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SENSE OF AGENCY AND INTENTIONAL BINDING

How does the brain link voluntary actions with their consequences?

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A Luca,

Perché la mia felicità può dirsi tale

solamente quando la condivido insieme a te.

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LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
AG	Angular Gyrus
AlHS	Alien Hand Syndrome
AnHS	Anarchic Hand Syndrome
ANOVA	Analysis of Variance
ASD	Autism Spectrum Disorder
BCs	Baseline Conditions
BDI-II	Beck Depression Inventory
BNE-2	Brief Neuropsychological Examination
BOLD	Blood Oxygenation Level Dependent
CI	Confidence Intervals
CM	Comparator Model
CBS	Corticobasal Syndrome
DA	Dopamine
DLPFC	Dorsolateral Prefrontal Cortex
DAED	Dopamine Agonist Equivalent Daily Dose
ECs	Experimental Conditions
EEG	Electroencephalography
FAB	Frontal Assessment Battery
fMRI	Functional Magnetic Resonance Imaging
H & Y	Hoehn and Yahr
IADL	Instrumental Activities of Daily Living
IB	Intentional Binding
IPC	Inferior Parietal Cortex
JE	Judgement Error

LDED	Levodopa Equivalent Daily Dose
mJE	mean Judgement Error
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
NPI	Narcissistic Personality Inventory
NS	Negative Symptoms
OCD	Obsessive-Compulsive Disorder
PAC	Primary Auditory Cortex
PET	Positron Emission Tomography
PFC	Prefrontal Cortex
PMD	Psychogenic Movement Disorders
PPC	Posterior Parietal Cortex
Pre-SMA	Pre-Supplementary Motor Area
tDCS	Transcranial Direct Current Stimulation
PS	Positive Symptoms
PMD	Psychogenic Movement Disorder
PDQ-8	Parkinson's Disease Quality of Life
SEM	Standard Error of Mean
SMHA	Sensorimotor Hand Area
SCPs	Slow Cortical Potentials
SMA	Supplementary Motor Area
SMC	Supplementary Motor Complex
SoAg	Sense of Agency
TMS	Transcranial Magnetic Stimulation
TMT	Trial Making Test
UPDRS-III	Unified Parkinson Disease Rating Scale

ABSTRACT

The feeling of generating and controlling external effects through our own actions is known as Sense of Agency (SoAg). When we act we are generally in control of what we are doing and, therefore, we are aware and responsible for both our actions and their consequences. For many years, researchers have tried to identify appropriate measures to study the SoAg. It has often been investigated using explicit tasks in which participants verbally reported if they felt they were the authors of a certain effect. However, in our everyday life, we experience a continuous flow of actions and their effects, and we do know that we are the authors of an action without interrogating ourselves about it or constantly making explicit judgments. Therefore, the use of implicit measures seems to better reflect the complex agency dimension. A very famous and reliable implicit measure is represented by Intentional Binding (IB). This effect occurs when a temporal compression between a voluntary action and its sensory consequence is observed (i.e., actions are perceived as occurring later than they really do, while the sensory effect is perceived as occurring earlier). The effect is limited to voluntary actions; in fact, IB is absent or reduced for situations in which the action is not driven by volition (e.g., passively-induced movement). Since its discovery, IB has been considered a valid quantitative index of SoAg and has been applied to study agency, both in healthy individuals and in clinical populations. In the light of this implicit measure, the aim of the

research presented here was to examine the SoAg from different perspectives, in order to provide new penetrating insights to comprehend this phenomenon. After the implementation of a new paradigm to measure IB (Study I), four main intriguing facets have been explored. In Study II, the main focus was to investigate the development and the evolution of the SoAg across the lifespan. Results indicated that SoAg follows a U-inverted shape, with children and elderly showing a reduced SoAg as compared to adult participants. Subsequently, the neural underpinnings of SoAg have been investigated (Study III), uncovering the important contribution of the pre-supplementary motor area (pre-SMA) in the perceived action-effect linkage. In Study IV the multisensory nature of the SoAg was explored, highlighting its supramodal nature and demonstrating how SoAg is governed by the same rules at the root of the multisensory integration. After having shed light on these different aspects in healthy populations, the last experiment (Study V) investigated the SoAg in the clinical domain, specifically referring to Parkinson Disease (PD) as a target pathology because of its characteristic difficulty in planning and initiating voluntary actions. Findings showed a reduced SoAg in this clinical population.

The results obtained from all the experiments included in the present thesis have been discussed in light of current theories of SoAg.

RIASSUNTO

Nella vita di tutti i giorni, mediante le nostre azioni, contribuiamo a indirizzare l'esito del nostro comportamento. In quanto agenti decidiamo quali azioni mettere in atto, valutando e giudicando nel contempo l'impatto e le possibili conseguenze che esse avranno sul mondo esterno e sulle persone che ci circondano. Tale capacità di giudizio e di valutazione delle conseguenze delle proprie azioni viene definita in letteratura come agentività (o *Sense of Agency*: SoAg), caratteristica essenziale della natura umana. Ad oggi, il modello sperimentale dominante per lo studio del SoAg è basato su paradigmi di tipo esplicito, chiedendo ai partecipanti di giudicare se un determinato evento sensoriale è causato dalla loro propria azione o dall'azione di un altro agente. Tuttavia, nonostante questi paradigmi siano stati molto utilizzati in letteratura, essi sono stati criticati in quanto non sembrano catturare l'esperienza implicita di *agency* che accompagna le nostre azioni quotidiane. Le esperienze quotidiane di *agency* infatti non coinvolgono necessariamente giudizi espliciti. Frequentemente si compiono azioni intenzionali in maniera quasi automatica, senza dover necessariamente pensare al fatto che 'io' sono stato l'autore di una determinata azione; basti pensare all'azione di prendere un bicchiere d'acqua quando abbiamo sete o di guidare. In questi casi si ha SoAg anche senza fornire alcun tipo di giudizio esplicito. Le misure implicite forniscono dunque un modo alternativo e migliore per esplorare e quantificare la vera natura

del SoAg. Ad oggi, una delle più famose e utilizzate è l'*Intentional Binding* (IB), ovvero la compressione dell'intervallo temporale che si instaura tra un'azione volontaria e l'effetto sensoriale prodotto.

Nella presente tesi si è deciso di utilizzare l'IB come misura implicita in quanto fenomeno molto robusto e replicato da molti studi. Traendo vantaggio da questo tipo di paradigma, il presente lavoro di ricerca ha avuto l'obiettivo di contribuire alla comprensione di alcuni meccanismi neuro-cognitivi sottostanti il SoAg. Dopo l'implementazione di un nuovo paradigma per la misurazione dell'IB (Studio I), sono stati presi in esame quattro differenti aspetti. Nello Studio II si è cercato di comprendere come il SoAg si sviluppi e si modifichi nell'arco di vita. I risultati hanno mostrato come il SoAg sembri seguire una traiettoria di sviluppo, venendo acquisito gradualmente nel corso dell'ontogenesi e 'decrementando' in età più avanzata. Successivamente, lo Studio III si è focalizzato sul tentativo di identificare le basi neurali di tale fenomeno, evidenziando un contributo cruciale dell'area pre-supplementare motoria. Nello Studio IV è stato fornito un contributo rilevante alla comprensione della natura multisensoriale del SoAg, corroborando le attuali evidenze scientifiche che suggeriscono come il SoAg sembri essere governato dalle stesse regole che stanno alla base dell'integrazione multisensoriale. Infine, nello Studio V, l'attenzione è stata rivolta all'ambito clinico, considerando un gruppo di pazienti con malattia di Parkinson, caratterizzata da un disturbo nella pianificazione e nel controllo delle azioni volontarie. Questi pazienti hanno presentato un SoAg significativamente ridotto rispetto ai controlli sani.

I risultati ottenuti dagli esperimenti descritti in questa tesi sono stati discussi alla luce delle attuali teorie proposte per lo studio del SoAg.

GENERAL OVERVIEW

Our voluntary actions are typically accompanied by a Sense of Agency (SoAg; Haggard & Tsakiris, 2009). We feel that we can choose and control our own actions and through them the outside world. We also feel that we are responsible for them. Although the SoAg plays a relevant role in our society given the profound impact on the legal system (Haggard & Tsakiris, 2009; Frith, 2013; 2014), its comprehension is still far from being exhaustive and a number of relevant questions are still unanswered. Some of these include: (1) does the SoAg change across our lifespan? Can children and elderly be considered responsible for their actions in the same way as adults? (2) what are the neural areas underlying the SoAg? (3) can the SoAg be considered a multisensory supramodal mechanism? (4) is the SoAg modified when the individual is affected by certain diseases characterized by a lack of voluntary control over one's own actions? This thesis attempts to address these questions by investigating the mechanisms underlying the SoAg from a neurocognitive perspective and by adopting an implicit measure to study the SoAg, that is to say the Intentional Binding effect (IB: Haggard, Clark & Kalogeras, 2002).

The present work is composed of two main parts: one theoretical and the other experimental. The first part, composed of two chapters, offers an in-depth introduction to the SoAg (Chapter 1) and to Intentional Binding (IB; Chapter 2) as an implicit measure to study SoAg. The second part concerns the outline of the experimental work. By taking advantage of IB as a reliable implicit measure of SoAg, in Study I (Chapter 3) a new paradigm, with the aim to reliably assess IB in both healthy and clinical populations, overcoming the main limitations linked to the methodologies currently adopted, is proposed. Utilizing this new paradigm, IB was replicated in a group of young adults. This methodological advance was then used in the second study to address the question of how agency develops and changes across the lifespan (Chapter 4). Agency plays an important role in society because it is strictly bound to the idea of responsibility for one's own actions (Haggard & Tsakiris, 2009; Frith, 2013; 2014). However, if the agent is a child or an older person, the feeling of being responsible for the consequences of a given action may differ from what an adult would feel: as a matter of fact, executive functioning represents the essential prerequisite for the emergence of SoAg (Haggard, 2008; Haggard & Tsakiris, 2009) and the frontal lobe is known to be the neural substrate for these abilities (Stuss & Levine, 2002). Many studies have revealed how vulnerable the frontal lobe is to structural and neurochemical changes occurring with age (e.g., e.g., Fuster, 1993; Giedd, Blumenthal, Jeffries, Castellanos, Liu et al., 1999; Raz, 2000; Casey, Tottenham, Liston & Durston, 2005): in fact, while the frontal lobe must still reach its full full maturation during childhood, in old age it starts to slowly deteriorate. This evolution is usually characterized by changes in executive functioning (e.g., West, 1996; Zelazo & Müller, 2002). Along this line, the findings described in Chapter 4 showed that children and elderly did show a different pattern of results – namely a decreased SoAg - as compared to that in young adults, suggesting that an intact functioning of frontal lobes is indeed required. However, although SoAg and IB have been extensively studied from a behavioural point of view, their neural bases remain relatively unexplored and the possible frontal lobe contribution hypothesis advanced in the second study has remained only highly speculative. Therefore, in the third part of the present thesis (Chapter 5) transcranial direct current stimulation (tDCS), a non-invasive neuromodulation technique (Dayan, Censor, Buch, Sandrini & Cohen, 2013), was adopted to shed light on the possible role of the frontal lobe with regard to the SoAg. In particular, the pre-supplementary motor area (pre-SMA), a brain region known for its key role in action planning and initiation (Nachev, Wydell, O'Neill, Husain & Kennard, 2007), was considered as potentially implicated in the phenomenon. The right primary auditory cortex (PAC) was also targeted as a control area and modulated with the same parameters within participants, as a region potentially involved in the processing of the auditory effects of the action. A significant reduction in IB was observed only after modulation of the pre-SMA, which thus supported the causal contribution of this prefrontal area in the perceived linkage between action and its effects. No involvement of the area implicated in the processing of the sensory effects produced by the action (here, the PAC) was detected, suggesting that the perception of sensory effects in IB does not take place in the primary sensory areas, supporting the idea that SoAg might be supra-modal in nature. Taking as a reference point the crucial contribution of the pre-SMA, the subsequent experiments (Study IV and Study V) were then performed to additionally provide indirect evidence of pre-SMA involvement in the experience of agency. Specifically, Study IV (Chapter 6) aimed to test the 'supramodality hypothesis' advanced in Study III. The findings supported the view according to which the SoAg would follow the same rules at the root of multisensory integration, providing additional behavioural evidence regarding the multisensory nature of the SoAg. In addition, the results indirectly supported the crucial implication of the pre-SMA and its key-role in binding intentional action to their sensory consequences, independently of the specific sensory nature of those effects. The findings also supported the hypothesis that pre-SMA might indeed represent a crucial station for the integration of incoming sensory information from the primary sensory cortices. In Study V the potential clinical implications of the SoAg were then examined (Chapter 7) by considering a disease characterized by pre-SMA hypo-activation, such as PD. Compared to matched healthy controls, the PD patients showed a reduced SoAg, providing further indirect evidence of pre-SMA contribution to the SoAg.

A general discussion contextualizing the results obtained by the studies presented in this thesis will be presented in Chapter 8 (but see also 'Discussion' sections for each experimental chapter).

PART I

THEORETICAL BACKGROUND

CHAPTER 1

THE SENSE OF AGENCY

In our everyday life many actions are performed in order to achieve specific goals. The cognitive neuroscience of action has mostly focused on the brain mechanisms responsible for voluntary movements control (e.g., Castiello, 2005; Kalaska, 2009). In contrast, the subjective experience of voluntary action has been partially neglected by the literature (Haggard, 2005; 2008). In regard to this latter point, it can be said that voluntary actions are characterized by two specific psychological components: *intention* and *agency* (Haggard, 2008). The vast majority of studies has focused on the first aspect, that is on the relation between intention and voluntary action, showing that motor acts are preceded by preconscious brain activity, which reaches awareness only in later stages, just before action execution (e.g., Libet, Gleason, Wright & Pearl, 1983; Haggard & Eimer, 1999; Soon, Brass, Heinze & Haynes, 2008). However, as human agents in the world, our actions do not end with the mere motor act, as they also imply effects in the external environment. It is at this point of the chain of events that agency plays its role, referring to the link between the voluntary execution of movements and their effects, experienced as external sensory consequences (Haggard, 2008). In order to exemplify the chain, it is best to use a common situation that each of us can relate with: after a very bad day at work, all we need when we finally arrive at home is to listen to some good music. Such storyline can be broken up into the two above-mentioned processes characterizing our voluntary actions. The *volitional* part corresponds to the shaping of the intention (e.g., listening to the music), which subsequently implements the corresponding motor program in order to achieve our goal (e.g., arm movements to reach the button in order to switch on the radio). The *agency* part is inserted subsequently, when our movements are then associated with the expected consequences (e.g., feeling the music). Such auditory reafferences contribute to the feeling that we have been the authors of that action.

This specific experience of oneself as the agent of one's own actions and subsequent consequences has been defined as SoAg (Haggard & Tsakiris, 2009). SoAg has been a topic of interest mainly to philosophers (Gallagher, 2000; de Vignemont & Fourneret, 2004; Pacherie, 2008), but over recent years it has also received attention from psychology and cognitive neuroscience researchers because of its great impact on both the single individual and on the society in general. As a matter of fact, SoAg is deeply entwined with our everyday notions of freedom and responsibility and is intrinsic to ethical and law questions concerning responsibility and guilt (e.g., Moretto, Walsh & Haggard, 2011; Haggard & Chambon, 2012). Indeed, when we voluntarily perform actions, we feel responsible for them and for their consequences. The fact that individuals are aware of their actions is a central feature of democracies and, it is on these bases that the guilt of a crime can be legally established. Moreover, there are some neurological and psychiatric pathologies characterized by a ‘compromised’ SoAg. For example, psychotic patients report that their actions are not their own, but are rather imposed on them by some other agents (for a review, see Moore & Fletcher, 2012). Therefore, the study of SoAg can be crucial for the investigation of clinical disorders characterized by a lack of voluntary control of actions and can provide insights pertinent to all of us, helping to define the boundaries of the responsibility of voluntary actions.

This chapter will provide an overview on the state of the art knowledge on the most relevant findings regarding SoAg.

1.1 MODELS UNDERLYING THE SENSE OF AGENCY

Two main models have been proposed to describe the underlying neurocognitive mechanisms responsible for the SoAg. The *Comparator Model* (*CM*; Wolpert & Ghahramani, 2000) suggests that SoAg arises mainly from processes underlying motor control and is inferred *retrospectively*, after the action has been performed, on the basis of the external consequences of the action. The *Apparent Mental Causation Theory* proposed by Wegner (Wegner & Wheatley, 1999; Wegner, 2003), which focuses on situational cues, suggests that SoAg arises when external events are consistent with our intentions. This dichotomy has, nevertheless, been outdated in favour of more recent models, such as the *Two Step Model* (Synofzik, Vosgerau & Newen, 2008) and the *Cue Integration Theory* (Moore, Wegner & Haggard, 2009; Moore & Fletcher, 2012; Synofzik, Vosgerau & Voss, 2013) according to which both internal and external cues are thought to influence the SoAg.

1.1.1 THE COMPARATOR MODEL

The *CM* was originally conceived as a model of motor learning and motor control (Wolpert & Ghahramani, 2000); however, it can also provide a useful framework for explaining the SoAg (e.g., Blakemore, Wolpert, & Frith, 1998; Blakemore, Frith, & Wolpert, 2001). According to this hypothesis, two types of internal models are implemented in the central motor system, the *inverse* and *forward* models. The *inverse* model has the main function of selecting the appropriate motor commands for achieving the desired goal. At the same time, a copy of the motor commands (i.e., the efference copy) is used by the *forward* model to predict the sensory consequences of the action. In case of a match between the predicted and the actual outcome, the action is experienced as self-performed; in case of incongruence another agent is considered the author of the action (Figure 1.1). In other words, SoAg is strong when there is a close match between the predicted and the actual sensory consequences of an action, and it is reduced when predicted and experienced consequences do not match. According to this model, SoAg necessarily occurs after the action has been performed, when the sensory evidence about the consequences of an action becomes available. Within the *CM*, the sensory feedback is only required for comparison purposes and does not *per se* carry the critical information for emergence of the SoAg.

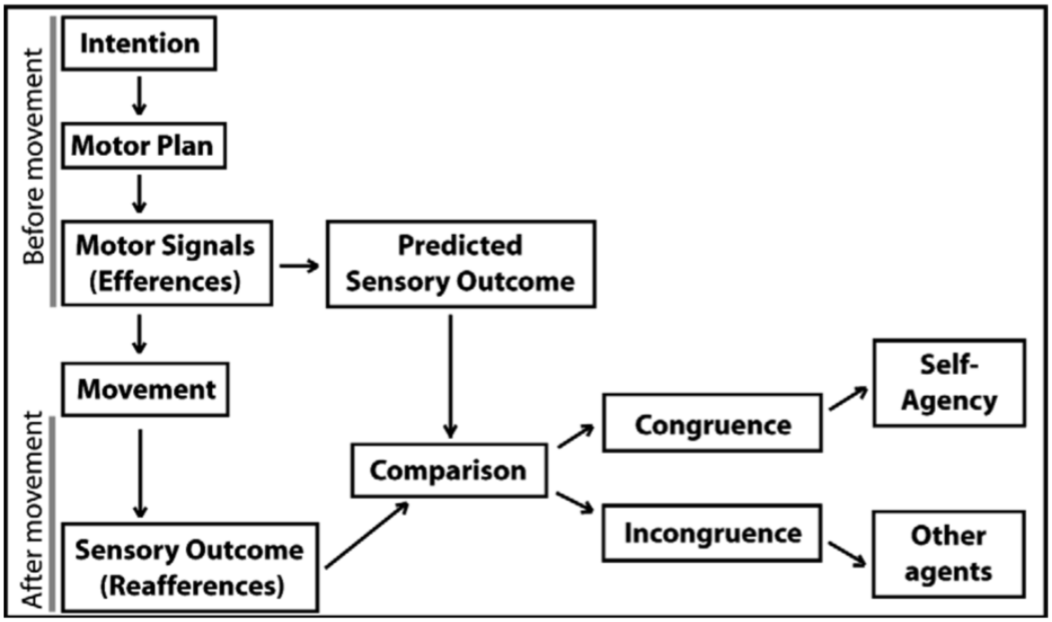


Figure 1.1. *The comparator model of the experience of agency (adapted from David et al., 2008).*

This view has received considerable empirical support from both behavioural and neuropsychological studies, as well as from investigations on its neural correlates (e.g., Voss, Ingram, Haggard & Wolpert, 2006; David, Newen & Vogeley, 2008). A pioneer experiment was conducted by Nielsen (1963) who asked participants to draw a line on a piece of paper; they could either see their own hand or an 'alien hand' (i.e., the experimenter's hand) drawing the line. In particular, the alien hand's movements spatially deviated from the participant's own movement.

Interestingly, participants adjusted their own movement to the false visual feedback without being aware of the adjustment.

Since 1963 many adaptations of this manipulation have evolved. Up to now, the experimental design usually implemented to test the *CM* consisted in inserting spatial (e.g., Fourneret & Jeannerod, 1998; Farrer, Franck, Georgieff, Frith, Decety & Jeannerod, 2003; Synofzik, Their & Lindner, 2006) and temporal (e.g., Leube, Knoblich, Erb, Grodd, Bartels et al., 2003; MacDonald & Paus, 2003) discrepancies between an action and its sensory effect. Taking as an example a typical spatial task, participants usually receive distorted visual feedback of their hand moving a joystick. When the movement of the virtual hand does not correspond to the participants' movement or when an angular bias is introduced between the participant's and the virtual hand's movement, participants tend to attribute it to another agent. Overall, these studies demonstrated that the SoAg is gradually reduced as temporal or spatial discrepancies increase. The *CM* has been adopted also to study abnormalities of action awareness (see Paragraph 1.4.1).

Although the *CM* dominates SoAg research basing its strength on several convincing behavioural and neuroimaging findings (for a review see: David et al., 2008), it has been criticized because it is unable to explain some aspects of SoAg (Synofzik et al., 2008; Vosgerau & Synofzik, 2012; Synofzik et al., 2013), such as the role of emotional valence of sensory effects or personal beliefs about an action.

Recent empirical studies within the motor prediction framework suggests a more complex picture that enhances the role of stages preceding the actions, such as action selection and preparation to the SoAg (Wenke, Fleming & Haggard, 2010; Chambon & Haggard, 2012; Chambon, Sidarus & Haggard, 2014). What is important here, as compared to the *CM*, is the intention-action link (i.e., the process through which intentions are transformed into specific actions), rather than the action-effect one. SoAg would, therefore, depend on *prospective* signals arising from internal circuits of action preparation, rather than on a post-hoc, retrospective comparison between predicted and current states of the environment, as postulated by the *CM*. SoAg could, therefore, be generated *prospectively*, before the actual outcome of actions is known (Figure 1.2).

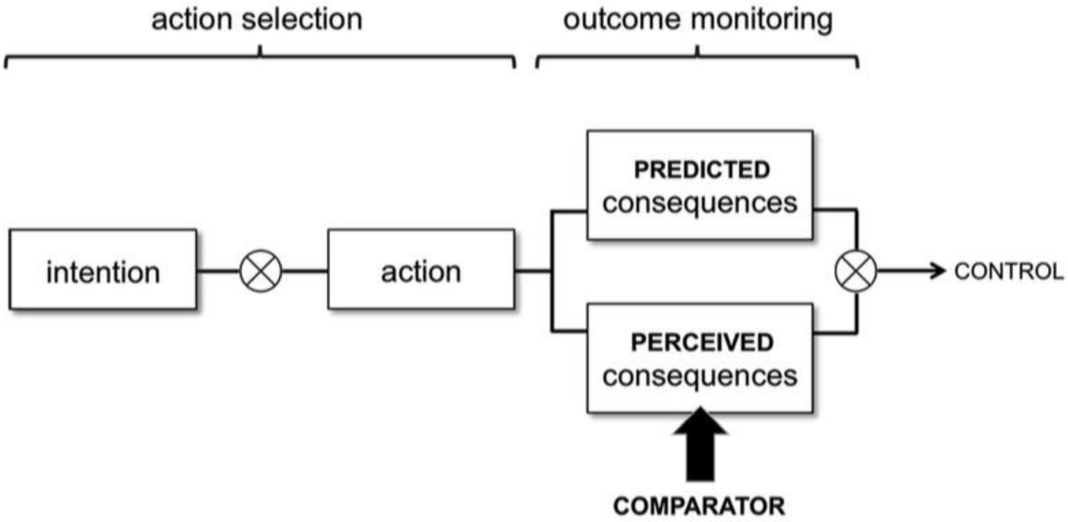


Figure 1.2. *The reviewed CM of the experience of agency (adapted from Chambon, Sidarus et al., 2014). The action-selection processes operate between the formation of the initial intention and action execution.*

Evidence supporting this view comes from studies in which the action selection variable (i.e., selecting between alternative actions) was manipulated (for a review, see: Chambon, Sidarus et al., 2014). For example, Wenke et al. (2010) investigated this component of the SoAg using an experimental design dissociating action selection from action–outcome matching processes. Participants were asked to respond to a left- or right-pointing arrow with a left or right key-press, respectively. Responding to the target caused the appearance of a colour patch afterwards. Participants had to judge how much control they felt over the patch of colour that followed their key-press. Prior to the directional target, a subliminal, unknown prime was presented, whose arrow directions were either identical ('compatible condition') or opposite ('incompatible condition') to the subsequent target direction. The colour presented depended on whether the participant's action was compatible or incompatible with the preceding subliminal prime, but did not depend on the prime identity or the chosen action alternative alone. Participants reported a stronger sense of control over the effects of an action (i.e., the colours) that were compatible with the preceding primes than over colours that followed prime-incompatible actions. Importantly, this effect was not due to predictability of action outcomes, since the relation between the key-press action and the colour outcome was always equally predictable. Rather, the stronger experience of control could only be explained by the fluency of the action selection (i.e., by an internal signal influenced by the prime–target relation), which necessarily occurs prior to movement. Results from this study and from other action priming experiments suggest that the SoAg is not merely due to *retrospective* matching occurring after the effects of action, but is also partly *prospective*, arising at the action selection stage (for similar results, see also Damen, van Baaren, & Dijksterhuis, 2014).

1.1.2 THE APPARENT MENTAL CAUSATION MODEL

The importance of postdictive, external cues (e.g., background and context-related information like thoughts and beliefs) is emphasised in the *Apparent Mental Causation Theory* or *Inference Model* (Wegner & Wheatley, 1999; Wegner, 2003). Here, SoAg arises when three principles are met: of *priority*, *consistency* and *exclusivity*.

Accordingly, in order for the SoAg to arise, the thought – or the intention - has to (i) appear prior to the action (*priority*); (ii) be consistent with the action itself (*consistency*) and (iii) no alternative causes have to be present (*exclusivity*). Therefore, the simply co-occurrence of outcomes coherent with the agent's intentions would be sufficient for the emergence of the SoAg (Figure 1.3).

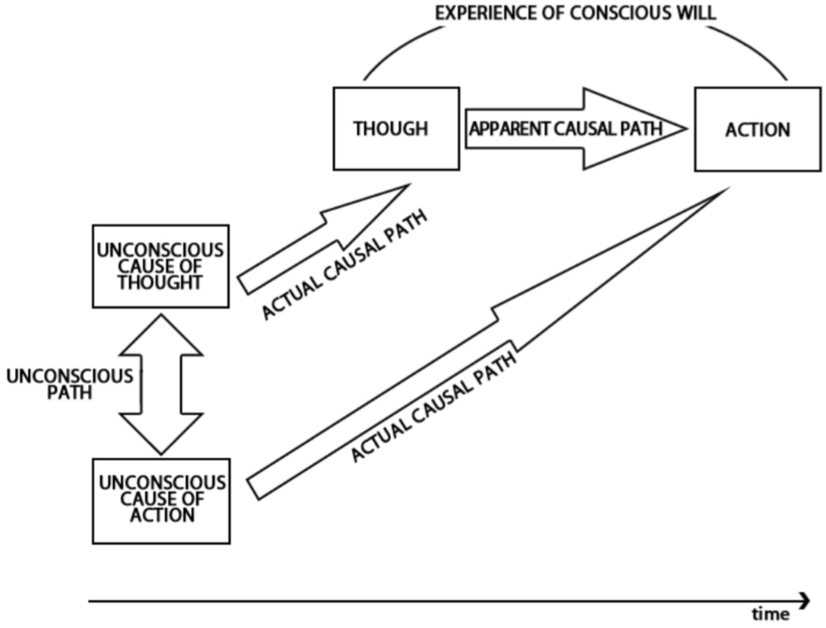


Figure 1.3. *The apparent mental causation model (adapted from Wegner & Wheatley, 1999).*

Similar to the *CM* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001), if the intention (here, the predictive element) to produce an outcome matches the actual sensory consequences following one's own action, individuals perceive causal responsibility for those consequences. If the intention mismatches with the outcome, a reduced SoAg is experienced. However, contrary to the *CM*, intentions depend only minimally on motor signals. Indeed, the cues are independent of action execution and the actual execution of a voluntary action is not necessary to SoAg. It is the match between prior conscious thoughts and the observed outcome of the action that makes the agent infer retrospectively that he/she was at the origin of the sensory event.

Support for the *Apparent Mental Causation Theory* comes from a study by Wegner and Wheatley (1999) who induced a false SoAg for movements that participants did not perform, priming them with thoughts relevant to a movement made by a confederate and making them rate the action as self-caused. These findings suggest that individuals are not intrinsically informed about their own actions, and rather rely on inferential processes to make sense of them. Therefore, the inferential view does not give any special role to efferent information internal to the motor system in generating the experience of action. Similarly, Johansson, Hall, Sikström, and Olsson (2005) presented participants with photographs of two faces. The participants had to choose the most attractive one. The photograph chosen was presented again to the participants, who were asked to explain the reason for their choice. When the Authors covertly manipulated the photographs by switching the chosen and non-chosen cards, they found that in case of a mismatch between the initial choice and actual outcome (i.e., when the cards were switched) the participants failed to notice the difference, and nevertheless explained a choice they in fact did not make. Evidence for this theory has also been provided by further studies which used priming to manipulate thoughts about the effect of an action before it was performed (e.g., Wegner, Sparrow & Winerman, 2004; Aarts, Custer & Wegner, 2005; Aarts, Custers & Marien, 2009; Moore, Wegner et al., 2009; Sato, 2009; Nahab, Kundu, Gallea, Kakareka, Pursley et al., 2011).

1.1.3 THE TWO-STEP MODEL

Since both the *predictive* (i.e., internal motoric signals: *CM*; Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001) and *postdictive* (i.e., external and situational cues: the *inference model*, Wegner & Wheatley, 1999; Wegner, 2003) theories have major limitations and do not exhaustively depict the complexity of the SoAg, Synofzik et al. (2008) proposed a *Two-Step Model* of the SoAg in order to account for both internal and external factors. This model includes a basic perceptual level - the Feeling of Agency (*FoAg*) - and an explicit level – the Judgment of Agency (*JoAg*) (Figure 1.4).

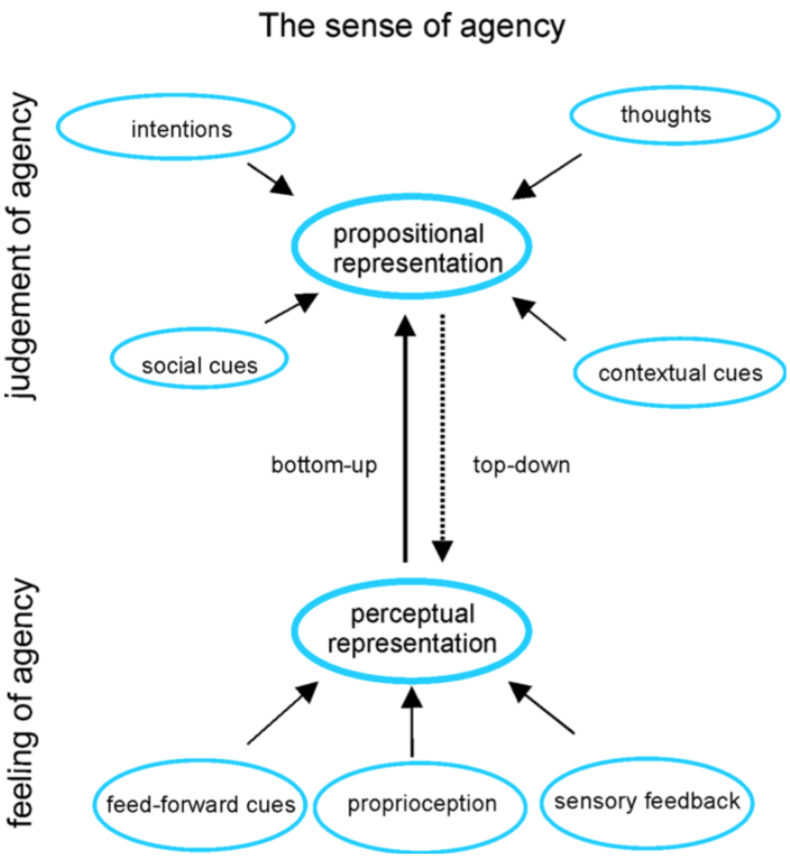


Figure 1.4. *The Two-Step model (adapted from Synofzik et al., 2008).*

The *FoAg* consists in sensorimotor processing and is affected by the match/mismatch between the internal forward model and the actual sensory feedback. Here, an action or a sensory event is merely classified as self- or not-self-caused and no external attributions are possible at this level. Subsequently and based on the *FoAg*, a judgment is formed at the *JoAg* level. Here, also contextual information, like background beliefs or information about the environment, are taken into account. For example, a mismatch detected at the *FoAg* level triggers the primary feeling of not being the author of a certain event and subsequently, at the *JoAg* level the search for the actual agent occurs.

1.1.4 THE CUE INTEGRATION THEORY

The *Two-Step* account (Synofzik et al., 2008) described in the previous section does not provide any criteria defining how cues are selected and integrated to shape the SoAg. In order to fill theses gaps, the *Cue Integration Theory* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013) has been proposed (Figure 1.5). Accordingly, in order to determine the cause of a sensory event, the brain must integrate information from multiple cues within a *Bayesian* model (Moore, Wegner et al., 2009; Moore & Fletcher 2012). Thus, these cues are weighted, depending on their availability and their reliability in a given situation, to produce the SoAg, with most weight being given to the most reliable cue. Usually predictive signals, such as internal predictions, provide the fastest and most reliable information about one's own actions. However, when predictive cues are weak or imprecise, other cues, like post-hoc ones (i.e., action feedback or the affective action outcome) receive a higher weight. It seems straightforward that the extent to which the *FoAg* and the *JoAg* contribute to the SoAg depends on an interplay of interacting cues.

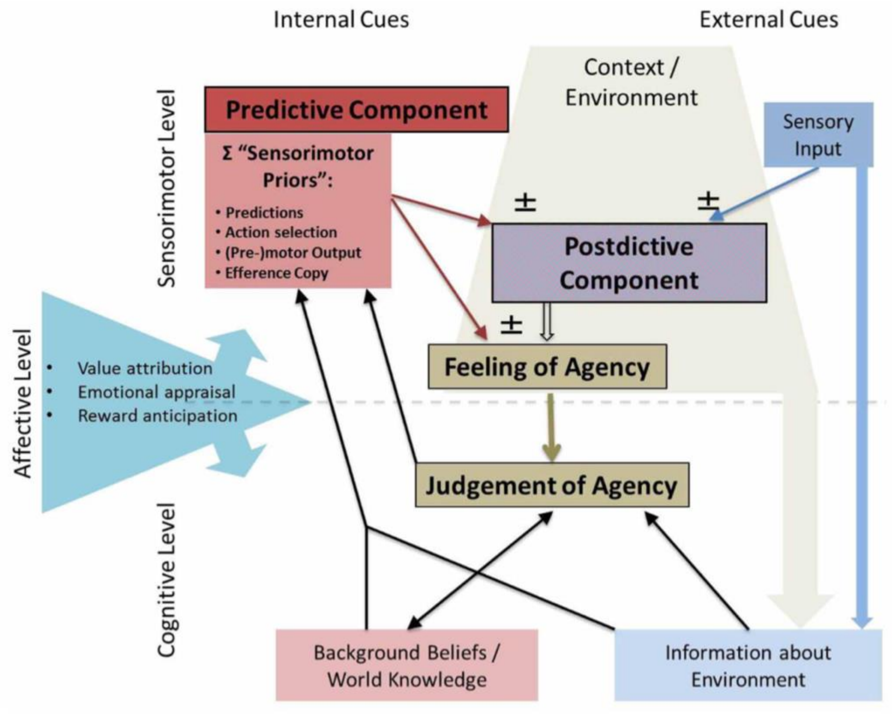
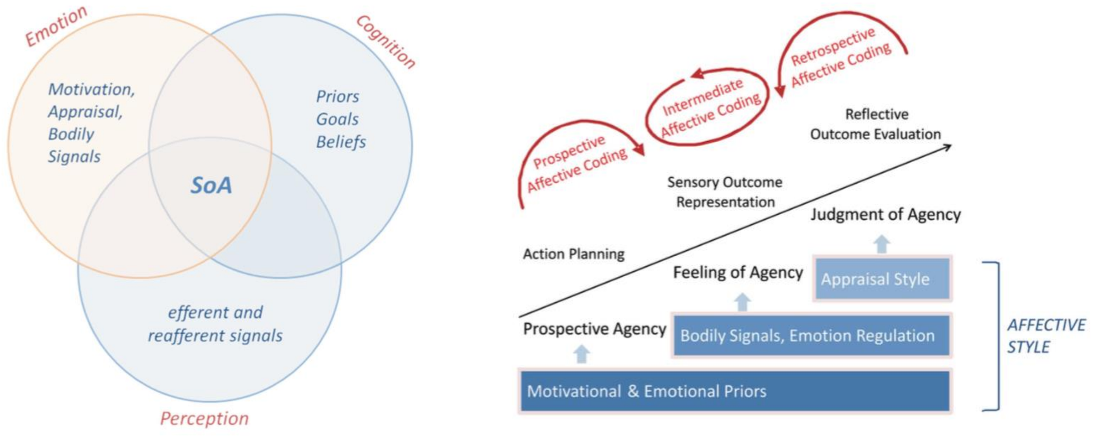


Figure 1.5. *The Cue Integration Theory (adapted from Synofzik et al., 2013).*

As showed in Figure 1.5, the sensorimotor predictive cues (i.e., the so-called 'sensorimotor priors') can be modulated by cognitive cues, like background beliefs. For instance, motor processing can be influenced using priming (Wegner et al., 2004; Aarts et al., 2005) or prior beliefs induced by contextual information (Desantis, Roussel & Waszak, 2011). In addition, the *FoAg* is determined by postdictive cues in a sensorimotor format, like the visual feedback of one's action (Synofzik, Their, Leube, Schlotterbeck & Lindner, 2010). Both *predictive* and *postdictive* components can contribute to the *FoAg*. The *JoAg* is then based on the *FoAg* and takes into account cognitive cues, like background beliefs, and information about the environment. At both levels (i.e., the *FoAg* and the *JoAg*), the cue integration process can be modulated by affective components (e.g., affective valence of the action outcome (Wilke, Synofzik & Lindner, 2012). However, evidence supporting the notion of optimal cue integration is still scant (e.g., Moor, Wegner et al., 2009; Desantis et al., 2011; Bednark & Franz, 2014; see Paragraph 2.1). This framework is also suited to explain various psychopathological disorders of agency (Moore & Fletcher, 2012; see Paragraph 1.4.1).

Although a growing body of literature has started to consider the importance of a *combination* of *different* cues to capture the entire complexity of the SoAg (e.g., Moore, Wegner et al., 2009; Synofzik et al., 2010; Moore & Fletcher, 2012), these models only partly consider emotional dimension. Indeed, up to the present moment, the potential role played by emotions has been largely neglected in the field of agency research. In fact, agency and emotions constantly interact in our daily life and agency could therefore change according to the emotional valence of an action's outcomes. To fill this gap, Gentsch and Synofzik (2014) thus proposed the *Affective Coding of Agency* model (Figure 1.6), as an essential extension of the *Cue Integration Theory* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013). Accordingly, SoAg is influenced by a combination of sensorimotor, cognitive and emotional cues (Wilke et al., 2012; Takahata, Takahashi, Maeda, Umeda, Suhara et al., 2012; Yoshie & Haggard, 2013; Gentsch, Weiss, Spengler, Synofzik & Schütz-Bosbach, 2015).



A. B.

Figure 1.6. *The Affective Coding of Agency (adapted from Gentsch & Synofzik, 2014). Panel A: the contribution of emotional cues with sensorimotor and cognitive cues in the formation of the SoAg. Panel B: the influence of emotional cues at different stages of agency processing.*

In addition, affective coding of agency may be differentially altered in various neuropsychiatric diseases (e.g., schizophrenia vs. depression), thus helping to explain the dysfunctions of agency experiences in these diseases (Gentsch & Synofzik, 2014).

1.2 CURRENT MEASURES TO STUDY THE SENSE OF AGENCY

The objective quantification of the SoAg, especially in a laboratory setting, is not an easy endeavour. Given the high relevance and complexity of this phenomenon, researchers have struggled to find appropriate measures to study the SoAg. In the ensuing sections explicit and implicit testing attempts will be reviewed.

1.2.1 EXPLICIT MEASURES

For many years, the most common approach to the study of agency has involved explicit judgements. Using self-reported judgments, participants were asked either to report whether a particular sensory event (e.g., the appearance of a symbol on a computer screen) was caused by their own action or by the action of another agent (e.g., Wegner & Wheatley, 1999; Sato & Yasuda, 2005; Tsakiris, Haggard, Franck, Mainy & Sirigu, 2005; Daprati, Wriessnegger, Lacquaniti, 2007), or to report how much control they felt for producing an outcome (e.g., Metcalfe & Greene, 2007; Preston & Newport 2010; Yomogida, Sugiura, Sassa, Wakusawa, Sekiguchi et al. 2010). Usually, when a spatial (e.g., Daprati et al., 2007) or temporal (Wegner & Wheatley, 1999; Farrer, Bouchereau, Jeannerod & Franck, 2008) congruence between one's own action and its sensory feedback is detected, agency is self-attributed.

Although having significantly contributed to shedding light on factors influencing the conscious SoAg, the self-report approach presents some limitations. Indeed, it is well known from social psychology that explicit measures are sensitive to different biases, such as the use of explicit strategies, social desirability, expectations and beliefs about the task, to mention some of the most relevant ones (Podsakoff & Organ 1986; Woolfolk, Doris, & Darley, 2006; Gawronski, LeBel & Peters, 2007). In addition, explicit tasks are influenced by limits related to introspection and subjectivity insights (Wolpe & Rowe, 2014), making their use problematic especially in patients and special populations – such as children and elderly - introducing confounding factors. Furthermore, the explicit attribution is self-biased in itself: participants consistently overestimate their actual agency over external events (e.g., Daprati, Franck, Georgieff, Proust, Pacherie et al., 1997; Tsakiris, Hesse, Boy, Haggard & Fink, 2007).

1.2.2 IMPLICIT MEASURES

The majority of investigations have utilized tests requiring explicit reports of agency. However, given the abovementioned limitations, the creation of implicit tasks has become crucial for exhaustively characterizing the SoAg. This is especially true if we also consider the fact that our everyday experiences of agency do not generally involve explicit judgements and we usually feel in control of what we are doing without explicitly reflecting upon it. Therefore, implicit measures provide an important and alternative way of quantifying SoAg, and may be better suited to capture its complexity. In fact, one of the main advantages of implicit tasks is that they do not require explicit attributions and intentional access, making them particularly suitable to study agency in clinical samples. Up to now, a number of implicit measures of the SoAg have been proposed, like the *kinematic* of movements (Fourneret & Jeannerod, 1998; Knoblich & Kircher, 2004), *sensory attenuation* Blakemore et al., 1998; Blakemore, Wolpert & Frith, 2000) and *IB* (Haggard et al., 2002). The *kinematic* of movements provides a detailed mathematical characterization of body movements through space and time, including linear and angular displacements, velocities and accelerations. Therefore, it can reveal the underlying, implicit properties of our actions that cannot be verbally reported otherwise. In addition, it can be used to demonstrate goal-directed behaviour in the absence of awareness (Fourneret & Jeannerod, 1998; Knoblich & Kircher, 2004) since it captures subtle adjustment in motor commands that otherwise would go unnoticed by researchers. *Sensory attenuation* refers to the fact then that the effects of one's voluntary actions are characterized by a reduced behavioural and neural response in terms of perceived intensity as compared to externally triggered effects (Blakemore et al., 1998; 2000). For example, the activity of the primary somatosensory cortex was found to be diminished in response to self-produced compared to external touch (Blakemore et al., 1998). Similarly, in the auditory and visual modality, electroencephalography (EEG) studies revealed a reduction in the amplitude of the N1 event-related potential following self-generated auditory events or visual stimuli (for recent reviews, see Waszak, Cardoso-Leite & Hughes, 2012; Hughes, Desantis & Waszak, 2013). With regard to the clinical populations, the absence of sensory suppression in patients suffering from hallucinations (Blakemore, Smith, Steel, Johnstone et al., 2000) is considered evidence for the role of this implicit measure in SoAg (Frith, Blakemore & Wolpert, 2000; Ford & Mathalon, 2004).

Within the context of the present research, however, there is yet another implicit measure, namely the *IB* (Haggard et al., 2002). This effect refers to the finding that a voluntary action and its following sensory effect are perceptually attracted toward one another in time, as compared to when both events occur in isolation. Chapter 2 will describe in detail the features and the mechanisms underlying this fascinating phenomenon.

1.3 NEURAL BASES OF THE SENSE OF AGENCY

Until now, the brain network hypothetically subserving the SoAg has not had a clear anatomical characterization, given inconsistent results obtained through discrepant experimental situations (see Paragraph 1.2 of this Chapter; for reviews, see David et al., 2008 and Sperduti, Delaveau, Fossati & Nadel, 2011).

In order to present the complexity and the heterogeneity of the phenomenon, in the next sections the most important findings regarding the neural correlates of the *retrospective (*Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001*)*, *prospective* (Chambon, Sidarus et al., 2014) and *inference* (Wegner & Wheatley, 1999; Wegner, 2003) accounts of the SoAg will be reviewed. It is worth noting that all these studies involve explicit tasks, which are the most common paradigms in the SoAg scenario and unfortunately investigations on the neural correlates of implicit measures of agency, namely the IB effect, have been restricted to a handful of studies summarized in Chapter 2 (Paragraph 2.4).

1.3.1 NEURAL BASES OF THE RETROSPECTIVE ACCOUNT

With respect to the *CM* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001; see Paragraph 1.1.1), the **posterior parietal cortex** (PPC) and the **inferior parietal cortex** (IPC) are the brain regions usually activated by explicit tasks asking participants to judge whether their own action is responsible for a specific sensory event (e.g., Fink, Marshall, Halligan, Frith, Driver et al., 1999; Farrer & Frith, 2002; Farrer et al., 2003). However, these areas usually appear to be involved mainly in conflicting, non-agency rather than in agency conditions according to studies in both patients and healthy participants (e.g., Spence, Brooks, Hirsch, Liddle, Meehan et al., 1997; Sirigu, Daprati, Pradat-Diehl, Franck & Jeannerod, 1999; Farrer & Frith, 2002; Farrer, Franck, Frith, Decety, Georgieff et al., 2004). For example, in a study by Farrer and Frith (2002), the IPC area appeared to be more active when participants attributed a visual event to another person rather than to themselves, while being aware of causing an action was associated with activation in the anterior insula. Likewise, a Positron Emission Tomography (PET) study (Farrer et al., 2003) observed that activity in IPC increased with the level of discrepancy between the executed and the observed action on the screen. Similarly, activity in the right **angular gyrus** (AG) correlates with the magnitude of the discrepancy between the intended and actual effects of the action (Farrer et al., 2003). The involvement of AG was also confirmed by a functional magnetic resonance imaging (fMRI) study (Farrer, Frey, van Horn, Tunik, Turk et al., 2008) where loss of agency was found to correlate with blood oxygenation level dependent (BOLD) response in the AG. Overall, increased activations of PPC and IPC in general, and AG in particular, were detected when participants explicitly rejected agency over an outcome. The Authors of those studies suggested that these regions could be involved in the comparison between the efference copy of the intended action and the actual sensory outcome. Any mismatch between these signals give rise to the explicit awareness of non-agency. Going beyond a correlational approach, also virtual lesions studies by means of transcranial magnetic stimulation (TMS) have investigated the role of the IPC and the adjacent parietal areas in SoAg (MacDonald & Paus, 2003; Preston & Newport, 2007; Ritterband-Rosenbaum, Karabanov, Christensen & Nielsen, 2014). A noticeable difference between the imaging findings and some of the brain stimulation results is that whereas the former consistently report higher activity of the IPC with increasing levels of external perturbation (e.g., when participants do not experience agency; Farrer & Frith, 2002; Farrer et al., 2003; Nahab et al., 2011), the latter seem to suggest that disrupting this region modulates agency relatively unspecifically regardless of whether the observed movement is externally generated (e.g., a manipulated movement) or not (e.g., a self-controlled movement) (e.g., Ritterband-Rosenbaum, Karabanov et al., 2014).

The **cerebellum** is another brain area implicated in signalling discrepancies between predicted and actual sensory consequences of movements. Blakemore et al. (2001), by means of PET showed increased cerebellar activation as a function of the delay between predicted self-generated tactile sensations via a robotic arm and actually experienced sensations.

Thus, both the cerebellum, PPC, IPC and AG appear to be plausible candidates as neural correlates of the *CM*. However, the cerebellum, unlike the PPC, does not seem to be necessarily associated with the actual comparison of predicted and actual signals or the detection of violations (Blakemore et al., 1998). Indeed, Sirigu et al. (1999) showed that patients with damage to the parietal lobule are no longer be able to differentiate their own hand movements from those of another agent. A similar phenomenon has not been reported for cerebellar patients.

In addition to the mentioned regions, other areas, within the frontal network, seem to be active in external-agency conditions, even though there are not enough findings to drawn definitive conclusions (Sperduti et al., 2011; e.g., the pre-SMA and the dorsolateral prefrontal cortex – DLPFC - Fink et al., 1999). On the other hand, brain areas such as premotor regions, primary somatosensory cortex and insula (e.g., Sperduti et al., 2011; Farrer & Frith, 2002; Farrer et al., 2003) appear to be more active in self-agency. Indeed, the introduction of a discrepancy between the subjects' hand movements and the visual feedback provided to the participants appears to modulate activity in the insular region: the smaller the discrepancy is, the higher the activation of the insula, which was also associated with an increased feeling of causing the movement.

1.3.2 NEURAL BASES OF THE INFERENCE ACCOUNT

The study of neural bases of the *inference account* (see Paragraph 1.1.2; Wegner & Wheatley, 1999; Wegner, 2003) has received little attention, despite its role in the emergence of agency. Only two studies have explicitly addressed this issue (Dogge, Hofman, Boersma, Dijkerman & Aarts, 2014; Renes, van Haren, Aarts & Vink, 2015). Dogge et al. (2014), using EEG, provided the first insight into the neural bases underlying agency inferences. Participants completed a computerized task in which they pressed a button followed by one of two colour words ('red' or 'blue') and rated the agency they experienced over the colour produced (i.e., to what extent they felt their key press caused the presented colour word to occur). Before executing the action, participants were explicitly instructed to verbally produce the colour or were briefly presented with a prime (e.g., the colour word). Functional connectivity between parietal and frontal areas was observed during low agency experiences in trials in which goals mismatched with the outcome. On the other hand, the coupling within frontal areas was observed during high agency (i.e., when participants thought they were the authors of the produced colour), suggesting that the frontal network was not involved in case of mismatching outcomes that were not ascribed to participants. Subsequently, using functional magnetic resonance imaging (fMRI), Renes et al. (2015) observed that the experience of self-agency was associated with increased activation in the medial prefrontal cortex, bilateral (medial) superior frontal cortex and the left inferior parietal lobule. Therefore, the inference account of agency seems to recruit higher cortical regions, such as the prefrontal cortex (PFC), more related to conscious monitoring (Slachevsky, Pillon, Fourneret, Pradat-Diehl, Jeannerod et al., 2001).

1.3.3 NEURAL BASES OF THE PROSPECTIVE ACCOUNT

Also the *prospective account* (see Paragraph 1.1.1, Chambon, Filevich & Haggard, 2014; Chambon, Sidarus et al., 2014) has received scant attention. Chambon, Wenke, Fleming, Prinz and Haggard (2013) using fMRI dissociated action selection processes from action-outcome matching by subliminally priming responses to a target arrow using a paradigm similar to that of Wenke et al. (2010) described in Paragraph 1.1.1. Results highlighted a network involving both left DLPFC and left AG. In particular, AG was active in case of non-agency conditions, when mismatches between prime and actual response to the target were detected, consistently with the other studies described in the Paragraph 1.1.1 (e.g., Farrer et al., 2003; Farrer, Frey et al., 2008), suggesting that AG codes for lack of agency. Interestingly, AG activation predicted the 'magnitude' of agency: indeed, only for incompatible trials, activity in the AG decreased as the sense of control over outcomes increased. In addition, activity in the AG, always in incompatible trials, was negatively correlated with activity in the DLPFC, which might provide conflict resolution between action alternatives by reducing activations for incompatibly-primed responses. In other words, DLPFC *activation* would reflect willed action, while its *deactivation* would signal dysfluency in the selection of willed action, resulting in a diminished sense of control over action effects. On the other hand, AG not only accounts for the *CM* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001) by monitoring mismatches between actions and outcomes, but also codes for prospective agency, by real-time monitoring action selection processes coming from DLPFC in advance of the action itself, and independently of action outcomes to finally shape agency.

Subsequently, Chambon, Moore & Haggard (2014) combined single-pulse TMS over left IPC and left DLPFC, with subliminal priming of action selection and judgements of control over action effects. The results confirmed and extended the findings from the previous fMRI study (Chambon et al. 2013), showing for the first time that the contribution of IPC to the SoAg includes early and prospective components related to action preparation and execution, which do not depend on processing at the time of action outcomes. No effect on DLPFC was observed.

Altogether, these studies suggested a functional subdivision of IPC: its *ventral* part would be more involved in retrospectively monitoring the link between the action and its consequences (e.g., Farrer, Frey et al. 2008), while its *dorsal* component would be more involved in monitoring the linkage between intention and action, prior to action execution and independent of action consequences (Chambon et al. 2013; Chambon, Filevich et al., 2014; Chambon, Moore et al., 2014; Chambon, Sidarus et al., 2014). In addition, the IPC appears to be a candidate area for the neural implementation of the *Cue Integration Theory* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013), playing a crucial role in monitoring the consistency between various action-related signals and action selection fluency may be one such cue.

1.3.4 CONNECTIVITY STUDIES

The experience of agency requires the integration of information generated at different brain sites. But how do these regions communicate? To date, only a few studies have investigated agency as the result of a network of functionally connected brain regions (David, 2012). For example, David, Cohen, Newen, Bewernick, Shah et al. (2007) asked participants to indicate perceived control over actions based on congruent or incongruent movement feedback. Increased functional connectivity was observed between the pre-motor cortex, cerebellum, and PPC when movements were correctly identified as externally generated, and between the insula and somatosensory cortex when movements were correctly classified as self-generated. Then Nahab et al. (2011) identified two main networks. The first one, the *leading network*, consists primarily of the left anterior inferior parietal lobe, the right supramarginal gyrus, the right temporoparietal junction and the anterior insula. This network would convey information to a *lagging network* consisting mainly of the cingulate, posterior inferior parietal lobe and the prefrontal lobe. The former is the first to become active and is likely to be involved in mismatch detection between motor predictions and sensory action effects; the *lagging* network translates, later in time, the outcomes of this comparison into a conscious agency experience. Although the aforementioned connectivity studies provide a first glimpse into neural dynamics underlying the SoAg, they deal with agency processes informed by motor predictive signals. However, as seen before in Paragraph 1.3.2, parietal and frontal regions are also associated with the inference account (Wegner & Wheatley, 1999): indeed, inferences depend heavily on functional connectivity between these regions (Dogge et al., 2014). This is due to the fact that both motor prediction and inference involve a comparison between predicted and actual outcomes (Dogge et al., 2014).

A recent EEG study (Ritterband-Rosenbaum, Nielsen & Christensen, 2014) identified an IPC-pre-SMA network in which SoAg is associated with stronger coupling from IPC to pre-SMA. When participants experienced agency over their movements coupled activity is present. In other words, IPC supplies the pre-SMA with information about a mismatch of sensorimotor and visual information after the movement has been performed. Attribution of agency (self vs other) does not depend on a pure increase or decrease activity in a single cortical area. Instead, it is the coupled activity in a specific frequency band within this network that determines SoAg. Very recently, Kang, Im, Shim, Nahab, Park et al. (2015) used EEG power spectrum measures and phase coherence of alpha, beta, and gamma frequency bands to estimate neuronal activity and functional connectivity. They found that the alpha band was the most closely correlated with SoAg modulation, in particular within the anterior frontal regions. The degree of desynchronisation was higher at greater levels of control and the functional connectivity was lower as the participants felt that they could control their virtual hand. This suggests that the system might be more active when there is a lack of agency. Indeed, under normal circumstances, the self-agency system is '*in equilibrium*' since for the vast majority of time the outcomes produced by one's own actions match with the actions performed. However, when the action does not match what was intended, the discrepancy is quickly detected and agency system is activated (Kang et al., 2015). These anterior frontal regions were also functionally connected with other cortical regions (e.g., the middle central, parietal, temporal, and occipital lobes in the right hemisphere), supporting the idea that frontal regions may be a sort of central hub receiving various types of information, such as sensory information and state estimation between self-movements and perception, adjusting motor output. This functional connectivity between frontal and other cortical areas was particularly modulated by beta and gamma bands. The study showed that alpha band activity is the characteristic neural oscillation of SoAg, which suggests that the neural network within the anterior frontal area may be important in the generation of SoAg.

To sum up, connectivity studies are relevant in order to assess how the different areas involved in the SoAg relate to one other. Although these studies are increasing, there is still much work to be done in order to identify the processing pathways that integrate information coming from these areas to support agency.

1.4 THE CLINICAL SIDE OF THE SENSE OF AGENCY

Two main general classes of dysfunctional agency can be broadly distinguished, as a consequence of (i) more diffuse neural changes underlying mental illnesses or (ii) focal neurological lesions (for a review, see: Moore & Fletcher, 2012). The following sections will provide a brief review of the main pathologies characterized by a lack of the SoAg

1.4.1 SCHIZOPHRENIA

Schizophrenia represents an outstanding 'pathophysiology model' within agency field (Synofzik et al., 2013). Indeed, patients suffering from schizophrenia report unusual experience of control over their actions. They may either feel that external forces are controlling their actions, or they may feel in control of events that are actually not caused by their own actions. SoAg functioning in this population has been mainly investigated using explicit judgments tasks. Usually, patients with delusions of control show difficulty in self-attribution of the sensory consequences of a given action, resulting from a mismatch between internal predictions and the actual sensory feedback. Therefore, these problems of agency may be linked to a deficit within the *CM* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001), namely in the internal forward model (e.g., Frith & Done, 1989; Blakemore et al., 1998; Blakemore, Smith et al., 2000; Frith, Blakemore &

Wolpert, 2000; Blakemore et al., 2001; Blakemore, Wolpert & Frith, 2002; Shergill, Samson, Bayn, Frith & Wolpert, 2014). According to this idea, patients would attribute any deviant sensory information – no longer compensated by internal predictions – to external sources rather than to themselves. This mechanism can also be explained by referring to the *Cue Integration Theory* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013). For example, according to the cue integration approach, schizophrenic patients with delusions of influence - who have a reduced reliability of motor predictive signals - would mostly rely on post-hoc information about their actions (e.g., visual feedback) rather than on internal sensorimotor cues in order to establish the source of agency (Synofzik et al., 2010).

Another line of research has examined the ability of these patients to attenuate self-induced sensory events and has shown that patients suffering from misattributions do not exhibit the normal reduction of neuronal response to self-generated, as compared to externally generated stimuli (Ford & Mathalon, 2004). This view has received further confirmation by studies involving perceptual decision tasks, showing that perceptual ratings were not decreased for self-induced sensory attenuation (Blakemore et al., 2000; Shergill et al., 2014). Interestingly, different pattern of results has been reported between patients with positive (PS) and negative symptoms (NS). Indeed, NS-predominant schizophrenia shows markedly diminished SoAg (Maeda, Takahata, Muramatsu, Okimura, Koreki et al. (2013) as compared to patients with PS who, on the other hand, present an ‘exaggerated’ SoAg (Maeda, Kato, Muramatsu, Iwashita, Mimura et al., 2012). Such differences suggest that dopamine (DA) plays a key-role: in fact, PS are characterized by a hyper-DA state, which woul boost agency experiences, contributing to ‘excessive’ SoAg experiences (Maeda et al., 2012). In contrast, NS in schizophrenia seem to be caused by a deficiency of DA circuitry (Maeda et al., 2013), which would reduce the SoAg.

1.4.2 OBSESSIVE-COMPULSIVE DISORDER

Another clinical profile in which SoAg appears to be potentially ‘compromised’, although neglected in the current literature, is the obsessive-compulsive disorder (OCD), where ‘dysfunction’ of awareness and control of motor actions are at the core of the phenomenological expression of this disorder. Specifically, obsessions are intrusive and uncontrolled thoughts, whereas compulsions regard the urgency to performed stereotyped mental or physical actions, both of which significantly impair everyday functioning. In particular, OCD patients exhibit *sequelae* mainly related to action planning and execution: a study conducted by Gentsch, Schütz-Bosbach, Endrass & Kathmann (2012) showed a lack of predictive self-attenuation. Specifically, in the EEG signal the typical reduction of N1 amplitude following self-generated sensory outcomes in healthy people (e.g., Blakemore et al., 1998; 2000) was absent in these patients, which did not rather seem to be able to distinguish between self and externally generated visual events. Within this context, the lack of sensory suppression of N1 component - after voluntary action generation of visual feedback - exhibited by patients indicates deficient internal motor predictions.

1.4.3 AUTISM SPECTRUM DISORDER

Knowing whether it is me or another agent that is producing and controlling a particular action is fundamental in order to establish self-other boundaries. Difficulties in this regard could lead to subsequent impairments in understanding the perspective of other individuals, a peculiarity of Autism Spectrum Disorders (ASD). In addition, ASD are characterized by impairments in motor planning, monitoring and prediction (for a review, see: Gowen & Hamilton, 2013). Based on these assumptions, an impairment on the agency domain might be predicted. However, until now, literature has reported mixed results, with studies showing either preserved or impaired SoAg (for a review, see: Zalla & Sperduti, 2015). According to a recent review by Zalla & Sperduti (2015), impairment in the SoAg might be featured by a reduced reliance on internal prospective signals, generated at very early stages of action selection and planning (Chambon, Sidarus et al., 2014) along with spared retrospective mechanisms (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001).

1.4.4 PSYCHOGENIC MOVEMENT DISORDER

Psychogenic movement disorders (PMD) are featured by involuntary movements (e.g., tremor, dystonia, corea), for which patients usually report a lack of control, in the absence of structural, metabolic, or neurological disease. Changes within SoAg have been reported in these patients (Pareés, Brown, Nuruki, Adams, Navare et al., 2014): using a classic 'force matching' paradigm, patients were required to match a force delivered to their index finger either by pressing down directly on their finger or operating a robot to press down on their finger. PMD patients showed reduced sensorimotor attenuation with respect to healthy controls. Subsequently, Macerollo, Chen, Pareés, Kassavetis, Kilner et al. (2015) extended these findings by exploring sensory evoked potentials, showing that patients are characterized by reduced sensory attenuation at onset of self-paced movement.

1.4.5 NEUROLOGICAL DISORDERS

Also many neurological disorders have been associated with modifications of agency (for a review, see: Kranick & Hallett, 2013). For example, in *Alien Hand Syndrome* (AlHS), patients deny that the limb is paralyzed and behave as it is not, sometimes claiming that it moves. The affected limb is in this respect not under full voluntary control and its actions are associated with a diminished SoAg (Moore & Fletcher, 2012). Similarly, the *Anarchic Hand Syndrome* (AnHS) is characterized by goal-directed movements performed without volitional control (Marchetti & Della Sala, 1998). A recent study conducted by Jenkinson, Edelstyn, Preston & Ellis (2015) provided the first direct examination of agency modifications in parietal-type AnHS demonstrating that it is not a mere deficit of motor control. In contrast to AlHS, in AnHS the hand is perceived as belonging to the person, but there is also a strong feeling of the hand being out of control, with its own will and responding to external cues. What is lacking is the sufferer's sense of being able to control or stop it (Moore & Fletcher, 2012). Also *tic disorders* are characterized by a lack of control over voluntary actions (Moretto, Schwingenschuh, Katschnig, Bhatia & Haggard, 2011): sudden, repetitive and stereotyped movements, experienced as a voluntary response to an urge, are at the core of this neurological disease. The experience of intention in these patients was delayed in proportion to disease severity, and Authors interpreted these results as symptom of a dissociation between motor intentions and sensory feedback.

As has emerged from this brief review, modifications of the SoAg characterize a wide range of disorders. Although much work has yet to be done, clinical disorders showing modifications of SoAg nevertheless represent an essential first window of insight into the neurocognitive mechanisms underlying this phenomenon.

1.5 TAKE-HOME MESSAGE

The review presented in this chapter shows how SoAg has become a hot topic within the cognitive neuroscience field, as evident from the increasing number of relevant articles published in the very recent years (David, Obhi & Moore, 2015). Indeed, many researchers have shown interest in this topic in view of the impact that SoAg has on individuals and on our society in general. Up to now, significant progress has been achieved with regard to models which significantly contribute to the understanding of the cognitive processes underlying agency in healthy individuals. Most importantly, thanks to this advance, a new window was also opened to the exploration of agency 'dysfunctions'. The fact that SoAg can be impaired in certain diseases has then suggested the existence of a neural substrate for this phenomenon. Here, although many efforts have been made to shed light on brain regions supporting the SoAg, a heterogeneous picture has emerged. Indeed, a scatter distribution of areas within our brain has been shown to be implicated in the processing of agency. One of the main factors which might have contributed to such a mixed picture is the different tasks and techniques usually adopted. Nevertheless, considering all these pieces of evidence together, it seems quite clear that frontal areas are more involved during agency attribution, while the parietal regions seem to be more implicated during loss of agency. However, the complexity of agency cannot be reduced to simply 'turning on' and 'turning off' of particular areas. To obtain a more compelling view of how SoAg works, connectivity studies are needed.

However, up to now the few connectivity studies present in the scientific overview are still incomplete because of the limited number of brain regions considered or, more critically, because brain regions associated with the implicit feeling of agency have been omitted. In fact, the vast majority of studies utilized explicit measures, which have several intrinsic limitations and might have, in some way, introduced confounding factors. Therefore, it appears that a straightforward consensus on the neural underpinnings of agency has yet to be reached and, despite many advancements, much work is still needed to fully appreciate the potentiality of such intriguing phenomenon.

In the following chapter, the IB effect will be considered as an implicit measure of SoAg. The possible adoption of this measure in routine investigations of agency, especially combined with neuroimaging techniques, could provide a suitable tool for optimal investigations of agency, both in healthy individuals and in clinical populations (Wolpe & Rowe, 2014).

CHAPTER 2

INTENTIONAL BINDING

Our voluntary actions influence the way people subjectively experience time (Haggard et al., 2002). For this reason, time perception represents nowadays one of the most important implicit measures for studying the SoAg (Tsakiris & Haggard, 2005). More than a decade ago Haggard et al. (2002) observed that voluntary actions and their sensory consequences are perceived as temporally shifted together in time. This effect has been called Intentional Binding (IB). Using the Libet clock method (Libet et al., 1983) - an external metric usually used to report one's own internal subjective experience of willing – Authors examined participants' awareness of actions and sensory effects. Participants had to watch a clock hand marked with conventional intervals (5, 10, 15, etc.), which rotated very fast (one rotation every 2560 ms) on an experimenter-generated clock-face. Their task was to report the time onset - in other words, where the clock hand was - when a particular event happened. In this study, Authors obtained a *baseline* measure of people's awareness of four main events: (1) a voluntary action: participants were instructed to press the spacebar whenever they felt the urge to do so and to report the clock hand position at the time of their action; (2) an involuntary action: participants had to report the time onset of a muscle twitch in the finger triggered by a TMS pulse over the motor cortex; (3) a click-sound produced by the discharge of the TMS coil, directed over an area of cortex where it would have not induced involuntary movements; (4) a 100-ms sound. They also obtained *agency* measures. In these agency conditions, two events were presented in each trial: the voluntary action, the involuntary movement and the sham TMS click were always followed by the 100-ms sound, after a fixed interval of 250-ms. In this case, participants had to report either when they perceived the occurrence of the first (i.e., their voluntary, involuntary action or the TMS click) or the second event (i.e., the sound). When comparing the *agency* trials (the ones with two events) with the baseline trials (where only one event was present), Haggard et al. (2002) observed that participants' awareness of voluntary actions in agency conditions, when followed by the sound, was delayed as compared to the baseline condition where only the voluntary action was present. This effect was called *action binding*. On the other hand, awareness of tones preceded by such voluntary actions was perceived earlier as compared to the baseline condition where only the tone was present. This other effect was named *effect binding*. In contrast, awareness of involuntary, TMS-induced movements was shifted earlier in time, away from the tone, whereas awareness of the consequent tone was shifted later in time, away from the TMS-induced movement. Awareness of sham TMS clicks and tones following such clicks did not change relative to baseline. This bias to perceive actions and effects closer in time than they actually are has been observed only when the first event was intentional (Figure 2.1). Indeed, it did not happen when the first event was unrelated to the participants' will. For this reason, IB is considered a reliable implicit measure of agency.

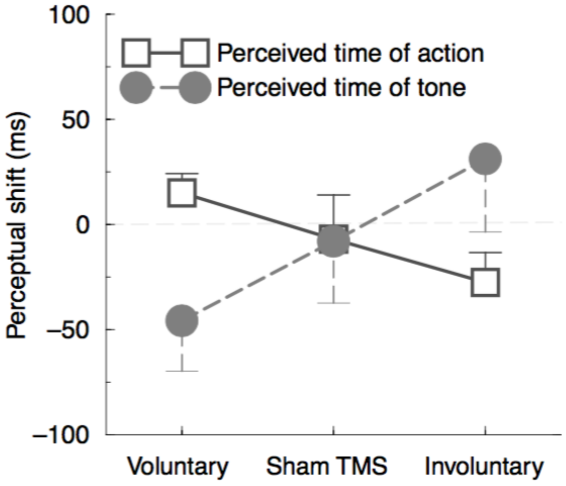


Figure 2.1. *The classic pattern of IB (adapted from Haggard et al., 2002). The perception of onset of voluntary actions was shifted later in time and the perception of tone onset was shifted earlier. This was not the case for involuntary actions induced by TMS, which showed the opposite effects.*

Until now, IB effect has been confirmed in many other studies and since its discovery it was successfully adopted to study agency in healthy people and clinical populations (for a review, see: Moore & Obhi, 2012).

The following sections will focus first on literature investigating the cognitive models underlying IB, and then a description of the principal factors potentially influencing IB will be provided. In the end, results coming from studies focusing on the neural correlates of IB and involving clinical populations will be described.

2.1 THE LINK BETWEEN INTENTIONAL BINDING AND THE SENSE OF AGENCY

Understanding the link between IB and SoAg requires many steps. The ***first*** one is to ***consider the models proposed to explain the SoAg and attempting to verify if they are able to account for IB as well***. Starting with the first model discussed in Chapter 1 (the *CM*: Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001; see Paragraph 1.1.1), IB was shown to be produced by dedicated motor control mechanisms that predict the sensory consequences of an action. Indeed, IB requires (i) an efferent signal, similar to the motor command posited by predictive models and (ii) reliable temporal relations between action and effect (Haggard et al., 2002), like predictive models learning the relation between motor command and sensory consequence. Support for this view has been provided by different studies (e.g., Haggard & Clark, 2003; Tsakiris & Haggards, 2003; Engbert & Wohlschläger, 2007). For example, Haggard and Clark (2003) tested this hypothesis by inserting occasional involuntary movements using TMS. Participants made voluntary key presses whilst watching the Libet clock. In some blocks TMS was randomly applied over motor cortex to disrupt the completion of some of these intentional actions by triggering an identical involuntary movement. Some actions were therefore intentional (i.e., the action precisely matched the participant's intention) and some were not (i.e., the action did not precisely match the participant's intention). Authors reported that the participants' intention to produce the auditory tone gave rise to the IB effect. However, if the intention was interrupted by an involuntary movement, followed by an identical tone, no IB occurred. In other words, disrupting intentions significantly weakened IB. These results show that the efferent signal involved in pressing the button has a critical role in IB. An intention, without the motor act, followed by the appropriate effect (the tone) is not sufficient. Therefore, predictive models have a critical role in constructing the conscious experience of an action.

However, IB is not only explained by the *CM*, but also by an *inferential* process (Wegner & Wheatley, 1999; Wegner, 2003). Indeed, Moore and Haggard (2008) investigated the contribution of both *prediction* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001) and *retrospective inference* (Wegner & Wheatley, 1999; Wegner, 2003) to the action component of IB. In order to isolate the contribution of these two processes, Authors devised a modified version of the Libet clock method, by varying the probability of action outcomes. The outcome could be *predictable* - the action triggered a tone in 75% of trials – and *unpredictable* – the key press produced a tone in 50% of trials. The contribution of *predictive* mechanisms was confirmed by an increase in action binding on 'action only' trials (i.e., in the absence of action outcomes) in the 75% vs. 50% conditions. Indeed, prior knowledge of the action–outcome association led to a predictive form of IB. Conversely, the contribution of *retrospective inference* was confirmed by an increase in action binding on 'action + tone' vs. 'action only trials', only in the 50% condition. Here, the contribution of prediction was minimal because the outcome was unpredictable. Therefore, the increase in binding on 'action + tone' trials could only have been due to the presence of the tone. This suggested that the tone retrospectively triggered a shift in the perceived time of action. Taken together, the results showed that action binding depends both on a *predictive* process - since it occurs even in trials in which tones are absent, in a situation where the action is highly predictive of a tone - and on *inferential* process, as action binding occurs even when the action is not strongly predictive of a tone, as long as the tone event occurs. Moore and Haggard (2008) demonstrated in this way the contribution of both internal sensorimotor prediction and external action outcomes to the SoAg. This dual contribution of internal motoric signals and external, situational cues was also demonstrated by Moore, Wegner et al. (2009). Using a priming paradigm, they investigated how supraliminal primes might alter the experience of the relation between actions and their effects. They considered two movement conditions: voluntary and passive. Prior to the movement in each condition participants were presented with a prime: a high or low pitch tone. The movement then produced, after a brief delay, a high or low pitch tone. They found that IB was increased when primes were congruent with the outcome. However, the effect was different in accordance to the type of movements: extrinsic cues were most effective for involuntary movements. On the other hand, when an internal agency cue existed within the motor system, as in voluntary movements, alternative external cues to agency have a reduced impact on action experience. These results suggest that such cues are not additive, but interactive and that their relative influence is determined by their reliability (for similar findings within SoAg, see Aarts et al., 2005). For this reason, Moore, Wegner et al. (2009) proposed that a *Bayesian* cue integration process might explain the IB effect.

Wolpe, Haggard, Siebner and Rowe (2013) provided direct evidence for the contribution of *Cue Integration Theory* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013). According to the cue integration hypothesis, IB could result from using both events (e.g., the internal motor cue and the external sound) as informative cues. The time estimates are based on a weighted average of the two events, in which the weight of each cue is determined by its reliability. Authors tested the contribution of cue integration to the perception of action and its sensory effect in IB, by manipulating the sensory reliability of the sensory outcome (e.g., the tone), that is, the tone intensity relative to a background white noise. Results provided support to the cue integration hypothesis for the action binding phenomenon: when sensory uncertainty is high or in the absence of sensory feedback, the perception of action relies more on these internal representations, thereby reducing action binding. However, tone binding is not supported by the cue integration process. On the other hand, it seems that tone binding depends on a 'pre-activation' mechanism (Waszak et al., 2012). Accordingly, the neural representation of a predicted sensory event, such as a sensory outcome following a voluntary action, is activated prior to its occurrence since its perceptual representation has already been pre-activated by internal motor signals. On the other hand, in the case of non-anticipated stimuli the signal accumulation would take longer to reach the threshold of awareness (Wolpe, Haggard et al., 2013). Other data are also consistent with the cue integration model. Desantis et al. (2011) investigated IB by considering the role played by the involvement of another potential agent, in different conditions: (i) participants were unsure whether they or a confederate had produced an outcome; (ii) participants were told that they had produced the outcome; (iii) participants were told that the confederate had produced the outcome. They found classical IB in the uncertain condition (i), where there was no explicit instruction concerning the author of the action. They also found that IB was increased when participants were led to believe an outcome was contingent on their own behaviour (ii), compared to a condition in which they were led to believe that the outcome was caused by the confederate (iii). These results suggest that when the conditions is uncertain participants use internal cues (e.g., sensorimotor information) to attribute agency, consistent with the idea that these internal cues receive higher weighting. However, if external cues to agency are compelling, these may over-ride the sensorimotor information.

2.2 NECESSARY CONDITIONS FOR INTENTIONAL BINDING

IB occurs only if certain conditions are satisfied. The vast majority of studies focused on the conditions that are necessary and sufficient in order for IB to happen. Haggard et al. (2002), for example, investigated the role of *temporal contiguity* and *temporal predictability*, by varying the delay between the key-press and the subsequent tone (250, 450, or 650 ms). Participants had to judge the time onset of the tone, both in separate fixed blocks - in which all trials involved a single interval - and in three additional blocks containing a randomized combination of all intervals. Authors observed that IB was modulated by *temporal proximity* and *predictability*: a stronger IB was observed for fixed than for randomized intervals and for short than long intervals. The fundamental role of causality has been suggested also by other studies (e.g., Engbert & Woschläger, 2007; Engbert, Woschläger & Haggard, 2008; Cravo, Claessens & Baldo, 2009; Moore, Lagnado, Deal & Haggard, 2009; Cravo, Claessens & Baldo, 2011). Recently, Kawabe, Roseboom & Nishida (2013) have shown that IB depends on a time window (starting from the onset of the action and extending over a certain period) in which the signals related to the action (i.e., internal agency cues) and its effect (effect-related signals) have to be integrated. If the delay between an action and its effect increases, the integration of the effect with the action would be less likely because this effect would occur outside this time window; as a consequence, the SoAg would be affected. In addition to causality, another important factor that needs to be present for the occurrence of IB is *intentionality* (see: Moore & Obhi, 2012 and Paragraph 2.3.3). For example, when participants do not directly experience the voluntary act of a movement (e.g., a key-press) but passively experience it, IB does not occur (e.g., Haggard et al., 2002; Wohlschläger, Engbert & Haggard, 2003). Taken together, both conditions – causality and intentionality - seem to play a key role in IB.

Other studies do not support this view. For example, Buehner and Humphreys (2009) have shown that the causal relation between an action and its consequence is more important than intentionality for the phenomenon to occur (see also: Buehner, 2012; 2015). In addition, reliable temporal relations also appear to be unnecessary, as temporal binding has been reported in studies employing unpredictable intervals between action and effect, including intervals longer than one second, well beyond the brief temporal window in which predictive forward models related to motor planning are thought to operate (e.g., Humphreys & Buehner, 2009; 2010; Ebert & Wegner, 2010; Poonian & Cunnington, 2013). However, these discrepancies seem to be related to methodological differences: indeed, these studies measured IB via numerical estimates or by asking participants to reproduce the interval between two event (see Chapter 3 for a detailed description of the current paradigms to measure IB).

Despite controversy over the underlying mechanisms, IB has been used as a proxy for the SoAg in several studies (for a review, see Moore & Obhi, 2012).

2.3 FACTORS MODULATING INTENTIONAL BINDING

As described in the previous sections, IB seems to arise from the same cognitive mechanisms responsible for the emergence of the SoAg. However, in order to fully disentangle the linkage between IB and SoAg, a further ***second step*** is required, that is ***to investigate whether the factors related to agency are also able to affect IB***. If this is the case, further supporting the notion of IB as an effective implicit measure of agency would be provided. Recent findings have indeed suggested that the IB effect, like the SoAg (e.g., Aarts et al., 2005; 2007; Wenke et al., 2010; Damen et al., 2014), can also be influenced by several contextual, situational and personal factors. The next section will examine the factors which contribute to shape IB in the attempt to shed light on the supposed link between IB and agency.

2.3.1 RESPONSIBILITY AND EMOTIONS

As mentioned in Chapter 1 (Paragraph 1.1.4) emotions have received little attention within SoAg field (for a review, see: Gentsch & Synofzik, 2014). Nevertheless, recent studies aimed to investigate how emotions modulate IB. Indeed, our actions typically aim at positive rather than negative outcomes and are reward-directed. Therefore, one might expect that IB should vary with the valence of action outcomes. For example, Moretto, Walsh et al. (2011) focused on the relation between voluntary action and both the moral and emotional consequences of action. They embedded the IB task within standard moral and economic dilemmas in order to understand how the context and effect of the action can modulate IB. Authors observed enhanced temporal compression when an action was followed by a moral rather than a merely economic outcome, suggesting that responsibility plays a crucial role for our SoAg. In addition, the binding of picture-effects towards actions was stronger for more than for less negative outcomes. In other words, people experience strong linkage of actions to their effects when actions are morally and emotively important, and produce important outcomes. However, opposite results have been shown by Yoshie and Haggard (2013) investigating whether SoAg in general – and IB in particular - might be altered by the emotional content of action outcomes (e.g., emotionally negative, positive and neutral sound). Contrary to Moretto, Walsh et al. (2011), reduced temporal binding between actions and consequences eliciting negative emotional vocalizations was observed (Yoshie & Haggard, 2013). Yoshie and Haggard (2013) have suggested that a possible explanation for this controversial pattern of results could be found in the experimental manipulation: indeed, in Moretto, Walsh et al. (2011) the moral and non-moral effects may have been by-products of a general influence of magnitude on arousal or salience, rather than an effect of valence, as in Yoshie and Haggard's study (2013). Support for Yoshie and Haggard's results comes then from another study in an economic context which showed reduced IB when participants lost money compared to when they gained or retained money (Takahata et al., 2012). Similarly, priming participants with positive pictures compared to neutral ones seems to lead to an increase of the IB effect (Aarts, Bijleveld, Custers, Dogge, Deelder et al., 2012).

Subsequently, Barlas and Obhi (2014) extended this research area trying to understand whether perceived pleasantness - a factor which is potentially shaped by cultural differences - can affect the IB. They tested western and non-western participants and examined the effect of pleasantness of action effects (e.g., consonant and dissonant piano chords) on both control ratings and IB. Authors made two main predictions: (i) perceived pleasantness of consonant chords would have produced higher feelings of control and liking ratings as well as stronger binding effect compared to the dissonant ones; (ii) as consonant and dissonant chords are based specifically on western tonal structure, a greater effect of consonance in the western group compared to the non-western group was hypothesized. As expected, both western and non-western groups showed greater control ratings for pleasant (consonant) compared to unpleasant (dissonant) outcomes. The IB effect, on the other hand, appeared to be stronger for the pleasant consonant compared to the unpleasant outcomes in the western group only. In other words, the western group showed stronger SoAg over more pleasant outcomes at both low and high levels of agency while the non-western group displayed the same effect only at the high level. This result is in line with other studies in literature showing that cultural differences in the degree of self-evaluations and self-enhancement become more evident with implicit measures, while explicit measures might not reveal any such difference (see: Barlas & Obhi, 2014). Therefore, agency may be differentially affected by the cultural background of participants.

2.3.2 PERSONALITY TRAITS AND INDIVIDUAL EXPERIENCES

In order to better understand whether IB is linked to agency, it is necessary to investigate other factors modulating the magnitude of the effect, such as personality traits (Hascalovitz & Obhi, 2015). For example, narcissistic traits are associated with increased dominance and egocentricity, and therefore one might expect that individuals characterized by this profile exhibit a high degree of agency and sense of control. Hascalovitz and Obhi (2015) tried to explore this aspect. Using the narcissistic personality inventory (NPI: Maxwell, Donnellan, Hopwood & Ackerman, 2011), a well-known index of sub-clinical narcissism in social psychological research, they recruited healthy participants and based on their scoring, they divided them into three groups: high, middle, and low NPI score. Results showed that different NPI scores were indeed associated with changes in the magnitude of IB. Namely, individuals with higher and middle NPI scores displayed levels of effect binding greater than those with low NPI scores. Overall, these results provide the first evidence that different scores on a personality trait are associated with differences in the degree of binding of effects.

Another type of intrinsic factor impacting on the SoAg via IB is the recall of personal episodes. For example, Obhi, Swiderski and Farquhar (2013) investigated whether activating memories of depression, associated with feelings of loss of control, alters the magnitude of IB, as compared to activating memories of the previous day, or a baseline condition in which specific memories were not activated. Results showed that IB was significantly weaker after remembering a depressing episode than in the other conditions, indicating that the memory of an episode characterized by a negative mood alters the IB effect. Also the perception of personal power appears to influence the IB effect, showing that IB is significantly affected by low-power perception (Obhi, Swiderski & Brubacher, 2012).

2.3.3 INTENTIONS AND BELIEFS

Intention attributions have been showed to modulate temporal perception of voluntary actions and their sensory effects (Wohlschläger, Engbert et al., 2003; Wohlschläger, Haggard, Gesierich, & Prinz, 2003; Moore, Teufel, Subramaniam, Davis & Fletcher, 2013; Poonian & Cunnington, 2013). For example, Wohlschläger Haggard et al. (2003) measured the estimated onset time of actions that participants either executed themselves or observed being executed by someone else or by a machine. In three experiments, the estimates of the machine actions always differed from those of self- and other-generated actions, whereas the latter two were indistinguishable. According to the Authors (Wohlschläger Haggard et al., 2003), this result could be due to the fact that participants usually attribute intentions to other biological agents but not to machines. Strother, House, & Obhi (2010) agree with this view: in their study participants performed the IB task in pairs and both participants were instructed to prepare and execute a key press during each trial, provided that the other participant had not pressed the key first. If participants were not the first to produce a press they were instructed to passively move their finger in concert with the other's press. Similar binding effect for self-generated and other-generated actions was observed, even when only one participant of the pair was instructed to plan and generate the action. These results are interpreted in the context of shared action representations: observing the act of another person activates the representations of these actions in the observer's brain which mediates binding (Strother et al., 2010). Furthermore, the temporal feature of intention (e.g., distal and proximal) impacts on IB, too (Vinding, Pedersen & Overgaard, 2013). Participants were instructed to act either immediately or to wait a certain time-interval before acting, when they experienced the intention to act. IB was significantly enhanced for distal (i.e., delayed) intentions compared to proximal intentions, indicating that the former leads to stronger SoAg. In a subsequent study (Vinding, Jenen & Overgaard, 2015), a series of delays between intention and action was included. Results showed that, again, delayed and proximal intentions have a different impact on IB. Indeed, the occurrence of both action and tone was reported earlier in the delayed conditions compared to the proximal conditions and this did not differ across delays for delayed intentions.

The perception of the sensory consequences of one's own actions is also modulated by *beliefs* about the cause of the sensory event. Indeed, IB is stronger when participants believe that they are responsible for the outcomes as compared to when they believed that another person is the cause (Desantis et al., 2011; Haering & Kiesel, 2012). These results, together with some other related studies (Aarts & van den Bos, 2011; Dogge, Schaap, Custers, Wegner & Aarts, 2012), clearly indicate that beliefs and IB are related.

2.3.4 OTHER TYPES OF INFLUENCES ON INTENTIONAL BINDING

Many other factors interact with our actions and contribute to shape agency. For example, our actions are often selected among different alternatives and we can freely choose what we desire; other times we decide on our own what to do, but we can also execute what other people tell us to do, for instance when we are at work. In other occasions, something unexpected happens and we are forced to inhibit what we were doing before that event. All these aspects characterize our actions and therefore have an impact on them.

Haggard and Cole (2007), for example, examined the influence of attention on IB. They considered a task in which participants were not informed which event to judge (either the action or the effect) until the end of the trial. This clearly prevented the participant from strategically attending to one of the two possible critical events (e.g., action or effect). They observed that IB was stronger when participants were unable to direct their attention to an action or an effect as compared to a condition in which they knew what to attend to. This result suggests that IB might not be dependent on focussed attention to a particular event.

When a voluntary action has to be inhibited at the very last moment Haggard, Poonian and Walsh (2009) observed that the usual temporal compression effect disappears and turns into a sort of repulsion. On the other hand, the magnitude of binding is greater when people have the possibility to choose between more than one options. Indeed, Barlas and Obhi (2013) varied the number of action alternatives (e.g., seven possible buttons compared to one and three possible button presses) that participants could select from and determined the effects on IB. Participants made self-paced button presses while viewing the classical Libet clock and reported the perceived onset time of either the button presses or consequent auditory tones. They observed that increasing the number of choices increased the sensation of agency. In addition, IB does not change between intentional and instructed actions (Wenke, Waszak, & Haggard, 2009), suggesting that we feel agency for actions and events both when we decide to perform them, and also when we are externally instructed to.

2.4 NEURAL BASES OF INTENTIONAL BINDING

Over the last decade many experiments have investigated IB from a behavioural point of view. Besides the studies which appealed a role of dopaminergic (Moore, Schneider, Schwingenschuh, Moretto, Bhatia et al., 2011) and glutammatergic pathways (Moore, Turner, Corlett, Arana, Morgan et al., 2011) (see next Paragraph), the underlying neural mechanisms are still not well understood, since only a few studies have explicitly considered the neural bases using different techniques within the cognitive neuroscience field.

The first study appeared in 2010 and was carried out by Moore, Ruge, Wenke, Rothwell and Haggard. Using theta-burst TMS they inhibited neural activity in two target regions, potentially implicated in IB: the sensorimotor hand area (SMHA) concerned with motor execution and sensorimotor feedback (Moore, Ruge et al., 2010; Weiller, Jüptner, Fellows, Rijntjes, Leonhardt et al., 1996) and the pre-SMA, known to be involved in cognitive aspects of internal movement generation and with the conscious urge to act (Fried, Katz, McCarthy, Sass, Williamson et al., 1991; Picard & Strick, 2001). As control site, they chose the sensory leg area. The Authors used the Libet clock method (Libet et al., 1983), but differently from other previous studies (e.g., Haggard et al., 2002; Haggard & Clark, 2003; Moore, Wegner et al., 2009), the voluntary action was followed by a cutaneous somatosensory stimulus (a mild shock) to the right little finger, instead of an auditory tone. Authors found that theta-burst TMS over only the pre-SMA significantly reduced the overall IB in respect to the control area (i.e., the sensory leg area). Testing each shift separately, Authors observed that pre-SMA stimulation only affected the effect binding component. Disruption of the SMHA with TMS did not significantly reduce binding relative to the control area. Taken together, the results of Moore, Ruge and colleagues (2010) suggest that pre-SMA contributes to the SogA. In order to overcome the fact that TMS did not explore effects of stimulating different sub-regions within the SMA complex, Kühn, Brass and Haggard run an fMRI study (2013). The Authors used a time interval paradigm to measure IB: participants had to judge the duration of the interval between an action (an active key press or a passive finger movement applied by the experimenter) and its effect (a tone) while being scanned. Differently from Moore, Ruge and colleagues (2010), the Authors observed a cluster in the left SMA proper, extending into the dorsal pre-motor cortex whose intensity activation correlated more strongly with judgment errors when performing an active movement rather than when the movement was passive. Further, Jo, Wittmann, Hinterberger and Schmidt (2014) adopted EEG in order to evaluate a possible correlation between IB and readiness potential. Authors found that self-initiated movements following negative deflections of slow cortical potentials (SCPs) resulted in a stronger binding effect, especially regarding the perceived time of the consequent effect. These results provide the first direct evidence that the early neural activity within the range of SCPs affects perceived time of a sensory outcome that is caused by intentional action. All together the present data highlight the crucial role played by frontal areas in IB.

Since the involvement of parietal regions in non-agency conditions using explicit measures (Fink et al., 1999; Farrer & Frith, 2002; Farrer et al., 2003), very recently Khalighinejad and Haggard (2015) investigated the contributions of both frontal and parietal areas to SoAg by combining tDCS and IB. Anodal stimulation of the left AG reduced effect binding, in line with other studies where AG activation is routinely associated with lack of agency, rather than with experience of positive agency (Farrer & Frith, 2002; Farrer, Frey et al., 2008; Sperduti et al., 2011). However, anodal stimulations over left DLPFC decreased IB, contrary to the fact that this area is normally thought to facilitate intentional action (Rowe, Hughes, Nimmo-Smith, 2010). No significant difference between cathodal and sham stimulations has been detected. In order to clarify the role of the DLPFC, in a subsequent study (Khalighinejad, Di Costa & Haggard, *in press*), Authors investigated whether such area may contribute to SoAg when participants select between multiple actions. Results found that anodal stimulation over DLPFC increased binding of actions towards outcomes, but only in tasks where participants endogenously selected between alternative actions.

2.5 THE CLINICAL SIDE OF INTENTIONAL BINDING

Another approach to study the potential link between IB and SoAg has been the characterization of the subjective experience of action in patients showing control and production deficits. The first study was conducted by Haggard, Martin, Taylor-Clarke, Jeannerod et al. (2003) in a group of schizophrenic patients and showed that the IB effect was significantly stronger in patients, with temporal intervals between actions and their consequence shorter than for controls. The findings of Haggard et al. (2003) have been then replicated by Voss, Moore, Hauser, Gallinat, Heinz et al (2010), using the modified probabilistic binding task implemented by Moore and Haggard (2008), in order to reveal the mechanisms responsible for the patients' deficits. They examined the contribution of *predictive* (Blakemore et al., 1998; Wolpert & Ghahramani, 2000; Blakemore et al., 2001) and *postdictive* signals (Wegner & Wheatley, 1999; Wegner, 2003). Results showed that schizophrenic patients lacked the *predictive* component of action awareness, showing a shift on 'action only' trials, regardless of the probability of tone occurrence. Importantly, the schizophrenic deficits in predicting the relation between action and effect were strongly correlated with severity of positive psychotic symptoms (i.e., delusions and hallucinations). Furthermore, the patients showed an exaggerated *retrospective* binding between action and tone, shifting the perceived time of action whenever the tone occurred, relative to when it did not occur. As such, their experience of agency appeared to be driven by immediate sensory evidence that a tone followed a particular action, without any reference to an internal model specifying the prior probability of a tone given an action. Conversely, in the control group, IB of actions towards tones arose almost entirely from predictive mechanisms. Therefore, the hyper-binding effect might have been due to an increase in the contribution of external agency cues, reflecting their reliance on retrospective mechanisms rather than predictive ones. These results could be explained referring to the *Cue Integration Framework* (Moore, Wegner et al., 2009; Moore & Fletcher, 2012; Synofzik et al., 2013). SoAg is dominated by the most reliable source of information. In schizophrenic patients, unreliable internal sensorimotor prediction may explain the stronger retrospective contribution to IB. No matter whether SoAg tasks are explicit or implicit, patients with schizophrenia are more likely than healthy controls to attribute the source of distorted or ambiguous visual feedback of an action to themselves (e.g., Daprati et al., 1997; Haggard et al., 2003; Synofzik et al., 2010; Voss et al., 2010; Maeda et al., 2012; Franck, Farrer, Georgieff, Marie-Cardine, Daléry et al., 2014; see also Paragraph 1.4.1). On the other hand, prodromal patients experiencing symptoms pointing towards a psychotic disorder but without a canonical diagnosis, show stronger predictive action binding (i.e., hyper-prediction) relative to controls (Hauser, Knoblich, Repp, Lautenschlager, Gallinat et al., 2011). This pattern of results suggests that the predictive deficits in IB could change during the progression of schizophrenic illness. The Authors suggested that these findings, hyper-prediction in the psychotic prodrome and hypo-prediction in schizophrenic illness, are consistent with recent models emphasising the role of gluttamatergic and dopaminergic pathways in the brain (Hauser et al., 2011). In fact, in the early stages of the disease, the excessive prediction is secondary to aberrant prediction error signalling, mediated by gluttamatergic pathways. This leads to excessively strong predictions. Subsequently, dysregulation of dopaminergic neurotransmission in the later stages of the disease adds noise to the prediction error signal and would explain the transition from excessive prediction in psychotic prodrome patients to disrupted/noisy predictions in patients with schizophrenia.

The hyper-binding effect observed in schizophrenic patients has also been induced in healthy controls following infusion of the drug ketamine (Moore, Turner et al., 2011), a useful drug model of schizophrenic illness since in healthy adults it produces a state similar to the disturbances of schizophrenia. This exaggerated effect was driven primarily by an increase in action binding, rather than effect binding. Subsequently Moore et al. (2013), used the probabilistic IB paradigm (Moore & Haggard, 2008; Voss et al., 2011; Hauser et al., 2011) to study the effects of ketamine on predictive action binding in healthy participants. Replicating previous results (Moore, Turner et al., 2011), ketamine appeared to significantly increase the magnitude of action binding – in particular the predictive contribution to action binding - an effect which closely resembles the performance of patients with prodromal symptoms of schizophrenia, reported in a previous study (Hauser et al., 2011). Therefore, ketamine may best reproduce a state resembling the psychotic prodrome, rather than established schizophrenic illness.

Given its potential as implicit measure of SoAg, IB has been adopted also to study disorders characterized by deficits in the performance or in the experience of willed action. For example, in 2010, Moore, Schneider et al. studied SoAg within the framework of PD, a motor pathology affecting voluntary motor control. Disturbances in willed behaviour in this disease are both a consequence of the disease itself, but also a common side-effect of dopaminergic treatment used to ameliorate the symptoms. Therefore, Authors were interested not only to understand how these patients experience agency but also to elucidate the role of DA in this phenomenon. Authors tested both healthy controls and patients ON and OFF dopaminergic medication on the same day. Results showed that both PD patients and healthy volunteers showed the IB effect but that the overall binding did not differ between PD patients OFF and healthy controls. This result suggests that PD itself is not associated with abnormal SoAg, since an increased of SoAg was present only in patients ON dopaminergic medication, indicating that changes in SoAg could be caused by dopaminergic medication used to treat the disease. Two possible explanations have been postulated by the Authors: first, the hyper-binding might have been linked to an overdosing of the ventral striatal DA system, that is crucial for instrumental learning. Indeed, in the earlier stages of the disease, DA in the dorsal striatum is more severely depleted than in the ventral striatum (Dauer & Przedborski, 2003). Therefore, cognitive functions supported by the dorsal striatum are improved by dopaminergic medication, while cognitive functions supported by the ventral striatum are worsened by dopaminergic medication because of the overdose. Second, the exaggerated binding found in PD patients ON medication could have been driven by a change in dopaminergic prediction error signalling, augmenting the strength of action-outcome associations. This hypothesis is also consistent with other data showing that IB is sensitive to an associative learning mechanisms where a key role is played by the prediction error (Moore, Dickinson & Fletcher, 2011). This hyper-binding effect is similar to that observed in schizophrenic patients (Haggard et al., 2003; Voss et al., 2010). In fact, in both diseases, there is a dysregulation of DA system and dopaminergic medication in PD patients is known to induce psychotic-like symptoms (Cummings, 1991). Later, in 2013, Wolpe, Moore, Rae, Rittman, Altena et al. studied an other group of patients characterized corticobasal syndrome (CBS) with multimodal brain imaging. Patients showed increased action binding only for the more affected hand and this effect was also correlated with the severity of alien limb and apraxia. Tone binding, on the other hand, was normal, suggesting a preservation of sensorimotor prediction for awareness of action. Structural neuroimaging analyses showed the behavioural variability in patients was related to changes in grey matter volume in pre-SMA, and changes in its underlying white matter tracts to prefrontal cortex. Moreover, changes in functional connectivity at rest between the pre-SMA and prefrontal cortex were proportional to changes in binding. These behavioural, structural and functional results converge towards the idea of a key-role of the frontal network for altered awareness and control of voluntary action in CBS.

Kranick, Moore, Yusuf, Martinez, LaFaver et al. (2013) investigated patients with psychogenic movement disorders (PMD), characterized by abnormal movements for which patients deny volition. Overall, the Authors demonstrated reduced action-effect binding in patients with PMD. Findings are also consistent with a recent study by Pareés et al. (2014), reporting both a loss of sensory attenuation in these patients and a subjective experience of being unable to control their motor symptoms. Diminished motor behaviour is also commonly reported in ASD (Gowen & Hamilton 2013). Specifically, motor difficulties in this population concern motor planning, monitoring and prediction. Sperduti, Pieron, Leboyer and Zalla (2014) tested IB using a time interval paradigm in a group of ASD people, observing that participants with ASDs exhibited reduced IB, suggesting an altered SoAg.

Taken all together, these results showed that IB represents an invaluable tool for the study of disorders of agency, suggesting specific changes in mechanisms of motor control and awareness of action for several major neurological and psychiatric disorders.

2.6 TAKE-HOME MESSAGE

A considerable number of studies have been undertaken in an effort to elucidate the intriguing relationship between IB and the SoAg (for a review, see: Moore & Obhi, 2012). In the previous sections the most relevant findings have been highlighted, helpful to understand why IB is considered an implicit measures of agency. From the literature review, it has been shown that IB might be explained by the same cognitive mechanisms underlying the SoAg. Specifically, the roles of *predictive* and *retrospective* processes in producing IB have been elucidated. In addition, different internal and external higher-order contextual factors have been proved to modulate the degree of IB. Not only IB was able to objectively describe essentials aspects of agency in healthy people, but also in clinical populations, providing a resourceful tool in clinical settings. It must be said that some researchers rather suggest to consider IB as a special case of general cause-effect processing (Buehner, 2015) and recommend great caution in interpreting it in terms of intentional processes. However, IB nowadays represents a promising tool to discover the most implicit aspects of agency, impossible to explore by means of explicit measures.

In the second part of the present thesis, the experimental results obtained by administering IB will be outlined.

PART II

THE EXPERIMENTS

CHAPTER 3

STUDY I

DEVELOPMENT OF A NEW EXPERIMENTAL PARADIGM TO ASSESS INTENTIONAL BINDING

3.1 INTRODUCTION

The first time Haggard and co-workers (Haggard et al., 2002) discovered the IB effect, the classical *Libet clock method* (Libet et al., 1983) was adopted. This method originally implemented by Libet and colleagues (1983) was conceived to study the relationship between the electrophysiological brain activity associated with voluntary movements and conscious intentions. Please, see Chapter 2 for a detailed description of both the methodology and procedure used to measure IB. Subsequent to Haggard's initial work (2002), Engbert, Wohlschläger, Thomas and Haggard (2007) introduced the *time interval* paradigm, a method to implicitly assess SoAg, aiming at directly capturing the relationship between action and effect. Participants had to estimate how long the interval between an action and its effect had lasted in milliseconds and these were recorded by an experimenter. As compared to the *Libet* *clock paradigm*, which requires temporal estimates based on the perceived time of a single event (i.e., the action and its effect separately), the *time interval* paradigm involves direct numerical judgements of the time interval between action and effect (e.g., Engbert et al., 2007; 2008; Cravo et al., 2009; Humphrey & Buehner, 2009; Kühn et al., 2013; Sperduti et al., 2014). This method has reproduced the basic properties of IB, such as its dependence on intentional action: in other words, the duration of the interval between voluntary action and its ensuing sensory effect is perceived as shorter than the interval between an involuntary movement and the same effect. However, this methodology is susceptible to a range of subjective biases (Poulton, 1979). For example, when asked to judge the interval between an action and its consequence, participants can give shorter estimates based on their beliefs, and not because they actually experienced them together (Cravo et al., 2011). Similar findings have also been obtained using a time interval *reproduction* task (e.g., Humphreys & Buehner, 2010; Poonian & Cunnington, 2013), where participants, after being exposed to temporal intervals between their own action and a subsequent tone, had to reproduce the intervals by holding down a key. Instead of using verbal estimates of the interval (e.g., Engbert et al., 2007; 2008; Cravo et al., 2009; Humphrey & Buehner, 2009; Kühn et al., 2013; Sperduti et al., 2014), motor responses are required.

Although the abovementioned methods are the most commonly adopted to investigate the IB and led to an increasing knowledge of it, other psychophysical methodologies have been introduced in the very last years. For example, Cravo et al. (2011) proposed a method based on *simultaneity judgments*, where participants were asked to rate whether a flash occurred at the same time as a tone. More in detail, participants were exposed to a tone after executing a voluntary action and a temporally independent flash, and had to judged whether the two stimuli (i.e., tone and flash) were simultaneous or not. IB was revealed when participants made 'synchrony' judgements for visual references occurring prior to the auditory consequence of movement, indicating that they perceived the later auditory tone to be synchronous with the earlier visual flash. The year after, Nolden, Haering & Kiesel (2012) introduced the method of *constant stimuli*, where participants had to compare a standard interval between a voluntary action and a visual effect with a tone. More in detail, they had to judge if the tone was shorter or longer than the interval between the key press and the visual stimulus. Also this method reproduced the classical IB effect.

Altogether the reviewed studies, using a number of different experimental paradigms, speak in favour of the existence of the IB effect, providing its validation as converging on a similar pattern of results, namely that action and effects are perceived as temporally attracted towards each other. However, *the Libet clock* method (Libet et al., 1983) offers several advantages in the study of IB. ***First***, as compared to the other methods - requiring direct numerical judgments of the time interval between action and effect (Engbert et al., 2007; 2008; Cravo et al., 2009;

Humphrey & Buehner, 2009; Humphreys & Buehner, 2010) - the *Libet clock* methodology allows for a disentangling between action binding (i.e., the shift of the action towards the tone) and effect binding (e.g., the shift of the tone towards the action). These two aspects of IB seem indeed to rely on different mechanisms (Moore, Ruge et al., 2010; Wolpe, Haggard et al., 2013; see Paragraph 2.1). ***Second***, mixed results have been reported regarding the question whether IB increases or decreases with increasing interval duration between voluntary action and its effect. Indeed, with the *Libet clock* methodology, IB decreases when the action–effect intervals increase (e.g., 450 and 650 ms), highlighting the role of causality in IB (see Paragraph 2.2). Differently, the *time interval* paradigm and the method of the *constant stimuli* have produced results with intervals up to 4 seconds (Humphreys & Buehner, 2009; Nolden et al., 2012). The *simultaneity method* proposed by Cravo et al. (2011), despite subjected to a smaller variability in IB estimates, does not allow to study the action binding since participants are usually asked only to evaluate the perceived time of auditory stimuli.

However, the *Libet clock* method has also its detractors. Indeed, although it has been successfully used in a large number of studies investigating IB (e.g., Haggard & Clark, 2003; Moore & Haggard, 2008; Moore, Wegner et al., 2009; Moore, Schneider et al., 2010; Barlas & Obhi, 2013; Wolpe & Rowe, 2014; Khalighinejad & Haggard, 2015), this paradigm has been the topic of several debates and has been criticized in many aspects (e.g., Gomes, 2002; Pockett & Miller, 2007). Although the aim of the present work goes beyond a mere description of every single methodological problem, the most important limitations could be ascribed to the following aspects. (i) The process of action control may be directly influenced by the clock structure. In particular, the participant may act in response to a particular clock positions, rather than in a truly self-generated manner (Engbert et al., 2007). (ii) When judging the position of a clock hand people could have systematic preferences for specific clock positions because of the predictability of number sequence. (iii) In addition, it has long been known that there are substantial inaccuracies in determining the timing and position of moving objects (Moutoussis & Zeki, 1997; van de Grid 2002). As an example, it has been shown that the comparison between a moving object (e.g., a clock hand) and an abrupt event (e.g., an auditory tone) can lead to spatiotemporal illusions, resulting in a moving object that is perceived as being ahead of its original position when the abrupt event occurs (Nijhawan, 1994; Cravo & Baldo, 2008). (iv) Finally, the rotating clock method could raise some problems with particular populations, like children and elderly people, given the fact that the acquisition of both clock and time knowledge changes and improves with age (Vakali, 1991). Indeed, the clock knowledge taps into a wide range of cognitive abilities, including EFs (Shulman, 2000). As many of these executive frontal processes are affected in pathological populations where the SoAg is 'compromised' (e.g., Haggard et al., 2003; Moore, Schneider et al., 2009; Sperduti et al., 2014), the clock method is far from being the best choice. In order to try to avoid all the above-mentioned limitations, the present work aims at developing a new and more suitable paradigm to assess IB, by taking the method developed by Soon et al. (2008) as a reference point. More in detail, Soon et al. (2008) were interested in studying the neural underpinnings underlying human conscious motor intentions. In order to investigate these processes, they decided to implement a modified version of the *Libet task* (Libet et al., 1983), by using letters instead of the classical clock. Taking inspiration from their method, to avoid the number sequence bias, a stream of familiar letters was used in the present study, in a non-alphabetic – therefore unpredictable - order. In this way, both the problem of the predictability given by the clock structure and the inaccuracy in time judgments occurring with rotating stimuli (van de Grind, 2002), can be avoided.

In this chapter the methods and the procedures are common to all the experiments included in the present thesis. Exceptions will be reported within each experimental chapter.

3.2 METHODS

3.2.1 PARTICIPANTS

Twenty-five participants (18 females; age range: 22 to 29; mean age in years: 23.37, SD: 1.74; education in years: 16.71, SD: 0.99) were enrolled in the experiment. All participants were right-handed, as measured by the Edinburgh Handedness

Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked of neurological and psychiatric pathologies. The study was conceived according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Padua. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study.

3.2.2 STIMULI, APPARATUS AND PROCEDURE

The experiment took place in a dimly illuminated room. The stimuli were presented on a 17-inch monitor controlled by a Pentium four PC programmed with E-Prime 2 (Psychology Software Tools, Pittsburgh, PA). The participants were seated comfortably in a chair at a viewing distance of 60 cm from the monitor. They were asked to passively observe a stream of unpredictable white, capital consonants at the centre of a black screen. In order to prevent the participants from responding immediately after the occurrence of the letters, a series of randomized white numbers was displayed before the letters' presentation (Figure 3.1). Each number and letter was presented separately and lasted for 150 ms, without time gaps in between. At the end of each trial, a set of response options (called 'response mapping') appeared on the screen. Five letters were presented on the screen, which included the target letter (i.e., the letter that was on the screen at the actual appearance of the event of interest), two letters immediately before and two letters immediately after the target letter during the stream of letters. All the letters within the response mapping were presented in a different random order. After each trial, the participants had to choose the correct consonant using the keyboard with their left hand. A 'response mapping' has been introduced in order to avoid the significant involvement of a memory retrieval component in the task. The experiment consisted of four baseline conditions (BCs) and six experimental conditions (ECs), for a total of ten conditions (Table 3.1).

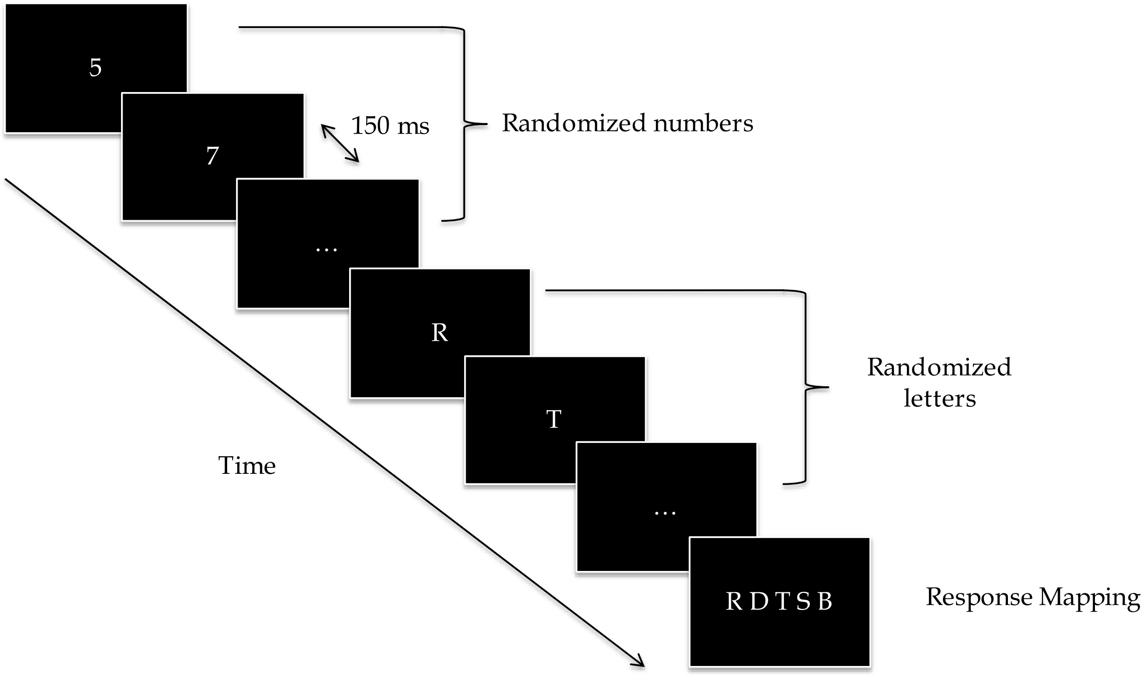


Figure 3.1. *Schematic illustration of the task structure. Participants passively observed a stream of numbers and letters that was updated every 150 ms. The frame with ". . ." here represents the continuous flow either of numbers or letters. After the appearance of the event of interest (e.g., voluntary action, involuntary action, tone, control tone) a response mapping was presented and participants chose the letter that was on the screen at the occurrence of the event of interest (e.g., voluntary action, involuntary action, tone, control tone).*

Table 3.1. *Conditions (Baseline and Experimental) and the judged event by the participants in each condition.*

Condition	Judged Event
Baseline Conditions	
1) Voluntary Action	Voluntary Action
2) Involuntary Action	Involuntary Action
3) Tone	Tone
4) Control Tone	Control Tone
Experimental Conditions	
5) Voluntary Action – 250 ms – Tone	Voluntary Action
6) Voluntary Action – 250 ms – Tone	Tone
7) Involuntary Action – 250 ms – Tone	Involuntary Action
8) Involuntary Action – 250 ms – Tone	Tone
9) Control Tone – 250 ms - Tone	Control Tone
10) Control Tone – 250 ms - Tone	Tone

Among the BCs, only one event occurred per condition (e.g., voluntary action, involuntary action, tone, control tone). For the ECs, two events occurred per condition. The time interval between the first event (the voluntary action, the involuntary action, or control tone) and the second event (tone) was set at 250 ms.

Among the BCs (Figure 3.2), only one event among voluntary action, involuntary action, tone, or control tone occurred per condition. The participants had to remember which consonant was on the screen when:

1) they made a free voluntary key-press with their right index finger (acting as a baseline for voluntary action condition). Here, participants had to wait until the letters' appearance before responding, in order to avoid response anticipation (i.e., a key-press performed immediately after the trial onset);

2) they felt their right index finger being passively moved down by a mechanical device (acting as a baseline for involuntary action condition), applied to the right index finger of the participants. The device was connected and activated by computer at a random interval after the trial's onset. When the computer gave the input, the key and, consequently, the right index finger moved down, giving the participant the same physical perception as the voluntary key-press;
3) they heard an auditory stimulus presented through headphones (1,000 Hz, 100-ms duration; baseline for tone condition: tone);
4) they heard another auditory control stimulus presented by headphones (same duration as the tone but with a different pitch; baseline for tone control condition: the control tone).

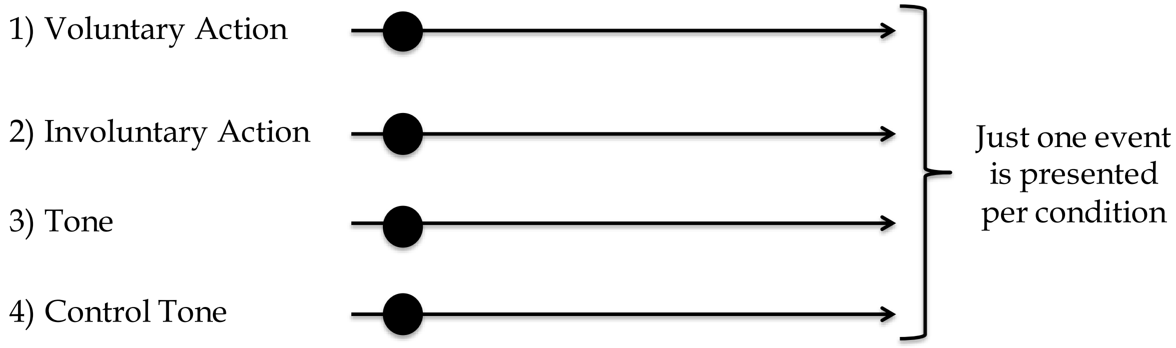


Figure 3.2. *Schematic representation of the BCs in which only one event (i.e., voluntary action, involuntary action, tone, control tone) occurred per condition. While viewing the stream of numbers and letters participants had to remember which consonant was on the screen when: (1) they made a voluntary key-press; (2) they felt their right index finger moved down passively; (3) they heard the tone; and (4) they heard the control tone.*

For the ECs, two events occurred per condition (Figure 3.3). The participants had to judge:

5) the onset of the voluntary action that produced the tone;
6) the onset of the tone caused by the voluntary action;
7) the onset of the involuntary action that was followed by the tone;
8) the onset of the tone activated by the involuntary action;
9) the onset of the control tone that was followed by the tone;
10) the onset of the tone activated by the control tone.

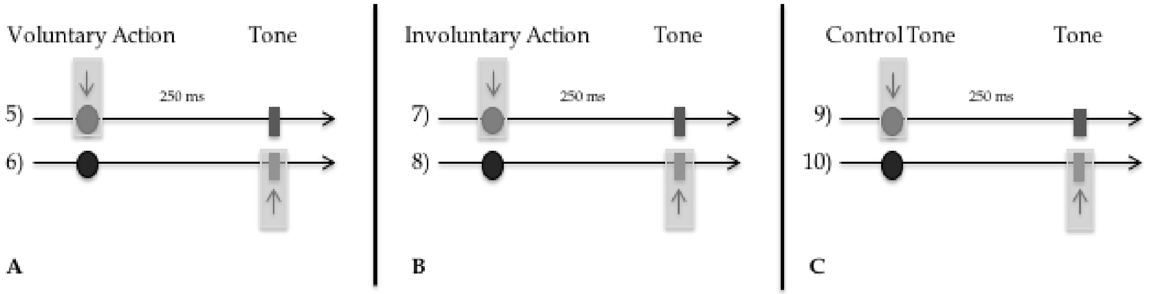


Figure* 3.3.** *Schematic representation of the Ecs.* ***(A) *Participants judged the letter that was on the screen either when they made the voluntary action (5) or heard the tone (6).* ***(B)*** *Participants judged the letter that was on the screen either when they felt their right index finger moved down passively (involuntary action; 7), or heard the tone (8).* ***(c)*** *Participants judged the letter that was on the screen either when they heard either the control tone (9) or the tone (10).*

Time interval between the first event (the voluntary action, the involuntary action, control tone) and the second event (tone) was set at 250 ms. Conditions involving the 'involuntary action' and 'control tone' were introduced as control conditions, in order to exclude the possible presence of IB in such conditions and investigate whether the results obtained for the voluntary action with the new paradigm were specific to SoAg. In all conditions, the stimuli were presented randomly, between 3 and 8 s after the trial onset. The stream of letters stopped randomly between 1.5 and 5 s after the event of interest. Thirty-three trials per condition were administered, for a total of 330 trials. The first three trials of each condition were discarded to allow for familiarization and were not included in the analysis. Each participant performed all of the conditions (BCs and ECs) in a different, random order over a single session.

3.2.3 DATA ANALYSIS

3.2.3.1 CALCULATION OF THE INTENTIONAL BINDING

For each trial, a judgment error (JE) was calculated, which is the difference between the actual time of occurrence of the judged event and the perceived time of its occurrence. A negative JE was interpreted as anticipatory awareness of events (i.e., the participants perceived the event happening *before* it really did), while a positive JE was interpreted as delayed awareness (i.e., the participants perceived the event happening *after* it really did). The obtained value could be 0 (the participant chooses the correct letter, that is the letter that was on the screen at the actual appearance of the event of interest); +1 (the participants chooses the letter that was immediately after the target letter); +2 (the participants chooses the second letter after the target letter); -1 (the participants chooses the letter that was immediately before the target letter); -2 (the participants chooses the second letter before the target letter). Each of these values was then multiplied by 150 (i.e., the actual duration of each letter on the screen) and then a final mean judgment error (mJE), including both negative and positive values, was calculated (Table 3.2). Baseline judgments usually vary widely both across people and groups (Haggard et al., 2002; Haggard et al., 2003) and may reflect individual strategies in the attention paid to the letters. In order to control for such individual differences, the differences between the mJE of an identical physical event in two different contexts (the BCs and ECs) were calculated (i.e., the perceptual shifts) by subtracting the mJE of each event in the BC (voluntary action, involuntary action, tone, or control tone) from the mJE of the same event in the EC. For example, the shift of the action towards the tone (i.e., action binding) was calculated by subtracting the mJE of the voluntary action in the BC from the mJE of the voluntary action in the EC, whereas the shift of the tone towards the action (i.e., effect binding) was found by subtracting the mJE of tone in the BC from the mJE of the same tone in the EC. Therefore, calculating the perceptual shifts was important to control for the cross-modal synchronization judgments, which differ widely across individuals. Finally, an overall binding measure (e.g., Haggard et al., 2002; Haggard & Clark, 2003) was also computed by combining the first (i.e., the action binding) and the second event (i.e., the tone binding). By calculating 250 ms - (action binding – effect binding), the obtained value represents the perceived linkage between an action and an effect, and provides an implicit measure of SoAg.

Table 3.2. *Schematic illustration to calculate IB*

Trial	**JE**	**JE * 150 ms**
1	0	0
2	0	0
3	0	0
4	0	0
5	-1	-150
6	-1	-150
7	-1	-150
8	0	0
9	0	0
10	0	0
11	1	150
12	1	150
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	-2	-300
21	1	150
22	1	150
23	1	150
24	0	0
25	0	0
26	0	0
27	0	0
28	0	0
29	1	150
30	1	150
31	0	0
32	0	0
33	-1	-150

3.2.3.2 STATISTICAL ANALYSIS

Analyses have been carried out by using both Statistical Package for Social Sciences (SPSS) and R software package (http://cran.r- project.org). Violin plots with a Kernel distribution applied were used to represent data (Allen, Erhardt & Calhoun, 2012).

To analyse data two main analyses were run:

1) paired-sample *t*-tests were used to compare the mJE of a certain event in the BC with the mJE of the same event in the EC. For example, the mJE of a voluntary action in the BC was compared with the mJE of the voluntary action in the EC;
2) in order to control for individual differences, perceptual shifts were calculated using repeated-measures Analysis of Variance (ANOVA) with 'type of context' (voluntary, involuntary, sensory) and the 'judged event' (either the first or the second) as within-participants factor. Greenhouse-Geisser correction was applied to the degrees of freedom of F statistics when the Mauchly's Test of Sphericity showed that the sphericity assumption was violated (alpha level: $p < 0.05$). Post hoc comparisons were then used to explore the means of interest and Bonferroni correction for multiple comparisons was applied (alpha level: $p < 0.05$).

3.3 RESULTS

Table 3.3 summarizes the mJEs, the perceptual shifts, and the overall binding. Using paired-sample *t*-tests, significant differences were only observed within the context of voluntary action [voluntary action in the BC vs. voluntary action in the EC, t_{24} = - 4.29, $p < 0.001$, 95% confidence intervals (CI): -79.09, -27.71, mean: -53.4 ms; tone in the BC vs. tone in the EC, $t_{24} = 5.86$, $p < 0.001$, 95% CI: 52.19, 109.01, mean: 80.6 ms] (Figure 3.4). Actions were therefore perceived later when followed by a tone, as compared to the BC, in which only the action was presented (Figure 3.4, left). Differently, a tone was perceived earlier when it was activated by the action, in comparison to a BC where only the tone was presented (Figure 3.4, right).

***Table* 3.3.** *mJEs, perceptual shifts and overall binding.*

	Judged Event	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Baseline Conditions				
1) Voluntary Action	Voluntary Action	20.8 ± 12.49		
2) Involuntary Action	Involuntary Action	62.6 ± 12.89		
3) Tone	Tone	41.2 ± 11.14		
4) Control Tone	Control Tone	35 ± 9.69		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	74.2 ± 15.43	53.4 ± 12.45	116 ± 18.59
6) Voluntary Action - Tone	Tone	-39.4 ± 12.64	-80.6 ± 13.77	
7) Involuntary Action - Tone	Involuntary Action	65.4 ± 11.77	2.8 ± 7.81	222.8 ± 18.38
8) Involuntary Action - Tone	Tone	16.8 ± 18.22	-24.4 ± 17.65	
9) Control Tone - Tone	Control Tone	25.2 ± 9.68	-9.8 ± 9.11	235.4 ± 18.53
10) Control Tone - Tone	Tone	16.8 ± 11.77	-24.4 ± 14.99	

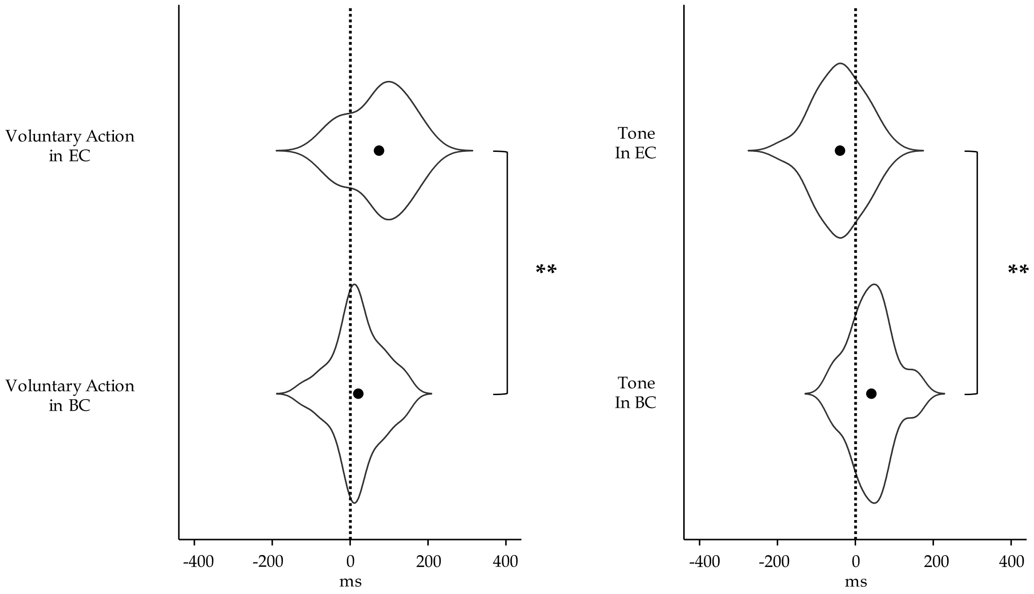


Figure 3.4. *Violin plots representing the distribution of each participant's mJE. The dashed lines stand for the actual onset of the event of interest. The black dots represent the mJE of the whole sample. On the* ***left*** *side, differences in the mJE of voluntary action in BC vs. EC are depicted. Here participants perceive the onset time of voluntary action later when it is followed by the tone (voluntary action in EC), as compared to the BC in which only the action is presented (voluntary action in BC). On the* ***right*** *side, differences in mJE of tone in BC vs EC are represented. Here, participants perceive the onset time of the tone earlier when it is activated by the voluntary action (tone in EC), in comparison to the BC where only the tone is presented (tone in BC). ** indicates the significant difference between BC and EC (p < 0.001)*

In order to calculate the perceptual shifts repeated-measures ANOVA was run. First, no main effect of 'type of context' was found, $F(2, 48) = 0.17$, $p = 0.846$, $\eta^2_p = 0.074$, while the effect of the 'judged event' was significant, $F(1, 24) = 19.03$, $p < 0.001$, $\eta^2_p = 0.442$, with a shift of the first event towards the second (15.47 ms; 95% CI: 1.85, 29.08) and vice versa (-43.13 ms; 95% CI: -67.37, -18.89). In addition, a significant interaction between these two factors emerged, $F(2, 48) = 17.74$, $p < 0.001$; $\eta^2_p = 0.425$ (Figure 3.5). We thus conducted a *post-hoc* analysis applying Bonferroni correction for multiple comparisons, in order to examine the interaction in more detail. The *post-hoc* analysis revealed that the difference between the first and the second event judged was only significant in the case of voluntary action ($p < 0.001$). In addition, concerning the first judged event, a significant difference was observed for voluntary action in comparison with the involuntary action ($p = 0.001$) and the control tone ($p = 0.001$). Involuntary action and control tone were not significantly different ($p = 0.849$). Significant differences also emerged when comparing the second judged event (e.g., tone) ('voluntary action context' vs. 'involuntary action context', $p = 0.006$; 'voluntary action context' vs. 'sensory context', $p = 0.002$). The 'involuntary action context' and the 'sensory context' were not significantly different ($p = 1.000$). Such interaction occurred because voluntary actions led to a perceptual shift of action towards tone and vice versa, whereas this effect was reduced for the involuntary action context and for the sensory context. Additionally, the repeated-measures ANOVA found a significant effect of the overall binding (i.e., the perceived linkage between action and effect), $F(2, 48) = 17.74$, $p < 0.001$, $\eta^2_p = 0.425$. *Post-hoc* comparisons showed a significant difference in both the voluntary and involuntary contexts ($p < 0.001$). In addition, the 'voluntary context' and the 'sensory context' ($p < 0.001$) were also significantly different. No significant differences were detected between the 'involuntary context' and the 'sensory context' ($p = 1.000$).

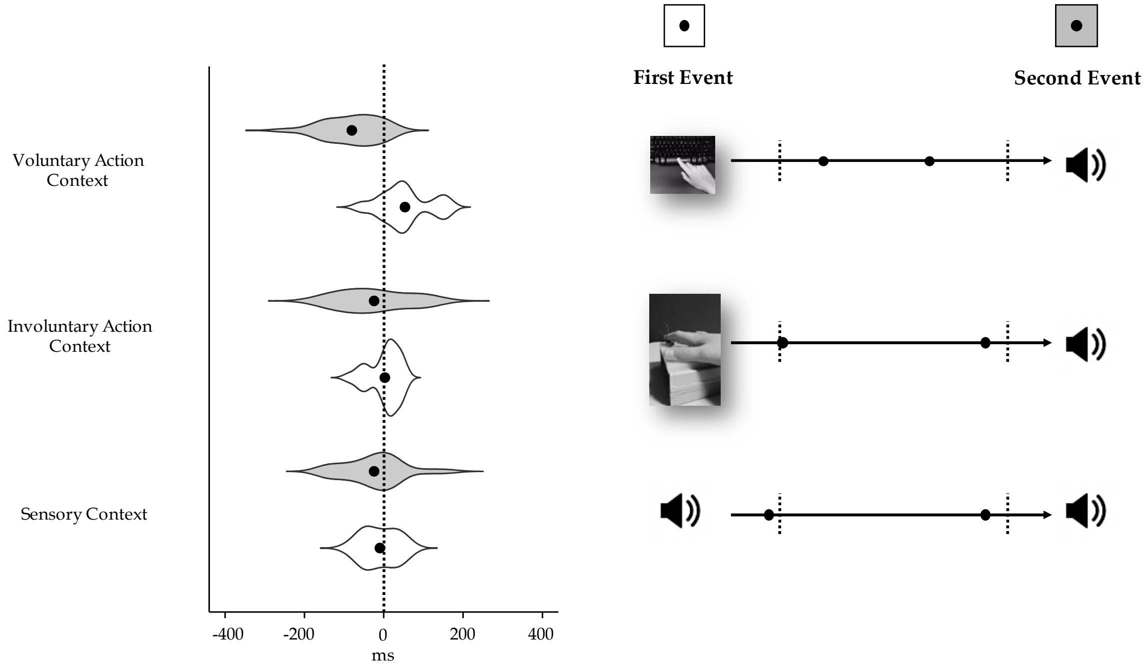


Figure 3.5. *On the **left** side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the perceptual shift of the first event towards the second one (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the perceptual shift of the second event towards the first one (i.e., the tone or effect binding). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the **right** side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the temporal compression occurs only within the voluntary context.*

In summary, temporal compression (IB effect) was only evident in the context of voluntary action. The overall binding data indicate that the participants perceived the interval between their action and its effect as significantly shorter than it really was, although no direct judgment of the time interval duration was requested.

Overall, results revealed that, when participants were actively causing the beep (i.e., the tone), which was always presented 250 ms after their voluntary action, the onset of the voluntary action was perceived as occurring later, as if the action was 'attracted' towards the tone. Analogously, the tone onset was perceived as 'bound' to the voluntary action. This temporal compression phenomenon was only present in the case of voluntary action; when the beep followed the involuntary action or another control beep (control tone), such compression did not occur.

3.4 DISCUSSION

The aim of the present study was to develop a new and reliable paradigm in order to study IB. In line with other studies in literature (e.g., Haggard et al., 2002; Moore, Wegner et al., 2009; Engber et al., 2007; 2008), the results reported here show that only voluntary actions were perceived as occurring later in time than they really were (i.e., as more adjacent to the following tone in temporal terms); on the other hand, tones were perceived as occurring earlier than they really were (i.e., closer to actions in time). Such temporal compression was limited to the context of voluntary condition, adding evidence to the fact that IB can be considered a valid implicit measure of agency. Indeed, no robust temporal compression and perceptual shifts occurred within the two control conditions, namely the involuntary and the sensory contexts. We considered these results as a proof of the IB effect.

With this new paradigm some of the methodological limitations of other approaches to IB (see Introduction) seem to be circumvented. For example, with respect to the *time interval* paradigm (Engbert et al., 2007; 2008; Cravo et al., 2009; Humphrey & Buehner, 2009; Humphreys & Buehner, 2010), the method described here does not only provide an overall measure of binding - like the time interval approach - but also and most importantly allows for a disentangling of action and effect binding. Indeed, these perceptual shifts seem to depend on different mechanisms (Wolpe, Haggard et al., 2013), and therefore it is preferable to obtain separate values for action end effect binding. Regarding the *Libet clock* paradigm (Libet et al., 1983), although it is the most used approach in the SoAg field, several aspects are still problematic (e.g., Gomes, 2002; Pockett & Miller, 2007). With the method proposed here, the most relevant issues have been overcome (e.g., predictability of number sequence). In addition, and most importantly within the context of the present thesis, the present methodology may be adopted to implicitly study agency in special populations (e.g., children, elderly, patients), who were 'untestable' before because of the confounders linked to the Libet clock methodology. We think that this paradigm might be applied for future research on IB, representing a reliable alternative to the methods used so far. This methodological advance will be used in the following experimental studies to answer other outstanding and open questions within the SoAg field.

CHAPTER 4

STUDY II

THE SENSE OF AGENCY ACROSS THE LIFESPAN

4.1 INTRODUCTION

Craik and Bialystok (2006) stated that "*there is a symmetry to our physical lives: we are independent and robust in youth and middle age, but dependent and frail in infancy and old age*". A similar patter of vulnerability across the lifespan has been also identified in our brain. Indeed, there is evidence of dramatic age-related modifications in our frontal cortex (for a review, see: West, 1996), which seems to be the last cortical area to mature in children and among the first one to be impaired in aging (e.g., Fuster, 1993; Giedd et al., 1999; Raz, 2000; Casey et al., 2005). Changes in brain structure and functionality inevitably impact on cognitive abilities: among these, EFs, which are mediated by frontal lobes' integrity and activity (Stuss & Levine, 2002), are primarily affected by such age-related changes. A considerable body of research shows convincingly that there are systematic, age-related improvements in EFs during childhood and adolescence, coinciding with a growth spurts in the maturation of the frontal lobes (Zelazo & Müller, 2002; Anderson, Anderson, Northam, Jacobs & Catroppa, 2001). Likewise, a decrease of EFs during normal aging, even in the absence of pathologies, has been demonstrated (West, 1996; de Luca, Wood, Anderson, Buchanan, Proffitt et al., 2003; Fisk & Sharp, 2004; Zalazo, Craik & Booth, 2004). Even more importantly in light of the present work, EFs are intimately linked to the concept of the SoAg. As a matter of fact, SoAg is defined as the ability of planning and controlling actions and through them the consequences in the external environment (Haggard & Tsakiris, 2009; see also Chapter 1). Therefore, SoAg is entitled to belong to the larger 'EFs family' supported by the frontal lobes. Indeed, the experience of agency requires (i) a plan to perform a goal-directed action and (ii) the identification of the consequences of our behaviour in the external world, while avoiding and inhibiting erroneous and maladaptive behaviours. With this in mind, one might expect that the SoAg follows an inverted U-shaped curve when considered across the lifespan. Up to now, the vast majority of investigations within the SoAg field has mainly focused on its cognitive and neural bases in healthy people and pathological populations (e.g., David et al., 2008; Moore & Obhi, 2012). However, how this capacity changes across the lifespan has been neglected so far. This represents an open and important issue to be explored, given the impact of SoAg in social and legal aspects of life. In fact, SoAg implies individual responsibility for the consequences of our own actions (Moll, Oliveira-Souza, Garrido, Bramati, Caparelli-Daquer et al., 2007; Frith, 2013, 2014) and in many countries, the law requires that a person is fully responsible and aware of the consequences of his/her actions (Moretto, Walsh et al., 2011; Haggard & Chambon, 2012; Frith, 2013; 2014). However, there are some exceptions to this 'rule'. For example, if the agent is a child, this feeling of being responsible for action consequences may not emerge in the same way as for healthy adults. Indeed, below a certain age, children are not considered responsible for their actions: the minimum age of responsibility is the topic of important legal debates and varies from 7–18 years old (Frith, 2013). The general idea is that children may not be considered as totally responsible for their own actions and consequently not fully entitled 'agents' since their frontal lobes are not completely matured (Moll et al., 2007; Mackintosh, 2011). In the same way, healthy elderly could 'loose' their agency: cognitive skills, motor and sensory speed and many other factors vary across lifespan and might impact people's feeling of agency (e.g., Baltes & Lindenberger, 1997; Li, Lindenberger, Hommel, Aschersleben, Prinz et al., 2004). A question that arises naturally is: how does agency present itself in these two populations? A study conducted by Metcalfe, Eich and Castel (2010) tried to resolve this issue, studying in particular the different metacognitive awareness of agency across the lifespan. They observed that young adults were the most sensitive to discrepancies in control over their actions compared to both children (8–10 years old) and older adults (mean age 75), suggesting that agency might follow a possible developmental trend. More recently, van Elk, Rutjens & van der Pligt (2015) investigated the development of illusory control and the SoAg in 7-12-year-old children and in young adults. They observed that the illusion of control decreased as children got older. In other words, adults tended to underestimate their actual performance, whereas children overestimated it. Conversely, the SoAg seems to be more stable across development. Indeed, in line with adult studies (e.g., Daprati et al., 1997; Farrer et al., 2003; Aarts et al., 2009), agency ratings for both adults and children were similarly affected by the congruence between performed and observed outcomes (e.g., when a temporal delay or spatial deviation was introduced). However, this last study did not consider older participants. Although both Metcalfe et al's study (2010) and van Elk's et al's (2015) studies were the first to investigate age-related differences in the SoAg, these investigations used explicit agency measures, which may be influenced by different biases, such as prior expectations and beliefs about the task (e.g., Gawronski et al., 2007). As seen in Chapter 1, these explicit measures say very little about the experience of agency, since they do not reflect or capture the feeling of agency that accompanies normal voluntary actions. Other investigations tried to shed light on the emergence of agency, but focussing only on a particular developmental period or considering other aspects related to the agency phenomenon. For example, studies focusing on the sense of the body (body awareness; for a review, see Rochat, 2010) and on the phenomenon of action-effect learning (Elsner & Aschersleben, 2003; Eenshuistra, Weidema & Hommel, 2004; Hauf, Elsner & Aschersleben, 2004; Elsner, 2007) have shown that (i) the sense of body is already present in the first few months of life. This would suggest that infants can indeed be considered agents in the world because they begin to gain control of their bodies and move voluntarily in the environment; (ii) action-effect learning seems to emerge even before the first year of age (Verschoor, Weidema, Biro & Hommel et al., 2010) even if other studies suggest that only 5-year-old children can report a mature experience of agency (Shultz, Wells & Sarda, 1980; Astington, 2001; Lang & Perner, 2002). However, all of the aforementioned studies are characterized by two important limits: (i) they contradict the fact that volition, strictly linked to the concept of agency, matures late during an individual's development (Haggard, 2008), when the brain, in particular the frontal areas, reaches its full maturation (Giedd et al., 1999) and (ii) they focus on low-level processes implicated in agency, which are considered to be necessary conditions for the appearance of goal-directed behaviour and action control, but are not sufficient to explain SoAg's complexity, which is rather a more sophisticated process. No similar studies have focused on elderly people.

The general purpose of the present work is therefore to explore how IB, as an implicit measure of SoAg, can develop across the lifespan, by overcoming the limits of the verbal reports that characterize the explicit level of SoAg. Based on the facts that (i) frontal lobes and EFs seem to play a crucial role in agency and that (ii) they seem to follow an inverted U-shaped curve across the lifespan, we expect that children and elderly do not present the classical IB effect - as reflected by a reduced temporal compression between a voluntary action and the ensuing sensory effect -

as compared to the young adults due to their immature and impaired frontal cortical functioning, respectively.

4.2 METHODS

4.2.1 PARTICIPANTS

A total of sixty participants were recruited for this study. According to their age, they were subdivided into three subgroups: (1) a new group of twenty young adults (15 females; age range: 22 to 30; mean age in years: 23.75, SD: 2.53; education in years: 16.67, SD: 0.98); (2) twenty children (16 females; age range: 8 to 11; mean age in years; 10.05, SD: 0.94; education in years: 5.1, SD: 0.85); (3) twenty elderly (12 females; age range: 66 to 76; mean age in years: 69.75, SD: 3.39; education in years: 15.1, SD: 4.14). All participants were right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked neurological, neuropsychological and psychiatric pathologies. On the basis of these exclusion criteria, two elderlies (Mini Mental State Examination, MMSE < 24; Folstein, Folstein & McHugh, 1975) were excluded. In addition, one child was omitted because he was not able to finish the task. The final cohort consisted of 19 children (15 females; age range: 8 to 11, mean age in years: 10, SD: 0.94; education in years: 5.05, SD: 0.85) and 18 elderlies (11 females; age range: 66 to 76, mean age in years: 69.78, SD: 3.21; education in years: 14.78, SD: 4.25). The study was conceived according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Padua. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study. Informed consent for children was obtained from parents.

4.2.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Study I (Chapter 3). In this present study, associations between the measures of IB (i.e., overall IB, perceptual shifts) and cognitive abilities were analysed using non-parametric correlations (Spearman's rank correlation coefficient).

4.2.3 NEUROPSYCHOLOGICAL MEASURES

Children and elderly received basic neuropsychological screenings in order to exclude participants with cognitive issues, which might interfere with the task. The neuropsychological evaluation of children included assessment of: (i) problem solving and abstract reasoning using the Coloured Progressive Matrices (Italian standardization: Pruneti, Fenu, Freschi, Rota, Cocci et al., 1996); (ii) sustained and selective attention (Bells Test: Biancardi & Stoppa, 1997); (iii) divided attention (Trial Making Test: TMT; forms A, AB, and B; Scarpa, Piazzini, Presenti, Brovedani, Toraldo et al., 2006). The tests administered to elderly included: (i) the MMSE; (ii) the Digit Span for memory assessment (included in the Brief Neuropsychological Examination 2; BNE-2; Mondini, Mapelli, Vestri et al., 2011); (iii) TMT-A and TMT-B to assess the cognitive domain of attention and EFs (always included in the BNE-2); (iv) the Frontal Assessment Battery to evaluate frontal lobe functions and motor skills (FAB: Appollonio, Leone, Isella, Consoli, Villa et al., 2005).

4.3 RESULTS

4.3.1 RESULTS I: YOUNG ADULTS

Table 4.1 summarizes the mJEs, perceptual shifts, and overall binding. In order to calculate the perceptual shifts repeated-measures ANOVA was run. First, no main effect of 'type of context' was found, $F(2, 38) = 1.59$, $p = 0.216$, $\eta^2_p = 0.077$, while the effect of the 'judged event' was significant, $F(1, 19) = 31.94$, $p < 0.001$, $\eta^2_p = 0.627$, with a shift of the first event towards the second (22.58 ms; 95% CI: 7.66, 37.51) and vice versa (-55.42 ms; 95% CI: -81.74, -29.09). In addition, a significant interaction between these two factors emerged, $F(2, 38) = 21.37$, $p < 0.001$; $\eta^2_p = 0.529$ (Figure 4.1). We thus conducted a *post-hoc* analysis applying Bonferroni correction for multiple comparisons, in order to examine the interaction in more detail. Concerning the first judged event (i.e., the shift of the first event towards the second one), a significant difference was found for voluntary action in comparison with involuntary action ($p < 0.001$) and control tone ($p < 0.001$). Involuntary action and control tone were not significantly different ($p = 0.178$). Significant differences also emerged when comparing the second event (e.g., tone) ('voluntary action context' vs 'involuntary action context', $p = 0.034$; 'voluntary action context' vs 'sensory context', $p = 0.003$). Tone following the involuntary action was not significantly different as compared to the tone following the control tone ($p = 1.000$). The interaction occurred because voluntary actions led to a perceptual shift of action towards tone and vice versa, whereas this effect was significantly reduced for the involuntary action context and for the sensory context. In addition, the repeated-measures ANOVA detected a significant effect of the overall binding (i.e., the perceived linkage between action and effect), $F(2, 38) = 17.42$, $p < 0.001$, $\eta^2_p = 0.478$. *Post-hoc* comparisons showed a significant difference in both the voluntary and involuntary contexts ($p < 0.001$). In addition, the 'voluntary context' and the 'sensory context' ($p < 0.001$) were also significantly different. No significant differences were observed between the 'involuntary context' and the 'sensory context' ($p = 1.000$). In summary, temporal compression (i.e., the IB effect) was only evident in the context of voluntary action. The overall binding data indicate that the participants perceived the interval between their action and its effect as significantly shorter than it really was, although no direct judgment of the time interval's duration was requested.

Table 4.1. *mJEs, perceptual shifts and overall binding in young adults.*

	Event Judged	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Baseline Conditions				
1) Voluntary Action	Voluntary Action	10.5 ± 61.15		
2) Involuntary Action	Involuntary Action	70 ± 70.52		
3) Tone	Tone	53 ± 50.51		
4) Control Tone	Control Tone	48 ± 46.58		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	88.5 ± 76.64	78 ± 51.03	70.25 ± 73.13
6) Voluntary Action - Tone	Tone	-38.75 ± 61.62	-91.75 ± 66.91	
7) Involuntary Action - Tone	Involuntary Action	78.25 ± 13.52	8.25 ± 38.94	187.25 ± 105.2
8) Involuntary Action - Tone	Tone	10.5 ± 94.51	-42.5 ± 90.82	
9) Control Tone - Tone	Control Tone	29.5 ± 48.12	-18.5 ± 43.8	217 ± 111.05
10) Control Tone - Tone	Tone	21 ± 62.78	-32 ± 65.28	

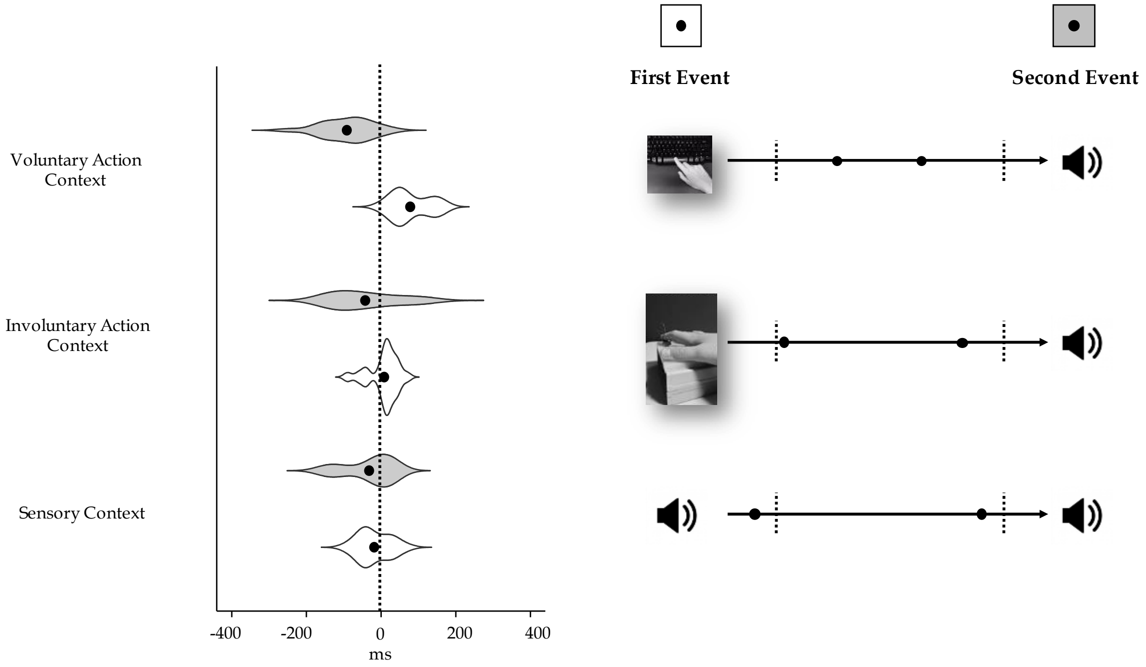


Figure 4.1. *On the* ***left*** *side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first event (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the tone). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the temporal compression occurs only within the voluntary context.*

Overall, our results revealed that, when participants were actively causing the beep (i.e., tone), which was always presented 250 ms after their voluntary action, the onset of the voluntary action was perceived as occurring later, as if the action was 'attracted' towards the tone. Analogously, the tone onset was perceived as 'bound' to its voluntary action. This temporal compression phenomenon was only present in the case of voluntary action; when the beep followed the involuntary action or another control beep, such compression did not occur.

4.3.2 RESULTS II: CHILDREN

All participants had an Intelligence Quotient above 100 and obtained normal scores on the TMT and Bells Tests. Means and SDs for all the neuropsychological measures are presented in Table 4.2.

Table 4.2. *Mean and SD of neuropsychological measures in children.*

	Mean	SD
Bells - Accuracy	128.35	8.14
Bells - Rapidity 30s	60.76	14.83
TMT-A	3.17	1.2
TMT-B	2.83	1.15
TMT-AB	3.06	1.16
CPM	113.85	11.93

SD: standard deviation; TMT: Trial Making Test; CMP: Coloured Progressive Matrices.

Table 4.3 presents children's mJEs, perceptual shifts and overall binding. As we did for results of Study I (Chapter III), we first compared the mJE of each event in the BC with the mJE of the same event in the EC using paired-samples *t*-tests. Significant differences were only detected in the perception of the tone in the ECs compared to the BCs, in which the tone was presented alone. However, these differences were not limited to the case of the voluntary action, $t_{18} = 4.23$, $p = 0.001$;

they also extended to the case of the two control conditions: involuntary action context, t_{18} = 3.40, p = 0.003, and sensory context, t_{18} = 3.7, p = 0.002. The tone (i.e., the effect/beep) was therefore perceived earlier when it followed the voluntary action, the involuntary action and the control tone, as compared to the BC. The perceptual shifts were also analysed in order to investigate IB. The repeated-measures ANOVA revealed no effect of 'type of context', $F(2, 36) = 0.107$, $p = 0.89$, $\eta^2_p = 0.006$, except for a main effect of the 'judged event', $F(1, 18) = 19.0$, $p < 0.001$, $\eta^2_p = 0.514$, with a shift of the first event towards the second one (1,23 ms, 95% CI: -13.29, 15.75) and vice versa (-51.75 ms, 95% CI: -70,47, -33.04). The interaction between the two factors was not significant, $F(2, 36) = 1.39$, $p = 0.26$, $\eta^2_p = 0.072$ (Figure 4.2), indicating that no temporal compression occurred for the voluntary action as compared to the other control conditions. When considering the overall binding, no differences were observed among the three contexts ('voluntary action', 'involuntary action' and the 'sensory context'), $F(2, 36) = 1.39$, $p = 0.26$, $\eta^2_p = 0.072$. The results showed that no IB was present in the 10-year-old children. Although a sort of minimal temporal compression seemed to exist in the case of voluntary action, it did not reach significance, when compared to the two control conditions. In addition, Spearman correlational analyses were conducted to examine the possible relationship between the implicit SoAg and neuropsychological measures. The only significant result emerged between the total temporal compression within the voluntary context and the TMT-A, $r = 0.467$, $p = 0.044$. The higher the score at the

TMT-A is, the larger the overall binding's value (i.e., reduced SoAg).

Table 4.3. *mJEs, perceptual shifts and overall binding in children.*

	Judged Event	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Baseline Conditions				
1) Voluntary Action	Voluntary Action	-20.79 ± 68.01		
2) Involuntary Action	Involuntary Action	82.63 ± 46.92		
3) Tone	Tone	78.16 ± 23.05		
4) Control Tone	Control Tone	81.58 ± 48.13		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	-5.79 ± 79.09	15 ± 76.08	170.26 ± 98.9
6) Voluntary Action - Tone	Tone	13.42 ± 70.77	-64.74 ± 66.7	
7) Involuntary Action - Tone	Involuntary Action	73.68 ± 59.55	-8.95 ± 43.48	211.05 ± 90.79
8) Involuntary Action - Tone	Tone	30.26 ± 60.72	-47.89 ± 59.82	
9) Control Tone - Tone	Control Tone	79.21 ± 34.65	-2.37 ± 51.22	209.74 ± 70.79
10) Control Tone - Tone	Tone	35.53 ± 53.98	-42.63 ± 50.2	

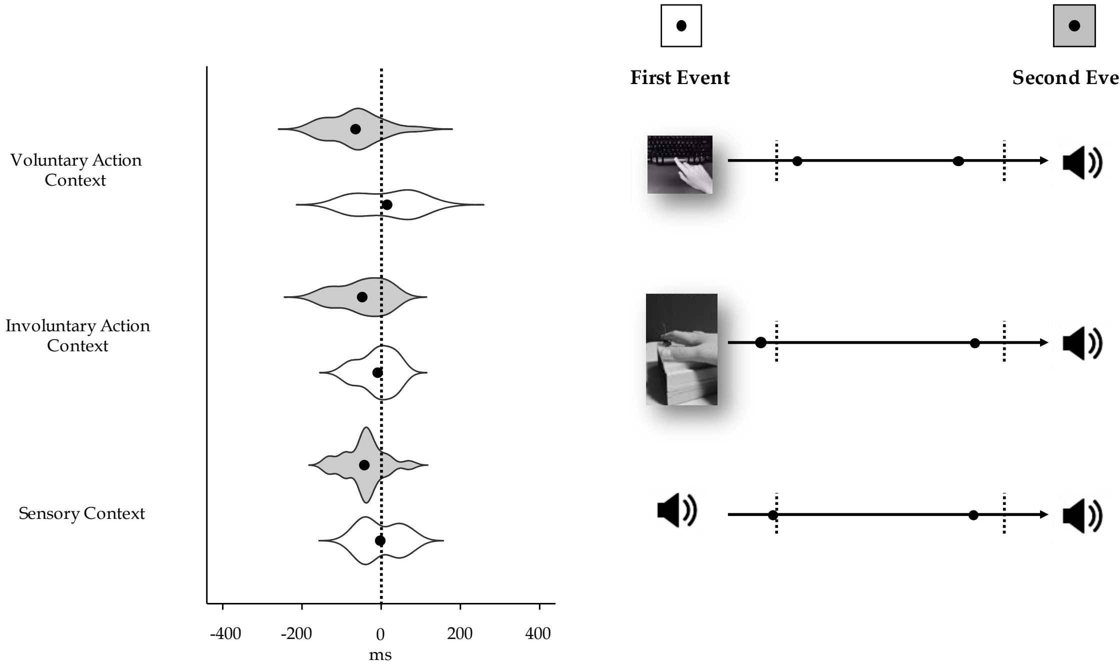


Figure 4.2. *On the* ***left*** *side, violin plots representing the distribution of each child's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first event (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the tone). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, temporal compression is not significantly different across the contexts (voluntary, involuntary and sensory context).*

4.3.3 RESULTS III: ELDERLY

All participants included in the final sample obtained normal scores on neuropsychological tests. Means and SDs for all the neuropsychological measures are presented in Table 4.4.

Table 4.4. *Mean and SD of neuropsychological measures in elderly.*

	Mean	SD
MMSE	29.11	1.02
Digit Span	6.00	0.84
TMT-A	33.22	10.3
TMT-B	102.12	48.46
FAB	17.28	0.96

SD: standard deviation; MMSE: Mini Mental State Examination; TMT: Trial Making Test; FAB: Frontal Assessment Battery.

Table 4.5 presents their mJEs, perceptual shifts and overall binding. As for children, we compared the mJE of each event in the BC with the mJE of the same event in the EC using paired-samples *t*-tests. Again, significant differences were only found in the perception of the tone in the ECs compared to the BCs. These differences were not limited to the case of the voluntary action, $t_{17} = 2.11$, $p = 0.05$; they also extended to the case of the two control conditions: involuntary action, $t_{17} = 6.25$, $p < 0.001$, and control tone, $t_{17} = 3.86$, $p = 0.001$. The tone was therefore perceived earlier when it followed the voluntary action, the involuntary action, or control tone, as compared to the BC where only the tone was presented. Perceptual shifts were also analysed in order to investigate IB. The repeated-measures ANOVA revealed a significant main effect of both 'type of context', $F(2, 34) = 13.97$, $p < 0.001$, $\eta^2_p = 0.451$ and the 'judged event', $F(1, 17) = 20.84$, $p < 0.001$, $\eta^2_p = 0.551$. Older participants tended to have a quite accurate temporal perception for events within the voluntary action context (2.36 ms, 95% CI: -23.33, 28.05) as compared to both the involuntary context (-43.06 ms, 95% CI: -57.34, -28.78; $p = 0.003$) and the sensory context (-42.08 ms, 95% CI: -61.17, -22.99; $p = 0.001$). No significant differences emerged between the temporal perception of the events within the involuntary action and the sensory contexts ($p = 1.000$). Regarding the 'judged event', the first event was shifted towards the second one (10.83 ms, 95% CI: -9.62, 31.28) and vice versa (-66.02 ms, 95% CI: -93.32, -38.72) ($p < 0.001$). However, the interaction between the two factors was not significant, $F(2, 34) = 0.63$, $p = 0.538$, $\eta^2_p = 0.036$ (Figure 4.3), indicating that no temporal compression occurred for the voluntary action as compared to the other two control conditions. When considering the overall binding, no differences were observed among the three contexts ('voluntary action', 'involuntary action' and the 'sensory' contexts), $F(2, 34) = 0.63$, $p = 0.54$, $\eta^2_p = 0.036$. Like in the case of children, the results showed that no IB occurred in elderly. No significant correlations were observed between IB and neuropsychological measures ($p > 0.05$).

Table 4.5. *mJEs, perceptual shifts and overall binding in elderly.*

	Event Judged	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Baseline Conditions				
1) Voluntary Action	Voluntary Action	-21.11 ± 91.37		
2) Involuntary Action	Involuntary Action	45.83 ± 61.91		
3) Tone	Tone	8.33 ± 56.12		
4) Control Tone	Control Tone	27.5 ± 58.04		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	23.06 ± 116.75	44.17 ± 94.19	166.39 ± 140.12
6) Voluntary Action - Tone	Tone	-31.11 ± 80.08	-39.44 ± 79.26	
7) Involuntary Action - Tone	Involuntary Action	48.33 ± 57.03	2.5 ± 39.34	158.89 ± 83.85
8) Involuntary Action - Tone	Tone	-80.28 ± 70.95	-88.61 ± 60.14	
9) Control Tone - Tone	Control Tone	13.33 ± 56.33	-14.17 ± 34.22	194.17 ± 91.22
10) Control Tone - Tone	Tone	-61.67 ± 72.11	-70 ± 77.04	

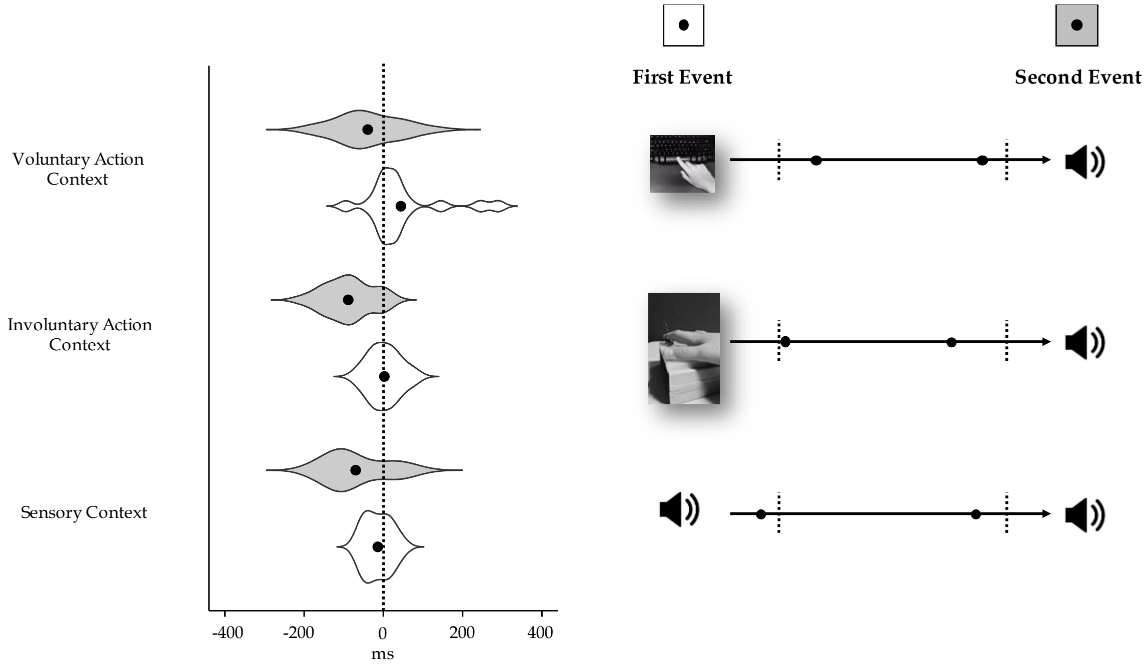


Figure 4.3. *On the* ***left*** *side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first event towards the second one (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the tone) towards the first one. The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, temporal compression is not significantly different across conditions (voluntary, involuntary and sensory).*

4.3.4 RESULTS IV: BETWEEN-GROUP COMPARISONS

In order to better understand the lack of IB in children and elderly, the degree of binding among the three groups was compared. Concerning BCs, using univariate ANOVA, no differences among the three groups were detected in the perception of voluntary action, $F(2, 54) = 1.17$, $p = 0.318$, or in the involuntary action, $F(2, 54) = 1.75$, $p = 0.184$. However, significant differences emerged in the case of tone, $F(2, 54) = 11.15$, $p < 0.001$, $\omega^2 = 0.26$ and control tone $F(2, 54) = 5.34$, $p = 0.008$, $\omega^2 = 0.13$. Regarding the temporal perception of tone, *post hoc* tests - with Bonferroni correction applied - revealed a significant difference between adults and elderly (-60 vs 8.33 ms respectively, $p = 0.011$, mean difference: 4.67, 95% CI: 8.18, 81.16) and between children and elderly (78.15 vs 8.33 ms respectively, $p < 0.001$, mean difference: 69.82, 95% CI: 32.88, 106.77). Regarding the temporal perception of control tone, a significant difference emerged only between children and elderly (81.57 vs 27.5 ms respectively, $p = 0.006$, mean difference: 54.08, 95% CI: 12.67, 95.49). As results show, participants widely differed on temporal perception of these baseline events, reflecting individual strategies in the attention paid to the stream of letters, in line with other studies (e.g., Haggard et al., 2003; Moore, Schneider et al., 2010). In order to control and remove such individual differences, perceptual shifts were analysed using 3 ('type of context') x 2 ('judged event') repeated-measures ANOVA, using the group (young adults, children and elderly) as between-factor. First, a non-significant main effect of group was detected, $F(2, 54) = 0.740$, $p = 0.482$, $\eta^2_p =$

0.027. Instead, significant main effects of both 'type of context', $F(2, 108) = 6.44$, $p = 0.002$, $\eta^2_p = 0.107$, and 'judged event', $F(1, 54) = 70.34$, $p < 0.001$, $\eta^2_p = 0.566$, were detected. Participants tended to have a general anticipated temporal perception regarding the events within the voluntary action context (-9.79 ms, 95% CI: -22.85, 3.27) as compared to both the involuntary (-29.53 ms, 95% CI: -39.41, -19.66; $p = 0.015$) and the sensory contexts (-29.94 ms, 95% CI: -39.43, -20.46; $p = 0.01$). No significant differences emerged between the involuntary and the sensory contexts ($p = 1.000$). Regarding the 'judged event', the first event was shifted towards the second one (11.55 ms, 95% CI: 2.37, 20.73) and vice versa (-57.73 ms, 95% CI: -71.19, -44.27; $p < 0.001$). Most importantly, the interaction between 'group', 'type of context' and 'judged event' was significant, $F(4, 108) = 3.99$, $p = 0.005$, $\eta^2_p = 0.129$. Differences between groups were significant only regarding the *action binding* within the voluntary action context (i.e., the shift of the voluntary action towards the tone, Figure 4.4). Specifically, action binding was significantly different between young adults and children ($p = 0.034$; 95% CI: 3.56, 122.44; mean difference = 63), but not between young adults and elderly ($p = 0.514$) and between elderly and children ($p = 0.728$). Also, the overall binding was compared among the three groups. No main effect of group, $F(2, 54) = 1.74$, $p = 0.186$, $\eta^2_p = 0.06$, was observed while a main effect of overall binding emerged, $F(2, 108) = 9.58$, $p < 0.001$, $\eta^2_p = 0.151$. Temporal compression within the voluntary action context was significantly different as compared to both the involuntary action context ($p = 0.007$) and the sensory context ($p = 0.001$). No differences emerged between the two control contexts, namely the involuntary and the sensory context (p = 0.600). Most importantly, a significant interaction between the overall binding and the group emerged, $F(4, 108) = 3.48$, $p = 0.010$, $\eta^2_p = 0.114$, (Figure 4.5). Young adults overall binding significantly differed from both children (p = 0.015) and elderly (p = 0.022) only in the case of the 'voluntary action context'. Total voluntary IB did not differ between children and elderly (p = 1.000). No differences emerged among groups in the case of the two control contexts (involuntary action context: children vs young adults, p = 1.000; children vs elderly, p = 0.293; young adults vs elderly: p = 1.000; sensory context: children vs young adults, p = 1.000; children vs elderly, p = 1.000; young adults vs elderly: p = 1.000).

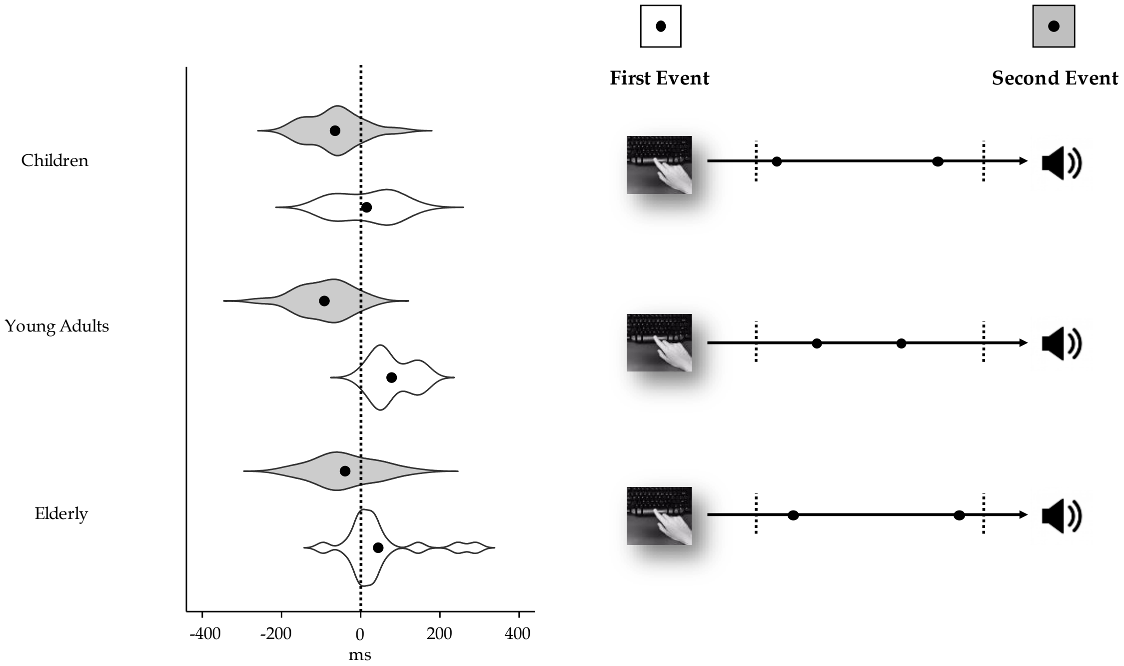


Figure 4.4. *On the* ***left*** *side, the graph shows the perceptual shifts within the voluntary action context for each group. The white violin plots depict the action binding (i.e., the shift of the the voluntary action towards the tone). Conversely, the grey violin plots represent the effect binding (i.e., the perceptual shift of the tone towards the action). The dashed line stands for the actual onset of the event of interest. The black dots stand for the mJE of each group of participants. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the total temporal compression is evident only within the group of young adults.*

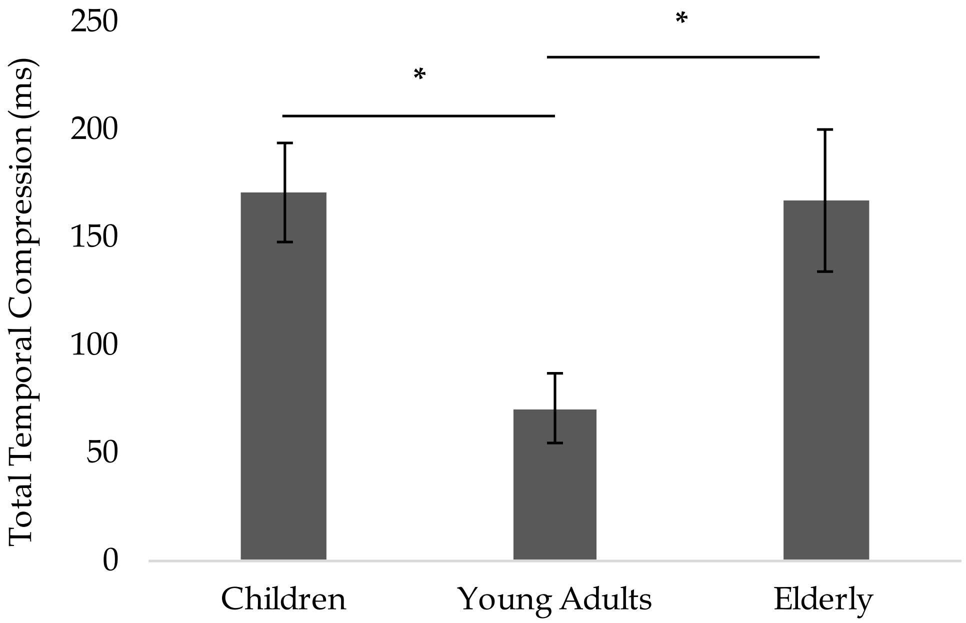


Figure 4.5. *Differences in the voluntary action overall binding among the three groups of participants. Error bars represent the standard error of mean (SEM) and * indicates the significant difference in overall binding among groups. Only adults present IB effect, showing an enhanced total temporal compression between voluntary action and its sensory effect. Smaller values indicate a stronger IB.*

4.4 DISCUSSION

The aim of the present study was to investigate the development and the evolution of the SoAg across the lifespan, using IB as an implicit measure, by taking advantage of its superiority over explicit tasks (e.g., verbal self-reports) (Wolpe & Rowe, 2014).

Results in the group of young adults replicate the findings of Study I (see Chapter 3). Again, only voluntary actions were perceived as occurring later in time than they really were (e.g., as more adjacent to the following tone in temporal terms); on the other hand, tones were perceived as occurring earlier than they really were (e.g., closer to actions in time). Such temporal compression was limited to the context of voluntary action. These results provide further support for the use of this new paradigm to examine IB.

As concern children and elderly, findings showed a reduction of the overall IB (i.e., larger values and absence of temporal compression), both in the context of 'voluntary action' and in the two control conditions ('involuntary action' and 'sensory context'). In both groups, the temporal occurrence of the tone in the ECs was significantly shifted towards the first event which triggered the auditory effect, independently of the type of the first stimulus (i.e., voluntary, involuntary or sensory). Why did this happen? Some possible explanations have been advanced. The first one refers to the *alerting system* (Petersen & Posner, 2012). Accordingly, the use of a warning signal prior to a target event produces, in young adults, a phasic change in alertness, preparing the system for the detection of an expected signal. Generally, reaction times improve following a warning signal. A similar phenomenon is also common in children. Indeed, considering the 'warning-signal hypothesis' (Droit-Volet, 2003; 2011), it has been shown that when target stimuli are preceded by warning signals, the amount of time required for stimulus processing decreases and accuracy improves. In fact, when children had to evaluate the tone in the ECs, judgment accuracy significantly increased in comparison to the BCs, in which only the tone was presented. In fact, in BCs children perceived the tone after its real onset (78.16 m). However, when the tone was activated by the voluntary action, it was perceived more accurately (13.42 ms). The same pattern also emerged when the tone followed the involuntary action (30.26 ms) and the control tone (35.53 ms).

Therefore, it has been speculated that children might have considered the first event (voluntary action, involuntary action, or control tone) to be a warning signal for the arrival of the subsequent tone. This ‘warning-signal hypothesis’ (Droit-Volet, 2003; 2011) finds confirmation in many developmental studies showing that a warning event can actually act as an attentional preparation cue and then leads to performance improvements. Therefore, the *alerting system hypothesis* (Petersen & Posner, 2012) seems to be suitable to explain children’s data. However, when considering elderly, this framework failed to provide a convincing account of the findings obtained in this sample. This is partially due to the fact that baseline temporal perception of the tone significantly differed between the two groups. More specifically, while children had a delayed temporal perception of the tone in BC (78.15 ms), elderly tended to be more accurate (8.33 ms). As seen before, in children the *alerting system hypothesis* seems to work since the values of the tone in ECs resulted to be more accurate as compared to the BCs. However, in older participants the first event could not be considered as a warning stimulus since in ECs the temporal perception of the second event (i.e., the tone) was worsened as compared to the BC, although being perceived earlier in time like in children. This is in line with other studies that demonstrated that older participants are not able to use temporal cues to improve performance (Vallesi, McIntosh & Stuss, 2009; Zanto, Pan, Liu, Bollingerm Nobre et al., 2011).

Another possible explanation that is worth taking into account refers to the *lack of inhibitory control*, which is suitable to explain both children (Diamond

& Doar, 1989; Rubia, Overmeyer, Taylor, Brammer, Williams et al., 2000; Durston, Thomas, Yang, Ulug, Zimmermann et al., 2002; Lorsbach & Reimer, 2011) and elderly data (Hasher & Zacks, 1988; Hasher, Zacks & May, 1999). In the present study, both children and elderly might have perceived the second event in the ECs earlier in time, as compared to the BCs, because they might have been influenced by the presence of the first event. In fact, when the tone is activated by the first event (voluntary action, involuntary action, or control tone) in the ECs, it is perceived earlier compared to the BCs. In other words, when children and elderly had to evaluate the second event in the ECs, it is likely that they were not able to disengage their attention from the irrelevant stimulus (i.e., the first event), which was therefore not well-inhibited. For this reason, the second event in ECs was perceived earlier compared to the BCs. Regarding children, this hypothesis finds confirmation in several classic developmental studies which have demonstrated that the ability to suppress irrelevant information becomes more efficient with age (Diamond & Doar, 1989; Rubia et al., 2000; Durston et al., 2002; Lorsbach & Reimer, 2011). As a matter of fact, performance on Stroop, flanker, and go/no-go tasks continues to develop over childhood and does not reach its maximum until 12 years of age or later (Carver, Livesey & Charles, 2001; Bunge, Dudukovic, Thomason, Vaidya & Gabrieli, 2002; Durston et al., 2002). Regarding elderly, one of the major theories of cognitive aging proposed that an important cause of age changes evidenced in cognitive tasks is the decline in the efficiency of inhibitory processes (Hasher & Zacks, 1988; Hasher et al., 1999). More in detail, older adults have difficulties in focusing on relevant information and, at the same time, in inhibiting attention to irrelevant contents. Aging resulted in poorer performance in a variety of paradigms that rely upon inhibitory processing, including stop signal task (Kramer, Humphrey, Larish, Logan, & Strayer, 1994), Stroop task (Houx, Jolles, & Vreeling, 1993), and antisaccade task (Butler, Zacks, & Henderson, 1999). The *lack of inhibitory control hypothesis* provides therefore a good framework to explain the shift of the tone towards the first event in both groups. In addition, with respect to kids, this hypothesis could better fit the obtained data as compared to the 'warning signal hypothesis' (Droit-Volet, 2003; 2011): in fact, in order to control the cross-modal estimations in timing judgments, we should consider the perceptual shifts and not just the difference between the BCs and the ECs. Figures 4.2 and 4.3 show that the second event seems to be influenced by the first one: the effect (e.g., tone) is perceived earlier towards the first event independently of the context, and the shift is numerically different between the first and the second event, with a greater shift for the second one. It is, therefore, more likely that children, like elderly, were unable to manage the interference caused by the first event and, consequently, to correctly evaluate the ensuing tone. Indeed, judging correctly the second event implies that attention has to be disengaged from the previously presented stimulus (i.e., the first event). In these cases, irrelevant information exploited resources that otherwise would have been available to process relevant information, which led to a decreased of the global performance.

Taken altogether, the lack of IB effect in children and elderly seems to be related to the fact that the task may be too difficult for them, as a result of their limited attentional control capacities (e.g., Brainerd & Dempster, 1995; Park & Reuter-Lorenz, 2009). However, participants reported normal scores on neuropsychological measures. Therefore, it is unlikely that the lack of effect could be simply due to issues with the task. In order to better understand the reduced IB in these two special populations, we proceeded to compare their data with those obtained in young adults. This helped us to answer the following question: did the lack of IB depend exclusively on the complexity of the task? If it was the case, when comparing data among the three groups, we should have found differences within all the three contexts (i.e., voluntary, involuntary and sensory). More precisely, both children and elderly should have differentiated themselves from young adults in all the three contexts. However, groups did not differ in terms of control conditions; rather, they only showed significant differences in the 'voluntary action' context, suggesting that the total temporal compression only characterizes adults' performance (Figure 4.5). On the other hand, when considering action and effect binding separately, children exhibited a reduced action binding (i.e., the shift of the action towards the tone) only as compared to adults (Figure 4.4). Children tended to be more focused on their voluntary actions, without taking into account the effects produced by them. This result might be explained by considering the two different processes implicated in action and effect binding (Moore, Ruge et al., 2010; Wolpe, Haggard et al., 2013). Effect binding seems to rely on a more general pre-activation mechanism (Waszak et al., 2012); the neural representation of a sensory outcome following a voluntary action is activated before its occurrence. When the predicted sensory event occurs, the perceptual threshold is reached faster than when the event is not predicted. On the other hand, action binding depends on both predictive motor control and inferential processes (Moore & Haggard, 2008). It might be possible that the pre-activation mechanism is already fully efficient in children, while mechanisms implicated in action binding might be still developing, though functioning in elderly. However, future studies are needed to shed light on this issue.

Data are also in line with literature regarding temporal perception. In adults, IB has been proved to be linked to the slowing down of the rate of an internal pacemaker (Wenke & Haggard, 2009). In kids and in older participants, studies indicate, on the contrary, the speeding up of the internal pacemaker (Droit-Volet & Wearden, 2002; Espinosa-Fernández, Miró, Cano, & Buela-Casal, 2003; Hancock & Rausch, 2010). In line with these findings, the increase in the speed of the internal pacemaker made kids and elderly to perceive their voluntary actions and their sensory effects to be further apart (i.e., a reduced IB).

In conclusion, the present study provides new insights into the comprehension of the developmental trajectory of SoAg. If we consider IB to be an ‘adaptive illusion’ that gives us a strong sense of causality and helps us to consider ourselves as responsible for certain effects, such an illusion does not seem to deceive children and elderly, maybe because the necessary cognitive skills, relevant for the SoAg to occur, have not been acquired yet or have started their ‘decline’. It is possible that children and elderly might not have shown IB because frontal areas, the most plausible ‘candidates’ as a neural substrate of

SoAg, are still developing or have started to deteriorate. For all of these reasons, it has been suggested that IB might be acquired gradually during ontogenesis, parallel with the maturation of the frontal cortical network, and might be lost in an advanced age. Since SoAg and IB seem to share the same common cognitive mechanisms and neural networks (e.g., David et al., 2008; Moore & Obhi, 2012; Kühn et al., 2013; Wolpe & Rowe, 2014), one might therefore speculate that, in conjunction with the reduction of IB, children and elderly also show a diminished SoAg, which does not allow them to understand the consequences of their actions. However, results reported here refer to IB, and speculations on SoAg remain limited. The possible hypothesis of a link between the reduced IB and the maturation or decline of frontal areas in children and elderly remains an open issue that needs to be tested by means of neuroimaging techniques. Future studies are required to confirm our hypothesis in order to provide a further step in the contextualization of SoAg dynamics throughout age.

CHAPTER 5

STUDY III

DISCOVERING THE NEURAL BASES OF THE 'AGENT BRAIN': A tDCS STUDY

5.1 INTRODUCTION

As seen in Chapters 1 and 2, the neural bases of the SoAg remain unclear. While the role of the AG (Farrer & Frith, 2002; Farrer et al., 2003; Farrer, Frey et al., 2008) and the DLPFC (Fink et al., 1999) have been constantly associated with non-agency conditions using explicit agency tasks, the neural underpinnings of implicit SoAg (i.e., IB) associated with agency conditions are not well understood. Very few studies have tried to explore its neural underpinnings, using different methods (see Paragraph 2.4). Kühn et al. (2013) and Jo et al. (2014) adopted correlational techniques (fMRI and EEG, respectively), while Moore, Ruge et al. (2010) used theta-burst TMS. These studies provided evidence that the frontal lobe, namely the supplementary motor complex (SMC), is involved; in particular, the latter research demonstrated that disruption of pre-SMA reduced IB. A very recent study by Khalighinejad and Haggard (2015) investigated the contribution of the AG – usually activated in non-agency conditions - to the SoAg, by mean of tDCS, showing that anodal stimulation of the left AG reduced IB. Always using tDCS, Khalighinejad et al. (*in press*) highlighted the potential role of the DLPFC to SoAg when participants had to select between multiple actions. However, the available evidence is still too scarce for drawing definitive conclusions on the neural bases of the implicit SoAg. This is especially true when considering that the same two well-validated paradigms (i.e., the rotating spot method – Libet et al., 1983 - and the time interval paradigm - Engbert et al., 2007; 2008; Cravo et al., 2009; Humphrey & Buehner, 2009; Humphreys & Buehner, 2010) have been used in the above studies, and both present several weaknesses (Gomes, 2002; Cravo et al., 2011; see Chapter 3 of the present thesis).

The aim of the present study is to collect new evidence on the neural bases of the implicit SoAg by focussing, in particular, on the contribution played by the pre-SMA. The reason behind this choice is linked to the fact that the experience of agency, as seen in Chapter 4, is strictly related to EFs, given that it requires (i) a plan to perform a goal-directed action and (ii) the identification of the consequences of our behaviour in the external world, while avoiding and inhibiting erroneous and maladaptive behaviours. In this sense, the involvement of pre-SMA becomes crucial, based on its relevant contribution to the executive functioning. This area is indeed considered to belong to the pre-frontal cortex and not to the motor cortex (Picard & Strick, 2001; Akkal, Dum & Strick, 2007; Nachev et al., 2007). Indeed, differently from the SMA proper, the pre-SMA has extensive connections with pre-frontal regions and is associated with the higher cognitive aspects of tasks (e.g., action planning and initiation). In addition to the previous findings obtained using TMS (Moore, Ruge et al., 2010), a very recent study conducted by Wolpe, Moore et al. (2013) also highlighted the importance of this area for the process under investigation. The Authors, using IB as an implicit marker of agency in patients with CBS, have underlined that patterns of functional connectivity between the pre-SMA and the prefrontal cortex in resting conditions seem to change according to IB effects, suggesting that a medial frontal–prefrontal network is necessary for awareness and control of voluntary actions. Pre-SMA has therefore been selected in the present study as the target area of stimulation to further verify its causal involvement in the complex phenomenon of SoAg. As compared to Moore, Ruge et al. (2010), tDCS (Dayan et al., 2013) was adopted for its potential use in the clinical practice. Indeed, establishing a causal relationship between the stimulated area and IB by means of tDCS might have direct clinical relevance for the treatment of certain neurological and psychiatric diseases in which SoAg is disrupted. tDCS could be therefore a suitable tool for intervening in these domains, enhancing awareness of voluntary action. The effects of non-invasive brain stimulation on IB have been tested in another sensory modality compared to that tested in the aforementioned study (Moore, Ruge et al., 2010), aimed to give additional evidence on the possible supra-modal nature of the effect. Specifically, unlike the quoted study that used a somatosensory feedback, the sensory effect produced by the voluntary action in our task was a tone, typically adopted in IB studies. In the present study, tDCS was firstly applied to healthy participants' pre-SMA. Secondly, in the same sample it was applied to a control region involved in processing action-auditory effects, i.e., the right PAC. In view of the findings provided by the previous TMS study (Moore, Ruge et al., 2010), we expect stimulation-dependent alteration of IB only when tDCS is applied over the pre-supplementary motor area (pre-SMA), with no contribution by the PAC.

5.2 EXPERIMENT I: tDCS over pre-SMA

5.2.1 METHODS

5.2.1.1 PARTICIPANTS

Fifteen healthy participants (11 females; age range: 20 to 29; mean age in years: 22.9, SD:1.9; education in years: 16.67, SD: 0.98) were recruited for this study. They all were right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked neurological, neuropsychological and psychiatric pathologies. In addition, they all met the inclusion criteria for participating in brain stimulation studies. The study was conceived according to the Declaration of Helsinki and adopted the safety procedures of non-invasive brain stimulation. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study. The study was approved by the Ethics Committee of the University of Padua.

5.2.1.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Study I (Chapter 3). The only difference regarded the number of conditions applied. In the present study, control conditions (i.e., the involuntary action context and the sensory context) were not included. Indeed, the main interest of the present investigation was direct to elucidate the brain bases of IB related to intentional actions. Therefore, only the voluntary action context was considered. The study consisted of two BCs and two ECs, for a total of four conditions. Participants underwent three stimulation sessions (sham-placebo stimulation and two active stimulations), separated by at least 24 h. The ordering for the stimulation conditions was counterbalanced across participants. To rule out alternative accounts of tDCS effects, a self-report questionnaire measuring mood and arousal was administered at both the beginning and the end of the experiment.

5.2.1.3 tDCS

tDCS was delivered through a battery-driven current stimulator (BrainStim; EMS Medical, Bologna, Italy), using a pair of surface saline-soaked sponge electrodes. The active electrode (4 x 4 cm) was placed over pre-SMA, which was localised with the EEG 10–20 system, with the centre of the tDCS electrode placed over the site of Fz (Hsu, Tseng, Yu, Kuo, Hung et al., 2011). The reference electrode (10 x 10 cm) was placed over the deltoid muscle of the right arm to exclude the confounding effects of the reference electrode. A constant current of 1.5 mA was applied for 20 min (including fade-in and fade-out times of 30 s each) in both the active stimulation conditions. In the sham condition, a 1.5-mA current was applied for 20 s at the beginning and end of the stimulation period. Testing sessions took place at the same time of the day to minimize circadian effects.

5.2.2 RESULTS

Table 5.1 summarises the mJEs, perceptual shifts and overall binding for sham, anodal and cathodal stimulations.

Table 5.1. *mJEs, perceptual shifts and overall binding for each stimulation protocol after pre-SMA modulation.*

Stimulation	Baseline Conditions	Event judged	Mean judgment error (ms) ± sd	Mean shift (ms) ± sd	Overall Binding (ms) ± sd
Sham	Voluntary Action	Voluntary Action	21.81 ± 52.95		
	Tone	Tone	23.18 ± 32.06		
Anodal	Voluntary Action	Voluntary Action	18.18 ± 56.03		
	Tone	Tone	24.09 ± 33.59		
Cathodal	Voluntary Action	Voluntary Action	33.64 ± 46.78		
	Tone	Tone	32.73 ± 32.71		
	Experimental Conditions				
Sham	Voluntary Action - 250 ms - Tone	Voluntary Action	95.45 ± 62.97	73.64 ± 48.77	125 ± 78.87
	Voluntary Action - 250 ms - Tone	Tone	-28.18 ± 55.92	-51.36 ± 47.15	
Anodal	Voluntary Action - 250 ms - Tone	Voluntary Action	39.55 ± 41.33	21.36 ± 51.59	181.82 ± 56.69
	Voluntary Action - 250 ms - Tone	Tone	-22.73 ± 47.98	-46.82 ± 40.33	
Cathodal	Voluntary Action - 250 ms - Tone	Voluntary Action	61.36 ± 57.85	27.73 ± 47.83	188.18 ± 68.3
	Voluntary Action - 250 ms - Tone	Tone	-1.36 ± 22.64	-34.09 ± 33.6	

In order to calculate the perceptual shifts a 3 ('type of stimulation': sham, anodal, cathodal) x 2 ('judged event': either the action or the tone) repeated-measures ANOVA was run. No main effect of the 'type of stimulation' was found, $F(2, 28) = 2.97$, $p = 0.067$, $\eta^2_p = 0.175$, whereas the effect of the 'judged event' was significant, $F(1, 14) = 41.3$, $p < 0.001$, $\eta^2_p = 0.747$, with a shift of the first event towards the second (40.91 ms; 95% CI: 19.74, 62.08) and vice versa (-44.09 ms; 95% CI: -58.02, -30.17; $p < 0.001$). More relevant, a significant interaction emerged, $F(2, 28) = 5.83$, $p = 0.008$, $\eta^2_p = 0.294$. In order to examine the interaction in more detail, post hoc analysis applying Bonferroni correction for multiple comparisons was run. The post hoc analysis revealed that type of stimulation influenced only the shift of the action towards the tone (i.e., action binding): in particular, sham stimulation was significantly different from anodal ($p = 0.007$) and cathodal ($p = 0.014$) stimulations (Figure 5.1). No difference was found between anodal and cathodal stimulations ($p = 1.000$) which both showed a reduced action binding compared to sham stimulation. Regarding the effect binding, no significant differences emerged among the stimulations (sham vs anodal: $p = 1.000$; sham vs cathodal: $p = 0.753$; anodal vs cathodal: $p = 1.000$).

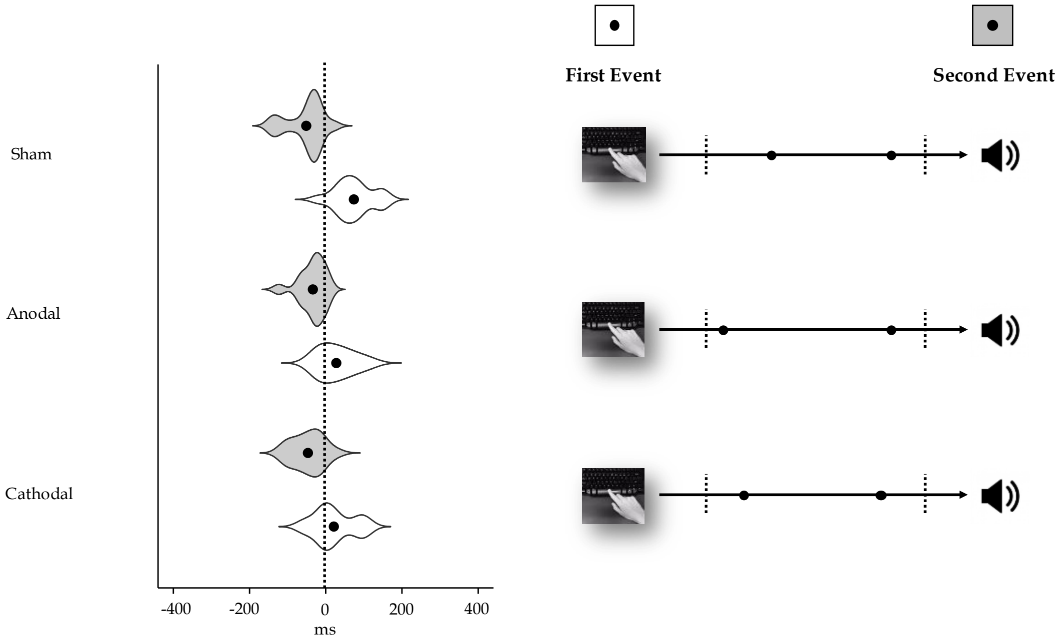


Figure* 5.1.** *On the* ***left *side, violin plots representing the distribution of each participant's mJE for the different stimulation protocols. The white violin plots depict the action binding. Conversely, the grey violin plots represent the effect binding. The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the temporal compression occurs only in the the sham stimulation condition.*

A one-way repeated-measures ANOVA was then calculated in order to study the effects of three tDCS stimulations (sham, anodal, cathodal) on the overall binding. Results showed a significant interaction, $F(2, 28) = 5.83$, $p = 0.008$, $\eta^2_p = 0.294$. Post-hoc analyses with Bonferroni correction for multiple comparisons revealed significant differences between the effects of sham tDCS and anodal tDCS ($p = 0.022$) and between sham tDCS and cathodal tDCS ($p = 0.043$) on the overall binding. Both anodal and cathodal stimulations reduced (i.e., higher values) the overall binding as compared to the sham condition, and did not significantly differ from each other ($p = 1.000$; Figure 5.2). Finally, to confirm that anodal and cathodal stimulations of pre-SMA affected primarily the experimental action condition and not the baseline action condition, the effect of the 'type of stimulation' on participants' judgement error in baseline action conditions was assessed using repeated-measures one-way ANOVA. No significant effect of stimulation type on baseline action condition was observed, $F(2, 28) = 1.033$, $p = 0.369$, $\eta^2_p = 0.069$.

Analyses of the self-report questionnaire measuring mood and arousal revealed no significant differences in any of the items as a function of stimulation conditions. With regard to the self-report questionnaire assessing the sensations experienced during the stimulation, sham and active protocols were found to be indiscernible.

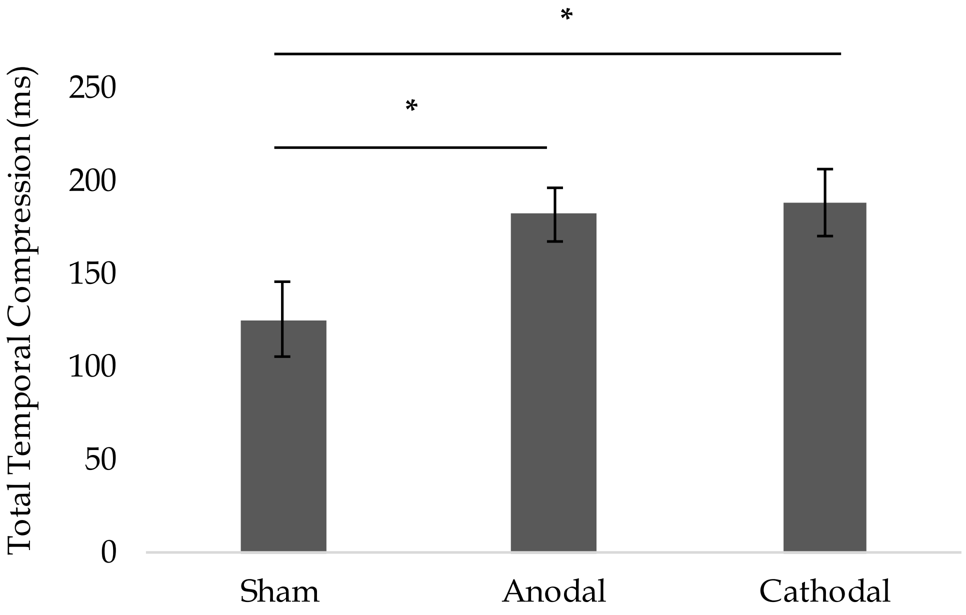


***Figure* 5.2.** *Differences of the overall binding among the three types of stimulation. Error bars represent SEM and * indicates the significant difference in overall binding among stimulation protocols. Only after sham stimulation the IB effect is still present. Conversely, both anodal and cathodal tend to reduce IB. Small values indicate a stronger IB.*

5.3 EXPERIMENT II: tDCS over the right primary auditory cortex

5.3.1 METHODS

5.3.1.1 PARTICIPANTS

Participants were the same as in Experiment I.

5.3.1.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Experiment I. Experiment II was run 1 month after Experiment I.

5.3.1.3 tDCS

In this experiment, all stimulation parameters were the same as in Experiment I, except for the placement of the active electrode (4 x 4 cm). This was placed over the right PAC, localized with the EEG 10–20 system and placed 1 cm inferior to the midpoint of C4 and T4 (Mathys, Loui, Zheng & Schlaug, 2010; Tang & Hammond, 2013).

5.3.2 RESULTS

Table 5.2 summarizes the mJEs, perceptual shifts and overall binding for sham, anodal and cathodal stimulations.

Table 5.2. *mJEs, perceptual shifts and overall binding for each stimulation protocol after PAC modulation.*

Stimulation	Baseline Conditions	Event judged	Mean judgment error (ms) ± sd	Mean shift (ms) ± sd	Overall Binding (ms) ± sd
Sham	Voluntary Action	Voluntary Action	27.73 ± 60.02		
	Tone	Tone	29.09 ± 40.04		
Anodal	Voluntary Action	Voluntary Action	53.64 ± 54.6		
	Tone	Tone	60.9 ± 50.79		
Cathodal	Voluntary Action	Voluntary Action	44.09 ± 63.9		
	Tone	Tone	42.73 ± 31.19		
	Experimental Conditions				
Sham	Voluntary Action - 250 ms - Tone	Voluntary Action	66.36 ± 81.06	38.64 ± 59.42	169.09 ± 92.63
	Voluntary Action - 250 ms - Tone	Tone	-13.18 ± 53.16	-42.27 ± 45.96	
Anodal	Voluntary Action - 250 ms - Tone	Voluntary Action	64.35 ± 61.37	10.72 ± 47.85	187.93 ± 82.68
	Voluntary Action - 250 ms - Tone	Tone	9.55 ± 47.36	-51.36 ± 56.98	
Cathodal	Voluntary Action - 250 ms - Tone	Voluntary Action	66.36 ± 57.13	22.27 ± 42.22	175 ± 66.55
	Voluntary Action - 250 ms - Tone	Tone	-10 ± 58.87	-52.73 ± 54.08	

In order to calculate the perceptual shifts a 3 ('type of stimulation': sham, anodal, cathodal) x 2 ('judged event': either the action or the tone) repeated-measures ANOVA was run. No main effect of the 'type of stimulation' was found, $F(2, 28) = 1.75$, $p = 0.192$, $\eta^2_p = 0.111$, whereas the effect of the 'judged event' was significant, $F(1, 14) = 21.93$, $p < 0.001$, $\eta^2_p = 0.610$, with a shift of the first event towards the second one (23.87 ms; 95% CI: 4.76, 42.99) and vice versa (-48.79 ms; 95% CI: -70.65, -26.92; $p < 0.001$). The interaction did not emerge as significant, $F(2, 28) = 0.309$, $p = 0.737$, $\eta^2_p = 0.022$, (Figure 5.2). A one-way repeated-measures ANOVA was then calculated in order to study the effects of the three tDCS stimulations (sham, anodal, cathodal) on the overall binding. Results showed no significant differences of tDCS stimulations, $F(2, 28) = 0.309$, $p = 0.737$, $\eta^2_p = 0.022$. Since the PAC was stimulated, a one-way repeated-measures ANOVA was run to assess the influence of tDCS on the temporal perception of tone in the BC. There was a significant effect of stimulation type on baseline tone condition, $F(2, 28) = 4.78$, $p = 0.016$, $\eta^2_p = 0.255$. Bonferroni correction showed that sham significantly differed from anodal ($p = 0.046$). Basically, anodal stimulation of the PAC reduced the temporal perception of the sound. No significant differences were detected between sham and cathodal ($p = 0.292$) and between anodal and cathodal ($p = 0.390$). Also for Experiment II analyses of the self-report questionnaires measuring mood and arousal and the sensations experienced during the stimulation revealed no significant differences as a function of stimulation conditions.

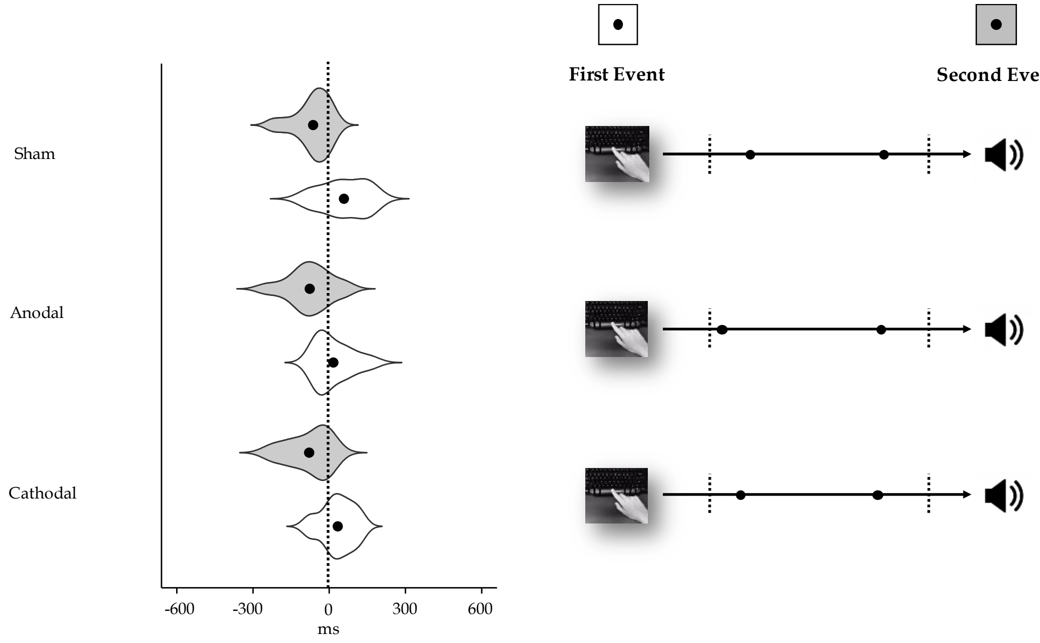


Figure* 5.2.** *On the* ***left *side, violin plots representing the distribution of each participant's mJE for the different stimulation protocols. The white violin plots depict the action binding. Conversely, the grey violin plots represent the participants' effect binding. The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants.*

5.4 DISCUSSION

In the present study tDCS was adopted to gain insights into the neural underpinnings of SoAg, using IB as implicit measure. Pre-SMA has been selected as a potential region involved in this phenomenon. Subsequently, PAC was also modulated, as a control area, given its key role in the processing of the auditory stimuli (Pickles, 2012), which here represent the effects of voluntary actions.

As we expected, results showed a significant reduction in IB only after stimulating the pre-SMA. In detail, sham stimulation significantly differed from anodal and cathodal stimulations, which both tended to reduce the overall IB, producing an inhibitory effect. Perceptual shifts were also analysed separately (action binding vs effect binding) as they seem to be mediated by different underlying mechanisms (Wolpe, Haggard et al., 2013). Only action binding (i.e., the shift of the action towards its auditory effect) was significantly reduced. Also in this case, sham stimulation differed from anodal and cathodal stimulations, which both tended to inhibit the shift of the action towards its effect. Unlike many previous findings in the motor domain, showing that cortical excitability is increased by anodal and decreased by cathodal stimulation (for a review, see: Jacobson, Koslowsky & Lavidor, 2012), polarity-dependent effects in behavioural measures were not observed, as both anodal and cathodal stimulations had an inhibitory effect on IB. Although this result could seem surprising at first sight (especially as regards the lack of facilitation for the anodal stimulation), the same inhibitory effect of both anode and cathode has been reported in other studies (Marshall, Mölle, Siebner & Born, 2005; Stagg, Jayaram, Pastor, Kincses, Matthews et al., 2011; Westgeest, Morales, Cabib & Valls-Sole, 2014; Zmigrod, Colzato & Hommel, 2014), which differed in many aspects from ours, thus making difficult to detect the reasons behind the lack of effects dependent on stimulation polarity. To test the hypothesis that longer durations of stimulation can somehow change the expected opposite anodal-excitation and cathodal-inhibition effects, additive analyses have been performed, similar to those described in the Method section, on data split into two halves (i.e., relative to the initial vs final parts of task performance). These new analyses did not confirm the above hypothesis as no significant difference between the two halves of the data was found (and for this reason they have not been reported in the Method's section). In this regard, one might incline to think that, beyond the importance of each single stimulation parameter in shaping stimulation-induced behavioural effects, these effects can emerge by complex interactions between a given combination of stimulation parameters, the targeted cognitive functions and the experimental tasks used to test these functions. However, the result pattern here observed confirms that the dichotomy between 'anodal-excitation' and 'cathodal-inhibition' in the cognitive domain is far from being considered unquestionable (for a review, see Jacobson et al., 2012), and that the reliability of polarity-dependent effects of stimulation, on both neural and behavioural levels, deserves to be investigated in more depth in future studies. Another possible explanation for this is based on the contribution of both SMA and pre-SMA in the perception of time (Lewis & Miall, 2003; Allman, Teki, Griffiths & Meck, 2014), as suggested by Javadi (2015). tDCS of the pre-SMA might have changed the expected duration of the delay and consequently reduced the SoAg. Anyway, the similarity between the effects of anodal and cathodal stimulation does not modify the meaning of the findings obtained by the present study, clearly indicating that the pre-SMA is likely to play a key role in the processing of IB. The pre-SMA seems therefore to give a crucial contribution to our feelings of being agents of our own actions. Indeed, inhibition of this area leads to a ‘weakening’ of IB, which may be interpreted as a decreased sense of control or agency. Moreover, our data support the view of distinct mechanisms underlying action and effect binding (Wolpe, Haggard et al., 2013). Perturbation of pre-SMA indeed altered only action binding, maintaining unchanged the effect binding: this peculiarity seems to keep participants more focused on their voluntary actions, ignoring however the produced sensory effect. Being more focused on the voluntary action itself, without considering the produced effects, suggests that SoAg might be decreased. The present data might also be discussed in light of the theories underlying the IB, which demonstrated that action binding, unlike effect binding, is supported by a *Cue Integration Theory* (Moore, Wegner et al., 2009; Wolpe, Haggard et al., 2013). In detail, estimation of time of action depends on an integration of two separate cues: the action and the sensory effect. The final estimate is then a weighted average, where the weight given to each cue depends on its reliability. In the absence of a sensory effect the perception of an action relies more on internal volitional signals, reducing therefore the action binding. On the other hand, unreliable information about the action event would lead to an over-reliance on its sensory effect and therefore increased binding of action. In our specific case, a reduced action binding was observed even if its effect was present. It might be possible that participants, who tended to concentrate only on their voluntary actions, behaved as if no sensory effect existed, reducing the shift of the action towards the effect. However, although such an interpretation is quite plausible, it should be treated with caution since we did not vary the probability of action's outcome and therefore we did not disentangle the specific contribution of these two sources of information for IB.

The present study adds several novelties to the study of SoAg, using IB as implicit measures. This is the first study attempting to elucidate the contribution of the pre-SMA by using tDCS. Two previous studies, using different neuroimaging methodologies (fMRI: Kühn et al., 2013; EEG: Jo et al., 2014), have investigated neural correlates and brain dynamics characterising IB, suggesting that the SMC might be a key brain region involved in this phenomenon. However, despite having put the bases for an initial understanding of the neural correlates of IB, these studies did not allow for a clear and definite comprehension of the role of SMC in the IB because only information correlative in nature was provided. To our knowledge, only one study tried to provide evidence for a causal involvement of the pre-SMA to the IB, adopting TMS (Moore, Ruge et al., 2010). Using somatosensory feedback, Authors targeted two areas thought to be involved in the cognitive aspects of internal movement generation and the sensory feedback: the pre-SMA and the SMHA, respectively. They found that TMS over the pre-SMA significantly reduced IB whereas no evidence was found for the involvement of SMHA in the phenomenon.

We decided to use tDCS for reasons relevant for both experimental research and clinical applications. As regard the first aspect, unlike neuroimaging methods this technique is able to demonstrate a causal link between a given stimulated area and a given behavioural effect - hypothesised to be mediated by that area. In addition, with tDCS it is easier to conduct placebo stimulation-controlled studies, as sham stimulation initially produces sensations similar to those produced by real stimulation without inducing changes in cortical excitability, a condition which is difficult to achieve with TMS because of methodological problems. As regards the clinical side, tDCS can be successfully used in this domain by virtue of the promising advantages it offers for the rehabilitation (e.g., more easily tolerated by participants, less expensive and potentially portable), especially when compared with other neurostimulation tools (Nitsche, Cohen, Wassermann, Priori, Lang et al., 2008).

Using tDCS we were able not only to replicate, but also to extend, the results obtained by Moore, Ruge et al. (2010). As the Authors previously claimed, we showed that modulation of pre-SMA reduces IB, with no direct contribution of the area which processes the effects of the action (i.e., the PAC in our study and the SMHA in Moore, Ruge et al., 2010). The confirmation of these results has relevant consequences on both methodological and theoretical sides. As regards the methodological implications, we were able to corroborate previous findings on IB with a different brain stimulation technique, which is usually described as having a lower spatial resolution than TMS. Similar results obtained with tDCS allow enlargement of the domain of application of the technique itself, which has already been shown to be a fruitful tool for experimental research in different domains (Penolazzi, Di Domenico, Marzoli, Mammarella, Fairfield et al., 2010; Penolazzi, Pastore & Mondini, 2013; Penolazzi, Stramaccia, Braga, Mondini & Galfano, 2014; Foerster, Rocha, Wiesiolek, Chagas, Machado et al., 2013).

As regards the theoretical implications, we extended the findings of Moore, Ruge et al. (2010) in many ways: (i) by adopting a new paradigm we successfully confirmed that pre-SMA contributes to IB; (ii) in our study the action effects were presented in the auditory modality, unlike in Moore, Ruge et al. (2010), who investigated the somatosensory modality. Therefore, although we did not directly test the two modalities through the same task, our results probably suggest that the effects of non-invasive brain stimulation on IB can be extended to another sensory domain (i.e., the auditory one); (iii) We did not find a contribution of the area implicated in the processing of the sensory effect produced by the action. This result is line with that of Moore, Ruge et al. (2010); however, as we found it in another sensory modality, it supports the supra-modality 'power' of IB, which is present independently of the type of the sensory feedback. It seems that the perception of the sensory effects in IB does not take place in the specific areas engaged in their processing (i.e., PAC and SMHA). Future studies should try to further verify this hypothesis, stimulating, for example, the whole SMC (both pre-SMA and SMA proper), which is a crucial station for the integration of the incoming sensory information, due to the fact that it indirectly receives sensory afferences from the primary sensory areas (Narayana, Laird, Tandon, Franklin, Lancaster et al., 2012).

Summing up, overcoming a correlational approach, the present study supports a causal contribution of pre-SMA in the functional genesis of SoAg, using tDCS. However, we cannot rule out the possibility that tDCS could also have affected neighbouring regions, anatomically and functionally linked to pre-SMA, and future studies, combining tDCS and neuroimaging techniques, will provide additional critical insights on this issue.

Our findings may have a strong relevance not only for scientists investigating motor, cognitive and neural mechanisms, but also for clinicians working with patients who present an altered awareness of action. For instance, exploring SoAg in PD (Moore, Schneider et al., 2010) and schizophrenia (Haggard et al., 2003), IB was found to be significantly stronger in patients than in controls. According to these findings, patients would tend to hyper-associate their actions and outcomes and to over-attribute the consequences of their movements to themselves. Based on our findings, showing that the active stimulation over pre-SMA reduced the temporal compression between actions and their effects (i.e., larger values of IB), tDCS might be, therefore, very useful in reducing this tendency in the above pathologies. In other words, tDCS might represent a novel therapeutic tool for those psychiatric and neurological pathologies in which the SoAg is disrupted.

CHAPTER 6

STUDY IV

THE SUPRAMODAL INTENTIONAL BINDING

6.1 INTRODUCTION

Our brain is immersed in a rich sensory environment. We live and act in a world constantly characterized by stimulations across multiple sensory modalities. The multisensory nature of everyday life allows for enhanced detection (Lovelace, Stein & Wallace, 2003), more accurate localization (Wilkinson, Meredith & Stein, 1996), and faster reactions (Diederich & Colonius, 2004) to stimuli. In addition to these highly adaptive benefits, the integration of information coming from different sensory systems is essential to provide a unified perception of our environment in order to control actions and its effects (i.e., SoAg). Following this line of reasoning, it might be possible that agency and IB can follow the same laws of multisensory integration (Eagleman, 2008). A crucial key requirement for multisensory integration is represented by the *'unity of assumption'* (Welch & Warren, 1980): stimuli presented in close temporal proximity, originating from a common source, are often integrated into a single, unified percept (McGurk & MacDonald, 1976; Shams, Kamitani & Shimojo, 2000; Ernst & Bülthoff, 2004). In other words, multisensory integration involves the merging of cues from different modalities into a single percept (Ernst & Bülthoff, 2004) and occurs only within a small temporal window around simultaneity, often called the *temporal window of integration* (e.g., Shams et al., 2000; Bresciani, Ernst, Drewing, Bouyer, Maury et al., 2005). It is clear that the temporal relation between the cause and the sensory effect plays a crucial role. IB potentially represents a way to confirm the *'unity of assumption'* (Rohde, Greiner & Ernst, 2014): action has to precede its sensory effect in a very brief temporal interval. Differently, if the sensory event precedes the voluntary action or the time interval between action and effect is too long, IB is violated, the unity assumption decreases and multisensory integration is prevented. Based on these assumptions, multisensory integration seems to be linked and central to the concept of agency. However, few studies have provided support for this. Indeed, the vast majority of investigations within the field of agency has neglected its multisensory nature (for a review, see: David et al., 2008; Moore & Obhi, 2012). Hypotheses on the reason why the multisensory nature of agency has been so far neglected lay on the fact that the reproduction of a setting of multi-modal stimulation mimicking the real world in the laboratory environment is extremely challenging. Nevertheless, the IB effect observed after voluntary actions has been robustly replicated using auditory, visual, and tactile modalities as sensory effects (e.g., Tsakiris & Haggard, 2003;

Engbert et al., 2007; 2008; Moore, Lagnado et al., 2009; Strother et al., 2010; Moretto, Walsh et al., 2011). All these studies suggest that the brain might contain a specific cognitive module that binds intentional actions to their effects, despite their disparate sensory nature and irrespective of differences in neural transmission times among the different senses. This mechanism is at the root of a coherent conscious experience of our own agency, independently of the sensory modality. However, in all these studies, Authors just changed the type of 'output', that is the sensory effect produced by participants' voluntary actions, always using visual stimuli as 'input' or reference point to report the temporal perception of the events - in particular, the latter point regarding the 'input' is specific for the studies which adopted the Libet clock methodology. This peculiarity has prevented to discover the actual multisensory nature of IB so far. Indeed, multisensory integration occurs not only when both the temporal order and the temporal window of integration are fulfilled, but also when different cross-modal stimulus combinations are assessed (Stein & Stanford, 2008). To the best of our knowledge, this issue has not been fully investigated yet. In order to shed light on this last aspect, the type of input has been varied: auditory stimuli were assumed as reference point to report the time onset of events. The question whether the use of auditory signals might alter the temporal perception of events in other sensory modalities - and therefore impact on IB – will be addressed. If IB is indeed a supramodal mechanism and follows the multisensory integration's rules, it should be present also modifying the type of sensory inputs.

6.2 EXPERIMENT I: the auditory-visual Intentional Binding

In the present experiment we modified the classical visuo-auditory paradigm usually adopted in the previous chapters. The main change regarded the type of input: indeed, instead of a stream of visual letters, participants listened to a series of auditory stimuli (e.g., syllables). As a consequence, also the type of sensory output has been modified and the classical auditory tone has been replaced by a visual stimulus.

6.2.1 METHODS

6.2.1.1 PARTICIPANTS

Twenty-two participants (14 females; age range: 20 to 33; mean age in years: 25.32, SD: 3.39; education in years: 17.45, SD: 1.77) were enrolled in the experiment. All participants were right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked neurological and psychiatric pathologies. The study was conceived according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Padua. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study.

6.2.1.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

The procedure was the same of that described in Study I (Chapter 3). Only the stimuli used and their duration changed. In particular, we have been forced to modify their exposure time in order make the stimuli high discriminable, avoiding possible confounders. Instead of the stream of visual letters usually adopted, participants were asked to listen to a stream of unpredictable syllables presented through headphones. Each syllable was presented separately and lasted for 250 ms, without time gaps in between. Only a subset of syllables has been selected in order to avoid that, during the auditory presentation, two syllables in sequence gave rise to a meaningful word. In order to prevent the participants from responding immediately after the occurrence of the syllables, the visual numbers used in the previous studies have been replaced by a continuous sound of randomized duration, which was played before the syllables' presentation. As sensory effects, instead of an auditory stimulus, a visual stimulus was adopted, namely a coloured circle, which lasted on the screen for 200 ms. The response modality was the same of that used in Study I (Chapter 3).

The experiment consisted of four BCs and six ECs, for a total of ten conditions. As in Study I (Chapter 3), among the BCs, only one event among voluntary action, involuntary action, visual stimulus, or control visual stimulus occurred per condition. The participants had to remember the syllable that they heard when: (1) they made a free voluntary key-press with their right index finger (acting as a baseline for voluntary action condition); (2) they felt their right index finger being passively moved down by a mechanical device (acting as a baseline for involuntary action condition), applied to the right index finger of the participants; (3) they saw a green circle which lasted for 200 ms (baseline for the visual stimulus); (4) they saw another circle (same duration as the visual stimulus but with a different colour – yellow – acting as baseline for the control visual stimulus). For the ECs, two events occurred per condition and the participants had to judge: (5) the onset of the voluntary action that produced the visual stimulus; (6) the onset of the visual stimulus caused by the voluntary action; (7) the onset of the involuntary action that was followed by the visual stimulus; (8) the onset of the visual stimulus activated by the involuntary action; (9) the onset of the control visual stimulus that was followed by the visual stimulus; (10) the onset of the visual stimulus activated by the control visual stimulus. Time interval between the first event (the voluntary action, the involuntary action, or the control visual stimulus) and the second event (the visual stimulus) was set at 250 ms. Please, see Figure 6.1 for a schematic representation of the experimental procedure.

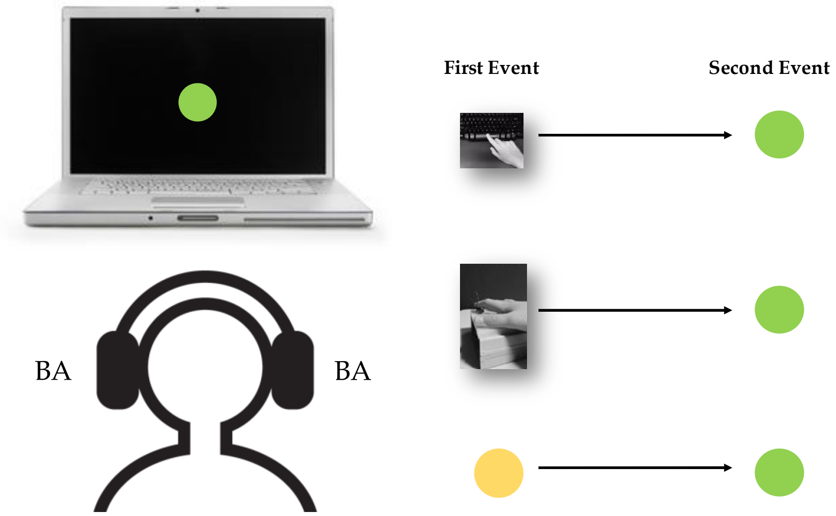


Figure 6.1. *Schematic representation of the task. Participants listened to a stream of unpredictable syllables while watching the black screen of a computer. In the ECs, the first event (voluntary action, involuntary action, yellow circle) was followed by a visual stimulus, namely a green circle. Participants had to judge which syllable they heard either when they were exposed to the first or the second event in separate conditions.*

6.2.2 RESULTS

Table 6.1 summarizes the mJEs, perceptual shifts, and overall binding.

Table 6.1. *mJEs, perceptual shifts and overall binding of the auditory-visual IB.*

	Judged Event	**mJE (ms) ± sd**	**Mean Shift (ms) ± sd**	**Mean Overall Binding (ms) ± sd**
Baseline Conditions				
1) Voluntary Action	Voluntary Action	10.11 ± 55.95		
2) Involuntary Action	Involuntary Action	20.45 ± 46.85		
3) Visual Stimulus	Visual Stimulus	26.89 ± 56.69		
4) Control Visual Stimulus	Control Visual Stimulus	17.04 ± 29.18		
Experimental Conditions				
5) Voluntary Action – Visual Stimulus	Voluntary Action	66.23 ± 94.23	55.3 ± 108.49	175 ± 125.83
6) Voluntary Action – Visual Stimulus	Visual Stimulus	7.2 ± 72.34	-19.7 ± 56.02	
7) Involuntary Action – Visual Stimulus	Involuntary Action	-15.91 ± 78.42	-36.36 ± 69.42	254.17 ± 110.31
8) Involuntary Action – Visual Stimulus	Visual Stimulus	-5.3 ± 93.67	-32.2 ± 82.11	
9) Control Visual Stimulus – Visual Stimulus	Control Visual Stimulus	-46.6 ± 69.94	-63.64 ± 63.53	303.03 ± 87.56
10) Control Visual Stimulus – Visual Stimulus	Visual Stimulus	16.29 ± 77.56	-10.61 ± 69.87	

Using paired-sample *t*-tests, significant differences were found within all the contexts. Regarding the 'voluntary action context', participants perceived the onset time of the voluntary action later when it triggered the visual stimulus in EC (i.e., the green circle) as compared to the BC in which only the voluntary action was present (voluntary action in the BC vs voluntary action in the EC, $t_{21} = -2.39$, $p = 0.026$; 95% CI: -103.4, -7.2; mean: -55.3 ms). Regarding the temporal perception of the visual stimulus (i.e., the green circle) following the voluntary action, it was perceived by participants earlier when it was activated by the voluntary action (7.2 ms) as compared to when it was presented alone (26.89 ms). However, the tendency did not reach the statistical significance, $t_{21} = 1.65$, $p = 0.114$; 95% CI: -5.14, 44.54; mean: 19.7 ms. Regarding the 'involuntary action context', the involuntary action was perceived earlier when it triggered the visual stimulus as compared to the BC in which participants had just to evaluate the temporal onset of the involuntary action [involuntary action in the BC (20.46 ms) vs involuntary action in the EC (-15.91 ms), $t_{21} = 2.46$, $p = 0.023$; 95% CI: 5.59, 67.14; mean: 36.36 ms]. This happened also within the 'sensory context': participants tended to perceive the control visual stimulus (i.e., the yellow circle) earlier in the EC (-46.6 ms) as compared to the BC (17.05 ms), $t_{21} = 4.7$, $p < 0.001$; 95% CI: 35.5, 91.8; mean: 63.64 ms. No differences were detected in all the other conditions ['involuntary action context': visual stimulus in EC vs visual stimulus in the BC ($p = 0.008$); 'sensory context': visual stimulus in EC vs visual stimulus in BC ($p = 0.484$)]. In order to calculate the perceptual shifts, repeated-measures ANOVA was run. First, a main significant effect of the ‘type of context’ was found, $F(2, 42) = 6.33$, $p = 0.04$, $\eta^2_p = 0.232$. In other words, participants tended to have a general delayed temporal perception regarding the events within the voluntary action context (17.8 ms) as compared to the involuntary context (-34.28 ms; $p = 0.024$) and the sensory context (-37.12 ms; $p = 0.016$). No differences were detected between these last two ($p = 1.000$). No main effect of the ‘judged event’ was found $F(1, 21) = 0.12$, $p = 0.732$, $\eta^2_p = 0.006$. Most importantly, a significant interaction between these two factors emerged, $F(2, 42) = 11.23$, $p < 0.001$; $\eta^2_p = 0.348$ (Figure 6.2).

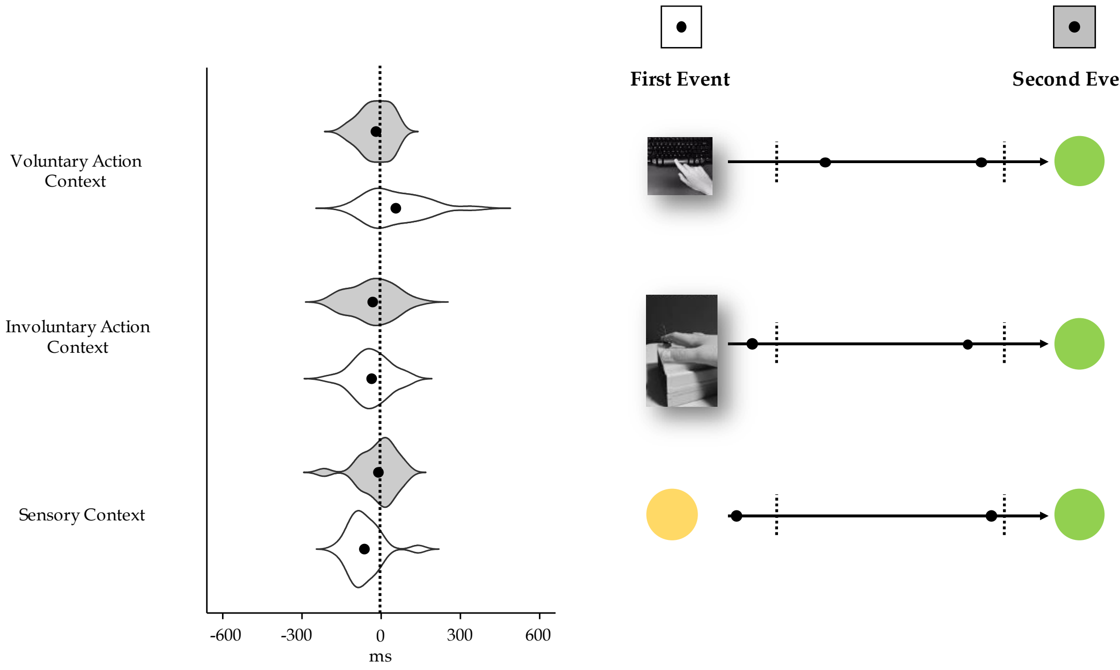


Figure* 6.2.** *On the* ***left *side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first judged event (i.e., the voluntary action, the involuntary action and the control visual stimulus). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the green visual stimulus). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the temporal compression occurs only within the voluntary context.*

A *post-hoc* analysis applying Bonferroni correction for multiple comparisons was conducted in order to examine the interaction in more detail. The *post-hoc* analysis revealed that the difference between the first and the second judged event was significant in the case of voluntary action ($p < 0.001$). In addition, concerning the first judged event, a significant difference was found for voluntary action in comparison with involuntary action ($p = 0.013$) and the control visual stimulus ($p =$

0.001). Involuntary action and the control visual stimulus were not significantly different ($p = 0.517$). No significant differences emerged when comparing the second judged event (e.g., the green visual stimulus) ('voluntary action context' vs 'involuntary action context', $p = 1.000$; 'voluntary action context' vs 'sensory context', $p = 1.000$; 'involuntary action context' vs 'sensory context', $p = 1.000$). Only voluntary actions led to a perceptual shift of action towards its visual stimulus (i.e., action binding). This effect was significantly reduced for the involuntary action context and for the sensory context. The one-way repeated-measures ANOVA found a significant effect of the overall binding (i.e., the perceived linkage between action and effect), $F(2, 42) = 11.23$, $p < 0.001$, $\eta^2_p = 0.348$. *Post-hoc* comparisons showed a significant difference in both the 'voluntary' and 'involuntary' contexts ($p = 0.04$). In addition, the 'voluntary context' and the 'sensory context' ($p < 0.001$) were also significantly different. No significant differences were found between the 'involuntary context' and the 'sensory context' ($p = 0.191$) (Figure 6.3).

In summary, the total temporal compression (i.e., IB effect) was evident in the context of voluntary action. The overall binding data indicate that the participants perceived the interval between their action and its effect as significantly shorter than it really was, although no direct judgment of the time interval's duration was requested.

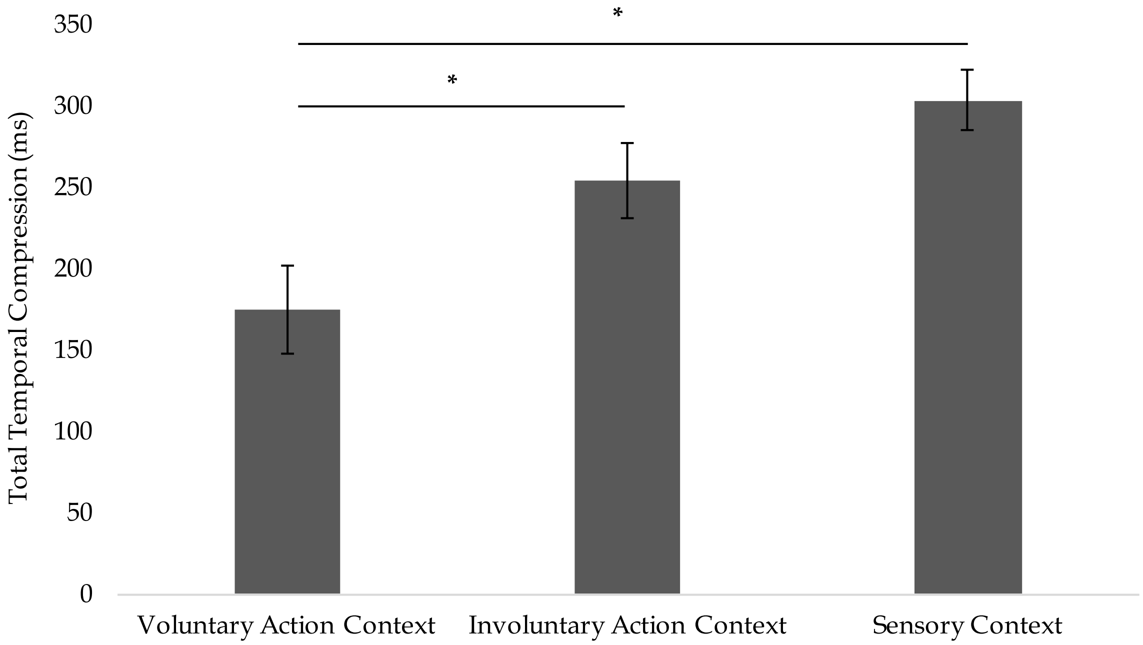


Figure 6.3. *Differences in the overall binding among the three contexts. Error bars represent SEM and * indicates the significant difference in overall binding among the three contexts. The temporal compression characterizing IB is only present within the voluntary action context. Small values indicate stronger IB.*

6.3 EXPERIMENT II: the time windows of the classical visuo-auditory Intentional Binding

A recent article by Danquah, Farrell and O'Boyle (2008) suggested that participants' judged timing of events is subject to both (i) systematic biases arising from the sensory modality through which they experienced the stimulus and (ii) the speed of the rotating clock hand. Experiment I explored the first issue and did not highlight differences when manipulating the type of sensory stimuli, corroborating and extending previous findings in literature and providing further support for the authenticity of IB as implicit measure of agency.

The following experiment focused on the second issue mentioned by Danquah et al. (2008): what happens if, using the classical paradigm adopted in the previous chapters, we slow down the presentation of the stream of letters?

6.3.1 EXPERIMENT II-A

6.3.1.1 METHODS

6.3.1.1.1 PARTICIPANTS

A new sample of twenty-two participants (16 females; age range: 20 to 29; mean age in years: 23.41, SD: 2.38; education in years: 15.64, SD: 2.7) were enrolled in the experiment. All participants were right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked neurological and psychiatric pathologies. The study was conceived according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Padua. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study.

6.3.1.1.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Study I (Chapter 3). The only difference was the duration of the visual stimuli: each number and letter remained on the screen for 250 ms, instead of 150 ms.

6.3.1.2 RESULTS I

Table 6.2 summarizes the mJEs, perceptual shifts and overall binding. Using paired-sample *t*-tests, the only significant difference observed regarded the sensory context [control tone in the BC (20.83 ms) vs control tone in the EC (-12.12 ms), t_{21} = 2.43, p = 0.024; 95% CI: 4.78, 61.13; mean: 32.95 ms].

Table 6.2. *mJEs, perceptual shifts and overall binding (Experiment II-A)*

	Judged Event	**mJE (ms) ± sd**	**Mean Shift (ms) ± sd**	**Mean Overall Binding (ms) ± sd**
Baseline Conditions				
1) Voluntary Action	Voluntary Action	62.88 ± 93.99		
2) Involuntary Action	Involuntary Action	32.95 ± 111.11		
3) Tone	Tone	26.14 ± 89.02		
4) Control Tone	Control Tone	20.83 ± 98.53		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	92.42 ± 107.49	29.55 ± 66.85	257.2 ± 130.69
6) Voluntary Action - Tone	Tone	62.88 ± 81.76	36.74 ± 105.3	
7) Involuntary Action - Tone	Involuntary Action	37.5 ± 110.16	4.55 ± 84.27	249.62 ± 118.76
8) Involuntary Action - Tone	Tone	30.3 ± 132.45	4.17 ± 82.28	
9) Control Tone - Tone	Control Tone	-12.12 ± 96.66	-32.95 ± 63.54	268.94 ± 85.57
10) Control Tone - Tone	Tone	12.12 ± 115.15	-14.02 ± 94.05	

In order to calculate the perceptual shifts, repeated-measures ANOVA was run. First, a main significant effect of the ‘type of context’ was observed, $F(2, 42) = 5.43$, $p = 0.008$, $\eta^2_p = 0.205$. In other words, participants had a general delayed temporal perception regarding the events within the ‘voluntary action context’ (33.14 ms) as compared to the ‘sensory context’ (-23.49 ms) ($p = 0.017$). No differences were detected between the ‘voluntary action’ and the ‘involuntary action’ contexts (4.36 ms) ($p = 0.392$) and between the ‘involuntary action’ and the ‘sensory’ contexts ($p = 0.206$). No main effect of the ‘judged event’ was detected $F(1, 21) = 0.337$, $p = 0.568$, $\eta^2_p = 0.016$. Also the interaction did not reach statistical significance $F(2, 42) = 0.173$, $p = 0.842$, $\eta^2_p = 0.008$ (Figure 6.4). Regarding the total temporal compression, the one-way repeated-measures ANOVA did not show a significant effect of the overall binding (i.e., the perceived linkage between action and effect), $F(2, 42) = 0.173$, $p = 0.842$, $\eta^2_p = 0.008$.

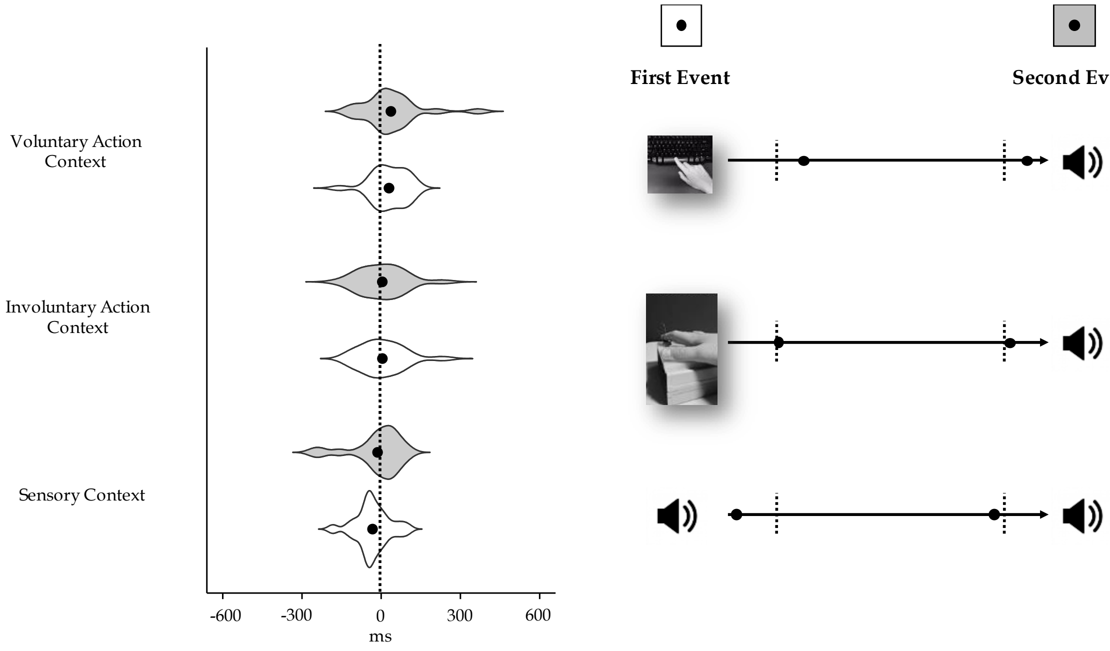


Figure 6.4. *On the **left** side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first event (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the tone). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the **right** side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, no differences emerge among the three contexts.*

6.3.1.3 RESULTS II: comparison between the auditory-visual and the visuo-auditory Intentional Binding

Since the timing of stimuli presentation was the same of Experiment I, we compared the degree of binding obtained in Experiment I and Experiment II-A. Concerning BCs, independent-samples *t*-test showed a significant difference only regarding the temporal perception of the voluntary action (t_{42} = 2.23, *p* = 0.031, 95% CI: 4.83, 98.96, mean difference: 51.89). More in detail, participants were more accurate in perceiving the temporal onset of the voluntary action using the auditory-visual IB (10.98 ms) as compared to the classical visuo-auditory paradigm (62.88 ms). We therefore analysed the perceptual shifts using 3 ('type of context') x 2 ('judged event') repeated measures ANOVA, with the 'type of paradigm' (auditory-visuo IB, visuo-auditory IB) as between-factor. First, a significant main effect of the 'type of paradigm' was observed, *F*(1, 42) = 4.42, *p* = 0.042, η^2_p = 0.095. Using the visuo-auditory IB, participants tended to perceive the onset time of events later (4.67 ms) as compared to the auditory-visual IB (-17.87 ms) (*p* = 0.042). In addition, a significant main effect of 'type of context', *F*(2, 84) = 11.12, *p* < 0.001, η^2_p = 0.209, was detected. Participants tended to have a general delayed temporal perception regarding the events within the 'voluntary action' context (25.47 ms) as compared to both the 'involuntary context' (-14.96 ms; *p* = 0.09) and the 'sensory' one (-30.3 ms; *p* < 0.001). No significant differences emerged between the 'involuntary action' and the 'sensory' contexts (*p* = 0.52). No significant main effect of the 'judged event' was detected *F*(1, 42) = 0.014, *p* = 0.907, η^2_p < 0.001, but the interaction between the 'type of paradigm', 'type of context' and 'judged event' was significant, *F*(2, 84) = 3.98, *p* = 0.022, η^2_p = 0.087. The only significant difference between the two paradigms emerged in the case of the effect binding within the voluntary action context (*p* = 0.032; 95% CI: 5.12, 107.76; mean difference = 56.44). The shift of the second sensory effect (i.e., either the the visual stimulus or the auditory tone) towards the voluntary action which triggered it, was only detected within the auditory-visual IB. Indeed, as depicted by Image 6.5, the effect binding within the visuo-auditory IB was delayed in time as compared to the effect binding within the auditory-visual IB.

Also the overall bindings were compared between the two paradigms. No main effect of the 'type of paradigm', $F(1, 42) = 0.412$, $p = 0.524$, $\eta^2_p = 0.010$ was found while the main effect of 'overall binding' emerged, $F(2, 84) = 5.32$, $p = 0.007$, $\eta^2_p = 0.112$: the temporal compression within the 'voluntary action context' was significantly different as compared to the 'sensory context' ($p = 0.005$). No differences emerged between the two control contexts, namely the 'involuntary' and the 'sensory' contexts ($p = 0.28$) and between the 'voluntary context' and the 'involuntary' one ($p = 0.406$). Most importantly, a significant interaction between the 'overall binding' and the 'type of paradigm', $F(2, 84) = 3.98$, $p = 0.022$, $\eta^2_p = 0.087$, was detected. More in detail, the overall auditory-visual IB significantly differed from the overall visuo-auditory IB ($p = 0.039$) only within the voluntary context. The total temporal compression characterizing voluntary actions was present only using the auditory-visual IB paradigm (Figure 6.6).

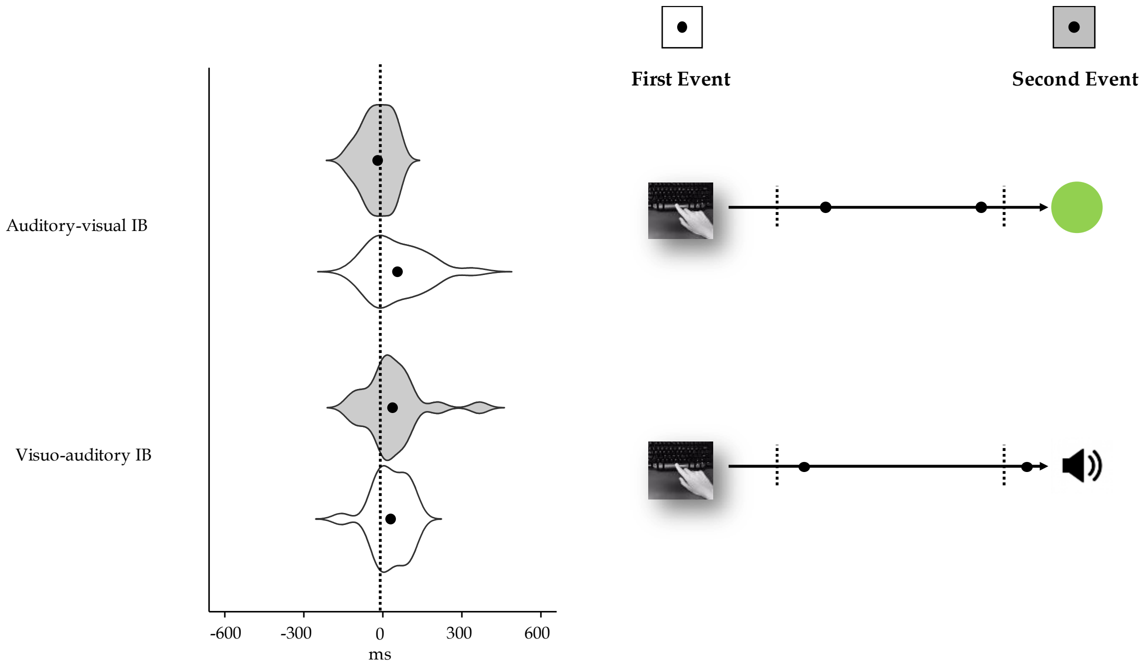


Figure 6.5. *On the* ***left*** *side, violin plots representing the distribution of each participant's mJE for the two paradigms within the voluntary context. The white violin plots depict the participants' action binding, while the grey violin plots represent the participants' effect binding (i.e., the visual stimulus for the auditory-visual IB and the auditory stimulus for the visuo-auditory IB). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the mean perceived event by the participants. As the image depicts, the temporal compression occurs only using the auditory-visual IB.*

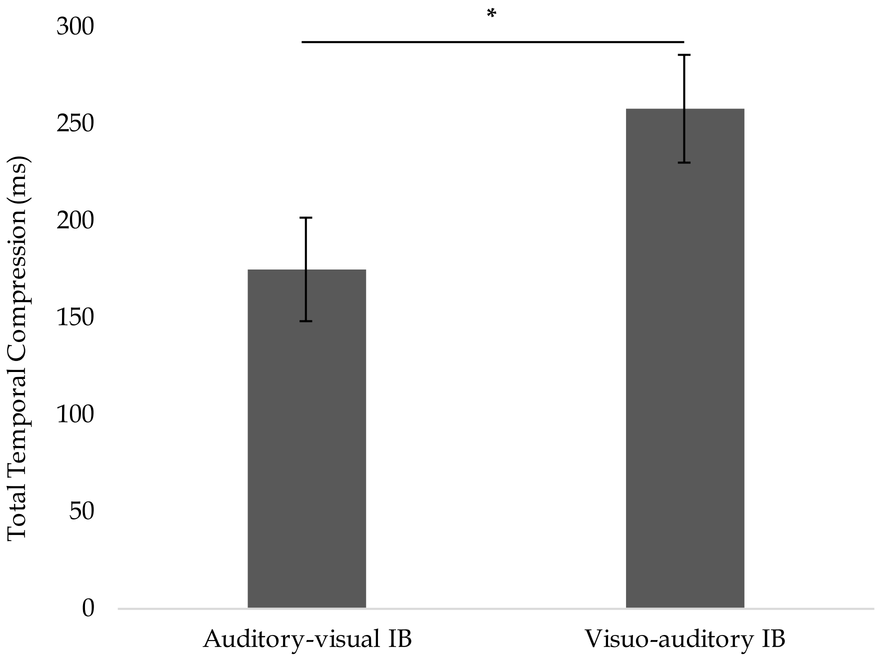


Figure 6.6. *Differences in the overall binding within the voluntary action context between the two paradigms. Error bars represent SEM and * indicates the significant difference in overall binding between the two paradigms. The temporal compression characterizing IB is only present when using the auditory-visual IB. Small values indicate stronger IB.*

Although the two paradigms involved different sensory modalities, making difficult a direct comparison of the obtained results, the findings of the present study show that when the stream of letters are slowed down using the classic visuo-auditory IB, the temporal compression disappears. Conversely, when the same duration is applied to a different modality (i.e., adopting the auditory-visual IB), the effect is still present. Using the classic visuo-auditory IB paradigm, it appears clear that the temporal window of visual letters' presentation plays a crucial role: IB appears when the letters last 150 ms each and disappear when they have a duration of 250 ms. In the next experiment an intermediate duration, that is 200 ms, was tested.

6.3.2 EXPERIMENT II-B

6.3.2.1 METHODS

6.3.2.1.1 PARTICIPANTS

Twenty-six new participants (18 females; age range: 21 to 31; mean age in years: 24, SD: 3.02; education in years: 16.81, SD: 1.39) were enrolled in the experiment. All participants were right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), had normal or corrected-to-normal vision, and lacked neurological and psychiatric pathologies. The study was conceived according to the Declaration of Helsinki and was approved by the Ethics Committee of the University of Padua. All participants were naïve as to the purpose of the experiment and gave their informed, written consent to participate in the study.

6.3.2.1.2 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Experiment II-A. The only difference was the duration of the visual stimuli. Each number and letter remained on the screen for 200 ms.

6.3.2.2 RESULTS

Table 6.3 summarizes the mJEs, perceptual shifts, and overall binding. Using paired-sample *t*-tests, the only significant difference was observed within the 'voluntary action context' [voluntary action in the BC (41.03 ms) vs voluntary action in the EC (73.33 ms), $t_{25} = -2.39$, $p = 0.025$; 95% CI: -60.15, -4.46; mean: -32.31 ms]. In order to calculate the perceptual shifts, repeated-measures ANOVA was run. No main significant effects of 'type of context', $F(2, 50) = 0.509$, $p = 0.604$, $\eta^2_p = 0.02$, and the 'judged event' $F(1, 25) = 1.098$, $p = 0.305$, $\eta^2_p = 0.04$ emerged. The interaction was not significant, too, $F(2, 50) = 2.11$, $p = 0.132$, $\eta^2_p = 0.078$ (Figure 6.7). Regarding the total temporal compression, the one-way repeated-measures ANOVA did not show a significant effect of the overall binding, $F(2, 50) = 2.11$, $p = 0.132$, $\eta^2_p = 0.078$.

Table 6.3. *mJEs, perceptual shifts and overall binding (Experiment II-B).*

	Event Judged	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Baseline Conditions				
1) Voluntary Action	Voluntary Action	41.03 ± 41.98		
2) Involuntary Action	Involuntary Action	61.28 ± 61.74		
3) Tone	Tone	45.38 ± 51.61		
4) Control Tone	Control Tone	41.03 ± 52.21		
Experimental Conditions				
5) Voluntary Action - Tone	Voluntary Action	73.33 ± 61.28	32.32± 68.94	203.59 ± 112.67
6) Voluntary Action - Tone	Tone	31.28 ± 77.72	-14.1 ± 72.67	
7) Involuntary Action - Tone	Involuntary Action	57.44 ± 56.26	-3.85 ± 53.9	245.9 ± 100.77
8) Involuntary Action - Tone	Tone	37.44 ± 91.29	-7.95± 93.73	
9) Control Tone - Tone	Control Tone	44.87 ± 97.6	3.85 ± 90.38	252.31 ± 112.95
10) Control Tone - Tone	Tone	51.54 ± 68.63	6.15 ± 76.64	

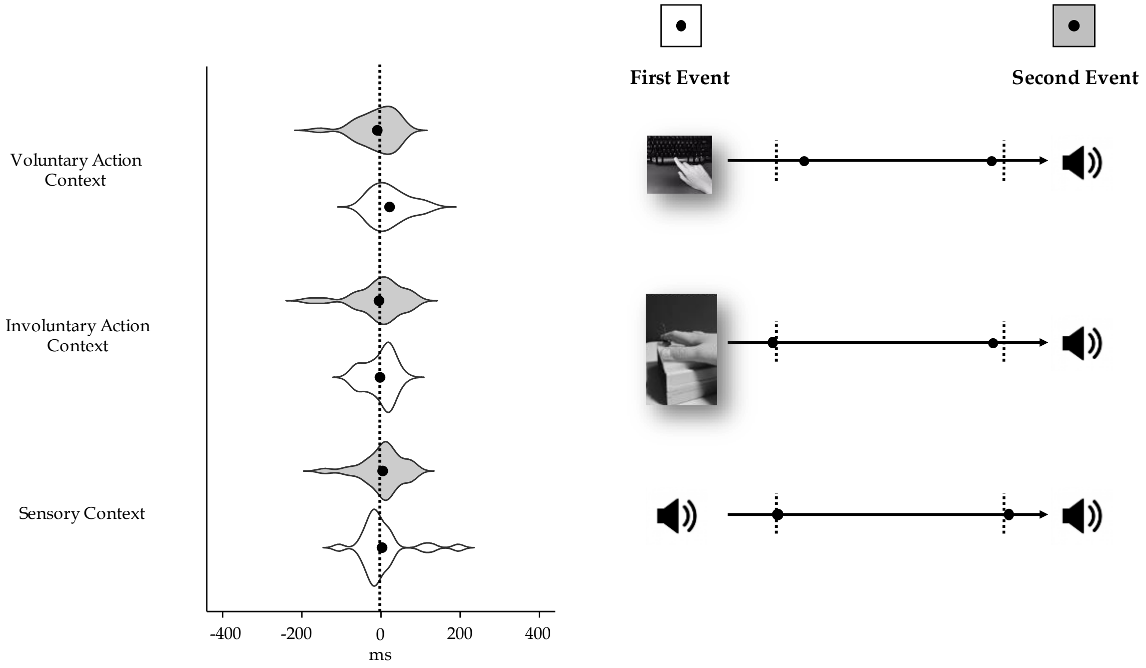


Figure 6.7. *On the* ***left*** *side, violin plots representing the distribution of each participant's mJE for the different contexts. The white violin plots depict the participants' perceptual shift of the first judged event (i.e., the voluntary action, the involuntary action and the control tone). Conversely, the grey violin plots represent the participants' perceptual shift of the second event (i.e., the tone). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of the whole sample. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, total temporal compression does not differ across the different contexts.*

6.4 DISCUSSION

The main purpose of the present series of experiments was to evaluate whether IB might be present even when changing the sensory modalities classically adopted to study the effect. The vast majority of investigations manipulated the type of sensory effect following a voluntary action, showing that the temporal compression characterising IB occurred irrespective of the sensory modality used (e.g., Tsakiris & Haggard, 2003; Engbert et al., 2008; Cravo et al., 2009; Ebert & Wegner, 2010). The present findings are in line with the existing literature, indicating that the illusion can be replicated in different sensory modalities and suggesting that IB is a reliable multisensory and supra-modal phenomenon, governed by the same principal rules at the basis of multisensory integration, that are the *temporal window of multisensory integration* Shams et al., 2000; Bresciani et al., 2005) and the *correct order of cause-effect* (Rohde et al., 2014). More precisely, IB appears when a voluntary action precedes its effect - irrespective of the sensory modality - in a close temporal proximity. These rules seem to be sufficient for the emergence of the multisensory IB. However, the concept of multisensory integration also implies that different combinations of cross-modal stimuli are assessed (Stein & Stanford, 2008). Therefore, in order to verify whether IB follows the same laws of multisensory integration, a further step is required, that is trying to see what happens, for example, when the sensory nature of the stream of visual stimuli - adopted to report the temporal perception of the events (e.g., the visual numbers of Libet clock, the stream of visual letters in our specific case) - is changed into another sensory modality (e.g., the auditory one). Do both the visual and the auditory streams of stimuli similarly influence the temporal perception of the events to be judged, causing the temporal compression characteristic of the IB? This would not only shed light on the real multisensory nature of IB, but would also provide hints to understand whether IB is a direct consequence of the adopted sensory modality, depending on the type of sensory stimuli used to report the temporal onset of the events. In all the IB studies which adopted the Libet clock method (e.g., Haggard et al., 2002; Tsakiris & Haggard, 2003; Haggard & Cole, 2007; Moore, Ruge et al., 2010; Moretto, Walsh et al., 2011), visual stimuli have always been used to report the temporal subjective experience of the events. However, it is well known that the visual system is more reliable for spatial rather than temporal resolution (e.g., Witten & Knudsen, 2005). Therefore, using visual stimuli to report the subjective onset time of events might have biased the judgments and contributed to the IB. On the other hand, audition is usually more reliable for the temporal aspects of perception (e.g., Repp & Penel, 2002; Bertelson & Aschersleben, 2003; Morein-Zamir, Soto-Faraco & Kingstone, 2003; Freeman & Driver, 2008). Therefore, one might expect that using auditory stimuli as reference point might prevent the appearance of IB, since people tend to be more accurate in determining the temporal onset of the events. In Experiment I we tried to understand this aspect by changing the nature of the sensory stimuli used as reference to report the onset time of events. Results showed that temporal compression (i.e., the IB effect) occurred also when auditory stimuli were adopted to report the temporal perception of the events. Most importantly, the total temporal compression characterizing IB occurred only within the voluntary context. Regarding the single perceptual shifts, only action binding was reproduced. An unexpected result was the lack of effect binding, which did not differ as compared to the other control conditions. More precisely, participants were really accurate to report the onset time of the second event and this prevented the perceptual shift. This result goes against the tide in respect to the vast majority of IB studies, showing a strong binding of auditory, visual and somatic effects towards actions and a weaker action binding (Haggard et al., 2002; Haggard & Cole, 2007; Tsakiris & Haggard, 2003; Moretto, Walsh et al., 2011). However, it is difficult to directly compare our results with those of these other studies because there are several differences in stimulus manipulation and procedure which might have influenced the results. One possible explanation might be that the second visual stimulus, independently from its trigger - voluntary/involuntary action or another visual stimulus - was better estimated because it was perceived as more intense - in line with Stein, London, Wilkinson & Price (1996) who reported that the perceived intensity of a visual stimulus is enhanced in the presence of a sound. Alternatively, the first event (either the voluntary/involuntary action or yellow circle) preceding the green one might act as a warning signal alerting participants that a visual stimulus was about to be presented, thus enabling them to be better prepared to temporal detect the upcoming circle (Zeigler, Grahaman & Hackley, 2001). Accordingly, participants responded accurately to the green circle since they were prepared for its arrival. Despite the reduced effect binding, the overall IB was nevertheless still apparent, even changing the type of sensory inputs and outputs. This result is extremely relevant since it demonstrates that IB is not only a reliable multisensory phenomenon, but also that it is supramodal, being able to arise (i) for different sensory stimuli produced by our voluntary actions and, most importantly, (ii) independently of the sensory stimuli adopted to investigate the phenomenon. In addition, the present findings contributed to characterize IB as an implicit measure of agency. Indeed, as active agents in the world, we everyday face with a multitude of multisensory stimuli. Therefore, the demonstration that IB is still present even when changing the type of sensory stimuli strengthens its relation with agency. In Experiment II-A and II-B we then studied the temporal windows within IB can occur. Using the classical visuo-auditory IB paradigm adopted in the previous chapters, the speed of the the visual letters was changed. Results showed that when the stream of letters was slowed down (e.g., 250 ms and 200 ms), the IB effect disappeared, as participants were quite accurate in detecting the temporal onset of the different events. These findings suggest that the temporal windows within the letters are presented are crucial for the emergence of the IB. In particular, the visuo-auditory IB occurs only when the stream of visual letter is set at 150 ms (see previous chapters).

To sum up, the present findings, in line with other studies in literature (e.g., Tsakiris & Haggard, 2003; Engbert et al., 2007; 2008; Cravo et al., 2009; Ebert & Wegner, 2010; Moretto, Walsh et al., 2011), suggest that SoAg may be considered as a reliable multisensory supra-modal mechanism, which is also evident when another combination of cross-sensory stimuli (e.g., auditory-visual IB) is tested.

Importantly, it appears to be necessary to adjust the timing of stimuli presentation accordingly to their sensory nature.

CHAPTER 7

STUDY V

REDUCED AWARENESS OF ACTION CONTROL IN PARKINSON DISEASE

7.1 INTRODUCTION

PD is a neurodegenerative illness characterized by prominent motor symptoms (e.g., bradykinesia, rigidity, tremor, and postural instability), which reflect, at least in part, a pathological loss of dopaminergic neurons in the ventral midbrain and nerve terminal degeneration in the striatum (Bernheimer, Birkmayer, Hornykiewicz, Jellinger & Seitelberger, 1973; Jankovic, 2008). However, PD is not a mere motor pathology since it is also characterized by a variety of symptoms which go beyond motor disturbances, such as cognitive decline especially affecting EFs (Elgh, Domellöf, Linder, Edström, Stenlund et al., 2009; Godefroy, Azouvi, Robert, Roussel, LeGall et al., 2010). PD is particularly interesting in the context of the SoAg research because of its characteristic disturbances in willed behaviour and motor cognition, including the difficulty of planning actions and establishing a link with their consequences (e.g., Hughes, Barker, Owen & Rowe, 2010; Hughes, Altena, Barker & Rowe, 2013; Wolpe, Nombela & Rowe, 2015). Up to now, only one study addressed this issue (Moore, Schneider et al., 2010), reporting that PD itself was not associated with abnormal SoAg. Interestingly, IB modifications in PD patients were caused by DA medication used to treat the disease. Indeed, according to the Authors, an overdose of DA in the ventral striatum – a key structure for instrumental reinforcement learning - would have caused a hyper-temporal binding, similar to what happens in schizophrenic patients with PS, where excessive DA activity leads to an over-association between intentional actions and external events (Haggard et al., 2003; Voss et al., 2010). Although the results of Moore, Schneider et al.'s (2010) are very attractive, suggesting a relevant contribution of DA in the SoAg, their interpretations might be questioned on several grounds. First, they assume that IB depends on ventral striatum's functioning. It is known that the ventral portion of striatum, given its extensive interconnections with the limbic part of the brain, plays an important role in the circuitry of reward-oriented behaviour (Haber, 2011). However, in Moore, Schneider et al.'s study (2010) actions did not produce salient or rewarded effects, minimizing the specific role of the ventral striatum in the linkage between action and its effects. Second, in PD the differential degeneration of DA between the dorsal and the ventral striatum is particularly evident especially in the early stages of the disease (Dauer & Przedborski, 2003; Haber, 2003). As the disease progresses, dopaminergic deficiency in the ventral striatum increases

(MacDonald, Monchi, Seergobin, Ganjavi, Tamyeedi et al., 2013). In the study of Moore, Schneider et al. (2010) the vast majority of patients at the time of testing were in an advanced phase of the disease, where it is likely that both the dorsal and ventral systems are suffering from DA depletion, making their pattern of results difficult to explain taking into account the *overdose theory*. Yet, available information about the effects of DA on SoAg in PD patients is inconclusive. In the present study special attention will be devoted to understand the role of DA in IB. As discussed in Chapter 2, IB is only observed for intentional actions and is mainly supported by the frontal SMA (see Chapter 5; Moore, Ruge et al., 2010; Kühn et al., 2013). In PD patients, the SMA – a key region associated with internal movement programming in the healthy brain (Picard & Strick, 1996) - is systematically poorly activated (e.g., Jahanshahi, Jenkins, Brown, Marsden, Passingham et al., 1995; Haslinger, Erhard, Kämpfe, Boecker, Rummeny et al., 2001; Sabatini, Boulanouar, Fabre, Martin, Carel et al., 2000), causing specific deficits in internal movement generation (Jahanshahi et al., 1995; Rowe, Stephan, Friston, Frackowiak, Lees et al., 2002). Indeed, PD patients often show specific impairments when relying on internal control processes (Siegert, Harper, Cameron & Abernethy, 2002; Michely, Barbe, Hoffstaedter, Timmermann, Eickhoff et al., 2012). Although dopaminergic therapy improves motor symptoms at all stages of disease, the effects of such treatments on PD-associated cognitive impairments are more complex. Previous studies investigating the effect of DA medication on EFs revealed inconsistent effects (for reviews see: Cools, 2006;

Dirnberger & Jahanshahi, 2013). Of particular interest in the context of the present study, deficits in higher internal motor control respond less well to dopaminergic medication (Michely et al., 2012), in line also with other studies (Feigin, Ghilardi, Carbon, Edwards, Fukuda et al., 2003; Kehagia, Barker & Robbins, 2010; Fasano, Daniele & Albanese, 2012; Narayanan, Rodnitzky & Uc, 2013). Based on these assumptions we hypothesized that PD patients on medication might show an opposite pattern compared as Moore, Schneider et al's study (2010), that is a reduced IB.

7.2 METHODS

7.2.1 PARTICIPANTS

Two groups of participants took part in the study. The first group (N = 13; 8 females; mean age: 54.39 years, SD: 5,62, range: 44-63; education in years: 13.77, SD: 3.83; average disease duration: 6.13 years, SD: 3.89; mean age at onset: 46.46 years, SD: 5.96) was recruited from the Parkinson and Movement Disorders Unit of the 'San Camillo' Hospital (Venice-Lido, Italy) and participants were all diagnosed with PD, according to the United Kingdom Parkinson's disease Society Brain Bank (Hughes, Daniel, Kilford & Lees et al., 1992; Gelb, Oliver & Gilman, 1999). Patients with atypical Parkinsonism as well as those who had clinically serious cardiovascular, metabolic and psychiatric diseases or neurosurgical procedures were not considered. We calculated Levodopa Equivalent Daily Dose (LDED) and Dopamine Agonist Equivalent Daily Dose (DAED) for each patient (Tomlison, Stowe, Patel, Rick, Gray et al., 2010). Clinical severity was graded using the Hoehn and Yahr (1967; H & Y) and the motor Unified Parkinson Disease Rating Scale (UPDRS-III; Fahn & Elton, 1987). Demographic data (age, gender and education level) and neurological details (age at onset, disease duration) were also collected (see Table 7.1).

Table 7.1. *Demographic data and clinical features of PD patients.*

	Mean	SD
Age	54.39	5.62
Education	13,77	3.83
Disease Duration	6.13	3.89
Age onset	46.46	5.96
LEDD	431.66	232.95
DAED	124.62	102.74
UPDRS TOT	21	4.58
H & Y	1.75	0.82
ADL	6	0
IADL	6.38	1.45
PDQ	5.46	3.73
BDI-II	5.62	4.87

SD: Standard Deviation; LEDD: Levodopa Equivalent Daily Dose; DAED: Dopamine Agonist Equivalent Daily Dose; UPDRS TOT: Unified Parkinson Disease Rating Scale Total; H & Y: Hoehn & Yahr; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; PDQ: Parkinson's disease quality of life; BDI-II: Beck Depression Inventory.

All patients participating in the study had a brain MRI with no otherwise clinically relevant structural alterations and were tested after medication. The time interval between medication administration and testing varied between 1 and 3 hours, such that patients were in a relative ON state. None of the participants showed therapy-related motor complications that could interfere with the study task. The second group was made up of sex- age- and education-matched healthy controls (N = 13; 5 females; mean age: 53.62 years, SD: 10.02, range: 30-66; education in years: 13, SD: 4.47). The inclusion criteria for all participants comprised an age < 65 years old (based on results obtained from the Study II - Chapter 4), intact visual and auditory senses, no current history of neurologic or psychiatric disease and no current history of drug or alcohol abuse. All the participants showed right-handed dominance (Edinburgh Inventory; Oldfield, 1971). The experimental sessions lasted approximately an hour. The ethics committee of the IRCCS San Camillo, Venice (Italy) approved the study, which was carried out in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all of the participants.

7.2.2 NEUROPSYCHOLOGICAL MEASURES

The neuropsychological protocol for PD patients included the MMSE and the Montreal Cognitive Assessment (MoCA: Nasreddine, Phillips, Bédirian, Charbonneau, Whitehead et al., 2005) to assess general cognitive functions. Attention/working memory domain was tested by the TMT (Giovagnoli, Del Pesce, Mascheroni, Simoncelli, Laiacona et al., 1996), Digit Span Forward and Corsi's Test

(Spinnler & Tognoni, 1987). EFs were evaluated by phonological fluency task (Novelli, Papagno, Capitani & Laiacona, 1986) and the Stroop Color/Word test (Caffarra, Vezzadini, Dieci, Zonato & Venneri, 2002). We used the Beck Depression scale (BDI-II) (Yamanishi, Tachibana, Oguru, Matsui, Toda et al., 2013) to evaluate the eventual presence of depressive symptoms (range score 0-63). We also administered the 8-item version of Parkinson's disease quality of life (PDQ-8; Jenkinson, Fitzpatrick, Peto, Greenhall & Hyman, 1997). In addition, abnormal functional independence was assessed by ADL/IADL. Standardized normative Italian datasets were used as comparative references to determine cognitive impairments. Regarding the control group, only the MMSE, Digit Span, TMT-A, TMT-B and Phonological Fluency task were administered.

7.2.3 STIMULI, APPARATUS, PROCEDURE AND DATA ANALYSES

All the materials, the procedure and data analyses were the same of those used and applied in Study I, described in Chapter 3. The only difference regarded the control conditions: only the 'sensory context' condition (i.e., that with the two sounds in sequence) was included, while the involuntary movement condition was excluded in order to reduce the necessary time to perform the task. Specifically, the 'sensory context' condition was added as control to investigate whether any deficit was specific to agency or indicated a more general deficit in timing judgements.

To correlate the IB score with clinical parameters such as the disease's duration, the motor UPDRS score and the age of onset, non-parametric correlations (Spearman's rank correlation coefficient) were run. To examine the effects of age and cognitive functions, these values were included as covariates in a subsidiary analysis.

7.3 RESULTS

Table 7.2 summarizes the mJEs, perceptual shifts, and overall binding in the two groups. Patients and controls did not differ in terms of age ($t_{24} = 0.241$, $p = 0.811$), sex ($X^2 = 1.39$, df = 1, $p = 0.434$) and education ($t_{24} = -0.557$, $p = 0.583$). Control and patient perceptual shifts were submitted to a repeated-measures ANOVA, with 'group' (patients vs controls) as between-subject factor, and the 'type of context' (voluntary action vs sensory) and the 'judged event' (first, second) as within-subject factors. A significant Group × Context × Event interaction was observed, $F(1, 24) = 5.42$, $p = 0.029$, $\eta^2_p = 0.184$. Only a main effect of the 'judged event' was detected, $F(1, 24) = 30.39$, $p < 0.001$, $\eta^2_p = 0.559$, with a significant shift of the first event towards the second one (23.65 ms) and vice versa (-56.25). No main effects of the 'type of context', $F(1, 24) = 1.17$, $p = 0.291$, $\eta^2_p = 0.046$, and 'group', $F(1, 24) = 0.89$, $p = 0.353$, $\eta^2_p = 0.166$ were found.

Table 7.2. *mJEs, perceptual shifts and overall binding for patients and controls.*

Group	Condition	Event Judged	mJE (ms) ± sd	Mean Shift (ms) ± sd	Mean Overall Binding (ms) ± sd
Patients	**Baseline**				
	1) Voluntary Action	Voluntary Action	-18.46 ± 74.96		
	2) Tone	Tone	18.85 ± 40.99		
	3) Control Tone	Control Tone	20± 42.67		
	Experimental				
	4) Voluntary Action - Tone	Voluntary Action	0 ± 85.54	18.46 ± 63.16	188.08 ± 86.28
	5) Voluntary Action - Tone	Tone	-24.62 ± 72.59	-43.46 ± 74.31	
	6) Control Tone - Tone	Control Tone	16.15 ± 41.84	-3.85 ± 39.54	189.23 ± 98.49
	7) Control Tone - Tone	Tone	-45.77 ± 85.14	-64.62± 85.11	
Controls	**Baseline**				
	1) Voluntary Action	Voluntary Action	-29.23 ± 95.13		
	2) Tone	Tone	53.85 ± 49.67		
	3) Control Tone	Control Tone	47.69 ± 48.59		
	Experimental				
	4) Voluntary Action - Tone	Voluntary Action	41.54 ± 123.35	70.77 ± 85.41	95.77 ± 97.12
	5) Voluntary Action - Tone	Tone	-29.62 ± 62.63	-83.46 ± 54.06	
	6) Control Tone - Tone	Control Tone	56.92 ± 40.24	9.23 ± 20.9	207.31 ± 99.43
	7) Control Tone - Tone	Tone	20.38 ± 107.62	-33.46 ± 96.34	

Examining the interaction in detail, *post hoc* comparisons did not reach the statistical power (Figures 7.1 and 7.2). We therefore analysed the overall binding across the two groups. A significant Group x Overall Binding interaction emerged, $F(1, 24) = 5.42$, $p = 0.029$, $\eta^2_p = 0.184$. The two groups differed exclusively regarding the voluntary action context ($p = 0.017$) (sensory context: $p = 0.646$) (Figure 7.3). Only healthy controls presented the classical total temporal compression, which did not emerge in the case of the control condition (i.e., the sensory context; $p = 0.003$). On the other hand, no differences between the experimental and the control conditions were detected in patients ($p = 0.973$). In a subsequently analysis controls and patients overall binding data were entered into a mixed analysis of covariance, with Age, MMSE, TMT-A, TMT-B, Digit Span and Phonemic Fluency as covariates in order to verify the role of age and cognitive performance on the obtained results. These additional analyses showed no interaction between overall binding and age, $F(1, 24) = 0.006$, $p = 0.81$, $\eta^2_p = 0.003$, MMSE, $F(1, 24) = 0.182$, $p = 0.673$, $\eta^2_p = 0.008$, TMT-A, $F(1, 24) = 0.169$, $p = 0.685$, $\eta^2_p = 0.007$, TMT-B, $F(1, 24) = 0.822$, $p = 0.374$, $\eta^2_p = 0.035$, Digit Span, $F(1, 21) = 0.01$, $p = 0.92$, $\eta^2_p < 0.001$, and Phonemic Fluency, $F(1, 23) = 0.025$, $p = 0.877$, $\eta^2_p = 0.001$. Regarding baseline judgments, patients' judgements of their actions or the tone in BCs were similar to those for healthy controls, suggesting analogous time judging abilities (baseline voluntary action: $t_{24} = 0.321$, $p = 0.751$; baseline tone: $t_{24} = -1.96$, $p = 0.062$; baseline control tone: $t_{24} = -1.54$, $p = 0.126$). The correlational analysis on the overall binding and the perceptual shift score showed no significant correlations between the performance and the disease's duration, the age of onset, the motor UPDRS score ($p > 0.05$) in PD patients. In addition, no significant correlations between any binding scores and any neuropsychological measures were detected ($p > 0.05$).

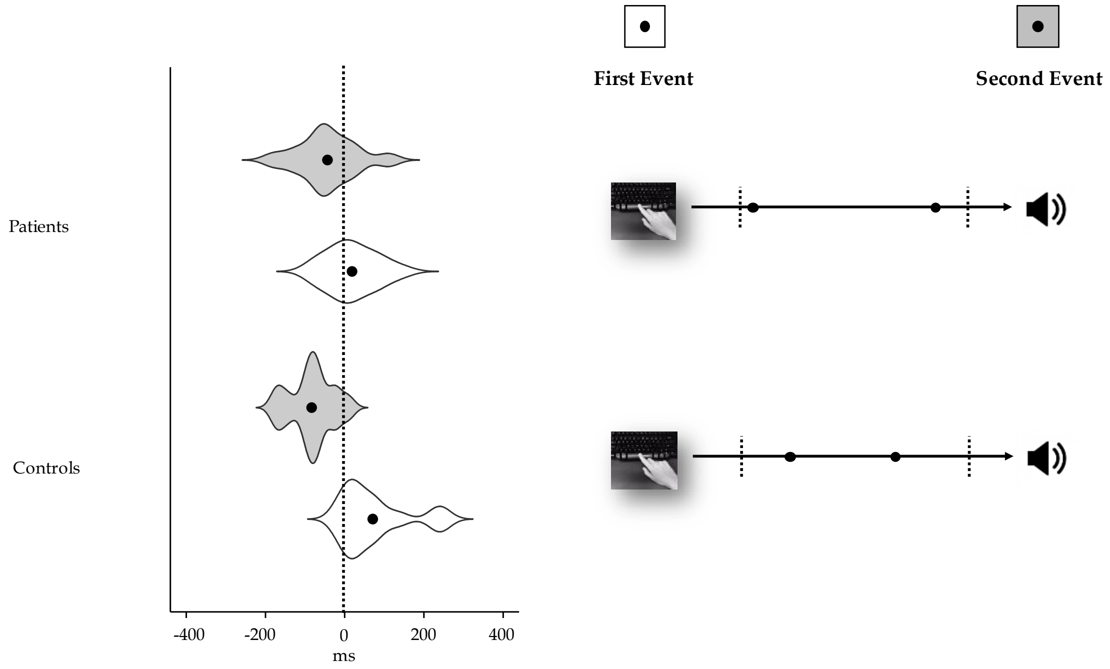


Figure 7.1. *On the* ***left*** *side, the graph shows participants' perceptual shifts within the* ***voluntary context****. The white violin plots depict the action binding (i.e., the shift of the the voluntary action towards the tone). Conversely, the grey violin plots represent the effect binding (i.e., the perceptual shift of the tone towards the action). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of each group of participants. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. As the image depicts, the total temporal compression is only evident within the group of controls.*

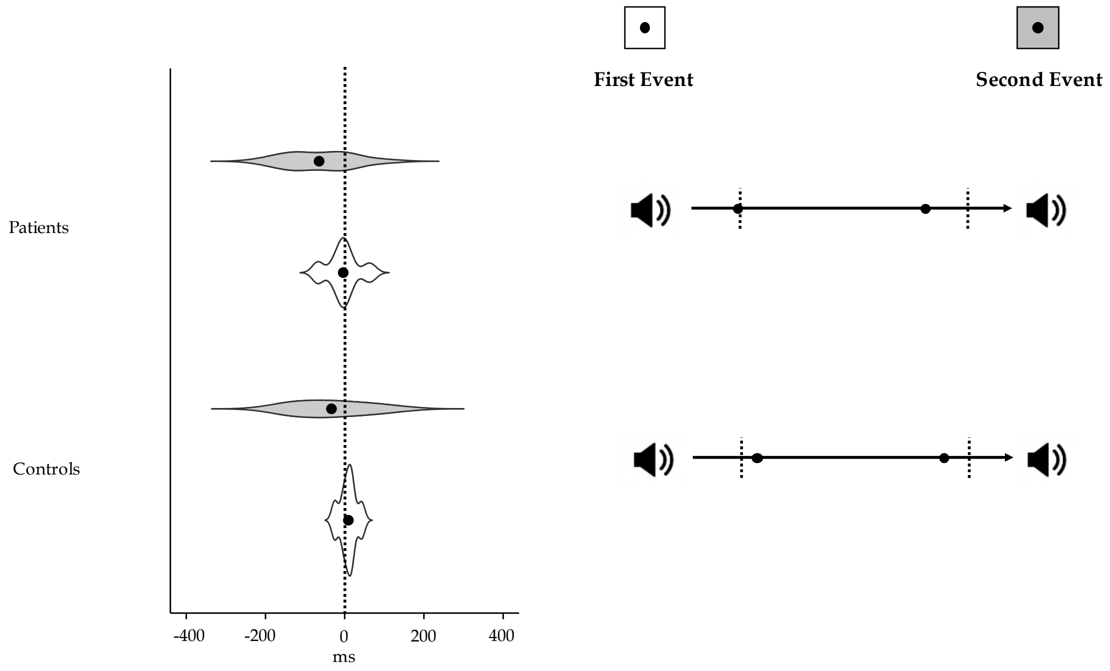


Figure 7.2. *On the* ***left*** *side, the graph shows the perceptual shifts within the* ***sensory context*** *for each group. The white violin plots depict the shift of the first sound towards the second tone. Conversely, the grey violin plots represent the effect binding (i.e., the perceptual shift of the second tone towards the first control tone). The dashed lines stand for the actual onset of the event of interest. The black dots stand for the mJE of each group of participants. On the* ***right*** *side, a schematic, graphical and symmetrical representation is depicted. Again, the dashed lines stand for the actual onset of the event of interest, while the black dots represent the perceived event by the participants. No significant differences emerge between the two groups.*

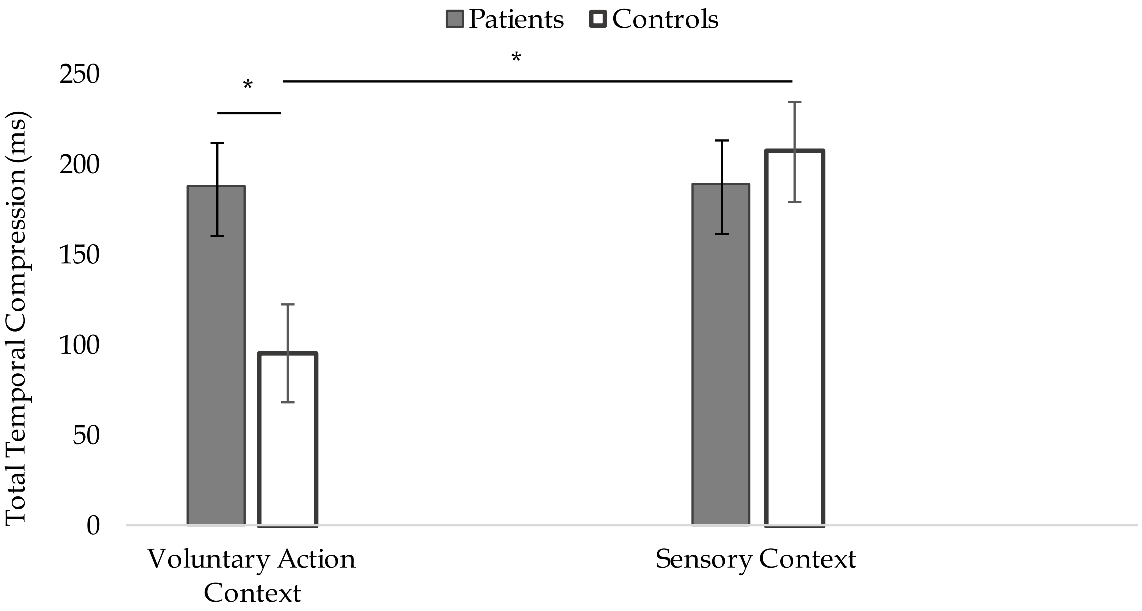


Figure 7.3. *Differences in the voluntary action and sensory overall binding between the two groups of participants. Error bars represent SEM and * indicates the significant difference in overall binding between and within groups. Only controls present the IB effect within the voluntary action context. No differences are detected between groups within the sensory context condition. Small values indicate stronger IB.*

7.4 DISCUSSION

The aim of the present study was to assess IB in a group of PD medicated patients in order to investigate the impact of dopaminergic treatment on the SoAg. The overall binding effect was significantly different in PD patients relative to control participants, highlighting a decreased temporal attraction of the perception of action towards a subsequent tone in PD patients. This lack of binding has been interpreted as an indicator of a decreased sense of control or agency over intentional actions. One might say that such behavioural change of binding might reflect poor attention to the task for the high levels of concentration required. However, PD patients demonstrated to perform the task quite well, despite its complex cross-modal nature. Indeed, patients' baseline judgments of actions and tones were similar to those of controls. In addition, a critical internal control came from the results of the sensory context (i.e., those with the two subsequent tones), which were not different from control participants. The significant findings regarded the overall binding, but not the single perceptual shifts, in line with the study run by Moore, Schneider et al. (2010). However, contrary to the mentioned study, the pattern of results was exactly the opposite. According to Moore, Schneider et al. (2010), like in schizophrenic patients (Haggard et al., 2003), DA would boost action-effect binding. Authors started from the assumption that IB is supported by the ventral striatum, which is supposed to be preserved from the DA loss in the very first phase of the disease. Therefore, cognitive functions supported by DA activity in this region (i.e., IB) are worsened by dopaminergic medication, inducing - instead of an impaired reduced temporal compression as expected by the excessive DA administration - a hyper-binding effect, as in schizophrenic patients who present an overactive dopaminergic system. However, if the overdose theory of the ventral striatum proposed by Moore, Schneider et al's (2010) was correct to explain their data, they should have expected an impaired performance and therefore a reduced - and not an increased - IB. This is also supported by evidence suggesting that the excessive

DA activity in schizophrenia is mainly associated with the dorsal and not the ventral striatum (Kegeles, Abi-Dargham, Frankle, Gil, Cooper et al., 2010; Sorg, Manoliu, Neufang, Myers, Peters et al., 2013). In addition, in PD the differential degeneration of DA-producing cells in dorsal and ventral striatum is particularly evident during the early stages of the disease. As the disease progresses, also the ventral part becomes deficient in DA, acting and reacting to DA in the same way as the dorsal part. In Moore, Schneider et al's (2010) the majority of patients at the time of testing was characterized by advanced stages of the PD disease, suggesting that both the systems were likely impaired. The overdose theory does not seem to be the ideal framework to consider in order to explain their results. Such over-association between a voluntary action and its sensory consequence in PD seems to be odd. Indeed, PD is characterized by an impairment in self-willed action initiation. Although DA administration is supposed to ameliorate the basic motor symptoms, the SoAg - as previously discussed in Chapters 1 and 3 – seems to belong to the EFs family and to reflect a more complex mechanism whose deficits cannot be restored with the simple dopaminergic therapy administration. Indeed, as previously reported in literature, deficits in higher internal motor control respond less well to dopaminergic medication (Feigin et al., 2003; Kehagia et al., 2010; Fasano et al., 2012; Michely et al., 2012; Narayanan et al., 2013). Our data are in line with these results, showing that DA is not able to restore these functions. Therefore, since IB is reduced in patients ON medication, one might also expect that PD itself is associated with a reduced SoAg. However, although this is highly likely, it remains only a speculation since patients OFF medication were not included in the present investigation, and future studies are required to verify this hypothesis.

To sum up, the present study showed that medicated patients presented a reduced IB as compared to controls. Most importantly, DA medication did not seem to improve this higher aspect of motor control (i.e., the awareness of action control). The reported inconsistencies between the present results and those of Moore, Schneider et al. (2010) might have resulted from different reasons, such as the heterogeneous patient populations, the different medication withdrawal methods administered as well as the paradigms and the protocols employed. Our data also support the hypothesis of Fern-Pollak, Whone, Brooks, and Mehta (2004) suggesting a differential motor and cognitive effect following medication withdrawal. Accordingly, these effects might arise from the possibility that DA modulates motor and cognitive function by different pathways, with motor functions being ameliorated through medication via nigrostriatal projections to motor cortex and cognitive functions predominantly influenced via mesocortical inputs to prefrontal cortex (see also: Mattay, Tessitore, Callicott, Bertolino, Goldberg et al., 2002). Hence, our findings add further support to the notion that EFs in higher order control of actions in PD may be related to neurotransmitter system dysfunction beyond the dopaminergic system, such as, e.g. acetylcholine, noradrenaline or serotonin (Marsh, Biglan, Gerstenhaber & Williams, 2009; Narayanan et al., 2013; Ye, Altena, Nombela, Housden, Maxwell et al., 2014; Ye, Altena, Nombela, Housden, Maxwell et al., 2015). Further studies are needed to disentangle this issue.

CHAPTER 8

CONCLUSIVE REMARKS

The feeling of being in control of the actions we make is a fundamental part of human experience and a is a *sine qua non* of a well-functioning society. Indeed, all civilized human cultures have the concept that individuals are responsible for their actions. Responsibility, in turn, takes both an individual dimension - since people have to deal and live with what they do - and a social dimension, as society may punish people for illegal actions. In lights of these relevant implications, a deep understanding of the SoAg seems to be mandatory.

The experimental work included in the present thesis aimed at extending the actual knowledge on the SoAg, capitalizing on an implicit measure, namely the IB effect. More specifically, the lifespan (Chapter 4), neural (Chapter 5), multisensory (Chapter 6) and clinical (Chapter 7) dimensions have been explored. The advances of the present thesis are several and multifaceted, with a significant potential for concrete applications.

A first novelty characterizing the present work was the development of a new method to investigate the implicit nature of the SoAg. This methodology showed its potential to 'catch' facets of agency processing - especially in particular populations (i.e., children, elderly and PD patients) - that otherwise would have remained uncovered if simply considering the explicit measures (see Chapter 1) and other implicit methodologies currently adopted to investigate IB (i.e., the clock paradigm – Libet et al., 1983 - and the time interval paradigms – see Cravo et al., 2011 for a brief review; see also Chapter 3 of the present thesis). With respect to the use of explicit measures, these are influenced by individual differences related to cognitive capacities or personality and to a lack of subjectivity insights. On the other hand, concerning the implicit measures, the paradigms currently adopted to study IB are still subject to a great deal of both support and criticism (see Chapter 3). For example, the time interval paradigm (e.g., Engbert et al., 2007; 2008; Cravo et al., 2009; Humphrey & Buehner, 2009; 2010) is not able to disentangle between action and effect binding, whereas the clock methodology taps into a wide range of cognitive abilities, including EFs, which are affected in populations with a 'compromised' SoAg. Therefore, the use of such tasks in these 'special' populations is far from being the optimal way to study the SoAg because of the possible confounders which might influence the results. In lights of these limitations, the introduction of a new methodology to be used especially in a clinical setting appeared to be necessary in order to elucidate the clinical side of the SoAg. In addition, detecting similar results (i.e., the IB effect) by means of another method allows the validation of IB as strong and reliable phenomenon, which is able to arise independently of the methodology used. The paradigm described in this work does not aim at replacing the previous ones (i.e., the Libet clock) which led to the discovery of IB (Haggard et al., 2002). However, the choice of a particular method has to take both studies' aims and the peculiarities of their sample (e.g., adults, children or patients) into account. For example, the new paradigm here proposed might lead to uncover agency processing in 'special' populations and might represent a possible prompt for the development of new tools in forensic domain. Future studies are needed in order to well characterize its potential, by testing larger samples.

By adopting this new methodology, SoAg was tested across the lifespan (Chapter 4) and in a group of patients with PD (Chapter 7). Results showed that children, elderly and PD patients presented a reduced SoAg as compared to matched controls. These data are relevant for two main reasons. First, our society condemns behaviours which have negative consequences on the external world or on other people. As a matter of fact, some populations, like those tested in the present thesis, present a lack of agency: this aspect should be carefully taken into account in the penal domain when establishing penalties. Second, these data shed light on the possible neural bases of the implicit SoAg. Indeed, considering the relevant role of EFs for a socially responsible conduct and the diminished SoAg in childhood, elderly and PD patients, a crucial role of the frontal lobe is expected. In the third study (Chapter 5), using tDCS, such hypothesis was tested and a causal contribution of pre-SMA in agency was observed. Indeed, modulation of such area in healthy participants reduced the SoAg. Even though the present thesis does not provide direct information about the brain mechanisms underlying the SoAg in children, elderly and PD patients, these findings seem to be in line with those obtained with tDCS in healthy participants. Indeed, the reduced SoAg might be linked to a still immature SMA in children (Crone, Donohue, Honomichl, Wendelken & Bunge, 2006) and to a SMA hypo-activation both in healthy elderly (Inuggi, Amato, Magnani, González-Rosa, Chiefo et al., 2011) and in PD patients. However, to fully account for this parallelism, future studies should combine behavioural data with advanced neuroimaging techniques in these populations. Another important result supporting, although indirectly, the possible involvement of the pre-SMA was obtained in Chapter 6 where the multisensory nature of the SoAg was explored. Here, findings showed that the temporal compression characterizing IB was still present independently of the sensory nature of actions' consequences and did not depend on the 'sensory nature' of the task: more precisely, the IB effect occurred even when changing the sensory modalities within the experimental task. These behavioural results would testify an indirect involvement of the pre-SMA, which seems to be crucially implicated in the action-effect linkage independently of the sensory nature of the effects (see Chapter 5 and Moore, Ruge et al., 2010). However, additional neuroimaging studies are mandatory in order to better define the supramodal role of the pre-SMA in the SoAg.

Findings reported in Chapter 6 are also relevant in order to open a new line of research within the agency field. Multisensory integration is a process known to occur not only for vision and audition – well explored within the SoAg – but also for other senses, like taste and smell (Driver & Spence, 1998; Stein & Stanford, 2008). With respect to smell, odours have a unique scientific potential: these stimuli are often consciously neglected, and their processing is mainly automatic, but able to modify the course of decisions and actions, partly because of their outstanding emotional power and social relevance (Stevenson, 2010). Odors are therefore of particular interest in studying agency for many reasons. First, they are omnipresent in our daily life and have been proved to modulate human behaviour exerting influence on cognitive domains and motor control (Spence, McGlone, Kettenmann & Kobal, 2001; Li, Moallem, Paller & Gottfried , 2007; Zucco, 2003; Porter, Craven, Khan, Chang, Kang et al., 2006; Tubaldi, Ansuini, Tirindelli & Castiello, 2008). Second, and most importantly, olfaction represents information affectively thanks to the strong overlap between olfactory cortex and limbic brain structures (Royet, Zald, Versace, Costes, Lavenne et al., 2000). This peculiarity of odors is crucial in the agency field since recent theories have underlined a link between SoAg and the affective domain (Synofzik et al., 2013; Gentsch & Synofzik, 2014). Very recently, some Authors (e.g., Moretto, Walsh et al., 2011; Haggard & Yoshie, 2013; Yoshie, Di Costa & Haggard, *in press*) tried to explore such issue by modifying the emotional or moral valence of auditory or visual stimuli. However, contrary to olfaction, audition and vision are not usually accompanied by the visceral feel of affective contact (Stevenson & Attuquayefio, 2013), not representing therefore useful senses to study the emotional side of agency. Odors, on the contrary, modulate neuronal responses within the amygdala in a stronger way (Royet et al., 2000), eliciting more intense affective self-report (Hinton & Henley, 1993) and emotional memories (Herz & Engen, 1996). Therefore, a deep understanding of the emotional dimension of agency might be reached using odors. Future studies are needed to confirm this hypothesis.

8.1 EPILOGUE

So, *"how does the brain link voluntary actions with their consequences?"* As stated by Haggard et al. (2002) *"the brain contains a specific cognitive module that binds intentional actions to their effects to construct a coherent conscious experience of our own agency"*. Altogether the pieces of evidence obtained from the present thesis indicate that the pre-SMA represents a crucial region within the SoAg. Such region would bind intentional actions with their sensory consequences, independently of their sensory nature. Sensory information would reach this region indirectly, namely via superior temporal sulcus for visual and auditory stimuli (Narayan et al., 2012). Its connections with the superior parietal lobule likely would indicate pathways responsible for cross modal sensorimotor transformations. Further neuroimaging and behavioural experiments are necessary to validate this proposal.

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