of equal sample sizes. The Kruskal-Wallis test is a required precursor for other nonparametric tests such as the Mann-Whitney test. A significant Kruskal-Wallis test indicates that at least one sample stochastically dominates one other sample. However, the test can not identify which sample is the source of the stochastic dominance. That is why other nonparametric tests had to be conducted following a significant Kruskal-Wallis test.

In our experiment, Kruskal-Wallis tests had been conducted in 3.3. between *ad10 pairings*, *ad20 pairings*, *se10 pairings* and *se20 pairings*. We could not use that test before because we only had two samples to assess.

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution. We used the Mann-Whitney U test in previous studies (i.e., Craddock et al., 2014 ; Renaux et al., 2017).
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.
- The **Cliff's Delta** statistic is a nonparametric effect size measure that quantifies the amount of difference between two groups of observations beyond p-value interpretation.

### 3.2. Statistical analysis :

#### 3.2.1. *Phase 1* :

Figure 22 shows visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1. There was no statistical difference between the two types of stimuli pairs ( $W = -.45$ ,  $p = .65$ ), nor between the *se10 pairings* and *se20 pairings* conditions (respectively,  $U = 166.00$ ,  $p = .36$  and  $U = 175.00$ ,  $p = .49$ ). Precisely, visual fixation durations were approximately the same for CS1-CS2 and CS3-CS4 presentations in *se10 pairings* and *se20 pairings*: 43.73% of visual fixation for CS1-CS2 in condition *se10 pairings* and 49.69% in condition *se20*

pairings; 45,24% of visual fixation for CS3-CS4 in condition *se10 pairings* and 49.58% in condition *se20 pairings*.

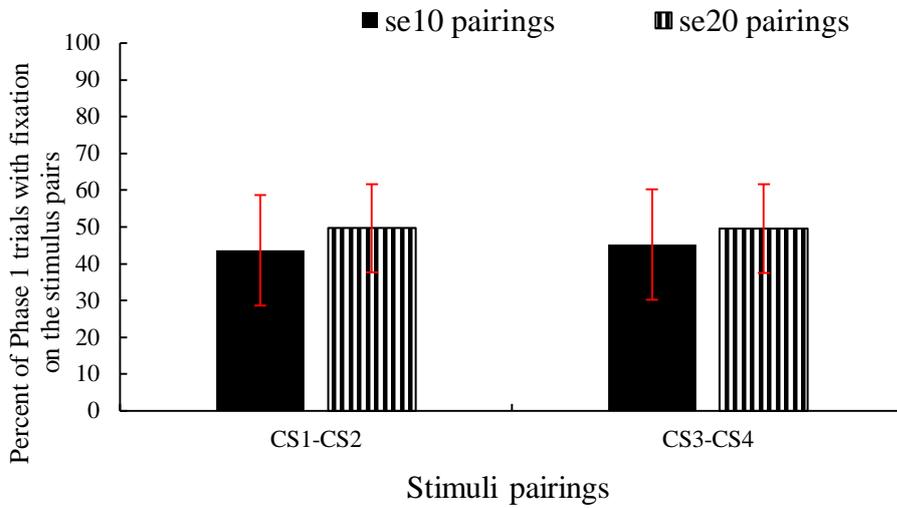


Figure 22. Mean percent of Phase 1 trial duration in which participants visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. Error brackets represent SEMs.

### 3.2.2. Phase 2 :

Phase 2 first order conditioning results are depicted in Figure 23. We observed higher responding to CS1 than to CS3 both in condition *se10 pairings* ( $W = 149$ ,  $p = .004$ , Cliff's  $d = 0.9$ ) and in condition *se20 pairings* ( $W = 151$ ,  $p = .005$ , Cliff's  $d = 1.0$ ). That means, all participants finally looked at the US zone after CS1 presentation and avoided the US zone after CS3 presentation. There was no interaction observed between Condition and Cue. Thus, SPC performances observed in Test were caused by Phase 2 conditioning.

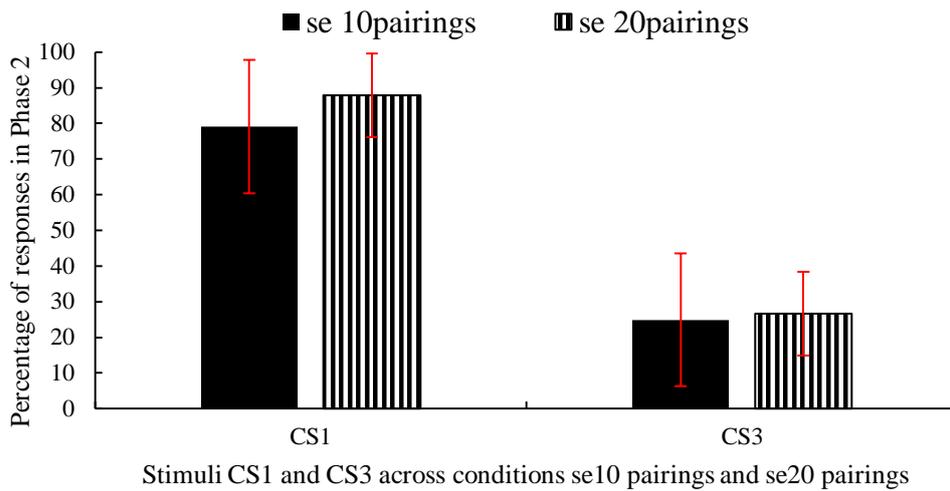


Figure 23: Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during Phase 2. Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 24 represents the number of participants exhibiting SPC responses at test. We observed high visual fixation times to the US zone after CS2 presentation. Precisely : in condition *se10 pairings*, visual fixation after CS2 presentation was observed in 16 of the 20 participants (i.e., 80%) compared to 14 of the 20 in condition *se20 pairings* (i.e., 70%), Fisher's exact test  $p = 1$ . More interesting, we observed a difference in visual fixation after CS4 presentation across conditions. In condition *se10 pairings*, visual fixation after CS4 presentation was observed in only 3 of the 20 participants (i.e., 15%) compared to 12 of the 20 in condition *se20 pairings* (i.e., 60%), Fisher's exact test  $p = .04$ .

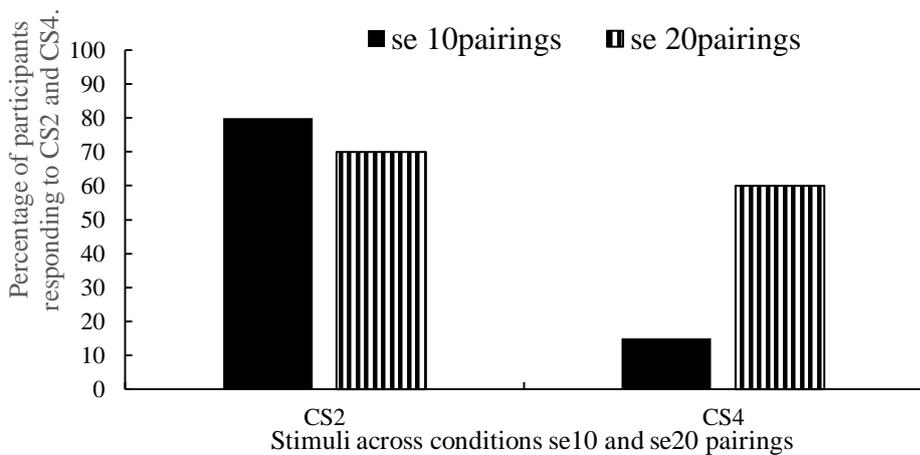


Figure 24. Percentage of participants during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of visual fixation to the video site during the CS4 test in conditions *se10 pairings* and *se20 pairings*.

### 3.3. Comparison between adults and seniors across 10 or 20 pairing presentations :

The present aim is to provide a comparison across the different groups in Chapters 4 and 5. Thus, we examined the visual fixation times for US zone for each participant of all groups and performed a Kruskal-Wallis (Khi2) test. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of means from more than two independent groups (4 groups), we obtained a sample size of at least 48 participants, with at least 12 participants in each group. In line with these recommendations, for these comparisons, we already had 80 participants, with 20 in each group. Thus, this analysis was properly powered.

#### *3.3.1 : Phase 1 :*

We observed significant differences of percentage of visual fixation in all groups for CS1-CS2 presentations (Khi2 : 22,13 ;  $p < .01$ ) and CS3-CS3 presentations (Khi2 : 19,88 ;  $p < .01$ ).

Specifically, between *ad10 pairings* and *se10 pairings*, CS1-CS2 presentation was more targeted by *ad10 pairings* compared to *se10 pairings* (U : 47,00 ;  $p < .01$ ) ; the same for CS3-CS4 presentations (U : 53,00 ;  $p < .01$ ). In addition, we observed such differences between *ad10 pairings* and *se20 pairings*. Precisely, CS1-CS2 presentation was more targeted by *ad10 pairings* compared to *se20 pairings* (U : 59,50 ;  $p < .01$ ) ; the same for CS3-CS4 presentation (U : 72,00 ;  $p < .05$ ).

Between *ad20 pairings* and *se10 pairings*, we observed differences of visual fixations on CS1-CS2 and CS3-CS4 presentations. Precisely, CS1-CS2 was relatively more fixated by *ad20 pairings* compared to *se10 pairings* (U : 129,50 ;  $p = .057$ ), and CS3-CS4 was more fixated by *ad20 pairings* compared to *se10 pairings* (U : 111,00 ;  $p < .05$ ).

Comparing *ad20 pairings* and *se20 pairings*, CS3-CS4 was relatively more fixated by *ad20 pairings* compared to *se20 pairings* (U : 130,00 ;  $p = .058$ ) ; there were no differences of visual fixation for CS1-CS2 presentation between *ad20 pairings* and *se20 pairings*.

Thus, we observed general differences of visual fixation on CS1-CS2 and CS3-CS4 presentations between adults and seniors. Surprisingly, such differences do not seem to infer on first order and second order conditioning.

### 3.3.1 : Phase 2 and Test :

First, we observed significant differences of percentage of visual fixation in all groups for ZUS ( $\text{Khi}^2 : 10,25 ; p < .05$ ) after CS2 presentation, and for ZUS ( $\text{Khi}^2 : 11,98 ; p < .01$ ) after CS3 presentation. Specifically, between *ad10 pairings* and *ad20 pairings*, ZUS was targeted more by *ad10 pairings* compared to *ad20 pairings* after CS2 presentation ( $U : 98,50 ; p < .05$ ). Thus, we can conclude that second order conditioning was more pronounced in adults exposed to the fewer number pairing presentations in Phase 1.

Between *ad10 pairings* and *se10 pairings*, we did not observe significant differences about visual fixation times.

Comparing *ad10 pairings* and *se20 pairings*, ZUS was targeted more by *se20 pairings* than by *ad10 pairings* after CS3 presentation ( $U : 146,00 ; p < .05$ ), which was unexpected because participants had to avoid ZUS after CS3 and CS4 presentations in order to avoid the aversive noise.

Comparing *ad20 pairings* and *se10 pairings*, ZUS zone was targeted more by *se10 pairings* compared to *ad20 pairings* after CS2 presentation ( $U : 109,00 ; p < .01$ ), while ZUS was targeted more by *ad20 pairings* compared to *se10 pairings* after CS3 presentation ( $U : 126,00 ; p < .01$ ). Here, we can conclude that rates of second order conditioning are better in *se10 pairings* compared to *ad20 pairings*.

Finally, ZUS was targeted more by *se20 pairings* compared to *se10 pairings* after CS3 presentation ( $U : 136,50 ; p < .05$ ), which was again an unexpected observation because participants had to avoid ZUS after CS3 presentation.

In conclusion, we demonstrated that the number of stimuli pairings in Phase 1 was a determinant in the establishment of SPC in adults and seniors.

## 4. Discussion

In summary, we observed higher rates of visual fixations on the US+/- area when CS2 was presented in condition *se10 pairings* compared to the *se20 pairings* condition. Moreover, many errors were observed among seniors: the elderly people had a tendency to look at the US+/- area during the presentation of CS3, and avoided this area when CS2 was presented in the *se20 pairings* condition. Thus, we find here the "ironic effect" described and named by Jacoby (1999): a high frequency of stimulus repetition among seniors does not improve their learning.

On the contrary, this repetition seems to have a disruptive effect on the conditioned response tested in our experiment in the young adults and in the elderly participants.

However, our results in Chapters 4 and 5 are not congruent with some geriatric studies focusing on the memory in seniors with or without senile dementia. Indeed, some authors agreed that large numbers of repetition of stimulus presentations to seniors without senile dementia is beneficial for their learning (Law, Hawkins, & Craik, 1988, Swick & Knight, 1997). Other authors have been implementing behavioral therapies using large amounts of repetition as a primary tool to maintain learning of patients with Alzheimer's disease, or with related dementia (Camp & Shaller 1989 ; Camp, 1989 ; Ferraro, Balota, et al. Connor, 1993). Indeed, we set up a behavioral program to recover writing skills for a senior who had a stroke (Renau, Rivière, & Nuchadee, 2017). The repetition exercise here consisted of writing on a sheet of paper the words spoken by the experimenter. The difficulty of the words was measured by its frequency in the current use of the French language. Reinforcers were social by the experimenter and consisted of additional time with the experimenter added based on the patient's performance at the end of the session. During this time, the experimenter spoke of various and varied subjects. When the patient wrote the word correctly, additional reinforcement time was added and the experimenter stated the next word. When the patient did not write the word, we verbally guided the correct answer and then repeated the word until it was well produced. Here, our goal was not to highlight the benefits of repetition, but rather to use it as a tool in the rehabilitation of a writing skill.

In the subsequent chapters, we will explore whether the 10 presentations of stimuli in phase 1 would be sufficient to establish SPC responding in seniors with neurodegenerative diseases such as Alzheimer. If we go back to the example of Camp and Shaller (1989), many trials were necessary to establish correct reminders concerning the association between faces and names of staff members of the hospital center. The authors explained that it was necessary to repeat visual stimuli because behavioral disorders related to senile dementia interfered with the learning of that discrimination.

## General Conclusion of Part 1

In that first part, we focused on the development of an SPC procedure which could be applied to both very young and elderly people. Chapter 3 tested two conditions A and B in which the distance between CSs presented in Phase 1 was manipulated. We observed a better rate of SPC when there was no distance at all between CSs presented in Phase 1. In chapters 4 and 5, we focused on the number of CSs pairings presented in Phase 1 by using 10 or 20 presentations in young and elderly people. In both groups, we observed better rates of conditioned responding during CS4 presentations with 10 than 20 pairings in Phase 1, while results concerning responses during CS2 presentations were disputable.

The central conclusion of these first three experiments is we created an SPC paradigm that worked successfully in young and elderly people without using any explicit instructions, except for “Sit down and look at the computer screen please” at the beginning of the experiment. These experiments were costly to us in terms of time and effort, but necessary for the execution of Part 2. As a result of this research, our final experimental procedure as used in Part 2 could be considered similar to the experimental procedures that have been used to test SPC in nonhuman animals. The main weaknesses that we should mention concern our experimental measures. Concerning anticipatory responses, we controlled the first eye gaze emitted by participants at the beginning of CS1 and CS2 presentations : participants had to look at the CS before targeting the US zone in order to obtain reinforcement. In this way, we could be certain that the first zone targeted after CS2 emission was the US zone or reinforcement was not delivered. Conversely, we did not record the first saccade after CS3 and CS4 presentations. It means that we didn't know where participants firstly looked at one specific zone after CS3 and CS4 occurrences. Thus, we can discuss zone preferences during CS3 and CS4 presentations, but we can not assume which zone had been targeted first.

## Résumés Partie 1

Ci-dessous un résumé en français de différents points abordés dans cette Partie 1.

### 1. Histoire du pré-conditionnement sensoriel :

Relatif à l'apprentissage associatif, le pré-conditionnement sensoriel (PCS) est considéré comme étant un conditionnement d'ordre supérieur dans la mesure où son établissement est plus complexe qu'un conditionnement dyadique de type CS-US. Pavlov (1927) a été le premier à démontrer ce phénomène par l'intermédiaire de procédures de conditionnement de second ordre (SC1-SI suivi des présentations SC2-SC1). Par la suite, Brogden (1939) a observé puis défini ce conditionnement de second ordre comme PCS. Ce type de conditionnement implique une première phase dans laquelle deux stimuli conditionnés sont présentés ensemble (Phase 1: SC2-SC1). Dans une seconde phase, un des deux stimuli est associé avec un SI provoquant une RI (Phase 2: SC1-SI). En test, la même réponse comportementale est observée après présentation de SC2, même si SC2 n'a jamais été directement associé au préalable avec le SI.

Depuis sa mise en exergue en 1939, le PCS a été examiné chez de nombreuses espèces animales. Chez l'humain, Brogden a toujours souligné la nécessité d'insérer des instructions dans les paradigmes expérimentaux afin d'observer ce type d'apprentissage associatif. En effet, les travaux de Brogden (1942, 1947) ont démontré que le PCS ne pouvait pas être observé chez l'humain sans utilisation d'instructions. Ainsi, de nombreuses études ayant pour objet d'étude l'établissement du PCS chez l'humain utilisent des instructions (pour exemples, Chernikoff et Brogden, 1949 ; Craddock, Renaux, Lefèvre, Nelson et Molet, 2014). À travers ce projet de recherche, nous voulions créer une procédure comportementale similaire aux paradigmes utilisés chez les autres animaux, afin d'observer du PCS chez l'humain sans utiliser d'instruction.

### 2. Attention visuelle et poursuite oculaire :

Nous avons utilisé un système de poursuite oculaire permettant d'enregistrer les temps de fixations visuelles comme mesure comportementale dans l'étude du PCS. L'attention visuelle est étudiée depuis des dizaines d'années (voir Von Helmholtz, 1925 ; James, 1981 ; Yarus, 1967, pour exemples), et est considérée aujourd'hui comme reflétant objectivement l'attention que porte un individu sur un stimulus ciblé (Duchowski, 2007). Concernant le conditionnement pavlovien, Kruschke, Kappenman, et Hetrick (2005) ont enregistré les fixations visuelles afin de tester le rôle de l'hypothèse attentionnelle dans le phénomène de blocage. Par l'intermédiaire de l'eye-tracking, les auteurs ont mis en évidence le défaut d'attention visuelle sur le stimulus

bloqué. De plus, Kaakinen, Hyönä, et Keenan (2002) ont démontré des préférences de fixation visuelle pour des stimuli considérés comme étant pertinents en comparaison à des stimuli non pertinents pour la survie de l'individu. En psychologie, l'attention visuelle enregistrée par les systèmes d'eye-tracking est souvent exploitée dans la reconnaissance des expressions faciales (Black et Yacoob, 1995) et à des fins commerciales (Wedel et Pieters, 2008). De nombreux chercheurs considèrent l'attention visuelle comme étant une mesure pertinente pour l'étude de populations n'ayant pas ou très peu accès au langage, tels que les bébés (Gredebäck, Johnson, et Hofsten, 2009) et les personnes âgées (Isaacowitz, Wadlinger, Goren, et Wilson, 2006).

Dans mon travail de recherche, l'attention visuelle a été la mesure commune des différents groupes expérimentaux (c.à.d. du bébé à la personne âgée). Ne nécessitant pas de compétences langagières pour être utilisée, cette mesure a été considérée comme étant pertinente auprès de nos populations ayant des défauts de stratégies verbales. En effet, un enfant non-verbal avec troubles autistiques n'aurait pas pu répondre à nos questions, mais pouvait regarder l'écran de l'ordinateur lors du paradigme expérimental. En ce sens, notre étude était similaire aux procédures comportementales utilisées chez les autres animaux.

### **3. Réponses anticipatoires et d'évitement dans le conditionnement pavlovien :**

Dans notre paradigme expérimental, les participants devaient anticiper l'apparition d'un SI+ et éviter celle d'un SI-. Pavlov (1927) avait observé des réponses anticipatoires de salivation (RC) avant présentation de la nourriture (SI+) après plusieurs présentations SC-SI. C'est ainsi que Pavlov argumentait de la valeur adaptative des réflexes conditionnés, la présence du stimulus pouvant être considérée comme une préparation à l'ingestion et digestion de la nourriture par l'organisme. Par exemple, la salivation émise avant présentation de nourriture permettrait de préparer l'organisme à recevoir de manière optimale la nourriture –favorisant ainsi la survie de l'individu.

Depuis les travaux de Pavlov (1927), de nombreuses études se sont penchées sur les réponses d'anticipation et d'évitement dans le domaine des comportements alimentaires, sexuels, addictifs, de fuites ou encore des expressions faciales (voir revue de Domjan, 2005). Nous considérons aujourd'hui ces réponses comme étant essentielles à la survie et à la reproduction d'un individu (voir pour exemple Cusato et Domjan, 1998) permettant à cet individu d'éviter tout stimulus dangereux présent dans l'environnement (voir pour exemple Myers, Cohn et Clark, 2005).

A travers ce projet de recherche, nous avons voulu observer ces réponses comportementales à travers différents groupes expérimentaux par l'anticipation d'un SI+ et l'évitement d'un SI-.

Notre hypothèse était d'observer ces réponses dans chaque groupe en raison de leur fonction adaptative.

#### **4. Contiguïté spatiale et conditionnement d'ordre supérieur :**

Afin de créer une procédure expérimentale pouvant observer du PCS sans utiliser d'instruction, nous nous sommes intéressés à plusieurs paramètres faisant l'objet de débats divers et de résultats contradictoires dans la littérature scientifique. En effet, puisqu'il fallait créer une procédure sans instruction chez l'humain, nous avons dû nous baser sur les recherches effectuées chez les autres espèces animales. Les notions de contiguïtés spatiales et temporelles sont souvent soulevées dans l'établissement de conditionnement de premier ordre et d'ordre supérieur. Les travaux relatifs à la contiguïté spatiale sont assez unanimes sur l'importance de la contiguïté temporelle entre deux stimuli. Nous développons dans le chapitre 2 en quoi ces études ont guidé nos choix concernant les intervalles de temps utilisés dans la procédure expérimentale créée.

Concernant la contiguïté spatiale, très peu étudiée dans le conditionnement d'ordre supérieur, quelques études mettent en exergue le rôle de la proximité entre deux stimuli (SC-SI) sur la fréquence d'apparition de la réponse comportementale ciblée. En effet, au plus le stimulus conditionné est physiquement proche du SI, meilleure est la réponse conditionnée observée en test (Wasserman et al., 1974 ; Cabrera and Vila, 1986 pour exemples). Concernant le conditionnement d'ordre supérieur, Rescorla et Cunningham (1979) ont démontré dans une tâche de second ordre apparentée au pré-conditionnement sensoriel le rôle de la contiguïté spatiale entre les SCs sur la réponse associative.

Néanmoins, aucune étude à notre connaissance ne s'est intéressée au rôle de la contiguïté spatiale dans le paradigme de PCS. Les résultats obtenus sont présentés et discutés dans le chapitre 3.

#### **5. Nombre de présentations de stimuli dans l'établissement de conditionnement d'ordre supérieur :**

Parallèlement au rôle de la contiguïté spatiale dans l'établissement de conditionnement d'ordre supérieur, le nombre de présentations de stimuli est également un sujet régulièrement controversé selon l'âge du participant ou de la présence de certains troubles développementaux. C'est pourquoi, nous nous sommes intéressés au rôle du nombre de répétitions des présentations de stimuli sur la réponse conditionnée auprès de jeunes adultes et de personnes âgées. L'objectif était de pouvoir déterminer par la suite un nombre optimal de présentations de stimuli similaires chez le jeune adulte et la personne âgée.

Chez le jeune adulte, il a été démontré qu'un nombre élevé de présentations de stimuli diminuait le taux de réponse conditionnée mesurée en conditionnement de premier ordre et d'ordre supérieur (Prewitt, 1967 ; Yin et al., 1994 ; pour exemples). Les travaux effectués chez la personne âgée controversent ces résultats. En effet, certaines études soutiennent le rôle fondamental de la répétition dans le maintien des performances de la personne âgée (Swick et al., 1997 pour l'exemple) alors que d'autres affirment le contraire (Camp et al., 1989). En ce sens, Jacoby (1999) affirme qu'un nombre excessif de répétitions peut avoir des effets « ironiques » sur les performances des personnes âgées, facilitant l'émission d'erreurs d'apprentissage.

Ainsi, les chapitres 4 et 5 avaient pour objectif de tester les performances de jeunes adultes ainsi que de personnes âgées avec une procédure expérimentale similaire variant le nombre de stimuli présentés en phase 1 de PCS.

Part 2 :

Influence of verbal behavior on conditioned responding.

## CHAPTER 1 : INTRODUCTION

Chapter 1 introduces (1) the development of verbal behavior in humans, (2) the role of verbal strategies in the establishment of SPC, (3) then the SPC task used in Part 2.

### 1. Development of verbal behavior in humans :

Humans are social animals, ordinarily living amidst one another. One social characteristic of humans is the use of written and oral words to communicate and likely to internally process information. We use the term verbal behavior in reference to all of these social behaviors. Lee (1981) considered language as a modulator of environmental-behavioral relationships, focusing on the language skills of children with autism spectrum disorders in comparison with children without developmental disorders. Indeed, language is often considered in terms of its structure (grammar, vocabulary, unobservable mental representations), rather than in terms of the objective environmental conditions influencing the speaker / writer to behave as she does. To support this point of view, Catania (1998) used the term "referent language" involved in the naming of objects by words and stipulated (p. 239):

« We also speak of language as if it were directed toward events or objects. We say that words or sentences refer to, deal with, speak of, call attention to, or are about things. The language of reference implicitly includes the direction from verbal behavior to environment. Every day language doesn't include words that emphasize the opposite direction. What if our everyday language has prejudiced us about the ways in which our verbal behavior works ? We hardly ever say that we utter nouns in the presence of the relevant objects or that sentences are occasioned by relevant events. Instead, we say that words refer to objects or that sentences are about events. There are good reasons for these usages ; ... [but] they may be misleading in an analysis of the behavior of speakers and listeners or reader and writers ».

#### 1.1. Verbal behavior considered as an operant :

Since Catania (1998), some authors refer strictly to language for the study of language skills (Baer and Guess, 1971), while others refer to a wide range of social behaviors such as gestures and mimicry (Hockett, 1968). In this line, Skinner introduced in 1957 in his famous book "Verbal Behavior" the concept of verbal behavior and defines it by its function rather than its structure. In contrast to the terms "language" and "language competence", verbal behavior refers to a speaker's behavioral response to the environmental conditions that establish and maintain that behavior. In my research, I therefore consider verbal behavior by its function whether this behavior is textual, oral or signed. Although this behavior is generally studied in

the form of voice or written responses, there are verbal behaviors internal to the individual that are difficult to be observed. Skinner (1957) devoted a whole chapter to internal verbal behaviors in which he developed how thought could be assimilated into verbal behavior, and maintained by its consequences on the individual himself (p. 449):

« The simplest and most satisfactory view is that thought is simply behavior – verbal or nonverbal, covert or overt. It is not some mysterious process responsible for behavior but the very behavior itself in all the complexity of its controlling relations, with respect to both men the behavior and the environment in which he lives. The concepts and methods which have emerged from the analysis of behavior, verbal or otherwise, are most appropriate to the study of what has traditionally been called the human mind ». Thus, our research focused on this type of verbal behavior defined as "rule-governed behavior" by Skinner in 1969. Rule-governed behaviors include verbal behaviors that affect the listener's (or the sender's) behavior, such as instructions, advice, or laws. From a behavioral point of view, the establishment and maintenance of these behaviors is complex because many factors encourage and maintain verbal behavior (Parrott, 1987). In addition, these behaviors have the characteristics of reflecting clearly defined reinforcement contingencies. For example, "Insert the coffee capsule and press the ON button" is a clear instruction to be followed in order to obtain coffee via a specific machine. More generally, ruled governed behaviors follow the contingencies  $SD : R \rightarrow SR$  (Skinner, 1969). For example, a behavior emitted by an individual is governed by the rules when he does not smoke in a place where smoking is prohibited, or when he follows GPS directions to find his way, or when he buys a product under the guidance of an expert salesman.

Verbal behaviors are governed by the rules and are acquired gradually throughout the life of an individual. According to Skinner (1957), the development of verbal behavior begins with babbling. In babbling, babies randomly emit a variety of sounds reinforced by parents / caregivers. As a result, the number of babbling increases and verbal behaviors are increasingly discriminated, with caregivers reinforcing more and more sounds recognizable in their native language. This is how the many random sounds of babies are shaped by the sounds of the caregiver's language and selected by its consequences.

### 1.2. Emergence of verbal behaviors in babies :

Indeed, from the first month of life, the baby can distinguish syllables like *pa* and *ba*. There are so-called 'tweets' emitted during the first two months of life, these tweets oscillating between the emission of tears and noises of satisfaction. Around the age of six months, the baby can recognize two-syllable words such as *papa* or *baba* and can also discriminate among the sounds

of many different languages. At this age, babies emit sounds composed of syllables such as *ba*, *da*, *pa* and can repeat them continually ('*dadadadadada*'), thus forming what we call babbling. Until the age of 9-10 months, babies can emit a variety of sounds suitable for different languages. Then, this variety will be extinguished to preserve only the sounds reinforced by the peers, sounds being generally part of their native language (Oller, 1981).

Fenson et al. (1994) showed that babies appeared to understand 20 to 30 words spoken by parents as young as 10 months of age. Such skills increase exponentially in the following months. Fenson et al. asked a large cohort of mothers to write the list of words that their babies seemed to understand by the babies' looking at the specific word item when it was pronounced by the mother. Subsequently, the first clear word spoken is issued around 12/13 months and is applied to many items. Gradually, the baby learns each word according to the item and the context in which the object is presented to form simple sentences at the age of 18 months when the repertoire of the child includes at least 50 words (Boudreault et al., 2007). These first sentences are generally composed of two to three words such as "Dada eat", and develop into complex sentences between 27 and 36 months.

### 1.3. Acquisition of verbal skills according to Denney's model (1982, 1984) :

The vocabulary of the child explodes between the age of 2 and 6 years when the child quickly learns the words associated with many items, up to 10 items per day (Anglin, 1996). With the beginning of schooling, researchers generally believe that verbal behavior further increases in quantity and complexity. The rate of acquisition of such skills by an individual gradually decreases with age, from age 30 onwards according to Denney's model (1982, 1984). According to this model, further enhancement of the verbal skills of an individual tends to decrease over the years, and eventually begins to decline (see Figure 25).

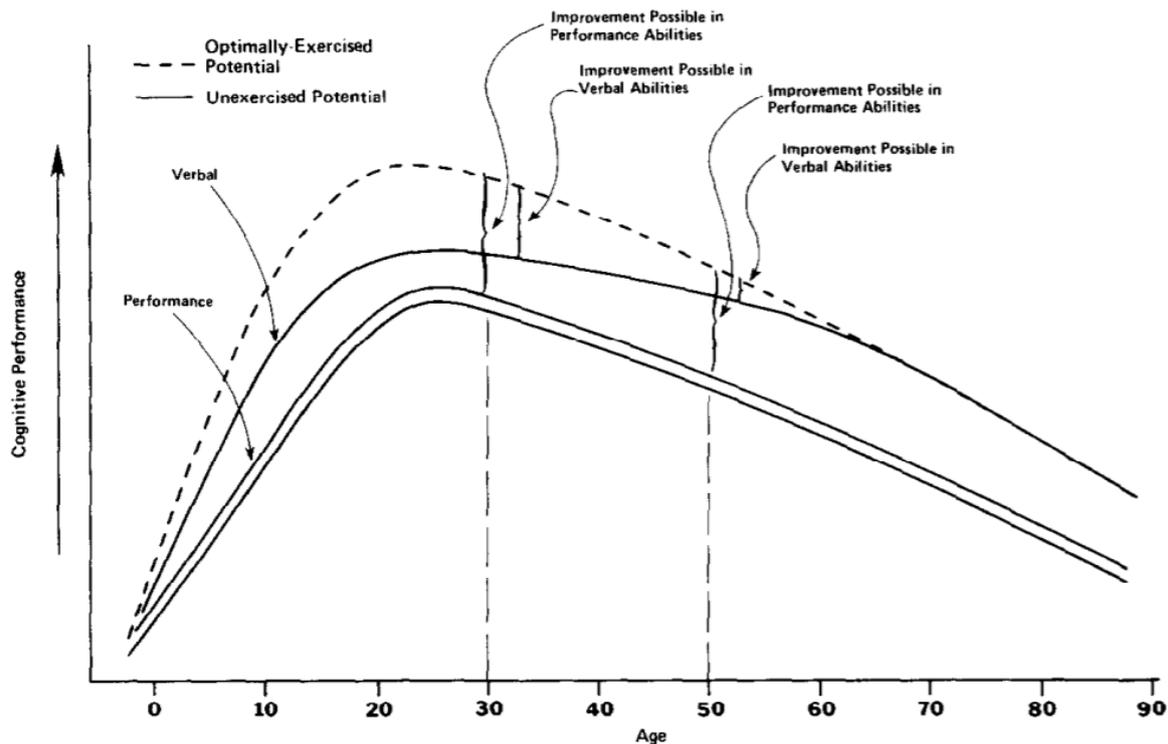


Figure 25 : Denney model, « Amount of improvement possible in both verbal performance abilities at the 30-year-old and the 50-year-old model.» from Denney (1984).

Concerning seniors, many studies showed the ultimate decrease of their verbal and cognitive performances compared to that of their younger selves (see chapter 5 of Part 1). If we consider the developmental studies previously presented, babies tested in our experiment (chapter 2 of Part 2) were aged between 4 and 9 months old and were at the babbling stage. The school age children presented in chapter 5 of Part 2 were in a developmental stage in which the number of verbal behaviors is expected to grow rapidly in number and complexity. Adults tested in chapters 3 and 4 of Part 1 had optimal verbal skills. Seniors tested in chapter 5 of Part 1 were expected to have poorer verbal skills than their younger counterparts. Finally, the dementia group of older people presented in chapter 4 of Part 2 was supposed to have the worst verbal performance, similar to that found in the babies. However, there is a need to criticize these developmental studies, which reflect the average performance of many individuals. Indeed, these models are based on observations made on large cohorts, with results used for a developmental standard.

#### 1.4. Development of verbal behaviors thanks operant procedures :

Other behavioral studies demonstrated that it is sometimes possible to have surprisingly good verbal behaviors expressed at early developmental stages and in end-of-life individuals. Also,

there are distinction changes in verbal behavior that emerge in the presence of developmental disorders such as autism spectrum disorders or disorders found in senile dementia.

Pelaez et al. (2011), for example, demonstrated that vocal imitation of new syllables was possible in infants between three and eight months of age. In this experiment, the baby was lying on a bed and one of the parents or caregivers was positioned above him. The task was to produce a sound in front of the baby with some upward intonation. When the baby repeated the sound, the parent strengthened socially by emitting another sound different from the first by physically stimulating the baby by caresses. In this manner, Pelaez et al. showed that many new sounds could be emitted in a few trials by babies aged three to eight months, just by reinforcing babies' variability of the sounds emitted during an interaction with a caregiver.

In young children with or without developmental disorders, many behavioral procedures also exist to improve their language skills. Sundberg and Michael (2001) reviewed the different results obtained through operant procedures on the emergence of verbal behaviors in children and adults with autism spectrum disorders. For example, Sundberg et al. (2000) used verbal guidance for verbal behavior in two non-verbal children with autism spectrum disorders. In this procedure, the educator has to verbally guide the child, "What is it?" while looking at an item, and the child has to answer with a word for the designated item. If the child did not utter the appropriate word (i.e., if no word is emitted, or if an incorrect word is emitted), the educator repeats the word until the child pronounces it correctly. A reinforcer is delivered according to the performance of the child. The verbal guidance "What is it? " is faded as the child's correct answer increases. Thus, Sundberg et al. (2000) noted the emergence and the increase of spontaneous verbal behavior in those two initially non-verbal children.

Moreover, the learning of verbal behaviors is also possible in seniors, even after a cerebral vascular stroke. For example, we implemented a behavioral procedure aimed at increasing the verbal behavior of an elderly person hospitalized in a geriatric center after a stroke (Renaux et al., 2017). We worked on the writing of words dictated by an educator by gradually shaping the frequency of use of the words by the elderly person. The beginning of the interventions consisted of the patient's writing simple words such as "the" and "I". As the patient's performance progressed, we made the written work requirement more difficult by using less frequent words such as "president" or "secretary". The task was to spell out a word that the patient had to write. If the patient wrote the word correctly, additional time for access to the reinforcing agent (e.g., a preferred book) was added and the educator named another word. If the patient did not write the word or was mistaken in the spelling, the educator verbally guided

the patient by repeating the word until the correct word was written by the patient. Thus, we observed a relearning of verbal behaviors of this patient, with performances maintained over time and visible on a follow-up six months after the end of care.

## **2. Verbal strategies in the establishment of SPC :**

Skinner (1969) stated that beyond its social aspects, verbal behavior (such as instruction) can affect behaviors initially governed by other reinforcing contingencies. One of the best ways to observe this effect is to compare the performance of individuals on an experimental task with or without instructions. If the behavior results diverge as a function of instructions, this reinforces Skinner's position.

### **2.1. Influence of instructions in experimental tasks :**

Several authors have studied the effect of human instructions in various reinforcement tasks. For example, Lippman and Meyer (1967) studied human performance on a fixed-interval reinforcement task. A group of participants who were not exposed to the authors' written instructions constituted a control group. The experimental group received a common set of written instructions during the experiment. The task was to accumulate points by pressing a response lever, a task that is considered reinforcing in humans (Weiner, 1964). Lippman and Meyer observed that patterns of behavioral responses differed according to the instructions given during the experiment. Indeed, when the instructions said that the points were going to be delivered for responses a certain time  $t$  after the last reinforcement, participants pressed significantly less on the response lever (typical pattern found in fixed interval reinforcement) compared to the other condition. On the contrary, when the instructions specified to the participants that the number of points would depend on the number of presses on the lever, authors observed more constant and higher rates of responses. Thus, Lippman and Meyer (1967) demonstrated that written instructions can modulate individuals' nonverbal behaviors, consistent with Skinner's (1969) views.

Bandura (1974) said there is a parallel between these instructions and modeling because verbal behaviors could 'model' the behavioral responses expected by the individual himself. Bandura's views imply that the reinforcement expected by an individual is decisive in the emergence of the person's behavioral responses. These written or verbal instructions are also considered to be rule-governed behaviors, as participants come to emit the expected behavioral responses more quickly when instructions are given (Buskist and Miller, 1986).

The improvement in performance obtained with instructions is all the more pronounced in deferred reinforcement procedures. It is easy to observe in everyday life behaviors that are reinforced in a delayed manner (Luciano, 2000). An employee will work every day to receive his pay only at the end of the month; students must do homework before a deadline followed by delayed feedback. When instructions are given concerning reinforcement contingencies, the behavioral response rates typically are higher. In this sense, Schlinger and Blakely (1987) classified rule-governed behaviors as events that alter the function of nonverbal behaviors. For example, before an aircraft takes off, a traveler on a plane receives the instruction "in case of a disturbance, place the yellow mask in front of your seat over your mouth and breathe normally". In this case, the instruction provides a very clear rule to follow in a particular context (i.e., in a danger situation) about a specific stimulus (i.e., the yellow mask). Without this instruction, we could anticipate that the individual might manipulate this object in a variable way, probably asking the steward about its functionality if there was still time to get help. Here the verbal instruction controls the delayed behavior that the traveler is to emit in case of danger.

### 1.3. Use of instructions in SPC procedures :

All of these studies led us to believe that verbal behaviors could also play a role in the observation of SPC in humans as opposed to nonhuman animals. Since Brogden (1939) highlighted SPC, relatively few studies have examined this phenomenon in humans. Brogden (1947, 1949) himself said that the observation of this second-order conditioned response required the use of written instructions given to participants. Without these instructions, no SPC could be observed in humans. Works of Jara et al. (2006) on a second order conditioning tasks (SOC) converged with Brogden's (1947, 1949) views. In their study, a disease name (CS1) was associated with serious health problems (US-). Subsequently, the name of a chemical substance (CS2) was associated with the name of the disease (CS1). A control condition was present with another disease name (CS3) causing different disorders and associated with another chemical substance (CS4). The question asked to the participant at the end of the experiment was to establish the cause of the health problems of a patient X suffering from CS1 or CS3 related disorders. Jara et al. found that most participants gave the correct name of the disease (CS1 or CS3) based on the health problems described. Participants could also give the name of the chemical (CS2 or CS4) associated with this disease (CS2 for CS1, CS4 for CS3). Jara et al. concluded that the observation of the conditioned second order response, evidenced by the responses to CS2 and CS4 was explained by participants' ability to form verbal strategies on causal tasks. More specifically, individuals were able to infer causal relationships between a cause and its consequence, thanks to the information given in advance.

However, in Part 1 we observed significant rates of conditioned responses, even despite our task lacking any explicit verbal or written instructions about the purpose of our experiment. One possible criticism is that participants might have created verbal strategies themselves, relevant to the experimental task they faced. We can not categorically refute this criticism because we did not operatively ask the participants if they had mentally created verbal strategies. Moreover, the observation of verbal behaviors internal to the individual is difficult to objectively assess. This is why our Part 2 is focused on SPC observations with individuals who have no verbal behavior, or who have distinct disability in verbal skills. To our knowledge, no study interested in SPC to date tested this phenomenon with this type of population.

### **3. Using an SPC Task**

This part presents the SPC task used among those next chapters of Part 2, in babies (i.e., chapter 2), autistic children (i.e., chapter 3) and elderly people with dementia (i.e., chapter 4). That procedure was detailed in Part 1, chapter 2 (see pages 31-46).

#### 3.1 Apparatus :

An eye-tracking system was used in conjunction with a conventional computer. Participants faced a computer screen (Dell Model Optiplex 7010) equipped with infrared cameras that monitored eye movements. The eye-tracking system (FaceLAB#5.1) recorded the participants' eye movements including both saccades and visual fixations. There was no physical restraint of participants' heads because the system was programmed to track the participants' visual focus, even when they moved their heads. Thus, participants only had to watch the computer screen. This system facilitated our providing participants with no explicit instructions. Importantly, eye gaze measure can be considered as one potential measure of attention and numerous researchers have reported longer duration fixations on task-relevant stimuli than irrelevant stimuli.

#### 3.2 Materials :

The CSs were four colored geometric shapes such as squares, triangles, circles and stars (red, blue, green, and yellow). For each participant, the CSs were randomly selected, combining a unique color and a unique shape. Thirty 2 s, video cartoon clips of pleasant scenes were used as the US+ and one of them, randomly selected without replacement, was presented immediately upon the participant looking at the target zone of the computer monitor on each CS1-US+ trial during Phase 2. Each video included action by cartoon characters such as Kung

Fu Panda, Dragons, or Kuzco. A single 2 s unpleasant sound was used as the US- and was emitted from the computer's two speakers if the participant looked at the target zone when CS3 was presented during Phase 2. The four colored geometric shapes were presented on the center of the computer screen. The 2 s presentations of the US+, presented in a 13 cm x 8 cm rectangle in a corner of the screen, and US- (the aversive noise) were both produced by the computer. The experimental procedure was controlled by Matlab 7.0 software, which was also used to analyze the data.

### 3.3 Procedure :

Participants were initially seated in front of a dark grey background computer screen. At the start of the experiment, four visual stimuli were randomly selected as CS1, CS2, CS3, and CS4 for each participant.

Phase 1 began with a sequence of ten simultaneous pairings of CS1 with CS2 and ten simultaneous pairings of CS3 with CS4 (see Results in chapters 4 and 5 of Part 1). These stimuli were presented simultaneously and spatially close (i.e., no distance between stimuli) to each other (see Results in chapter 3 of Part 1). To capture the attention of participants, cues initially appeared at random points along the edges of the screen and 'flew' to the center of the screen over 15 ms. On each trial, a pair of cues (CS2-CS1 or CS4-CS3) were presented horizontally aligned at the center of the screen. Which cue was to the left was randomly determined for each trial. Each cue pair then persisted at the center of the screen for 2 s. Each stimulus pair appeared ten times interspersed in a random order.

Phase 2 immediately followed Phase 1. CS1 and CS3 were individually presented in random order at the center of the screen, after entering the screen in motion as described above for Phase 1. When the US+ appeared at the termination of CS1, it was presented in a randomly selected specific zone of the computer screen (i.e., top right, top left, bottom right, or bottom left), but consistent on all trials for any given participant. During presentation of CS1, a solid line black 7 cm x 7 cm cross was presented in the US+ zone. Participants had to fixate on that zone before the cue presentation was over in order to obtain the short video clip; hence, the task was actually instrumental. If they failed to do so, the trial ended up and a new trial with CS1 began until the 'correct' response was emitted. After three correct responses to CS1, the cross was faded into a dotted line cross. Participants still had to look at the US+ zone to obtain the video clips. When CS3 appeared, participants had to look away from the US+ zone; otherwise the US- (i.e., an unpleasant sound) was emitted and a new trial with CS3 began. Phase 2 ended when a participant emitted three consecutive correct responses with the dotted

line cross for CS1 and three consecutive correct responses for CS3 without an intervening error. When participants reached this performance criterion, they were tested on CS2 and CS4. We used this criterion to be certain that CS1 was associated with the US+ and CS3 was associated with the US-: this first order conditioning was necessary to reveal any SPC established during Phase 1.

CS2 and CS4 were each tested once separately, entering in 'flight' from the edge as described for Phase 1. We used a single test trial for each cue to avoid extinction effects that would have permitted early test trials to reduce the sensitivity of subsequent test trials. The critical question was whether participants would anticipate the appearance of a movie clip when CS2 or CS4 was presented. Testing was in extinction; that is, even if participants looked at the US+ zone, no video clip nor aversive noise was presented. To avoid possible order-of-testing effects, we controlled for whether the first test trial was a CS2 or a CS4 presentation. For 10 participants in each condition, testing began with the CS2 trial followed by the CS4 trial; for the other ten participants in each condition, the order was reversed.

## CHAPTER 2 :

### SPC IN NON-VERBAL BABIES (4-9 months)

Babies participating in our experiment were aged between 4 and 9 months and were thus considered to be non-verbal individuals because the babbling emitted does not seem to have a social function. In addition, babies do not appear to use verbal strategies in their learning (Makin, 2007).

#### 1. Introduction :

##### 1.1. Demonstrations of associative learning in babies :

The study of Bhat, Galloway and Landa (2010) aroused our curiosity that associative learning had in fact been demonstrated in 6-month-old babies. The purpose of that study was to compare visual attention performances among a large cohort of babies, some of these babies being suspected of developing autism spectrum disorders. Thus, 25 babies without developmental disorders were compared to 25 other babies with risks of developing autistic disorders on a task of "object-social learning" (Bhat et al.). Early signs of autism spectrum disorders include non-response to social interaction, lack of attention to others, and lack of eye tracking during social interaction. These authors were therefore interested in ocular fixation times in infants in order to detect defects in visual fixations in social interactions as early as 6 months of age. In that experiment, babies were placed in a suitable chair in front of a joystick connected to a speaker device emitting music. The experimental task was to use a joystick to activate music clips. As soon as the baby was able to trigger the music, one of his parents socially reinforced that behavior. The visual fixation times on the parent's face and on the joystick were recorded. Bhat and al. observed a higher visual fixation time on non-social stimuli in high-risk infants compared to control-group infants. In addition, all of their babies had successfully used the joystick to access the music. The authors talked about associative learning between the joystick and receiving a reinforcing item (i.e., music in their experiment).

These results are also supported by many authors who focused on the development of memory in humans. Rovee-Collier (1997) underlined the differentiation between procedural memory and declarative memory, procedural memory being considered as primitive and the declarative as requiring the acquisition of social skills such as language. Rovee-Collier (1997) focused on the development of memory in individuals with developmental disorders, especially children with autistic disorders. Prevailing thought decades ago was that declarative memory should be deficient in these individuals who lack social skills. However, Rovee-Collier (1997) showed that learning requiring access to a declarative memory was found in children with autistic

disorders. The author thus concluded that declarative and procedural memory both followed the same developmental processes and that language skills were not necessary for this development. Today, it is thought that typical 3-month-old babies can quickly learn causal relationships (Rovee-Collier et al., 2001). These results led us to believe that an observation of SPC could be possible with human babies, although this type of conditioning has never previously been observed in this population.

### 1.2. Second order conditioning in infants rats (Cheatle and Rudy, 1978) :

Cheatle and Rudy (1978) demonstrated the existence of second order conditioning in infant rats. In that experiment, the researchers collected 29 babies at birth (D0) from a litter of female rats raised in the laboratory and tested them at the 7th day post-birth (D7). One of the first senses developed in the rat is olfaction. In that way, Cheatle and Rudy used a phylogenetically aversive odor for the baby rat (US-). In a first phase, a drop of lemon (CS1) was followed by the presentation of the aversive odor (US-). Then in a second phase, the drop of lemon (CS1) was followed by a drop of orange extract (CS2) in a single trial. Authors then assessed the exploratory behaviors to the different stimuli presented at the test, depending on the experimental conditions in which the baby rats were confronted. Indeed, a control group of baby rats was also confronted with a pairing of lemon (CS1) and orange (CS2) extracts without the CS1-US- pairing. Very quickly, Cheatle and Rudy observed that babies who had been exposed in the first phase to US- were approaching CS1 less and less when it was presented, compared to the control group. The same was found with the orange extract CS2. Thus, Cheatle and Rudy demonstrated first and second order conditioning in the 7-day-old rat, after pairing two conditioned CS1 and CS2 stimuli together, one having been previously exposed with an aversive odor US-.

The studies described above speaks to many questions concerning the establishment of associative learning at a very early developmental stage. Our behavioral task used discriminative auditory and visual stimuli for babies aged 4 months and older who do not have verbal strategies in their behavioral repertoire. The goal of this chapter, therefore, was to observe whether or not an SPC response occurred in an associative learning situation described as complex because it requires recall of associations CS2-CS1-US for individuals at a very early developmental stage. According to the hypothesis of verbal strategies in the establishment of associative learning, we should not observe such a conditioned response in human babies. Our behavioral procedure has been explained previously in Part 1. We used the same eye-tracking

system that allowed the baby to be free to move. No written or oral instructions were used during this experiment.

## **2. Participants :**

Twenty-four babies (11 girls and 13 boys/ 28 babies initially tested, 4 rejected because excessive crying) participated in this experiment, all aged between 4 and 9 months. The average age of participants was 5.79 months (SD : 1,60). No deficiency or developmental disorder was observed within these participants. In addition, the babies had no predisposition to developmental disorders such as autism spectrum disorders.

Each parent read and signed the consent form before the start of the experiment. Babies were placed on baby chairs in front of the computer screen so that each baby could watch the stimuli presented on the computer screen. The parent could stand behind the baby or behind a tinted window to observe the development of the experimental task.

Calibration of eye-tracking system was harder compared to calibration for typical adults. Indeed, for each baby we had to respect their sleep cycle and to choose with his/her parents the best time during awareness in order to have his/her attention for 30 minutes. For calibration, we used an amusing movie cartoon instead of typical red points that are used with typical adults. Thus, babies were motivated to look at calibration points before the beginning of the experiment. Unfortunately, we stopped the experiment for four babies who cried a lot after US-presentation during Phase 1. Thus, we present results for 24 babies instead of 28.

The babies were free to move in the babychair, as the eye-tracking system did not restrain him physically. If a baby began to cry, the experiment was momentary stopped and we waited for a quiet time to restart the experiment. The parent could also signal the experimenter to note suspicious or precursors of disruptive behavior in of their child.

## **3.Results :**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques.

### 3.1. Statistical issues :

Floor and ceiling effects were observed and the variance of results was artificially low within babies. Moreover, within participants our data did not exhibit normal distributions. Thus, we used nonparametric tests to analyze visual fixation times on the CS1-CS2 and CS3-CS4

presentations, and on the US zone. See below the statistical nonparametric tests used in order to illuminate the results of the experimental task with  $p (<.05)$ , used in Renaux et al. (2017) :

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution.
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.

### 3.2. Statistical analysis :

#### *3.2.1. Phase 1 :*

Figure 26 shows visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1 in babies. There was no statistical difference between the two types of stimuli pairs ( $W = -.49$ ,  $p = .96$ ). Thus, visual fixation durations were approximately the same for CS1-CS2 and CS3-CS4 presentations in babies: 83.42% of visual fixation for CS1-CS2 and 83.77% of visual fixation for CS3-CS4 presentation.

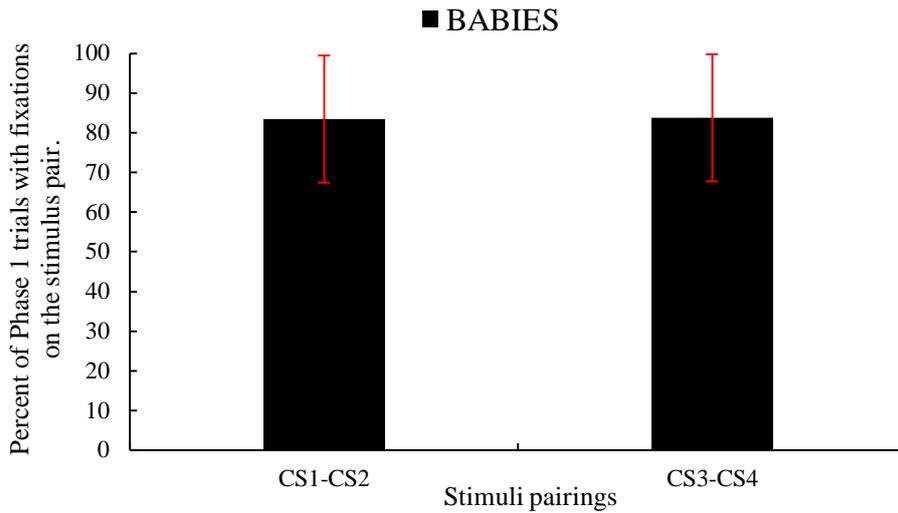


Figure 26. Mean percent of Phase 1 trial durations in which babies visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. Error brackets represent SEMs.

### 3.2.2. Phase 2 :

Figure 27 illustrated Phase 2 first-order conditioning results. We observed higher responses rates to CS1 than to CS3 in babies ( $W = 150, p = .004$ ). Thus, all babies looked at the US zone after CS1 presentation and avoided the US zone after CS3 presentation. No interaction was observed between Condition and Cue. That is, conditioned responses in CS2 and CS4 tests were caused by Phase 2 conditioning.

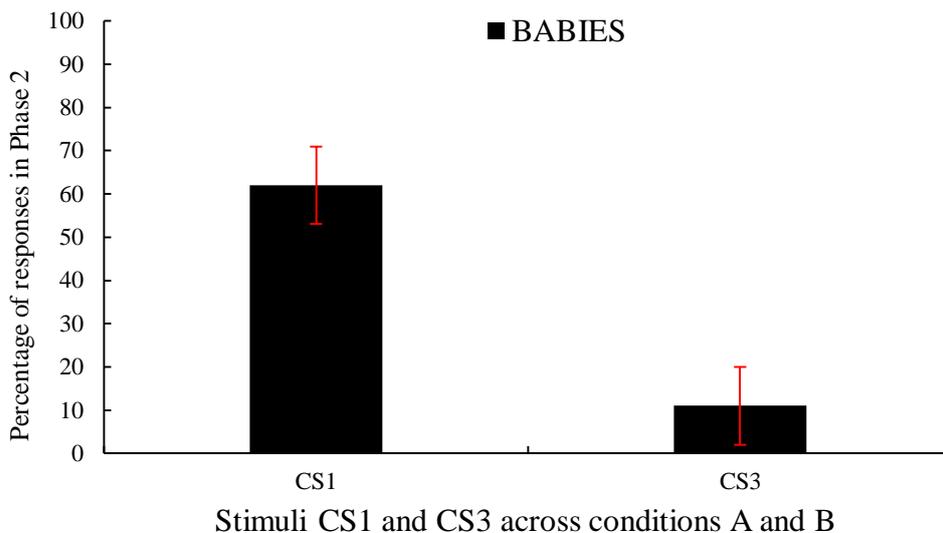


Figure 27: Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during Phase 2 in babies. Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 28 represents the number of babies exhibiting SPC responses at tests. We observed a SPC rate notably high because most of the babies looked more closely at the US+ zone when CS2 was presented than when CS4 appeared (Fisher's exact  $p = .04$ ). Precisely, visual fixation after CS2 presentation was observed in 21 of the 24 babies (i.e., 87,5%) ; visual fixation after CS4 presentation was observed in only 2 of the 24 babies (i.e., 8,33%). In this experiment, we demonstrated the existence of associative learning in individuals lacking language skills during the early developmental stages of their lives. These results will be compared to other experimental populations in chapter 5 of Part 2.

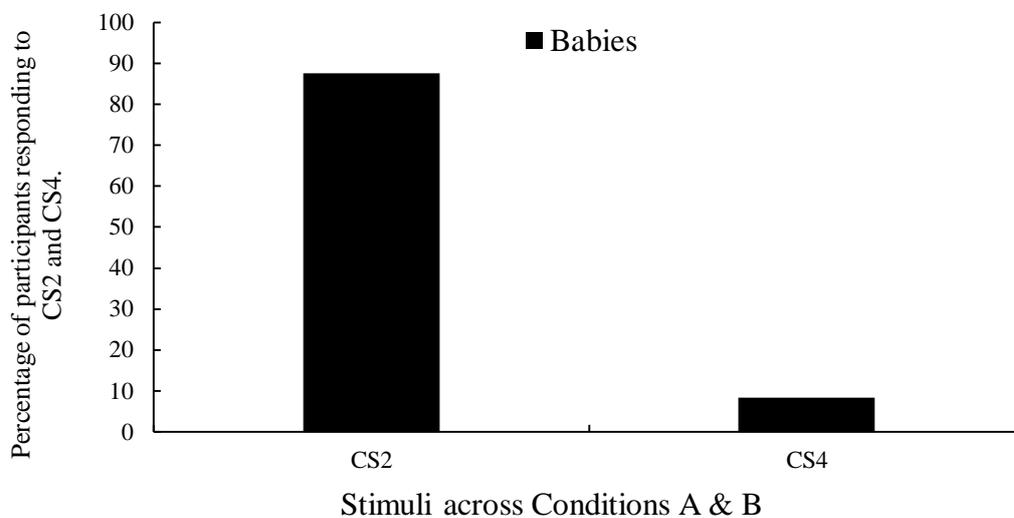


Figure 28. Percentage of babies during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of visual fixation to the video site during the CS4 test.

## 4. Discussion

In this chapter, we observed high visual fixation times for most of our babies in the US+ zone when CS1 and CS2 were presented. This means that first and second order conditioning can be observed in babies aged between 4 and 9 months, that is, the babies were able to anticipate the emission of an appetitive stimulus US+. Also, the visual fixation times on the US zone were lower when CS3 and CS4 were presented on the computer screen. This means that babies were able to avoid the aversive sound US-. Here, we demonstrated first and second order conditioning in babies aged between 4 to 9 months, by their avoiding an aversive stimulus US-. More generally, we demonstrated the existence of SPC in young individuals lacking language skills.

In comparison to previous mentioned studies, our results confirmed some specific works which observed second order associative learning in young rats (Cheatle and Rudy, 1978) or establishment of declarative memory in humans (Rovee-Collier et al., 2000). Here again, our results highlighted the establishment of skills using memory without verbal skills. Indeed, it seems that such associative learning does not depend on verbal skills in humans. Thus, we put forward the hypothesis that the verbal behavior is not a facilitator of the SPC response.

## CHAPTER 3 :

### SPC IN NON-VERBAL AND VERBAL AUTISTIC CHILDREN

In chapter 3, we tested one of the hypotheses concerning the establishment of SPC in humans. Indeed, this type of conditioning is generally explained by the use of verbal strategies in humans (Jara et al., 2006). Deficits in verbal strategies and more generally disorders in verbal skills have been demonstrated in verbal and non-verbal children with autism spectrum disorders (Anderson, Lord, Risi, DiLavore, Shulman, Thurm, ... and Pickles 2007, Baron-Cohen, Leslie and Frith 1985, Happé 1995, McEvoy Rogers and Pennington 1993, Mundy Sigman and Kasari 1990, Ornitz Guthrie and Farley 1977, Ungerer and Sigman 1987).

#### **1. Introduction :**

##### 1.1. Joint attention and verbal behavior in autistic children :

Anderson et al. (2007) studied a cohort of 205 children with autistic disorders aged 2, 3, 5 or 9 years old, assessing language skills using psychometric assessments and also assessing joint attention in each participant. Joint attention is considered as a core social skill based on basic visual discrimination and defined as the capacity to use eye contact and cues to coordinate attention with someone on a stimulus (Pelaez, 2009). In other words, it implies shared awareness of a stimulus. Anderson et al. (2007) observed a great variability in the results obtained and noticed a diversity of verbal disorders within the cohort ranging from disorders in verbal and non-verbal expression to failure to respond to simple instructions. Joint attention was one of the phenomena observed in that study and is an often observed in autistic children : children were asked to point a specific tool (e.g., a spoon), then they had to look at the tool before pointing to it for the experimenter. The authors demonstrated that the results of joint attention tests were good predictors of the child's future language level. In addition, authors found that the poorer the language skills, the more prone the child would be to emit socially inadequate behaviors, with these behaviors having a considerable negative impact on the life of the individual. Similarly, McEvoy et al. (1993) compared the verbal skills of children with autistic disorders to other school children without autistic disorders. Here, the executive function (i.e., how to solve a problem) and social communication were studied. McEvoy et al. found that children with autistic disorders had more difficulty in resolving tasks but persevered more than their peers without autistic disorders. Also, as already pointed out by Anderson and al. (2007), these authors observed a lack of joint attention in children with autistic disorders, as well as a defect in verbal communication with their peers. This lack of joint attention was also

found in 45-month-old children followed for 13 months who were suspected for autism spectrum disorders (Mundy et al., 1990). A correlation between joint attention capacity and the emergence of verbal behaviors were observed: the more the joint attention was deficient, the greater the delay in emergence of verbal behaviors. Thus, these authors considered visual attention as a good behavioral measure of autism in children, and they worked to improve joint attention in autistic children.

### 1.2. Categorization skills in autistic children :

In addition, Ungerer et al. (1987) studied receptive language and categorization skills in children with autistic disorders compared to peers without developmental disorders. The task was for the autistic child to put into boxes several items when they were subsequently presented one by one according to their shapes, colors and functions, then to name these items presented on flashcards. Ungerer et al. (1987) observed significantly lower performance in children with autistic disorders compared to the control group. Nowadays, we know that individuals with autistic disorders have developmental delays in many areas such as motor skills, communication and perception, at least during the first two years of life (Ornitz et al. 1977). Baron-Cohen et al. (1985) claimed that individuals with autistic disorders could not predict events or infer facial expressions of others. Happé (1995) modulated these conclusions by experimenting with social event anticipation tasks on individuals with autism spectrum disorders in comparison to individuals without developmental disorders. In that experiment, Happé observed that the learning of anticipatory behaviors (e.g., completing a story initiated by three flashcards presented in a specific order) was possible in individuals with autistic disorders, but that the acquisition time was longer compared to that observed in typical individuals. This author also pointed out that this acquisition was faster when the individual had good language skills. Happé's data suggested that establishment of anticipatory responses in children with autism spectrum disorders was possible, contrary to other studies (Ornitz et al., 1977 ; Baron-Cohen et al., 1985).

### 1.3. Associative learning in autistic children :

Moreover, some studies focusing on associative learning in children with autistic disorders challenged the results observed in previous studies (Bhat, Galloway and Landa, 2010, Preissler, 2008). For example, Preissler studied associative learning between words and images in verbal children with autistic disorders. The experimental task consisted of presenting an image of an item (e.g., a spoon) with the associated verbal word ("spoon"). The child had to repeat the word specific to the image of the item presented. Subsequently, these images were associated with

real objects, and the child had to name it. Preissler showed that verbal children with autistic disorders had performances similar to children without developmental disabilities in this discrimination task and in naming items. This study can not be readily generalized to our experiment because no stimulus had been associated with an unconditioned stimulus in Preissler's work. Similarly, Bhat et al. (2010) obtained the same results in a discrimination tasks similar to the study of Preissler by recording the visual fixation times of children with autistic disorders and varying social (e.g., human faces) and non-social stimuli (e.g., usual objects like a toy, a chair, or spoon). Thus, these authors demonstrated that associative learning between social and non-social stimuli was possible with autistic children, even though visual fixation times differed greatly across the nature of the different stimuli. Indeed, the visual fixation times were lower when a social stimulus was presented, compared to a non-social stimulus in autistic children compared to children without developmental disorders – which is a characteristic observed with autistic children who mostly have a preference for non-social stimuli compared to social stimuli.

To our knowledge, no prior research has used the SPC procedure with this population, despite the existence of many experimental works focused on the learning of verbal behaviors. For example, Sherer et al. (2001) developed a tool to teach the language skills to children with autism spectrum disorders. The goal of the authors was to develop these skills through the use of therapeutic videos. The child had to answer questions from a computer with different videos on various topics such as "What do you like doing on weekends?" or "What do you like to eat?". Audiovisual feedback was given to the child at the end of the test. In this experiment, the children were able to emit words from their behavioral repertoire as well as to make short sentences. The tools used in that experiment thus allowed the development and generalize of these skills with respect to various subjects as preferred food or preferred games (Sherer et al., 2001). Concerning the emergence of verbal behaviors in non-verbal children with autism spectrum disorders, the work of Koegel et al. (1987, 1988) introduced some possible behavioral therapies. Koegel et al. (1987) emphasized the importance of working on functional behavioral responses in individuals with autism spectrum disorders. These authors determined how to manipulate environmental variables, both in terms of antecedents and consequences, in order to facilitate the emergence of verbal behaviors with non-verbal children. For each child, experimenters used stimuli and natural reinforcers to train the verbal behavior for two hours a day. For example, a bottle of water was placed on the work table and the experimenter verbally guided the child to sound [o] for water later. Koegel et al. (1987) observed an increase in the number of verbal behaviors in children with autistic disorders, these children having been

initially non-verbal. Subsequently, Koegel et al. (1988) demonstrated the emergence of those verbal behaviors can be improved by first using topics of reinforcing conversations for the individual, then changing the themes within therapy. Thus, a preference assessment was conducted at the beginning of the session for each individual, and then worked on the verbal behaviors associated with the child's preferred reinforcer.

#### 1.4. In our experiment :

In this chapter, we tested two groups of children diagnosed as having autism spectrum disorders: verbal children and non-verbal children, all supported by ABA services. Because the establishment of SPC is presumably based on higher reasoning processes (Jara et al, 2006), and SPC had not found with children with autism spectrum disorders (Ornitz et al., 1977 for example), we expected not to observe this type of learning in our two experimental groups. However, because the use of verbal strategies had been proved facilitative for the establishment of associative learning (Broden et al., 1947, Jara et al, 2006), we hypothesized that the SPC rate observed would be higher in the verbal children in comparison to the non-verbal children. No comparison with children without developmental disabilities will be made in this chapter because there are important environmental variables separating these two populations. The experimental task for the two experimental groups was therefore the same as the one described before.

## **2. Participants**

Twenty-five children (7 girls and 18 boys) diagnosed as having autism spectrum disorder participated in this experiment, aged between 4 and 9 years old (mean : 7,02 years old ; SD : 2,2). The verbal skills of each child were assessed using the Peabody Picture Vocabulary Scale (PPVT©). Following the PPVT, each participant was placed in the experimental group "verbal" or "non-verbal" according to their performance (see Appendix 2).

Thus, 11 children (of 17 children tested) with autism spectrum disorders are part of the verbal group and 14 other children (of 19 children tested) were assigned to the non-verbal group. Each legal guardian first read and signed a consent form, and could also attend the session by standing behind a tinted window so that the child would not be disturbed by the presence of one of his parents. Each child could leave the experience at any time, not being physically restrained by the eye-tracking apparatus. The experimenter could also terminate the experiment if he saw a behavioral disorder emitted by the participant. For example, if a self-injurious behavior was emitted during the experiment, the experimenter ended the experimental task.

We excluded 11 autistic children (specifically, 6 verbal children and 5 non-verbal children) because of behavioral disorders. For the safety of participants, experimenters and materials, we stopped the experimental task when a behavioral disorder was emitted. Data of those 11 autistic children are not presented.

### **3.Results :**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of the means of two independent groups, we obtained a recommended sample size of at least 106 participants, with at least 53 participants per group. However, despite this recommended group size, in this study we managed to recruit only 25 participants, with 11 and 14 in each group. Hence, we conducted our analyses with nonparametric statistics to our interpretations of these results.

#### 3.1. Statistical issues :

For the same reasons explained in previous chapters, see below the statistical nonparametric tests used in order to illuminate the results of the experimental task with  $p (<.05)$  :

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution.
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.
- The **Cliff's Delta** statistic is a nonparametric effect size measure that quantifies the amount of difference between two groups of observations beyond p-value interpretation.

### 3.2. Statistical analysis :

#### 3.2.1. Phase 1 :

Figure 29 shows visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1. No statistical difference between the two types of stimuli pairs were observed ( $W = -.40$ ,  $p = .97$ ), nor between the *verbal* and *non-verbal* autistic children (respectively,  $U = 66.00$ ,  $p = .55$  and  $U = 73.00$ ,  $p = .27$ ). Visual fixation durations were approximately the same for CS1-CS2 and CS3-CS4 presentations in *verbal* and *non verbal* children: 44.57% of the visual fixation for CS1-CS2 in condition *verbal* and 43.92% in condition *non-verbal*; 43,92% of visual fixation for CS3-CS4 in condition *verbal* and 45.16% in condition *non-verbal*.

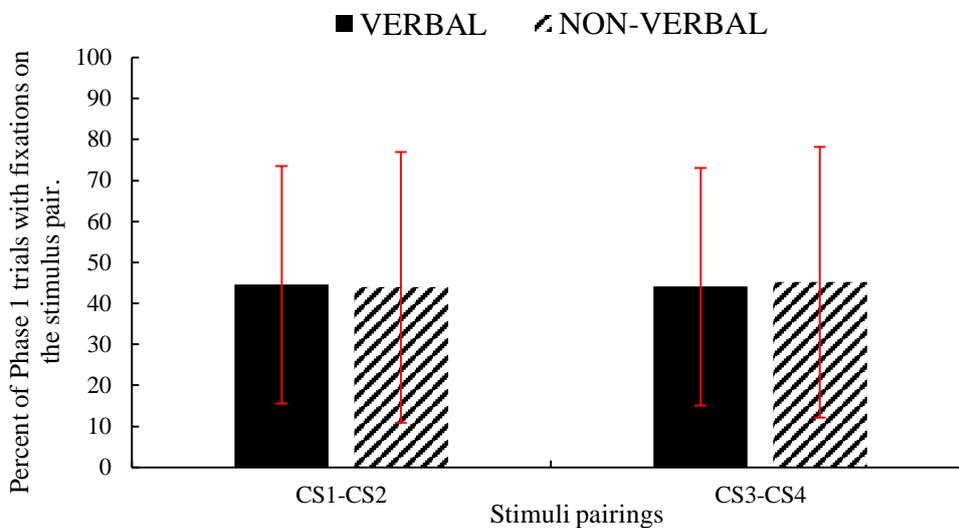


Figure 29. Mean percent of Phase 1 trial duration in which autistic children visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. Error brackets represent SEMs.

#### 3.2.2. Phase 2 :

Phase 2 first order conditioning results are illustrated in Figure 30. We observed greater responding to CS1 than to CS3 both in condition *verbal* ( $W = 144$ ,  $p = .003$ , Cliff's  $d = 0.9$ ) and in condition *non-verbal* ( $W = 147$ ,  $p = .004$ , Cliff's  $d = 0.9$ ). That means, all autistic children looked at the US zone after CS1 presentation and avoided the US zone after CS3 presentation. No significant difference was demonstrated between the two experimental groups of verbal or non-verbal children with autism spectrum disorders. In addition, there was no interaction observed between Condition and Cue. Thus, SPC performances observed in Test were caused by Phase 2 conditioning.

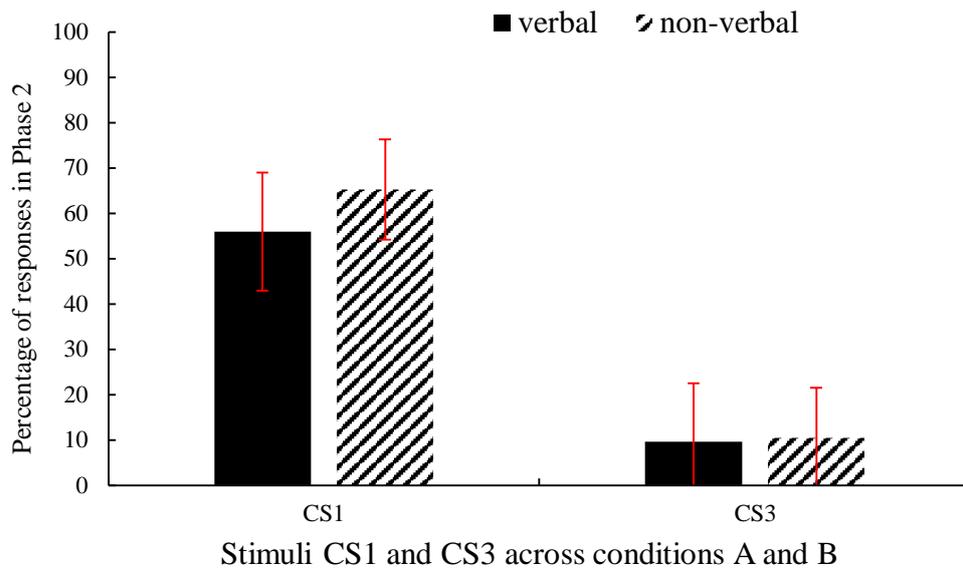


Figure 30: Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during Phase 2 in *verbal* and *non-verbal* autistic children. Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 31 represents the number of autistic children exhibiting SPC responses at tests. At the end of the second phase, both experimental groups showed high levels of visual fixation on the US+ zone when CS2 was presented. Precisely, visual fixation after CS2 presentation was observed in 9 of the 11 in condition *verbal* (i.e., 81,81%) compared to 8 of the 14 in condition *non-verbal* (57,14%), Fisher's exact test  $p = .44$ ). Visual fixation after CS4 presentation was observed in 0 of the 11 in condition *verbal* (i.e., 0%) compared to 1 of the 14 in condition *non-verbal* (i.e., 7,14%), Fisher's exact test  $p = 1$ . Thus, no significant difference was demonstrated between the two experimental groups of verbal or non-verbal children with autism spectrum disorders.

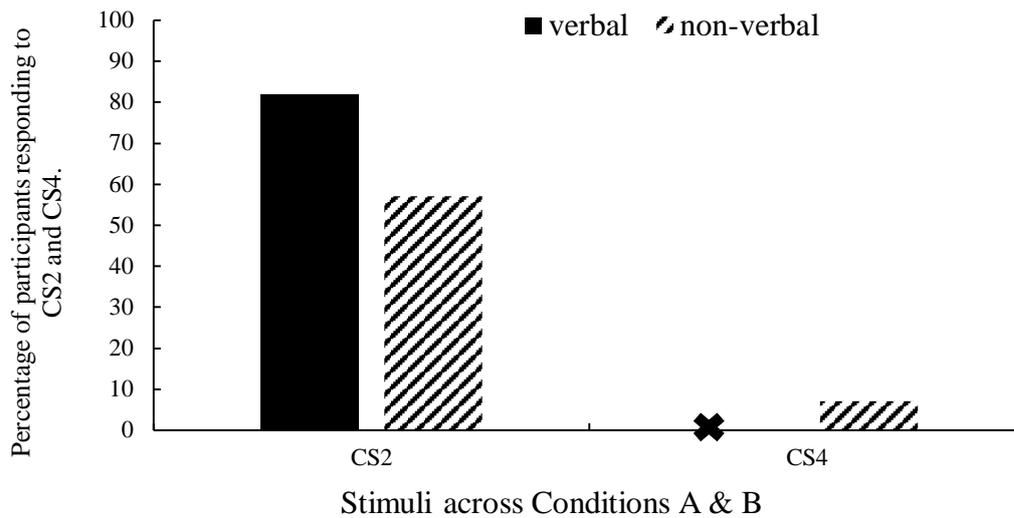


Figure 31. Percentage of autistic children during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of visual fixation to the video site during the CS4 test in conditions *verbal* and *non-verbal*.

#### 4. Discussion :

In this chapter, we observed high visual fixation rates in the US+ zone when CS1 and CS2 were presented to participants; demonstrating first and second order conditioning in verbal and non-verbal children with anticipatory responses to appetitive stimuli. In addition, we found that visual fixation rates were lower after the presentations of CS3 and CS4. This is also a demonstration of first and second order conditioning of aversive stimuli avoidance responses. Therefore, our data are consistent with some studies that have demonstrated the existence of second order associative learning between conditioned stimuli in children with autistic disorders (Bhat, Galloway and Landa, 2010, Preissler, 2008). In this experiment, we demonstrated the same type of learning with biologically critical stimuli (i.e., unconditioned appetitive and aversive stimuli).

Because we did not observe lower visual fixation rates in non-verbal children with autistic disorders compared to verbal children, verbal behavior does not appear to be beneficial for the establishment of SPC. From this point of view, our study did not support the work of Happé (1995) who stated that verbal behavior improves the skills of children with autism spectrum disorders. Indeed, our study showed that non-verbal children looked at the US+ area when CS2 was presented, and also avoided this area when CS4 appeared as did their peers with verbal skills. Therefore, these results supported our hypothesis that verbal behavior is not necessary for the establishment of SPC.

## CHAPTER 4 : SPC IN DEMENTIA

The increase of general cognitive deficits seen in dementia has led to the development of new tools using informant and performance screening methods to assess cognitive functioning in impaired individuals (Galvin, 2018). Specifically, evaluations of learning and memory in dementia patients have highlighted deficits in recall and attention compared to elderly controls (Grober and Buschke, 1987). Jointly, the observed decline in cognitive abilities is correlated with affective disturbances including emotional deficits and apathy, which are initially noticeable in patients with mild dementia (Derouesne, Thibault, Lagha-Pierucci, Baudouin-Madec, Ancrì, and Lacomblez, 1999).

### 1. Introduction :

#### 1.1. Respondent and operant conditioning and the elderly with dementia :

Despite the widely observed general cognitive decline seen in dementia, some behavioral learning is seen in dementia patients permitting the treatment of escape and aggressive behaviors (Rogers, Holm, Burgio, Granieri, Hsu, Hardin, and McDowell, 1999; Baker, Hanley and Mathews, 2006; Buchanan and Fisher, 2002). Moreover, training in occupational activities often enhances morning care routines like toileting or dressing and can reduce disruptive behaviors (Rogers, Holm, Burgio, Granieri, Hsu, Hardin, and McDowell, 1999). Escape and aggressive behaviors in nursing homes can be reduced by reinforcing appropriate behaviors (Baker, Hanley and Mathews, 2006) or with the use of music contingently delivered immediately after compliant behavior occurrences (Buchanan and Fisher, 2002). Such successful escape and appetitive conditioned behaviors can often be viewed within the framework of associative learning. In typical associative learning experiments with nonhuman, a conditioned signal (e.g., a tone or a flash light) precedes the occurrence of an unconditioned stimulus (e.g., an aversive electric shock) and subjects subsequently avoid the conditioned signal if possible. The dominant theoretical account of the conditioned avoidance is that it is acquired and maintained by a combination of respondent and operant conditioning (e.g., Dymond and Roche, 2009). First, respondent conditioning is implemented by the warning signal becoming a conditioned stimulus (CS) because of its prior pairings with the unconditioned aversive stimulus (US). Thus, avoidance responses occur in the presence of the CS because it evokes fear. Operant conditioning takes place when an avoidance response is emitted in the presence of the CS and is maintained by the escape from the CS and by the consequent reduction in fear. This learning is subsequently maintained by knowledge of the

relation between the avoidance response and the absence of the US (Dymond and Roche, 2009), involving multiple neural systems such as the cerebellum and the prefrontal cortex (Molchan, Sunderland, McIntosh, Herscovitch, and Schreurs, 1994), which are typically degenerated in dementia (Strich, 1956). Multiple correlations between degenerated brain areas and losses of cognitive abilities (Terry, Masliah, Salmon, Butters, DeTeresa, Hill and Katzman, 1991 ; Fischer, Gage, and Björklund, 1989) led researchers to think that associative learning could not be observed in patients with dementia.

However, some studies focused our attention on the use of experimental tasks based on operant conditioning. Spira and Edelstein (2007) conducted an experiment in order to evaluate operant conditioning in four typical elderly compared to four elderly with Alzheimer's disease, using a button-pressing task and a single subject design. In that study, the elderly had to seat in front of a computer screen connected to a joystick, with which they had to put coins into the box when coins are given. A coin-delivery mechanism was used in order to deliver reinforcers according to the elderly's responses constituting different reinforcement conditions. Indeed, Spira and Edelstein (2007) tested transitions in the elderly with *fixed ratio* (FR), *fixed interval* (FI) and *extinction* (EXT) schedules. Many previous studies have focused on the sensitivity to those schedules in typical adults (e.g., Hays, Brownstein, Haas & Greenway, 1986). Spira and Edelstein observed in both groups (i.e., typical elderly and elderly with dementia) the same patterns of operant conditioning according typical patterns demonstrated in typical adults. This was an interesting result because the elderly with dementia emitted the same conditioned responses compared to typical elderly people. In addition, the authors observed a higher sensitivity to the FI-EXT transition in the dementia group compared to the control group, which suggests that the elderly with dementia are more sensitive to the no-reinforcement schedule compared to the elderly without dementia. Such results supported the possible effectiveness of non-drug therapies for elderly with dementia. Gräsel, Wiltfang and Kornhuber (2002) reviewed numerous non-drug therapies in elderly with dementia, including the use of classical and operant conditioning. The authors encouraged the use of behavioral therapies that aim to recover lost skills elderly (e.g., reading, writing), or to enhance some abilities (e.g., use a specific tool of the home care) using operant conditioning. Many of those studies involve associative learning, even if the authors did not mention it. For example, Spira and Edelstein (2007) used a tone paired with a light before each trial in order to signify to elderly people that a new trial began and that coins are going to be delivered. Here, both tone (CS1) and light (CS2) were associated with the US+ (i.e., coins delivered). Thus, each participant was ready to pick up coins from the box as soon as

they heard and saw the light and the tone at the beginning of each trial. In that study, the goal of Spira and Edelstein was not to examine SPC, in that light and tone were always presented together and there was no test after tone or light presented alone. Thus, all that they examined was first order conditioning.

### 1.2. In our experiment :

Toward assessing associative learning in dementia patients, the present experiment used a SPC (Brogden, 1939) procedure implemented with an eye-tracking system. The use of an eye-tracking system facilitated our avoiding the use of instructions, which might have confounded learning with comprehension of verbal instructions. This point is important because of the possibility of instructions being misunderstood by participants with cognitive disabilities. The preparation also permitted participants to exit the experiment if they wanted because there was no physical restraint, and they would just have had to look away from the computer screen or close their eyes. To our knowledge, SPC has never before been examined in dementia patients. Basically, we asked whether such relatively complex learning (i.e., associative chains such as CS2-CS1-US) could be observed in dementia.

The present experiment examined SPC in two experimental groups: twenty typical elderly people (seniors [Sen]) and twenty elderly patients with a diagnosis of dementia (Dem). Exactly the same procedure was used in both groups.

## **2. Participants**

Twenty typical elderly (11 females and 9 males; 71 and 96 years old, mean age 87,0 years old, SD : 1,16) volunteers were assigned to the control group Senior. Each participant read and signed an informed consent form prior to the experiment.

Twenty patients with diagnoses of dementia (13 females and 7 males; 78 and 95 years old, mean age 88,8 years old, SD : 1,32) were assigned to the experimental group Dementia. Each participant passed a PATHOS© evaluation and presented severe dementia with lacks of verbal abilities and attention (see Appendix 3). PATHOS© provided a personal evaluation of the deficits and the specific needs of health care (Benhamou, Berti, Brodner, De Andres, Draisci, Moreno-Azcoita et Viel, 2008). A member of each dementia patient's family read and signed an informed consent form prior to the experiment.

Participants could exit the experiment if they wanted it, or if experimenters observed distressed behavior. In this study, only one participant had been excluded in the dementia group, because of a hypersomnia during the experimental task in Phase 1 (during which CS2-CS1 and CS4-

CS3 pairing presentations occurred). Results of the sleepy participant will not be presented in that chapter 4.

The experiment was approved by the University of Lille Institutional Review Board.

### **3.Results**

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size necessary to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of the means of two independent groups, we obtained a recommended sample size of at least 106 participants, with at least 53 participants in each group. However, despite this recommended group size, in this study we managed to recruit only 40 participants, with 20 in each group. Hence, we conducted our analyses with nonparametric analyses to our interpretations of these results.

#### 3.1. Statistical issues :

For the same reasons explained in previous chapters, see below the statistical nonparametrics tests used in order to illuminate the results of the experimental task with  $p (<.05)$  :

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution.
- **Fisher's exact test** : Fisher's exact test is a statistical significance test used in the analysis of contingency tables. Fisher's exact test is commonly used when sample sizes are small, although the test is efficient for all sample sizes. Thanks to Fisher's test, the significance of the data's deviation from the null hypothesis can be calculated rather than relying on an approximation that becomes exact only in the limit as the sample size grows to infinity, as with many statistical tests.
- The **Cliff's Delta** statistic is a nonparametric effect size measure that quantifies the amount of difference between two groups of observations beyond p-value interpretation.

### 3.2. Statistical analysis :

#### 3.2.1. Phase 1 :

Figure 32 illustrates visual fixation duration for CS1-CS2 and CS3-CS4 trials presented in Phase 1 in elderly people. There was no statistical difference between the two types of stimuli pairs ( $W = -.48, p = .63$ ). However, we observed significant differences of visual fixations between the *dementia* and *control*, (respectively,  $U = 48.00, p < .01$  and  $U = 45.00, p < .01$ ). Precisely, visual fixation durations were higher for CS1-CS2 and CS3-CS4 presentations in *control* compared to *dementia*: 84.45% of visual fixation for CS1-CS2 in condition *control* and 44.42% in condition *dementia* ; 84.44% of visual fixation for CS3-CS4 in condition *control* and 45.14% in condition *dementia*.

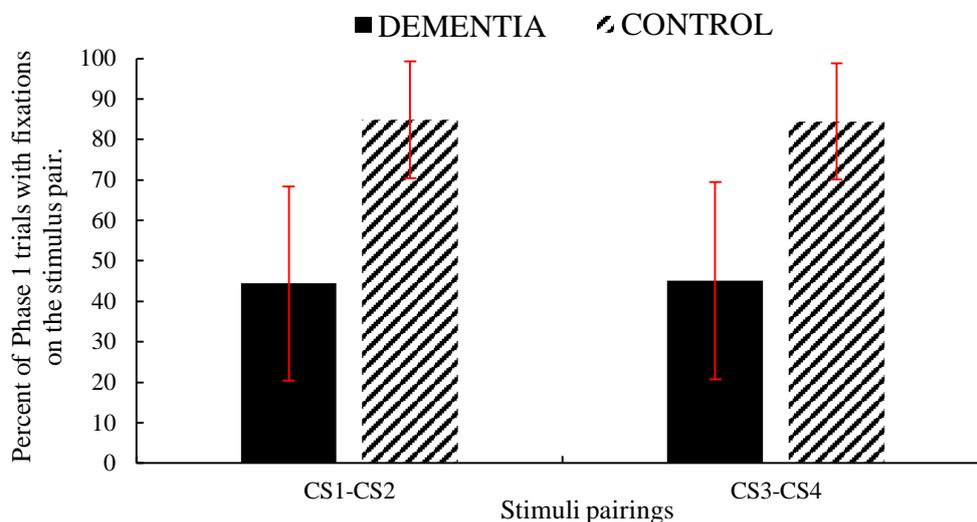


Figure 32. Mean percent of Phase 1 trial duration in which the elderly visually fixated on the stimulus pairs (CS2-CS1 and CS4-CS3) at the center of the screen. Error brackets represent SEMs.

#### 3.2.2. Phase 2 :

Figure 33 present Phase 2 first order conditioning results. Once again, we observed greater responding to CS1 than to CS3 both in condition *dementia* ( $W = 157, p = .003, \text{Cliff's } d = 1.0$ ) and in condition *control* ( $W = 143, p = .004, \text{Cliff's } d = 0.9$ ). That means, all participants finally looked at the US zone after CS1 presentation and avoided the US zone after CS3 presentation. Note that we did not observe differences between groups instead of the significant different visual fixation times in CS1-CS2 and CS3-CS4 presentation in Phase 1.

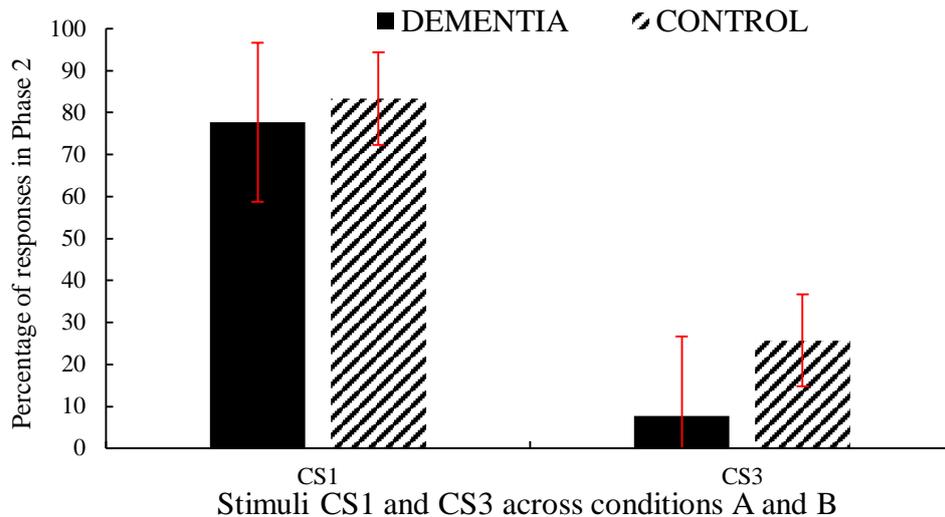


Figure 33: Mean percent of CS1 and CS3 trials with visual fixation to the US+ video site during Phase 2 in the elderly people (*dementia* compared to *control*). Error brackets represent SEMs.

### 3.2.3. Test of CS2 and CS4 :

Figure 34 represents the number of participants exhibiting SPC responses at tests. No significant difference between groups was found either for CS2 test trial (Fisher exact  $p = 1$  for both conditions). Precisely: in condition *dementia*, visual fixation after CS2 presentation was observed in 12 of the 20 participants (i.e., 60%) compared to 10 of the 20 in condition *control* (i.e., 50%). No significant differences between groups in the proportion of avoidance of the US zone was obtained for CS4 test (Fisher exact  $p$ 's = 0.75). Precisely: in condition *dementia*, visual fixation after CS4 presentation was observed in 1 of the 20 participants (i.e., 5%) compared to 2 of the 20 in condition *control* (i.e., 10%).

Thus, both groups learned both first order conditioning and SPC avoidance of the aversive US, and the two groups did so similarly.

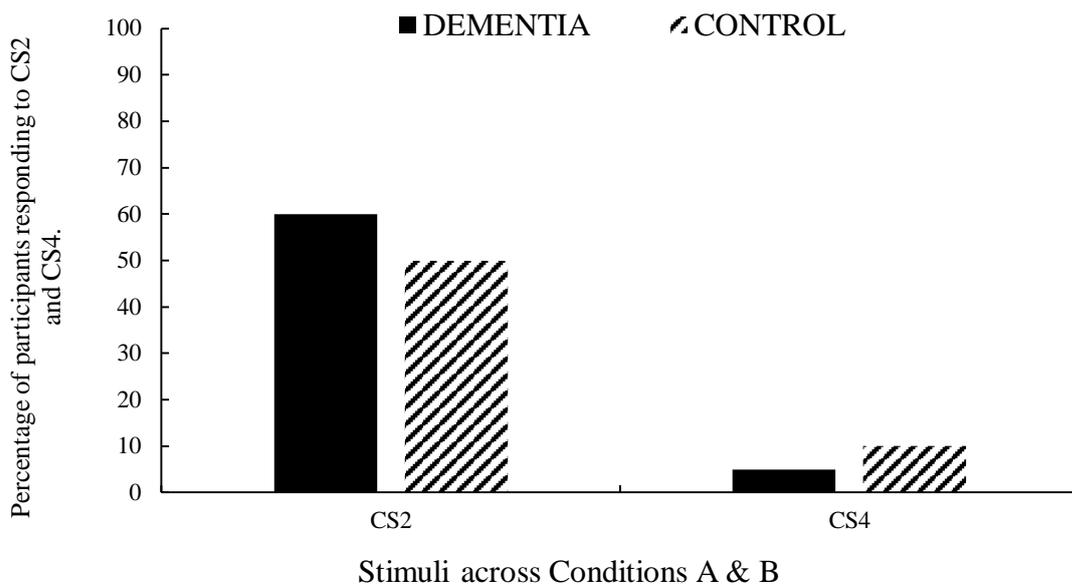


Figure 34. Percentage of elderly during the SPC test exhibiting visual fixation to the video site during the CS2 test and absence of visual fixation to the video site during the CS4 tests in conditions *dementia* and *control*.

#### 4. Discussion

The results showed that patients with dementia, like healthy elderly people, learn first order and higher order associations such as those required in SPC. SPC has an appreciable adaptive value (Kaakinen, Hyönä, and Keenan, 2002) in that it extends the number of CSs associated with a US to CSs that was never directly paired with the US in that, when a cue is actually paired with the US, all other cues previously associated with that cue will inherit the conditioned response. Trivially, this process allows avoidance of outcomes in the presence of cues that were never paired with an aversive US as well as contributing to rapid learning of events that predict safe or appetitive outcomes.

An ability of dementia patients to escape aversive stimuli has already been reported without referring to Pavlovian processes (Rogers, Holm, Burgio, Granieri, Hsu, Hardin, and McDowell, 1999; Baker, Hanley and Mathews, 2006; Buchanan and Fisher, 2002). Nevertheless, demonstrating SPC with dementia patients is, somehow, surprising in the sense that SPC is thought to call upon the representation in memory of the CS that was actually paired with the US (i.e., CS1). More specifically, if CS2 (which was formerly paired with CS1) evokes the US representation or the unconditioned response (UR) at test, it is presumably because CS2 evokes the representation of CS1 and consequently its association with the US or the UR (Rizley and Rescorla, 1972).

Interestingly, the current data shows not only the ability of dementia patients to use memorized associations on which new associations can be built, but they also show temporo-spatial abilities required for avoidance responses. Nearly all dementia patients in our study avoided US- by not looking at the US zone after CS4 presentation. The patients' strategy suggests that they could localize events in space and choose at what time to gaze at or away from the US zone. More generally, the current study seriously qualifies the assumption of impairment in dementia at least for basic associative learning and memory.

## Chapter 5: SPC across ages

In the previous chapters, we demonstrated in several populations first order and second order conditioning. The aim of the present chapter is to focus on the first and second order conditioning across several developmental groups (i.e., babies, children, adults and seniors).

### 1. Introduction :

#### 1.1. Piaget's assumption about Development :

Works by Jean Piaget (1896-1980) are very influential in French Contemporary Psychology, especially in the human development area. One of Piaget's goals was to determine how thinking developed in humans. His work was partially focused on studies of childhood in which he observed how children failed in a task before succeeding in it (Piaget, 1952, 1970, 1977). From his observations, Piaget described several developmental periods concerning the human cognitive development. A first period from birth to the age of 2 years is called the « sensorimotor period, » in which babies explore their environment by touching and tasting. By the end of that period, children begin to use appropriate words to identify items. A second period focused on ages between 2 and 7 years old, and is called « preoperative period ». Piaget stipulated that children in this period begin to use words in order to think and to communicate with someone else, using a simple logic around the age of 6 years old. A third period includes the ages between 7 and 12 years old, and is called the « period of concrete operations ». Here, children expand their vocabulary and use complex logic (e.g., mathematical processes like addition and division), and have a mental representation of familiar items. According to Piaget, deductive thought with complex learning is possible starting at 12 years old. In that final developmental period (called the « formal operation period »), young adults are able to imagine familiar and new items, mentally organize complex ideas, and solve complex problems.

#### 1.2. Verbal strategies and developmental models :

Other developmental models focus on verbal behaviors, which are the focus of our study. The development of verbal behavior in infancy was described in early pages of chapter 1. We highlighted Denney's model (1982, 1984), which stipulated that the number and complexity of verbal abilities increase with the beginning of schooling before gradually decreasing starting at 30 of age. Denney's (1984) model compares cognitive performance in humans aged between 0 and 90 years old. Generally speaking, we observe low cognitive performance at birth, which increases gradually up to about 20 years of age with training, and without training, although

training enhances the progress. Developmental approaches consider this enhancement to be a product of schooling provided by both academic situations and social interactions. After 30 years of age, Denney's model assumes that general performance gradually decreases. That decrease can be moderated by a performance training, although ultimately the decrease is inevitable. Denney's research caused him to modulate his model based on non-normative subjects who showed higher performances than expected based on their chronological age. For example, in select instances, the general performance of a senior could be better than that of a young adult's.

According to Denney's model and Piaget's work, we assumed that verbal abilities would differ across our experimental groups. Indeed, babies have a deficiency in verbal ability relative to adults, children at 5-6 years of age begin to develop their abilities, young adults have optimal verbal abilities, and seniors have better verbal abilities compared to children and babies but lower abilities compared to young adults. Because one hypothesis concerning the establishment of SPC is focused on the use of verbal strategies (e.g., Brogden, 1947, 1949 ; Jara et al., 2006), we might predict that there would be differences in conditioned responding across developmental groups. Specifically, if our experimental task required the use of such verbal abilities, adults and seniors should have better rates of conditioned responding, compared to babies and children.

### 1.3. In our experiment :

In the present chapter, we compare individuals of several developmental ages without developmental disabilities (i.e., without autistic children and elderly with dementia). The goal was to compare typical individuals who followed a typical developmental process. It is known that autistic children and the elderly with dementia do not follow the typical developmental states. We used specific evaluations according to the developmental disorders (e.g., ABLLS®-R for autistic children ; PATHOS© for the elderly with dementia). Thus, this chapter focuses on four developmental stages : babies, children, adults, and seniors.

## 2. Participants

This chapter compares four experimental groups :

- **Baby group** : Twenty-four babies (11 girls and 13 men , mean age 5,79 months , SD : 1,50) (i.e., chapter 1 of Part 2).

- **Children group** : Twenty typical children (13 girls and 7 boys , mean age 5,26 years old , SD : 0,51) enrolled at the kindergarten Prévert located at Lille (i.e., not presented in the previous chapters). None of these children had any developmental disability.
- **Adult group** : Twenty French university students (14 women and 6 men , mean age 23,8 years old , SD : 1,2) (i.e., chapter 2 of Part 1, condition ad10 pairings).
- **Senior Group** : Twenty French seniors (13 women and 7 men , mean age 69,55 years old , SD : 1,7).(i.e., chapter 3 of Part 1, condition se10 pairings).

All groups were examined using the same experimental task with the same eye-tracking system. Each participant or tutor's participant read and signed an informed consent form prior to the experiment. The experiment had been approved by the University of Lille Institutional Review Board.

### 3. Results :

All results were collected at the end of the experiment by the Matlab© software, and were analyzed with conventional statistical techniques. Using the G\*Power 3.1 software (Faul, Erdfelder, Buchner, & Lang, 2009), we calculated the estimated sample size required to observe an average effect ( $f = 0.5$ ) with an  $\alpha = 0.05$  and a power of 0.80. With the main analysis viewed as a comparison of the means of more than two independent groups (4 groups), we obtained a sample size of at least 48 participants, with at least 12 participants in each group. In line with these recommendations, for these comparisons, we already had 88 participants, with at least 20 participants in each group. Thus, this analysis was properly powered.

The goal of chapter 5 is to compare the percentages of visual fixation times among several experimental groups : babies, children, adults and seniors. Here, we will not present in detail the data already reported in the previous chapters for each group. The present aim is to provide a comparison across the different developmental groups. Thus, we examined on the visual fixation times for CS1-CS2/ CS3-CS4 zones and US zone for each participant of all groups and performed a Kruskal-Wallis test.

#### 3.1. Statistical issues :

As explained in the previous chapters, we used the statistical nonparametric tests below :

- A **Kruskal-Wallis test by ranks**, also called a one-way ANOVA on ranks, is a nonparametric method to test whether samples originate from the same distribution. This test is often used for comparing more than two independent samples of equal sample sizes. The Kruskal-Wallis test is a required precursor for other nonparametric

tests such as the Mann-Whitney test. A significant Kruskal-Wallis test indicates that at least one sample stochastically dominates one other sample. However, the test can not identify which sample is the source of the stochastic dominance. That is why other nonparametric tests had to be conducted following a significant Kruskal-Wallis test.

- The **Mann-Whitney U test** (also called the Mann-Whitney Wilcoxon) is a nonparametric test of the null hypothesis that is equally likely that a randomly selected value from one sample will be greater or lesser than another value selected from a second sample. The Mann-Whitney U test does not require that the data be normally distributed and is considered to be an efficient test to determine whether two independent samples come from the same distribution.

### 3.2. Statistical analysis :

#### 3.2.1. *Phase 1* :

First, we observed significant differences of percentage of visual fixation times in all groups for CS1-CS2 and CS3-CS4 zones (Khi2 : 25,42 ;  $p < .05$ ). Mann-Whitney test revealed that there was no difference of percentage of visual fixation times between babies and children for CS1-CS2 presentation (U : 223,00 ; NS) nor for CS3-CS4 presentation (U : 223,50 ; NS). In addition, there was no difference in the percentage of visual fixation times between babies and adults for CS1-CS2 presentation (U : 208,50 ; NS) and CS3-CS4 presentation (U : 226,00 ; NS). However, we observed a higher percentage of visual fixation times in babies compared to the elderly for both stimuli pairings CS1-CS2 (U : 62,00 ;  $p < .01$ ) and CS3-CS4 (U : 56,00 ;  $p < .01$ ).

Comparing children with adults, there was no difference in the percentage of visual fixation times for CS1-CS2 presentation (U : 152, 50 ; NS) nor for CS3-CS4 presentation (U : 167,00 ; NS). However, we observed higher percentage of visual fixation times in children compared to the elderly for CS1-CS2 presentation (U : 61,50 ;  $p < .01$ ) and for CS3-CS4 presentation (U : 47,00 ;  $p < .01$ ). The same was observed between adults and elderly. That is, we obtained higher percentage of visual fixation times in adults compared to elderly for CS1-CS2 presentation (U : 47,00 ;  $p < .01$ ) and for CS3-CS4 presentation (U : 53,00 ;  $p < .01$ ).

In conclusion, CS1-CS2 and CS3-CS4 presentations were more targeted by babies, children and adults, compared to the elderly.

### 3.2.2. Phase 2 and Test :

First, we observed significant differences of percentage of visual fixation times in all groups for US zone (Khi2 : 9,42 ;  $p < 0.05$ ). A Mann-Whitney test revealed that there was a general (i.e., all US zones pooled) difference in the percentage of visual fixation time between babies and adults (U : 129,5 ;  $p < 0,01$ ), and between children and adults (U : 129,5 ;  $p < 0.05$ ). There was no difference in the percentage of visual fixation time between babies and children (U : 210,00 ; NS), nor between babies and seniors (U : 204 ; NS), nor between children and seniors (U : 193 ; NS), nor between adults and seniors (U : 149,5 : NS). In conclusion, there are general differences of percentage of visual fixation times in Phase 2 and in Test between babies and adults, and between children and adults (see Figure 28) :

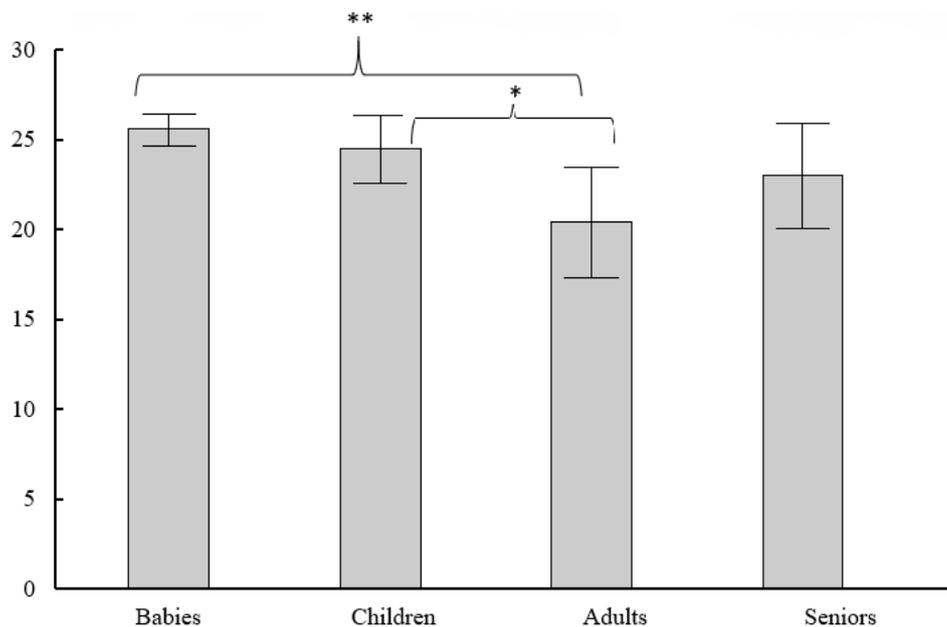


Figure 35 : Differences of percentage of visual fixation in Phase 2 and Test for all zones for each experimental group (Khi2 : 9,42 ;  $p < 0,05$ ), « \* » means  $p < .05$  , « \*\* » means  $p < .01$ .

Second, there were visual differences for all groups concerning fixation times on ZUS after CS1 presentation (Khi2 : 21,47 ;  $p < 0.01$ ), and after CS3 presentation (Khi2 : 30,07 ;  $p < 0.01$ ). Thus, we tested those differences between specific groups for the US zone previously noted. No analysis was conducted on other zones because Kruskal-Wallis test showed there are no overall differences of visual fixation times for these zones.

Specifically, ZUS was more targeted by children compared to babies after CS1 presentation (U : 133 ;  $p < 0.01$ ), whereas ZUS was more targeted by babies after CS3 presentation (U : 100 ;  $p < 0,01$ ). Thus, we can conclude that first order conditioning is more pronounced in

children than in babies because of the higher rate of responses for children on ZUS after CS1 presentation. However, we have to remember that all participants succeeded Phase 2 of the experimental task, showing clear establishment of first order conditioning. The results presented previously reveal that first order conditioning was better in children compared to babies.

Between babies and adults, ZUS was more targeted by adults compared to babies after CS1 presentation ( $U : 49,00 ; p < 0,01$ ), whereas ZUS was more targeted by babies after CS3 presentation ( $U : 130,00 ; p < 0,05$ ). Once again, we see that first order conditioning was more pronounced in adults compared to babies (i.e., better visual fixation on ZUS after CS1 presentation) despite first order conditioning having been demonstrated in all groups.

Between babies and seniors, ZUS was more targeted by seniors compared to babies after CS1 presentation ( $U : 147,00 ; p < 0,05$ ), whereas ZUS was more targeted by babies after CS3 presentation ( $U : 106,00 ; p < 0,01$ ).

Between children and adults, there were no other differences about US zone between children and adults, nor between children and seniors, nor between adults and seniors.

In conclusion, all participants reached the criterion of Phase 2, demonstrating a presence of first order conditioning. Nonetheless, ZUS was more targeted by children, adults and seniors compared to babies after CS1 presentation. That implies that first order conditioning was more pronounced with those three populations with respect to anticipatory responding. There was no other significant difference concerning first order conditioning after presentation of CS3, nor concerning the second order conditioning after CS2 and CS4 presentations.

#### **4. Discussion**

The aim of the present chapter was to compare the conditioned responses observed between four different developmental ages. A nonparametric ANOVA (i.e., Kruskal-Wallis test) found that there were only overall differences of visual fixation times during Phase 2 and Test between babies and adults, and between children and adults. That is, ZUS was targeted more by children, adults and seniors compared to babies after CS1 presentation, whereas ZUS was targeted more by babies compared to others after CS3 presentation. No other significant differences were detected concerning ZUS. We conclude that first order conditioning was more pronounced in children, adults and seniors after CS1 presentation than in babies, despite babies finally reaching the learning criterion of Phase 2. Moreover, those differences seemed to have no

influence on second order conditioning in babies because there were no significant differences between groups for visual fixation on ZUS after CS2.

Our results differed from prevailing developmental models (e.g., Denney 1984 model) in the sense that there were no differences in anticipatory responding (i.e., conditioned responses after CS1 presentation) across children, adults and seniors, nor for a second order conditioning (i.e., conditioned responses after CS2 and CS4 presentations) across all groups (i.e., babies included). Our results imply that verbal abilities are not necessary for the establishment of SPC, with this being demonstrated with different developmental groups characterized partially by distinctly different verbal abilities. One limitation of our study (developed in the General discussion) is that it does not assume one hypothesis concerning the establishment of SPC, but just questions the need for verbal abilities in the establishment of SPC.

## Résumés Partie 2

Ci-dessous un résumé en français de différents points abordés dans cette Partie 2.

### 1. Développement du comportement verbal

Les humains sont des animaux sociaux, vivant la plupart du temps les uns avec les autres. Une de leurs caractéristiques sociales est la communication, avec l'utilisation de mots oraux, écrits, gestuels, ou encore par l'intermédiaire de signes. En 1957, Skinner a introduit le terme de «comportement verbal» et l'a défini par sa fonction plutôt que par sa structure. Ainsi, le comportement verbal fait référence à la réponse comportementale d'un locuteur émise en fonction de conditions environnementales qui établissent et maintiennent ce comportement.

Skinner (1957) considère la « pensée » comme une réponse comportementale interne aux individus. Dans notre étude, nous nous sommes concentrés sur les « comportements gouvernés par les règles » (Skinner, 1969) qui ont un effet sur l'auditeur (ou l'individu lui-même), tels que les instructions, les lois et les conseils. Comme tout autre comportement (verbal), les comportements gouvernés par les règles se développent et se maintiennent tout au long de la vie des individus. Les bébés que nous avons testés étaient au stade de babillage, considéré comme un stade de « non raison » (Fenson et al., 1994). Selon les modèles de développement (comme Denney, 1984), les compétences verbales sont primaires pendant l'enfance et commencent à se développer avec le début de la scolarité pour atteindre une performance optimale vers 20-30 ans, suivie d'une diminution des capacités jusqu'à la fin de la vie.

Cependant, certaines procédures comportementales montrent une possible émergence et amélioration de ces capacités verbales, par exemple chez les enfants de 3 à 8 ans (Pelaez et al., 2011), chez les enfants autistes non verbaux (Sundberg et al., 2000) et chez les personnes âgées avec déficience verbale (Renaux et al., 2017). Ainsi, dans notre recherche, nous avons considéré les comportements verbaux comme des opérants.

### 2. Stratégies verbales et PCS :

Au-delà de son aspect social, Skinner (1969) a stipulé que le comportement verbal, tel que des instructions, pouvait affecter les comportements différemment de leurs contingences de renforcement initiales. Plus tard, Bandura (1974) affirmait que les comportements verbaux pouvaient moduler les réponses comportementales attendues par l'individu lui-même et / ou par l'expérimentateur. Des études telles que celles de Lippman et Meyer (1967) ont confirmé cette hypothèse en démontrant différents patterns de réponses en fonction des instructions données aux participants lors de la tâche expérimentale.

De tels travaux laissent penser que les comportements verbaux pourraient également moduler les réponses conditionnées observées dans les études se focalisant sur le PCS chez l'humain. Brogden (1942, 1947) a lui-même déclaré que les instructions étaient essentielles à l'observation du PCS. Ainsi, cet apprentissage associatif a été étudié chez des adultes typiques capables de lire des instructions données (voir, Craddock et al., 2014; Molet et al., 2010). Par exemple, Jara et al. (2006) ont utilisé une procédure de conditionnement de second ordre dans laquelle ils ont démontré que les individus étaient capables de former des stratégies verbales sur des tâches causales. Plus spécifiquement, les individus étaient apparemment capables d'inférer des relations de cause à effet entre cause et conséquence d'un événement, grâce aux informations données dans les instructions. En réalité, peu d'efforts ont été déployés pour déterminer si les instructions étaient réellement nécessaires dans cette tâche expérimentale.

Cependant, nos résultats développés dans la Partie 1 ont montré que le phénomène de SPC avait été observé sans l'utilisation d'instructions chez des individus typiques. Pour tester l'influence de stratégies verbales dans le PCS, nous avons répliqué notre procédure sur des individus dépourvus de compétences verbales tels que les bébés, ou présentant une déficience verbale observée chez les enfants avec troubles autistiques et les personnes âgées atteintes de démences.

# General discussion

## 1.SUMMARY AND CLINICAL APPLICATIONS

### 1.1 Resume of findings :

My work focused on a specific type of associative learning: Sensory preconditioning. Since its introduction by Brogden in 1939, few studies have studied this type of learning in humans. Furthermore, to our knowledge no study tried to observe SPC in individuals lacking of verbal abilities, whereas one of the theories concerning the establishment of SPC is based on the use of rule-governed behaviors in humans. In our experimental task, all participants were free to move and placed in front of a computer screen, where the task was to look at the screen. No instructions were issued because using instructions was not feasible with individuals with behavioral disorders such as nonverbal children with autistic disorders or elderly people with severe senile dementia. Thus, visual fixation time as the dependent variable allowed us to study of SPC in individuals at different developmental stages and being deprived/deficient in language skills.

Thus, for the first time in research, we sought to control the environmental parameters allowing the observation of a SPC response by repealing the use of written instructions during the experimentation (Part 1). In the first experiment (chapter 3 of Part 1), we demonstrated the role of spatial contiguity in the establishment of SPC by comparing the conditioned response rate in a condition in which stimuli were presented adjacently in phase 1 (i.e., condition B), compared to present distantly one another (i.e., condition A). The results indicated that closer spatial contiguity played a beneficial role in the observation of SPC. Then we were focused on the number of CS2-CS1 and CS4-CS3 pairing presentations in Phase 1 of the tasks, due to the results in the literature being controversial on this subject. Thus, we presented either 10 or 20 pairings of stimuli to different experimental groups, and subsequently found a better rate of SPC at test for the condition in which the stimuli had been presented only 10 times instead of 20. In addition, we found similar results in seniors, demonstrating that repetition of stimuli beyond 10 was not beneficial for the establishment of SPC in humans (see chapter 4 & 5 in Part 1).

The results obtained and presented in these first three chapters led us to develop a similar experimental task for the atypical populations tested in Part 2.

First we tested babies 4 to 9 months old who seemingly lacked any verbal abilities. We observed high levels of SPC in this population, with most babies correctly anticipating the onset of the US + and avoiding the US- (see chapter 2 of Part 2). Then we tested the same paradigm in verbal and non-verbal children all with autism spectrum disorders. Here, we did not observe

any differences in associative learning between the two populations, with SPC rates being high among all children (see chapter 3 of Part 2). Thirdly, we tested elderly people with senile dementia in comparison to a group of elderly people without senile dementia. Once again, we did not find any significant differences in the anticipatory responses of US+ and the avoidance response of US- in the two experimental groups (see chapter 4 of Part 2). Finally, we assessed the development of SPC across several developmental groups, ultimately challenging contemporary developmental models and general conceptions of human cognition (see chapter 5).

The overall results obtained suggest that verbal behaviors are not necessary for the establishment of complex learning that involves the establishment of associations between different conditioned stimuli. Moreover, we demonstrated that this type of learning is present in all populations tested, regardless of their developmental stages.

## **1.2 Clinical applications :**

That research was essentially an exploratory study in that SPC had not previously been tested with eye-tracking system while avoiding any instructions during the experimental task with atypical populations. That research was not funded, and I worked as a psychologist specialized in Applied Behavior Analysis for 3 years carrying for autistic children, adults with developmental disorders and elderly people with dementia. My research work can be applied to various clinical approaches – and I applied it in my clinical work among my findings.

### 1.2.1 Spatial contiguity and SPC :

In chapter 3 (Part 1), we demonstrated that rates of conditioned responses (i.e., avoidance and anticipatory responses) were better in a condition in which stimuli were presented contiguously in Phase 1, in comparison to a condition where there was a small space between those stimuli. Those results were innovative for the SPC study and congruent with other studies focused on the role of spatial contiguity in the establishment of associative learning. With respect to clinical applications, these results led us to consider a reorganization of the therapeutic environment in some circumstances. Indeed, in order to facilitate learning in individuals with disabilities, we can change the spatial organization of specific items used in learning. For example, if we trained an autistic child to associate one written word with its corresponding object, we should place the two stimuli very close to each other in order to facilitate the association learning, instead of separating them by a large distance. Obviously, this type of procedure could be used with any individual for any learning. In France, in typical classrooms written words/ written cues are always posted at a specific place on a wall, which is not a good location for some young

students. Indeed, every student learns in a different way with a specific speed of learning; and sometimes cues have to be replaced according to the needs of those students (e.g., a teacher can move a specific cue to place it next to the problem item for such students).

### 1.2.2. Impact of the number of pairing presentations :

In chapters 4 and 5 (Part 1), we observed better rates of avoidance responses after 10 pairing presentations rather than 20, in young and elderly people. Here, those surprising results underlined the futility of items repetitions in specific situations. For example, in geriatric institutes it is often used to say, “Repeat it, it’s an old man/woman”. Thus, you can hear most of the time the same speech repeated by caregivers to elderly people with dementia or without dementia (i.e., which means elderly without dementia who are hospitalized for physical disabilities). Our results supported the assumption that repetition of stimuli is not always a good solution for individuals. For example, we tried to train a typical bedridden elderly person to press an emergency button connected to his bed that would ring in the nurses’ office in case of emergency. We proceeded to train him in order to anticipate a real emergency. The prompt was a visual page full of instructions explaining how to use the emergency button. Nurses presented those instruction pages several times before pressing the emergency button for the bedridden elderly. In that study, if I observed a failure in the press button response, I asked myself several questions before asking the nurse to again present the same visual prompt:

- Is there a physiological cause? (i.e., sudden hearing and / or visual loss, dementia, etc.)
- Is the stimulus too complex for the individual ?
- Can I change the stimulus characteristics in order to make it more prominent ?
- Can I manipulate the consequences of the response associated with that stimulus ? (i.e., use of reinforcement)

Here again, the clinical questions concerning the role of repetitions on the patient’s training could be generalized to any individual on any learning task.

### 1.2.3. Our experimental task as training or verification tool for atypical populations :

Part 2 underlined the possibility of testing atypical populations on a experimental task that avoids the use of instructions. Specifically, we succeeded in testing babies, children, autistic children and elderly people with dementia all with the same apparatus on the same experimental procedure. The central benefit of our experimental task is that participants did not need to read/understand written or oral instructions that are often necessary in other studies focused on human learning.

In that sense, our experimental task could be used in various areas simply by changing the stimuli used. More generally, we could study the same avoidance and anticipatory responses in visual measures on various populations faced with different stimuli. In the present procedure, we used colored shapes as CS1, CS2, CS3 and CS4. For a clinical work, we could change the nature of those stimuli in order to facilitate the learning of some specific ability. For example, if we want to facilitate a training procedure in which a non-verbal adult had to learn the pedestrian traffic laws, we could change the CSs to cues relevant to the immediate task (e.g., red fire – “stop” – US- and green fire – “drive” – US+). Here we could check the anticipatory and avoidance responses by targeted the eye movements of that individual. Of course, that kind of learning would be only the first step in training the individual with respect to the traffic laws.

Such clinical applications could also be used in the treatment of phobias, and other pathologies characterized by an atypical aversion for specific stimuli. Here, our experimental task could be used as a verification tool thanks to the avoidance response objectively obtained from the eye movements of these individuals. For example, consider a woman with anorexia nervosa who developed an aversion for high-fat food and an excessive preference for salads (i.e., low protein rate food). We could replace our CSs with pictures of foods and observe the evolution of the anticipatory and avoidance responses in the anorexia woman, during behavioral therapy. Here, we could expect a decreasing rate of avoidance responses for high-fat food developing gradually as the treatment progressed.

## 2. LIMITATIONS AND CRITIQUES OF OUR EXPERIMENTAL TASK

A first issue concerning our research is the number of participants for each experimental group. In Part 1, we tested 40 adults in chapter 3 (i.e., 20 in each condition), 40 adults in chapter 4 (i.e., 20 in each condition) and 40 seniors in chapter 5 (i.e., 20 in each condition). In Part 2, we tested 24 babies in chapter 2, 25 autistic children (i.e., 11 verbal and 14 non verbal children) in chapter 3, 40 seniors (i.e., 20 typical elderly and 20 elderly with dementia) in chapter 4, and 20 typical children compared to other groups in chapter 5. Thus, we obtained results for only 229 participants. Obviously, it would have been better if the number of participants had been higher than 20 per condition for statistical reasons (e.g., ability to use parametric statistics), and if I could test other ages (e.g., 12-13 years old participants).

A second issue is that the results obtained in chapter 3, 4, and 5 of Part 1 have to be considered with caution due to my only examining the two specific experimental conditions tested. In chapter 3, I tested the role of spatial contiguity with only two experimental conditions A and B : stimuli separated with a small space (i.e., separation of 6 cm between stimuli) *versus* contiguous stimuli (i.e. 0 cm between stimuli). We observed better rates of conditioned responses when stimuli were contiguously presented, asserting that a closer spatial contiguity facilitated the establishment of SPC. It's important to say that we could test lots of other experimental conditions like different distances between the stimuli presented (e.g., 0, 2, 4, 6, and 8 cm) in order to observe the possible variations of conditioned responding. In chapters 4 and 5, we focused on the role of the number of pairing presentations in Phase 1 on the degree of conditioned responding. We asserted that rates of responses were better after 10 pairings compared to 20 pairings in Phase 1 for adults and seniors. It would be desirable in a future study to more widely manipulate the number of pairing presentations in Phase 1. Those ideas will be implemented by students in Master (University of Lille). For now, one Master class student is focusing on two additional conditions in which stimuli pairings are presented 30 or 40 times in typical adults. Those data will be considered for a future publication in which chapter 4 manipulations will be completed with two additional experimental conditions (i.e., with a total of 4 conditions 10, 20, 30 and 40 pairing presentations).

Another limitation of our experimental task, the main one in fact, concerns the assumption of the use of verbal strategies in the establishment of SPC. Some authors believe that verbal processes underlie associative learning, such as SPC (see Introduction of Part 2). My experiments (like other experiments) indicate that associative learning can occur without verbal processes. Of course, my data do not refute the possibility that some associative learning could

be mediated by verbal processes, only that this is not true for all associative learning. Furthermore, the lack of verbal skills of some subjects (e.g., babies, non-verbal autistic children, the elderly with dementia) strongly suggests that the learning these subjects evidenced was mediated by something other than verbal processes. Beyond that exclusion, the present experiment does not test or speak to what did mediate the learning that was observed (despite the hypotheses that are discussed in the next few pages).

Finally, one other limitation of our experimental is the non-use of other materials which could have been added to the eye-tracking system. Indeed, our experiment focused on anticipatory and avoidance responses, using US+ and US- as unconditioned stimuli. However, it would have been interesting to add some emotional assessment possibly with electrodermal measures in order to verify whether there were positive emotional reactions after US+ presentations and negative emotional reactions after US- presentations. In the present experimental task, although we observed significant anticipatory responses after CS1 presentations and significant avoidance responses after CS3 presentations, we only tested them with eye movements of the participants. Future research on the topic could consider the addition of materials like an electrodermal measuring device, and emotional trackers such as facial expressions that are recognized by computer systems. Also, we could test another avoidance response using an eye blink conditioning system, in which a air jet is emitted toward the eye of the participant. Of course, we would have to consider the ethics here, especially for individuals with disabilities and individuals more likely to develop aggressive behaviors after aversive stimuli presentations.

### 3. THEORETICAL ISSUES

The results observed in the several chapters here question some fundamental issues in associative learning. Because my thesis was an explanatory study, I did not advance any specific theory concerning the establishment of SPC. I simply discussed about one hypothesis concerning the necessary use of verbal strategies in the establishment of SPC. Here I very briefly propose some hypotheses concerning the possible observation of SPC specific to my work (see 1 and 2 below) and we could discuss about the subjective evaluation of verbal strategies (see 3 below).

#### 1. “Biological determinant” and individual survival :

##### 1.1. US+ and US- as biological determinants for participants :

The main surprising result of my work is probably the observation of similar conditioned responses in several highly divergent developmental groups. To my knowledge, no prior study focused on SPC with such a large variety of populations (i.e., babies, typical children, children with autistic disorders, typical adults, typical seniors, and seniors with dementia). One hypothesis concerning those results is suggested by the choice of unconditioned stimuli used in these experiments. Indeed, used as experimental measures the anticipation and avoidance responses are viewed as fundamentally necessary for the survival of organisms (Domjan, 2005). Here, we can hypothesize that the present CSs associated with US + and US- emissions have through associative learning become real "biological determinants" ostensibly for survival in all of the participants. Of course, we can imagine that our experiment was differentially perceived by each individual according to his/her developmental stage. Babies and elderly probably have never before been exposed to this type of task and material in a laboratory context.

##### 1.2. Respondent conditioning prior higher abilities :

Razran (1955) pointed out that associative learning was more prevalent in young children and other "underdeveloped" (Razran's term, 1955) species compared to adults. Indeed, Razran stated that young children used their primary abilities (i.e., conditioned reflexes) in learning tasks whereas adults, who are at a more advanced stage of development, used cognitive skills to solve the task. However, Razran wondered about his own results because they had not been replicated experimentally by other researchers. In our study, contrary to what Razran said, we do not find better rates of anticipation and avoidance responses among young children aged 5

to 6 compared with other experimental groups. However, we only demonstrated it within a SPC procedure.

### 1.3. Persistence of aversive conditioning :

Concerning rates of avoidance responses in all participants, many studies observed that aversive conditioning persists throughout an individual's life, more than with appetite reinforcement (Waters et al., 2017 ). This would suggest that aversive conditioning is essential for the survival of the individual, from an early age to the end. In their study, Waters et al. presented a CS1 geometric shape with US- aversive noise on several trials to young children, adolescents and adults. A fear conditioned response after the presentation of CS1 was observed in all three experimental groups, demonstrating the aversive nature of the sounds used as a US in their experiment. Waters et al. also observed that this conditioned fear persisted longer in children compared to other experimental groups, even after extinction treatment. Therefore, once again, we might assume that the US- used in our research was a powerful "biological determinant" for the survival of all participants with respect to a task using an avoidance response of an US- such as mine.

## **2. Compound stimulus and equivalence relations in the establishment of SPC :**

Another characteristic of our work is that we observed SPC without using written or oral instructions, unlike some studies in humans (e.g., Brogden, 1942, 1947; Jara et al. 2006; Craddock et al., 2014). The results we obtained concerning the role of spatial contiguity in the establishment of SPC (see Chapter 3 of Part 1) confirm the remarks of McLaren and Mackintosh (2000) on the role of compound stimulus in associative learning.

### 2.1. Use of compound stimuli in Mackintosh and al. (1991) and in our experiment :

In their review, the authors highlighted the many studies that have observed associative learning in nonhuman species using compound stimuli as linked by within-compound associations. For example, the Mackintosh, Kaye, and Bennett (1991) study used compound *versus* non-compound stimuli in rats by observing their approach behaviors. Here, different sensory stimuli were associated at the same time, and then one of them was followed by the occurrence of the appetitive smell of food. Mackintosh et al. (1991) thus observed approach behaviors on the two conditioned stimuli previously presented as a first phase compound stimulus, rather than when these two stimuli were presented separately. Beyond the role of spatial contiguity on SPC demonstrated in our experiment, we may also consider having introduced compound (CS2-

CS1) and (CS4-CS3) stimuli to the participants, since these two stimuli were adjacent and contiguous to each other. Other (see Figure 36):

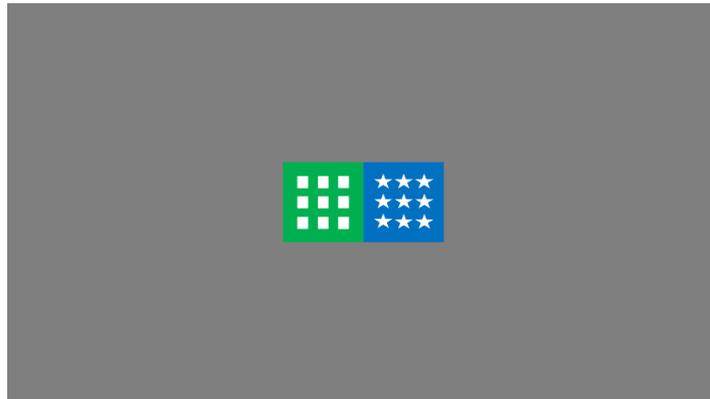


Figure 36: Example of CSs presented in Chapter 3 of Part 1, when there was no space between CSs.

## 2.2. Description of equivalence relations :

Therefore, we can question the formation of compound stimuli. How two stimuli close to each other could form a single compound configured stimulus? If we look at Figure 36, might a participant be visualizing one two-color stimulus, instead of two stimuli of different colors? One hypothesis concerns the equivalence relations. Pierce and Cheney (2013) illustrated equivalence relations in this example, p. 283-284:

« For most Americans, the flag is a significant symbol. When we see the flag, we may think of the United States, mother, and apple pie. This suggests that symbolic behavior involves the training of stimulus equivalence. The presentation of one class of stimuli (e.g., flags) occasions responses made to other stimulus classes (e.g., countries). This seems to be what we mean when we say that the flag stands for, represents, or signifies our country. Equivalence relations such as these are important aspect of human behavior. For example, in teaching a child to read, spoken words (names of animals) are trained to visual stimuli (pictures of animals) and then to written symbols (written words for animals). Eventually, the written word is then said to stand for (or mean) the actual object, in the same sense that the flag stands for a country. ». Thus, Americans regard their flag as a compound stimulus, not as a set of diverse and varied stimuli such as white stars, a blue rectangle, and red and white horizontal lines.

Three major equivalence relationships have been highlighted. First, we speak of a symmetry relation when a class A stimulus is interchangeable with a class B stimulus (if  $A = B$  then  $B = A$ ). More basically, we also talk about reflexivity when a stimulus A is found in A. Symmetry and reflexivity are considered as elementary laws. For example, we present a child with a

stimulus A (e.g., the number "2"). We speak of reflexivity if the child is able to show us the number "2" among several numbers "1; 3; 5; 2; 7 ". If the child is able to give two items {X; X} (= B) when we present him the stimulus A "2", we speak of symmetry relation. Finally, transitivity is the third equivalence relation between different stimuli. In this relation, if A = B and B = C then A = C. For example, we are talking about transitivity if the child is able to associate the word "two" (= C) with the number "2" (= A ) and the right amount {X; X}.

### 2.3. Test of equivalence relationships :

Such equivalence relationships have been studied many times in diverse animal species in the form of "Matching-to-sample" procedures (Catania, 1984). For example, reflexivity is tested in this type of procedure by presenting to the animal a specific geometric shape, which it must then find later among two geometrical shapes. Catania et al. (1989) studied equivalence relationships in young children through verbal behaviors. In a first experimental phase where the reflexivity was tested, the authors presented the child with a star in the center of the screen which he had to point out later among various added items (see Figure 37). The aim of Catania et al. was, among other things, to study the emergence and development of verbal behaviors in young children.

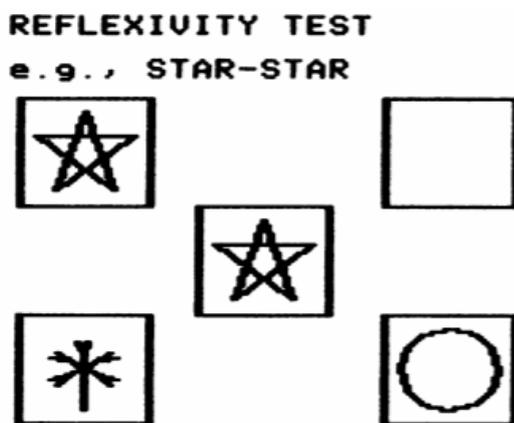


Figure 37: Example of Catania et al. (1989) experiment testing the reflexivity relation in children.

In our study, we can invoke the reflexive relationship because the CSs belonged to the same class of stimuli. For this, we must consider the two CSs forming a compound stimulus. Thus, our compound stimulus A presented in the first phase of SPC may have caused a second phase conditioned response mediated by one of its components CS1 or CS3, as well as in the test phase after presentation of its other component CS2 or CS4. As a result, we see opportunity of the equivalence relation of reflexivity "A (in the second phase of SPC) = A (found in tests)".

Although we can draw a parallel between reflexive relations and the establishment of associative learning such as SPC, we can not currently explain the formation of these equivalence relationships, which seem to be present as early as 4 months of life until old age.

### **3. Reflexions about verbal strategies :**

Finally, a large theoretical issue of my work concerns the study of verbal strategies. In the present research, I focused on verbal behaviors and verbal abilities, which were evaluated for autistic children and seniors with dementia – but not for all experimental groups. Obviously, it is pertinent to say that all verbal behaviors were not considered in that research. Here, I affirmed that verbal behaviors did not have an impact in the establishment of SPC, but there are limitations because I considered only one part of those verbal behaviors. As Skinner mentioned (1957), thoughts can be considered like any operants, but are difficult to observe. In adults, I certainly should have asked to participants what kind of logic process they followed to succeed the experiment – which I did not do it. That kind of questionnaire could not be used with atypical populations tested like non-verbal autistic children or seniors with dementia.

Also, I assumed that non-verbal populations have a profound lack of verbal strategies. Here again, we can entertain some opposing views because covert verbal strategies can not be objectively observed in these kinds of populations. It seems easy to imagine that there are other logic processes in non-verbal populations, associated with verbal strategies or with totally other kinds of deductive processes. The establishment of SPC in those atypical populations certainly concerns other strategies, inaccessible and misunderstood for now.

# Articles and communications

## 1. Articles

- **Renaux, C.**, Rivière, V., & Nuchadee, M.L.J. (2017). Increased writing performance using a shaping procedure with a patient with sequelae caused by cardiovascular accident. *Journal of Ageing Research and Healthcare, Vol2*, 32-39.
- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R. R. (2017). Role of spatial contiguity in sensory preconditioning with humans. *Behavioural Processes, 142*, 141-145.
- Nelson, J. B., Craddock, P., Molet, M., & **Renaux, C.** (2017). Recovery of attention with renewal. *Learning & Memory, 24*, 637-640.
- Craddock, P., Wasserman, J.S., Polack, C.W., Kosinski, T., **Renaux, C.**, & Miller, R.R. (2017). Associative structure of second-order conditioning in humans. *Learning & Behavior, 46*, 1-11.
- Craddock, P, **Renaux, C.**, Lefèvre, F., Nelson, J.B., Molet, M. (2014). Integration of multiple memories in sensory preconditioning. *Behavioral Processes, 108*, 94-97.

## 2. Communications

- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R.R. (2018, May). Associative learning in babies : Higher-order conditioning without verbal skills. Poster presented at ABAI San Diego, 25-27th May, USA .
- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R.R. (2018, February). Associative learning in non-verbal autistic children : Verbal processing hypothesized as a mediator of associative learning. Poster presented at ABAI Miami, 23-25th February, USA .
- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R.R. (2017, November). Number of stimuli presentations for the observation of sensory preconditioning. Oral Communication presented at International ABAI Paris, 14-15th November, France.
- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R.R. (2017, May). Spatial contiguity's contribution to the formation of associations between neutral stimuli. Poster presented at the ABAI Denver, USA.

- **Renaux, C.**, Rivière, V., Craddock, P., & Miller, R.R. (2017, May). Associative learning in dementia : Implications for the role of verbal strategies in associative learning. Poster presented at SQAB Denver, USA.

- **Renaux, C.**, & Rivière, V. (2015, November). *The use of eye-tracking system in experimental behavior analysis, Second-order conditioning in young children and elderly people, with or without verbal skills*. Poster presented at The new technologies at the services of Neurosciences, Lille, France.

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# Annexes

## NOTE D'INFORMATION DES PARTICIPANTS

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La durée de la passation est d'environ 10 minutes. Pendant cette période, vous serez amené à regarder différents stimuli qui apparaissent sur l'écran de l'ordinateur. Vos saccades oculaires seront enregistrées via un système d'eye-tracking, afin de déterminer post-test vos temps de fixations visuelles, et vos différentes poursuites oculaires. Cette expérience se déroule en 4 phases : une première phase de calibration nécessaire au bon fonctionnement de l'eye-tracking ; une seconde phase où deux stimuli apparaîtront de manière simultanée ; une troisième phase où un stimulus apparaîtra et sera suivi ou non d'un autre stimulus. Enfin, vous aurez une phase test composée de stimuli déjà observés.

Dans le cadre de cette recherche, un traitement de vos données va être mis en œuvre pour permettre d'analyser les résultats. A cette fin, les données vous concernant seront transmises au Promoteur de la recherche ou aux personnes ou sociétés agissant pour son compte. Ces données seront identifiées par un numéro de code et seront donc anonymes. Ces données sont donc susceptibles d'être utilisées dans le cadre de cette recherche et d'être traitées.

Vous êtes libre d'accepter ou de refuser de participer à cette étude. A tout moment, vous êtes en droit d'arrêter l'expérience sans encourir aucune responsabilité ni préjudice de ce fait.

Cette étude sera menée sous l'investigation de Charlotte Renaux et sous la supervision du Pr Vinca Rivière. Pour toute question relative à l'étude, les coordonnées de l'investigatrice sont :

Mme RENAUX Charlotte

charlotte.renaux.maeac@hotmail.fr

**Signature participant :**

**Signature proposant :**

## CONSENTEMENT DE PARTICIPATION

### MINEURS

Le laboratoire SCALab vous propose de participer à une tâche de fixation visuelle via un ordinateur équipé d'un système d'eye-tracking, dans le but d'étudier le conditionnement d'ordre supérieur. Cette étude est menée sous l'investigation de Charlotte Renaux et sous la supervision du Pr Vinca Rivière.

Nous vous informons que :

- Vous pouvez à tout moment interrompre votre participation sans avoir à le justifier.
- Vous pouvez prendre connaissance des résultats de l'étude dans sa globalité lorsqu'elle sera achevée.
- Les données recueillies demeureront strictement confidentielles.

Mr ..... et Mme ..... autorise / n'autorise pas leur enfant ..... à participer à l'étude présentée conjointement. (Rayer la mention non souhaitée)

Compte-tenu des informations qui m'ont été transmises :

*A remplir par le participant de plus de 12ans*

*cocher les cases appropriées en fonction de votre volonté (OUI / NON)*

	OUI	NON
<b>1) J'accepte librement et volontairement de participer à la recherche</b>	<input type="checkbox"/>	<input type="checkbox"/>

Fait le ..... / ..... / ..... à .....

Signature du participant :      Signature des parents :      Signature de l'investigateur:

### Appendix 1 : Informations and prior consent

Autism	N°	Gender	Age	Score EVIP@
	1	M	7.5	88//110
	2	M	6.7	84//116
	3	F	7.2	106//129
	4	F	6.8	95//124
	5	M	7.7	97//116
	6	M	6.5	88//122
	7	M	6.6	80//112
	8	F	6.9	59//91
	9	M	6;2	46//84
	10	M	9;8	84//84
	11	M	9;1	47
	12	F	9;7	36
	13	M	6;3	12
	14	F	7;2	20
	15	M	7;9	10
	16	M	7;8	27
	17	M	9;10	12
	18	F	8;1	26
	19	M	11;6	0
	20	F	6;2	32
	21	M	4.2	66
	22	M	5.1	64
	23	M	4.8	80
	24	M	8.6	71
	25	M	9.10	51

**Appendix 2** : Gender, age, and diagnosis of autistic children (Chapter 3 Part 2).

Patients Dem	N°	Gender	Age	PATHOS@
	01	F	88	534
	02	F	88	228
	03	F	91	614
	04	F	78	554
	05	F	95	234
	06	M	94	254
	07	M	80	240
	08	M	87	249
	09	F	81	170
	10	F	87	146
	11	M	93	86
	12	M	90	182
	13	F	94	267
	14	M	88	638
	15	F	88	235
	16	F	93	59
	17	F	93	212
	18	F	87	188
	19	F	91	57
	20	M	90	431

**Appendix 3** : Gender, age, and diagnosis of dementia participants (Chapter 4 Part 2).

# Abstract

Brogden (1939) demonstrated sensory preconditioning (SPC) in which two conditioned stimuli (CS) are paired in a first phase (Phase 1 : CS2-CS1), before pairing one of them with an unconditioned stimulus (US) (Phase 2 : CS1-US). SPC is said to have occurred when CS2 elicits the conditioned response (CR), despite the fact that it never having been directly paired with the US. In humans, Brogden (1942 ; 1947) emphasized as necessarily the use of explicit instructions in order to observe such an associative response. In the present study, we wanted to use an SPC procedure in humans similar to that used with other species, which means using procedures without any verbal instructions. We used visual fixation as the common measure of all of our experimental groups (i.e., babies, children, adults, seniors, and dementia patients). We examined the SPC procedure using eye tracking as our dependent variable in populations with verbal disabilities, like autistic children and elderly people with dementia, because visual fixation does not require verbal abilities to be implemented.

Our research focused on SPC among different conditioning variables (Part 1) and testing the role of verbal strategies on that kind of associative learning (Part 2). In addition, we observed that associative learning at several stages of development. First, we observed high rates of SPC in all experimental groups instead of impaired behavior that would have been consistent with predictions of developmental and psychopathological models about limited cognitive performance in very young, very old, and cognitively impaired subjects (i.e., autism and dementia). Some parallels with equivalence relations and adaptative functions are discussed.

**Keywords** : associative learning, SPC, visual fixation, spatial contiguity, repetition, development, verbal behavior.