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CHOOSING TO INHIBIT:

NEW INSIGHTS INTO THE UNCONSCIOUS MODULATION OF FREE-CHOICES

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Coordinatore: Ch.mo Prof. Giovanni Galfano

Supervisore: Ch.mo Prof. Umberto Castiello

Co-Supervisore: Prof. Chiara Begliomini

Dottorando: Tommaso Dall'Acqua

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LIST OF ABBREVIATIONS

AAL: Automated Anatomical Labeling

ACC: Anterior Cingulate Cortex

AI: Anterior Insula

AIC: Akaike Information Criterion

BA4: Brodmann Area 4

BA46: Brodmann Area 46

BMI: Body Mass Index

BOLD: Blood Oxygenation Level-Dependent

DDM: Drift Diffusion Model

dFMC: Dorsal Fronto-Median Cortex

DLPFC: Dorsolateral Prefrontal Cortex

dPFC: Dorsal Prefrontal Cortex

EEG: Electroencephalography

EPI: Echo Planar Imaging

ERPs: Event Related Potentials

FIR: Finite Impulse Response

fMRI: Functional Magnetic Resonance Imaging

FP: Frontopolar Cortex

FWE: Family Wise Error

FWHM: Full-Width at Half-Maximum

GLM: General Linear Model

GLME: Generalized Mixed Effects

GPi: Internal Segment of the Globus Pallidus

HRF: Hemodynamic Response Function

HR_{max}: Maximum Heart Rate

IFG: Inferior Frontal Gyrus

IPL: Inferior Parietal Lobule

ISI: Inter-Stimulus-Interval

ITI: Inter-Trial-Interval

LME: Linear Mixed Effects

$LOAD_{max}$: Maximum Watt Load

M1: Primary Motor Cortex

MFG: Middle Frontal Gyrus

MNI: Montreal Neurological Institute

MPRAGE: Magnetization Prepared Rapid Acquisition Gradient Echo

MVPA: Multivoxel Pattern Analysis

NCE: Negative Compatibility Effect

P: Precuneus

PCE: Positive Compatibility Effect

PG: Precentral Gyrus

PMC: Premotor Cortex

preSMA: Pre-Supplementary Motor Area

RAH: Reticular-Ascending Hypofrontality

RCZ: Rostral Cingulate Zone

REML: Restricted Maximum Likelihood

RFT: Gaussian Random Field Theory

RFX: Random Effects Analysis

ROI: Region of Interest

RP: Readiness Potential

RTs: Reaction Times

SFG: Superior Frontal Gyrus

SG: Supramarginal Gyrus

SPM12: Statistical Parametric Mapping 12

SSD: Stop Signal Delay

SSRT: Stop Signal Reaction Time

SST: Stop Signal Task

STN: Sub-Thalamic Nucleus

TR: Repetition Time

SYNOPSIS

In our daily activities, we all experience a certain degree of control over our behaviours and the more we feel 'in control' the more we are likely to describe our behaviours as self-generated or 'intentional'. Such intentional control refers to the capacity of humans to perform actions based on internal decisions and motivations, rather than external stimulation. Within the psychological debate on free will, this evidence raised the question on how 'free-choices' are taken when decisions are not dictated by immediate external imperatives. The core argument concerns whether voluntary actions follow a conscious intention to act or whether the feeling of being in control is just an epiphenomenon of unconscious neural mechanisms that are the true origin of behaviour.

Different components of a free-choice can be isolated and investigated. Participants can choose *what* action to make, *when* to make an action, or *whether* to make an action at all (Brass & Haggard, 2008). Each of these refers to a different aspect of free-choice, but all of them involve the presence of a choice between multiple available options. Studying voluntary responses in this manner and comparing them with action or inhibition in response to a specific external stimulus, allow us to obtain useful insights into the origin of endogenous decisions. Among these components, the decision about whether to act – the so called 'intentional inhibition' – has received less attention. Such decision can be taken at almost any stage during motor preparation, until a point of no return (Schultze-Kraft et al., 2016). Libet (1983) controversially suggested that last-moment decisions to inhibit an action involved a purely conscious form of 'free won't' (Libet, Gleason, Wright, & Pearl, 1983). However, alike voluntary actions, conscious decisions to inhibit might also depend on unconscious brain processes. For this reason, to what extent intentional decisions to inhibit are necessarily based on a deliberate choice is still an open question (Parkinson & Haggard, 2014).

The present thesis will examine how unperceivable – subliminal – information in the environment, physiological states of the body and ongoing pre-conscious fluctuations in brain activity contribute to generate voluntary decisions to act or to inhibit. Starting from the contemporary debate raging around free will and taking into account the most recent cognitive models of voluntary actions, the introductory section of the thesis will provide an overview on the basic concepts linked to volition (Chapter 1). Particular attention will be given to behavioural inhibition and how this component has been studied along a continuum from 'stimulus-driven inhibition' to 'intentional inhibition'. For each concept introduced, I will provide a review of the current state of the art regarding both the neural and behavioural mechanisms involved. In particular, I shall focus on previous research suggesting that making free-choices activate a specific network of brain activity.

Chapter 2 will review current evidence regarding how subliminal information in the environment and psychophysiological states act as modulators for free-choice mechanisms both at the behavioural and neural level. Indeed, there is consistent evidence concerned with the ability of subliminal stimuli to bias our free decisions by influencing the activity within the 'choice network'. Similarly, psychophysiological states such as the arousal have been shown to moderate a number of cognitive tasks including response inhibition.

The second part of the thesis will focus on the empirical work I have conducted to investigate some of the theoretical issues previously introduced. The experiment described in Chapter 3 exploits a 'Go/Nogo' paradigm assessing the effect of subliminal priming by highlighting the dramatic effect of congruent and incongruent subliminal information on reaction times and free-choices. As the first experiment validated the paradigm as a meaningful tool to disentangle between forced and free components of making choices in relation to subliminal processing, the functional magnetic resonance (fMRI) experiment described in Chapter 4 capitalizes on the same kind of manipulation. A region of interest (ROI) analysis was conducted to test whether the degree of intentionality of the response

and the information provided by subliminal information might modulate the activity within the 'free-choice network'. In Chapter 5 the effect of an increased level of arousal induced by physical exercise on the performance in the same task will be examined. The experimental section of the present thesis will end with Chapter 6 in which the neural underpinnings of the conscious generation of actions by means of multi-voxel pattern analysis (MVPA) has been investigated.

The thesis will end with a general discussion (Chapter 7). Here I shall rely on the evidence presented in the preceding experimental chapters to propose that free-choices are determined by the interplay between brain, body, and sensory environment.

SINOSSI

Nelle attività quotidiane, tutti noi percepiramo di essere in controllo delle nostre azioni e più ciò viene avvertito, più siamo inclini a descrivere i nostri comportamenti come 'intenzionali'. Questa sensazione di 'controllo intenzionale' si basa sulla nostra capacità di produrre azioni basate più su decisioni e motivazioni interne rispetto a decisioni e motivazioni guidate da eventi esterni. L'evidenza di ciò ha alimentato il dibattito relativo al 'libero arbitrio' stimolando la discussione su come sia possibile prendere delle decisioni unicamente endogene e non basate su indicazioni derivanti dall'ambiente circostante. Il problema principale riguarda la definizione dell'origine di questi meccanismi: le nostre azioni, quando eseguite intenzionalmente, sono prodotte da processi decisionali consci, oppure la nostra sensazione di essere 'in controllo' è solamente un epifenomeno dovuto a meccanismi neurali inconsci che determinano il successivo svolgimento dell'azione?

È possibile differenziare e studiare separatamente diverse componenti decisionali di un'azione intenzionale. Le persone possono scegliere *quale* azione fare, *quando* farla e *se* farla (Brass & Haggard, 2008). Ognuna di queste componenti fa riferimento a diversi aspetti delle azioni intenzionali ma tutte loro sottintendono la capacità di fare una specifica scelta tra molte alternative. Studiando in questo modo le azioni intenzionali e confrontando quest'ultime con le azioni guidate da stimoli esterni, è possibile ottenere utili indicazioni sull'origine delle nostre scelte. Delle tre componenti precedentemente descritte, la componente decisionale del *se* fare un azione – definita "inibizione intenzionale" – ha ricevuto minor attenzione in letteratura. La scelta di inibire un azione può essere presa a diversi stadi della programmazione motoria, fino a un "punto di non ritorno" dove l'azione non può più essere inibita efficacemente (Schultze-Kraft et al., 2016). Libet (1983) suggerì che la capacità umana di inibire un azione fino all'ultimo momento, sottintendesse la possibilità di una forma consapevole di "libertà di veto" (Libet, Gleason,

Wright, & Pearl, 1983). Tuttavia, come per l'origine delle azioni intenzionali, anche l'inibizione intenzionale delle azioni, potrebbe dipendere da processi cerebrali inconsci. Per questo motivo, la possibilità che la decisione d'inibire un'azione intenzionalmente sia necessariamente basata su una libera scelta è ancora argomento di forte dibattito (Parkinson & Haggard, 2014).

Alla luce di quanto detto, lo scopo di questa tesi è quello di esaminare il contributo della presenza di stimoli subliminali nell'ambiente circostante, degli stati psicofisiologici del corpo e delle fluttuazioni dell'attività cerebrale precosciente, nelle generazione delle decisioni intenzionali di inibire o produrre un'azione. Partendo dalla descrizione del dibattito sul libero arbitrio e prendendo in considerazione i più recenti modelli teorici sulle azioni intenzionali, il capitolo introduttivo fornirà una panoramica completa dei concetti relativi alla volontarietà nel controllo motorio (Capitolo 1). L'inibizione delle azioni verrà trattata con occhio di riguardo, introducendo la distinzione tra "inibizione intenzionale" e "inibizione guidata da stimoli esterni". Per ognuno dei concetti introdotti, fornirò una descrizione completa dello stato di avanzamento della ricerca sia dal punto di vista teorico sia dei correlati comportamentali e neurali coinvolti. In particolare mi concentrerò su un network di aree strettamente legate alla produzione di decisioni intenzionali.

Il Capitolo 2 esaminerà come gli stimoli subliminali e gli stati psicofisiologici del corpo possano agire da modulatori dei meccanismi legati alla produzione di azioni, sia a livello comportamentale che a livello neurale. Infatti, studi recenti concordano nel dimostrare come gli stimoli subliminali possano manipolare i processi decisionali legati all'azione influenzando l'attività di un specifico network di aree cerebrali. Allo stesso modo, gli stati psicofisiologici come l'*arousal* hanno dimostrato di moderare numerosi compiti cognitivi tra i quali anche l'inibizione delle azioni.

Sull base degli aspetti teorici introdotti nella prima parte della tesi, la seconda parte si focalizzerà sul lavoro sperimentale che ho condotto durante il dottorato di ricerca.

L’esperimento descritto nel Capitolo 3 utilizzerà un paradigma di "Go/Nogo" per evidenziare l'effetto drammatico della stimolazione subliminale sui tempi di reazione agli stimoli e sulle scelte volontarie di inibire o produrre un’azione. Poiché il primo esperimento ha potuto validare la fruibilità del paradigma come strumento di analisi delle componenti volontarie dell’azione ed inibizione, in relazione all'elaborazione subliminale, l'esperimento di risonanza magnetica funzionale (fMRI) descritto nel Capitolo 4 capitalizzerà sullo stesso tipo di manipolazione sperimentale. È stata condotta un'analisi su aree cerebrali di interesse (ROI) per verificare se il grado di intenzionalità della risposta e le informazioni fornite dagli stimoli subliminali possano modulare l'attività all'interno network di aree specifico. Nel Capitolo 5 invece, verrà esaminato l'effetto dell’aumento del livello di arousal indotto da esercizio fisico, sulla prestazione allo stesso compito. La sezione sperimentale della tesi terminerà con il Capitolo 6 in cui verranno esplorati i correlati neurali della generazione delle azioni mediante l’analisi multivariata dell’attività cerebrale (MVPA).

La tesi terminerà con una discussione generale (Capitolo 7) nella quale, basandosi sui risultati ottenuti nei precedenti capitoli sperimentali, verrà proposto come la capacità di scelta intenzionale tra l’esecuzione e l’inibizione di un’azione sia determinata dall’interazione tra cervello, corpo e l’ambiente circostante.

PART I

THEORETICAL BACKGROUND

CHAPTER 1

MAKING FREE-CHOICES: AN INTRODUCTION

During the tense, winner-take-all Uruguay vs. Italy World Cup's match in 2014, Luis Suárez, one of the world's best strikers over the past years, suddenly sank his teeth into the Italian defender Giorgio Chiellini's shoulder, earning himself a four-month ban. The postgame reactions were predictably inflamed and the questions abounded: what was Suárez thinking? Suárez himself struggled understanding why he could not avoid doing such an infamous and impulsive act. In later interviews he sought to explain how part of the way he plays is felt as unconscious, for better or worse, as if he need to "switch off" potentially interfering conscious thinking. Nevertheless, considering the multiple referees, the TV cameras and perhaps most dramatically, the millions of people watching on television worldwide, how does this "switching off" could have been so uncontrollable and unconscious? If so, should we consider him responsible for what he did? What were the necessary conditions for these accidents to occur? Philosophers, psychologists, neuroscientists or simply sport enthusiasts wondered about the variety of plausible answers to these questions because of the direct connection with the long-lasting debate on humans' capacity for free will.

1.1. The debate on free will

Do people have 'free will'? As healthy adults, from our subjective perspective we can vividly experience an intuitive sense of agency and intentionality across our life. Without considering reflex movements where behaviour is automatically driven by bio-mechanical urges from the body and occurs without a motor command (e.g., yawning, eye blinking), the origin of voluntary behaviour is perceived as 'from the inside': our conscious intentions

precede and cause the physical events that lead us to taking decisions and executing actions. In other words we feel 'in control' and in this sense, our will is experienced as free, a stance that inevitably leads to a dualism where the mind and the brain are separate, interacting entities (Caspar & Cleeremans, 2015). Although the folk-psychological definition of free will takes for granted the capacity for willed behaviour, there are many situations in which such dualistic view of mind-body causation simply does not hold, as for the Luis Suárez example mentioned above. Defining free will as the capacity of controlling one conscious behaviour give rise to many philosophical questions: what happen when voluntary – endogenous – actions are produced (or stopped) without explicit conscious awareness? Does this form of control imply the existence of free will? Is it a uniquely human capacity? (Frith, 2013).

In science the question whether 'free will exists or not' puzzled researchers for centuries and continues to stimulate interests because its implication in many fields of study, from philosophy to psychology and neuroscience (Kane, 1998). The precise definition of free will is heavily burdened with many ethical implications related to morality and responsibility. Across different cultures and societies people are considered causal agents and only who can decide and initiate her own course of action is judged responsible and deserve punishment (Haggard & Lau, 2013). Psychology's interests on free will have a long tradition starting from the genesis of experimental psychology (James, 1905). With the advent of behaviourism however, research lost its interest on the subject, partially because of the scepticism of psychology regarding the reliability of introspection for the study of human cognition. Only recently, in conjunction with the emergence of cognitive neuroscience, psychologists rediscovered the passion for the study of volition. Crucially, the focus has moved from the disheartening question of whether free will exist or not, to the scientifically approach centred on the mechanisms that govern voluntary actions (Baumeister, 2008; Brass, Lynn, Demanet, & Rigoni, 2013). For the first time in history, with

the improvement of brain imaging techniques, researchers had the possibility to correlate introspective data on the sense of conscious intention with objective measurements of brain activity. This combination has made volition an experimental issue, rather than exclusively philosophical (Haggard & Lau, 2013).

1.1.1. The scientific study of volition

Beginning with the ingenious Libet's experiment, research challenged the dualistic view of mind-body causation suggesting that conscious experience of one's intentions is an epiphenomenon rather than the cause of brain activity (Libet et al., 1983; Soon, Brass, Heinze, & Haynes, 2008). In the original formulation of the experiment participants, while watching a rotating hand clock, were instructed to produce an action (i.e., pressing a button) whenever they felt the 'urge' to do so, without any time restriction. At the same time electrodes were placed on the scalp to record electrical activity related to motor preparation. After the action was made, participants were asked to report the position of the clock in relation to when they first felt the conscious intention to move (W judgment) or the actual movement (M judgment). The authors showed that a slow negative potential shift in electroencephalography (EEG) activity in the frontal lobe (readiness potential – RP) was recorded approximately 200 milliseconds before participants' reports of the conscious intention to move (W judgment). The emergence of RP demonstrated for the first time that unconscious brain mechanisms predicts – and intuitively determined – voluntary actions, putting a final nail in dualism's coffin. Libet's interpretation left open the possibility that conscious awareness might have a more specific role in vetoing unwanted behaviour rather than determining action, moving from the concept of 'free will' to a capacity of a 'free won't' or intentional inhibition (Libet et al., 1983). However, unconscious brain activity has been recently recorded to precede, perhaps unsurprisingly, free intentions to stop actions, challenging the possibility for a free won't (Filevich, Kühn, & Haggard, 2013).

Is free will therefore a mere illusion? (Wegner, 2003). Although replicated in other forms (Fried, Mukamel, & Kreiman, 2011; Matsuhashi & Hallett, 2008) and with much more convincing time-scales (Soon et al., 2008) this class of experimental manipulations has been criticized because the unreliability of subjective timing judgments in such small window of time and for the possible confounding caused by the attentional demands required by the task (Lau, Rogers, Haggard, & Passingham, 2004; Trevena & Miller, 2002). According to recent bottom-up views of action generation, the conscious intention to move is not elicited by the RP, but merely depends on spontaneous fluctuations in neural activity that occasionally brings the motor system to the output threshold. For Schurger et al. (2012), the RP is merely an artefact produced by the averaging event-related potentials (ERPs) based on the reported W judgment (Schurger, Sitt, & Dehaene, 2012). On this view, voluntary actions happen to us, rather than us causing them.

Following Libet's ground-braking discoveries, researchers took advantage of two empirical methods to look into voluntary actions: first, through introspection, voluntary actions can be defined in terms of experience or the so-called 'first-person perspective'. Alike Libet's experiment (Libet et al., 1983) studies in this field are concerned with the definition of how people experience the sensory consequences of the intention to move and the sense of agency upon their actions (Chambon, Wenke, Fleming, Prinz, & Haggard, 2013; Decety & Lamm, 2007; Dogge, Schaap, Custers, Wegner, & Aarts, 2012; Haggard, Clark, & Kalogeras, 2002). Second, research on voluntary actions has been defined in terms of behaviour or 'the third-person perspective' (Frith, 2013). For the purposes of the present thesis the next section will review the current empirical knowledge on voluntary action espousing the 'third-person perspective'.

1.1.2. Defining volition from the third-person perspective

Since James original conceptualization, voluntary actions were contrasted with reflex actions, thus interpreting them on the basis of the third-person perspective. In James view, voluntary actions are performed purposefully because humans wish to fulfil desires, with the intention to fulfil certain goals (James, 1905). James' interpretation capture one of the major limits of the empirical approach to volition: voluntary actions are based on expectations of future reward guided by an internal set of goals linked to previous reinforcements and memories of past experiences. Intuitively, these processes are never under the control of the experimenter and the internal causes of behaviour are not experimentally tractable (Nachev & Husain, 2010).

Despite this intrinsic limitation, present research takes the viewpoint of the detached observer and typically uses paradigms that contrast actions that are controlled endogenously as opposed to reflex actions that are driven by external signals (Haggard, 2008; Keller et al., 2006; Krieghoff, Waszak, Prinz, & Brass, 2011; Mueller, Brass, Waszak, & Prinz, 2007; Waszak et al., 2005). Since a key feature of a voluntary act is that it cannot be predicted from the external context then the choices must be 'free' or endogenous. Neuropsychological findings such as the anarchic hand syndrome, give support to the basic dichotomy of external versus internal generation of actions. Patients with anarchic hand syndrome have distinct problems in intentionally controlling the movements of one hand, while the other hand is still under intentional control. Crucially, the 'anarchic' hand sometimes acts towards specific objects in the environment suggesting that it is under external control (Della Sala, Marchetti, & Spinnler, 1991).

Standard experimental paradigms manipulate the degree of voluntariness associated with an action by asking participants to produce 'free-choices'. In a typical condition, participants are required to produce a specific action in response to the appearance of a stimulus (e.g., press the left button when the red light turns on). In another

condition participants are instructed to 'free-choice' which action to perform between a number of alternatives (e.g., press the left or the right button when the green light turns on). In the latter – unconstrained – condition, each choice is not fully determined by the external stimulus and cannot easily be predicted. The second condition is thus clearly more voluntary and more 'free' and less predictable as a consequence (Frith, 2013; Frith, Friston, Liddle, & Frackowiak, 1991).

Arguably, the comparison of free-choices with externally guided choices within the controlled environment of the laboratory does not allow to draw a clear picture of how volitional control operates in everyday life situations: rather than being exclusively internally controlled or externally controlled, our actions lay in a continuum along the two extremes. However, the study of free-choices it has been very useful to produce theoretical speculations.

1.2. Past research on free-choices

Far from capturing the 'true essence' of human volition as it takes place in everyday life (there is an intrinsic paradox in asking a person to be voluntary), the scientific study of free-choices has the ability to isolate the key generative components of the intention toward action (Haggard, 2008). For this reason, an interpretative model has been put forward to provide a heuristic framework for the study of voluntary actions.

1.2.1. Voluntary actions: a model

A quick look at the recent literature on volition shows that voluntary actions cannot be studied as a unitary concept. Brass and Haggard (2008) proposed a model that distinguishes at least three major decisional components of the intentional choice: what, when and whether (Brass & Haggard, 2008). Further, each of this components have been related with distinct subjective experiences if considered from the first-person perspective

(Brass et al., 2013). The 'what' component discriminates between which actions to execute. It is usually investigated with paradigms in which participants are free to choose between many alternatives of actions (Lau, Rogers, & Passingham, 2006; Schlaghecken & Eimer, 2004). Since this decision requires participants to resolve the conflict among the available response options it is related to the subjective experience of 'conflict resolution' (Brass et al., 2013). The 'when' component relates to the decision of when to execute a predetermined action. Paradigms dealing with the 'when' component usually compare a condition in which participants gave a response at their own choice with a condition in which they are instructed to respond by an exogenous cue (Libet et al., 1983; Soon et al., 2008). This component is related to the subjective experience of 'urges' (Jackson, Meltzoff, & Decety, 2006). The third component (the 'whether' component) is concern with the intentional process of deciding whether to execute the action at all and it relates to the subjective feeling of 'disappointment' (Brass & Haggard, 2007). The latter component has been relatively less explored given the complexity of collecting empirical data on a mechanism that does not produce a behavioural output (as the action is intentionally inhibited) and there are no external stimuli that time-lock the decision process. However, paradigms have been created exploiting neuroimaging techniques.

Based on this theoretical approach in the next section behavioural and neuroscientific evidence for the What, When, Whether (WWW; Brass & Haggard, 2008) model of voluntary actions will be reviewed.

1.2.2. Neural and Behavioural correlates of free-choices

Several studies suggest that intentional and reflexed actions seems to be controlled by different neural pathways in the brain: while stimulus-driven actions are controlled via a lateral network including the parietal and the premotor cortex, voluntary control involves a number of brain regions within the frontomedian cortex (Jenkins, Jahanshahi, Jueptner,

Passingham, & Brooks, 2000; Krieghoff et al., 2011; Waszak et al., 2005). In particular, the rostral cingulate zone (RCZ) and the pre-supplementary motor area (preSMA) have been consistently shown to be involved in different aspects of intentional control of action (namely the 'what' and the 'when' components). Accordingly, the next section will review some empirical evidence in support of a functional (Krieghoff, 2009) and behavioural (Becchio et al., 2014) dissociation of these two components. Following, in the second part of the chapter an exhaustive description of the third component ('whether') will be provided.

1.2.2.1. Deciding what to do

In neuroimaging studies, when participants have to make free action choices, activity is typically seen in the dorsolateral prefrontal cortex (DLPFC). However, it is unclear whether the activity of this area reflected the attentional demands of action selection or the freedom of choice. To address this issue Lau and colleagues (2004) compared a free selection condition, where participants randomly choose a stimulus out of many alternatives, with a condition in which the selection was specified by the task. Crucially, the involvement of attentional and working memory demands was minimized across task conditions by using novel stimuli in each trial. Results showed that the activation of DLPFC was not significantly different in the two conditions. Consistently with other studies reporting activations in different parts of the frontomedian wall (Cunnington, Windischberger, Robinson, & Moser, 2006; Lau et al., 2006) they reported activation in the parietal cortex, the anterior cingulate cortex (ACC), the preSMA and the RCZ for the free selection condition (Lau, Rogers, Ramnani, & Passingham, 2004). These studies however often confound perceptual and motor factors inducing some inconsistency in the exact anatomical location.

Mueller and colleagues (2007) address the yet unsolved question of the differential role played by the preSMA and RCZ in internally guided actions if compared to cued conditions. They conducted an fMRI study asking participants to temporally bisect the interval between the stimulus displays by making left and right key presses at the midpoint of isochronous appearing signals (a sequence of '×' presented to the left or the right of the fixation point). In the internally guided condition, subjects selected left or right key presses determining the side on which the next stimulus would appear. In the externally guided condition, they had to react with a button press corresponding to the side where the preceding stimulus appeared. By means of this manipulation, the action and the perception of the action in the two conditions were balanced. From a cognitive perspective, however, they differ substantially. Results showed that the RCZ was activated differentially by internally as compared to externally guided actions. The preSMA showed an equal level of activity in both conditions and thus did not differentiate between the two modes of action (Mueller et al., 2007). This suggested a primary role for the RCZ in internally selected actions (the 'what' component). Since timing was identical in both conditions, the activity related to preSMA determined the right moment for the execution of the action (the 'when' component).

1.2.2.2. Deciding when to act

Ever since Libet's innovative experiment there has been great interest in discovering whether brain activity preceding the 'when' decision might be manipulated and/or predicted (Lau, Rogers, Haggard, et al., 2004; Soon et al., 2008). In this kind of experiment, conditions in which participants decided when to act are compared with trials in which the time of execution was externally triggered by external visual and/or auditory stimuli. Typical results include activations of different areas located in the frontomedian wall for internally versus externally timed actions (Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen,

2003; Deiber, Honda, Ibañez, Sadato, & Hallett, 1999; Wiese et al., 2004). Although further activity has been reported in the DLPFC, basal ganglia, parietal cortex and insula it has been proposed that this activations reflect attention, maintenance of the information and motor related processes due to random generation of button presses for the intentional but not for the externally timed conditions. In contrast, activations in the frontomedian wall are assumed to reflect processes involved in internal action timing. In the study of Deiber and colleagues (1999) participant performed intentional movements of the right finger (intentional condition). The movement of the finger produced a visual signal that was recorded. In a second condition participant watched the recorded movement and were required to move again the right fingers in response to each signal (externally triggered condition). During the task they collected fMRI data on four regions of interest of the frontomedian wall (preSMA, SMA, RCZ, ACC). Results showed that in the preSMA, RCZ and ACC activation was more extensive for the intentional condition if compared with the externally triggered condition (Deiber et al., 1999).

Other brain imaging studies used a different approach to investigate the when component of intentional action. In a recent study Lau and colleagues (2004b) used Libet's paradigm to investigate the brain correlates of the intentional generation of an action. In their version of the task, the authors required participants to either attend to the intention to act or at the actual implementation of the movement. By directing attention to the intention (or urge) to act they found an increase of preSMA activity if compared to the condition where participants were attending the bare movement (Lau, Rogers, Haggard, et al., 2004). This evidence clearly support the involvement of the preSMA in the 'when' decision.

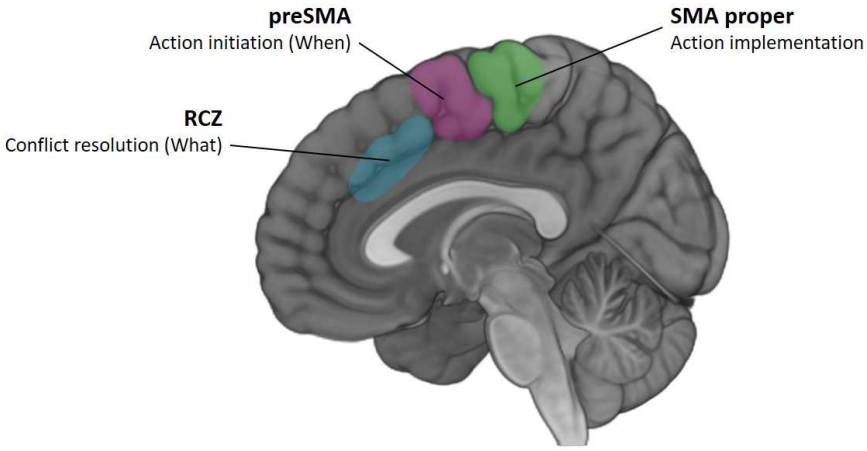

Figure 1.1: Schematic overview of brain regions in the frontomedian wall, along with their assumed functions within the 'WWW' model of intentional actions (Brass & Haggard, 2008). Image displayed in neurological convention. RCZ, rostral cingulate zone; preSMA, pre-supplementary motor area; SMA, supplementary motor area.

1.2.2.3. Dissociating the 'what' and 'when' components

Based on the aforementioned results, the activations reported to support the 'what' and the 'when' decisional component appear to be very similar, with most consistent activity within the RCZ and/or preSMA (Fig. 1.1). Although RCZ seems to be more involved in processing of 'what' decisions and the preSMA seemingly in 'when' decisions the evidence appears not very convincing. A recent study by Krieghoff and colleagues (2009) aimed to dissociate the neural correlates of internally selected and internally timed actions. Subjects were presented with a cue and had to decide as quickly as possible which action to perform and when to do so. Further, the two decisions were either taken voluntary or triggered by an external cue enabling the authors to differentiate between internal and external what and when decisions. Crucially they dissociated the moment at which the subjects had to make the decision of what to do and when to act, from the moment at which the subjects actually executed the action. Based on the results of Mueller et al. (2007) they hypothesized that the RCZ might be involved in deciding which action to perform, whereas

the preSMA might be involved in the decision of when to perform the action. The results of the whole-brain analysis revealed a functional dissociation between the two areas in the frontomedian wall. The RCZ was involved in the decision of which action to perform, whereas a brain region in the posterior frontal cortex, close to the preSMA, was sensitive to the when decision. Post-hoc analysis revealed an interaction between the 'what' and 'when' component in the area close to the preSMA, suggesting that the two processes are not completely dissociated, but are interdependent (Krieghoff, 2009).

Further evidence for a double dissociation of this component came from a recent studies of Soon et al. (2008). Using MVPA in a novel implementation of the Libet' task, the authors showed that brain activity occurring several seconds prior to the movement, allowed to predict both the choice (left or right button presses – 'what) and the timing ('when') of participants' responses. They showed that the frontopolar (FP) cortex and the precuneus (P) best predicted the 'what' decision while information related to the 'when' decision was decoded in the preSMA and SMA (Soon et al., 2008).

An elegant demonstration of how the 'what' and the 'when' subcomponent of intentional action can be dissociated up until their actual motor implementation came from a study of Becchio and colleagues (2014). In two consecutive experiments they explored the kinematic patterning that characterized reach-to-grasp movements in free and cued conditions. While in the first experiment compared voluntary and stimulus-driven movements directly, the second experiment investigated whether selective intentional components of intentional actions affected different characteristic of the reach-to-grasp movement. In the latter experiment the 'what voluntary' decision (conceptualized as a choice between small and large objects) was compared with a 'what constrained' condition, while the 'when' decisions for 'voluntary' and 'constrained' condition were mutually compared. Results showed that movement time was longer and maximum grip aperture was reached later in time for the 'what voluntary' compared to the 'what constrained'

condition. The influence of the when decision component was confined to the time of maximum grip aperture. This was reached earlier for 'when constrained' actions in comparison to 'voluntary' actions, indicating that the intentional selection of the timing of the action influenced the approach parameters. This behavioural results are the first evidence that the movement parameters of an action are distinctly modulated by the two subcomponent of intentional action, namely the 'what' and the 'when' component (Becchio et al., 2014).

To sum up, there is strong evidence for a functional dissociation of the 'when' and 'what' component both at the neural and at the behavioural level.

1.3. The importance of inhibition for everyday function

In everyday life, alternative action programs must be inhibited to achieve optimal goal-directed behaviour. Choosing whether to perform an action or not is a fundamental process that allows people to flexibly interact within a complex social environment. Without this ability, actions would be impulsive and would leave little space to correct misguided decisions. Sometimes such decisions might be taken ahead of time, such as when planning whether to go for a run in the morning or deciding to sleep an extra hour. Often, however, one has to take an in-the-moment decision to accomplish or to stop a motor plan that has already partially implemented. Football athletes for example, continuously regulate their interactions with other players by both deciding 'the best athletic feat' for that specific game phase, but also through being able to inhibit the motor plan in reaction to an opponent's unexpected move. In that circumstances an effective balance between action and inhibition could be a very important factor to decide that a predicted change in the environment will be inappropriate thus preventing the execution of the motor plan and any of its causal external effects.

Response inhibition is generally considered a prominent sub-component of cognitive control which is part of executive functions (Bari & Robbins, 2013; Veen & Carter, 2006). According to the past literature, the processes by which such higher-order supervisory system allows to halt a lower-order behavioural impulse, might arise from two possible mechanisms. On one hand, 'stimulus-driven inhibition' describes the ability to inhibit actions in response to some exogenous signals that are present within the physical environment or within the current set of appropriate social rules (Severens, Kühn, Hartsuiker, & Brass, 2012). On the other hand, in everyday life situations a more intentional mechanism might be recruited to withhold from executing a pre-potent action tendency, the so-called 'intentional inhibition' (Brass & Haggard, 2007; Filevich, Kühn, & Haggard, 2012).

1.3.1. The study of stimulus-driven inhibition

Most of what we know regarding inhibitory control has been investigated over the years employing paradigms that required participants to stop an ongoing behaviour in response to an external sensory stimulus (van den Wildenberg et al., 2010). In these tasks, desisting from action is a reactive response linked to the presentation of an unambiguous signal in the environment which directs the inhibition of the response, excluding any component of spontaneous choice of the individual, but just to implement the 'stop' instruction. In this respect, 'Go/Nogo' paradigms and 'Stop signal' tasks (SSTs) have been frequently adopted to investigate inhibition (Verbruggen & Logan, 2008).

In the Go/Nogo paradigm participants are exposed to one of two cues that instruct them to either act or withhold action. Usually 'go' stimuli are presented in a sequence, in alternation with 'nogo' stimuli, triggering the inhibition of a tendency to respond, a phenomenon termed 'action restraint'. The Go/Nogo task manipulates action pre-potency by varying the probability of 'go' and 'nogo' cues (Eimer, 1993). For example, increasing the

frequency of 'go' cues in a block of trials, would boost the urge toward action so that participants would be more ready to act. As a consequence also the level of inhibition required to withhold the response at the appearance of the 'nogo' cue would be increased.

Differently, the SST (Logan, 1994) requires an active search for the 'stop signal' to trigger inhibition for an already started action, eliciting a process of 'action cancellation' (Bari & Robbins, 2013). In a classical SST, participants are forced to respond to well-defined go stimuli presented on every trial, while they are required to halt key presses in response to a pre-instructed external stop signal that might appear just after the go stimulus. The time between the 'go' and the 'stop' signals is defined as the stop signal delay (SSD). By varying this delay it is possible to manipulate the likelihood of a successful inhibition of the response. With a longer SSD the action program is interrupted later and stopping becomes more difficult. As a consequence commission errors are more likely to occur. This experimental manipulation allows to calculate the stop-signal reaction time (SSRT) which is a measure of efficacy of the inhibitory processes (Logan, 1994; Logan & Cowan, 1984). The SSRT provides information on how quickly the inhibition process can be applied successfully before action execution. A shorter SSRT means more effective inhibition.

1.3.1.1. The neural correlates of stimulus-driven inhibition

The electrophysiological correlates of response inhibition have been widely investigated. In the Go/Nogo task, go cues produce smaller N2 and P3 components than nogo cues (Eimer, 1993). A high false-alarm rate (i.e., acting when participants should inhibit) has been correlated with smaller nogo-related N2 components if compared with a lower false alarm rate. This suggests that the amplitude of the N2 component reflects the intensity of the inhibition capacity (Falkenstein, Hoormann, & Hohnsbein, 1999). In the same fashion, experiments using the SST indicated that N2 and P3 components are crucial for response inhibition meaning that stop signals increase the components' amplitude

compared to the go trials (Kok, Ramautar, De Ruiter, Band, & Ridderinkhof, 2004). Moreover the N2 and P3 components related to stop signals are considerably larger when stop signals are infrequent: in this condition since the impulse toward action is stronger, inhibition processes need to be more powerful (Ramautar, Kok, & Ridderinkhof, 2004).

Externally-driven inhibition has been commonly associated with increased activity in the fronto-basal ganglia network as revealed by fMRI studies (Duann, Ide, Luo, & Li, 2009; Jahanshahi, Obeso, Rothwell, & Obeso, 2015; see Fig. 1.2). In the SST, successful stopping is associated with activation in the dorsal prefrontal cortex (dPFC), the inferior frontal gyrus (IFG, mostly in the right hemisphere), the preSMA and the basal ganglia (most prominently the dorsal striatum and the sub-thalamic nucleus – STN; Aron, 2011; Bari & Robbins, 2013). Although the IFG, STN, and preSMA areas seem necessary for response inhibition, the nature of the functional connection among these areas is debated. While direct connections between IFG and STN are frequently reported (Aron, 2011), some studies suggest a direct connection exclusively between IFG and preSMA with further projections of the preSMA to the STN (Duann et al., 2009; Jahanshahi et al., 2015). SSRT strongly correlates with IFG, but less with preSMA (Aron et al., 2007), so the precise role of the latter area might be more general in response inhibition paradigms, reflecting processes of action monitoring and conflict-detection.

Although we have extensive knowledge regarding the 'stimulus-driven' processes, we know little regarding the 'intentional' processes that can be involved with inhibitory control.

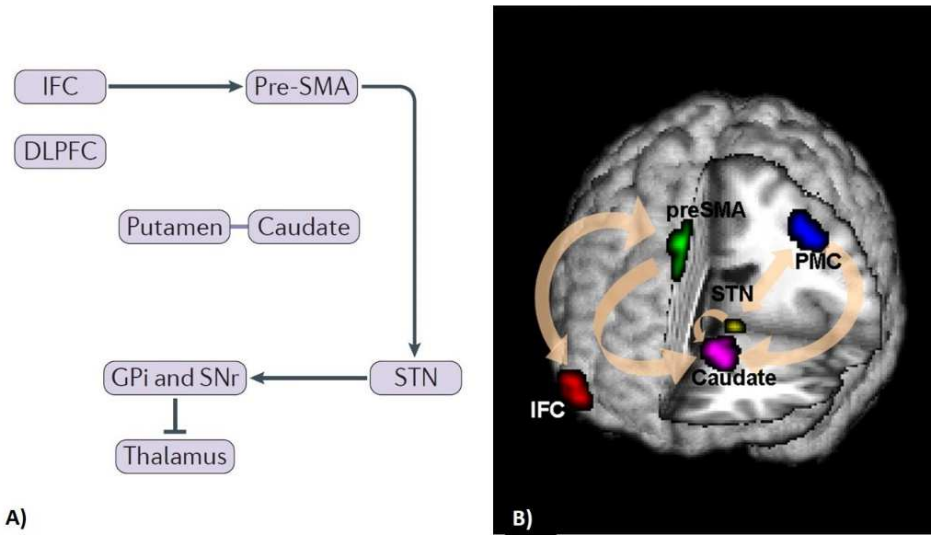

Figure 1.2: Panel 'A' depicts the fronto-basal ganglia pathway mediating inhibitory control according to Jahanshahi et al., (2015). Stimulus-driven inhibition, which is automatic and habitual, is proposed to be mediated by the hyperdirect cortico–subthalamic–pallidal–thalamo–cortical pathway. For clarity, some connections are not shown (modified from Jahanshahi et al., 2015). Panel 'B' depicts the functional connections reported in Duann et al., (2009). The analysis showed that the preSMA and PMC are interconnected with the caudate head and the STN. The IFC showed reciprocal connection with the preSMA but not with other structures (taken from Duann et al., 2009). Image displayed in neurological convention. DLPFC, dorsolateral prefrontal cortex; GPi, internal segment of the globus pallidus; IFC, inferior frontal cortex; preSMA, pre-supplementary motor area; PMC, premotor cortex; SNr, substantia nigra pars reticulata; STN, sub-thalamic nucleus.

1.3.2. The study of intentional inhibition

According to the 'whether' component of the 'WWW' model of voluntary actions (Brass & Haggard, 2008; Haggard, 2008), by means of the so-called 'intentional inhibition' we are able to make an endogenous self-determined decision to stop our actions (Filevich et al., 2012) up until the very last moment (Schultze-Kraft et al., 2016). Since, in everyday life we rarely receive an external stimulus telling us to withhold action, such decisions are most likely taken on a voluntary basis. In this view, intentional inhibition captures the 'free' process of deciding between intentionally performing or intentionally inhibiting a planned action without an immediate external signal instructing us to do so.

In sports such as volleyball, for example, we may see an approaching ball which automatically triggers the response to hit back. However, we may realise at the last moment that there is a possibility that the ball will land outside the court. We could then decide to inhibit our motor plan and let the ball pass with the hope it will land beyond the lines. During this sequence of events, since the signals from the environment are ambiguous the decision to inhibit is made endogenously.

1.3.2.1. Challenges in intentional inhibition research

Despite the extensive information concerning stimulus-driven inhibition, the concept of intentional inhibition has been relatively ignored in previous research. Two main reason could be at the basis of this evidence: first, because of the complexity in designing experiments capable of a rigorous study of intentional inhibition as a separate construct. Second, because previous research considered intentional inhibition and stimulus-driven inhibition as single and indivisible concepts.

1.3.2.1.1. Making a free-choice

To intentionally inhibiting an action participants must be able to make an intentional – free – choice to stop the ongoing action program. Arguably, this is rather a complex condition to reproduce in the laboratory. Scientifically rigorous experimental paradigms necessarily introduce a number of constrains on participants' decisional processes and/or on the behaviour itself. Instructing participants to be 'spontaneous' is a quite counterintuitive request, and represents the one of the major criticisms for all the research in this field. Although this intrinsic limit, 'free-choices' to inhibit can still be objectively studied in the laboratory setting by contrasting intentional action and inhibition choices with responses in which one particular response must be made following an external instruction (Haggard, 2008).

1.3.2.1.2. Pre-decision and post-decisions

Inhibition is conceptualized to be an active process. To be effectively studied however, the inhibition of a response must follow a prepotent action impulse to suppress. Intuitively, without an active 'urge' toward the action an active inhibition of the very same action cannot be studied. Stimulus-driven paradigms can manipulate this 'tendency' by increasing the number of go trials and presenting participant unexpected nogo, or stop, signals. However, intentional inhibition paradigm cannot include stop signals. For this reason, guarantee this prerequisite may represent a challenge for intentional inhibition research. Nevertheless experimental paradigms must somehow assure that an action has been prepared before the participants' free decision of stopping it. One possibility could be push participants to act frequently, so that they can develop a strong impulse toward action, and then present well-defined 'free-choice' stimuli where participants have to take an in-the-moment decision whether to act or to inhibit (Kühn & Brass, 2009; Parkinson & Haggard, 2014). Alternatively, to encourage action preparation experimental paradigms can provide strict time limits to responses or provide unpleasant consequences (e.g., an annoying sound) when an error is made in action trials (Kühn, Haggard, & Brass, 2009; Lynn, Demanet, Krebs, Van Dessel, & Brass, 2016).

1.3.2.1.3. The lack of behavioural output

The study of intentional inhibition is also challenging because as the action is inhibited does not produce measurable behavioural outcomes such as reaction times, error rates or movement kinematics. Due to these factors, intentional inhibition has been widely investigated through neuroimaging techniques with the aim to define whether intentional and externally-driven inhibition rely on the same neural mechanisms or not (Schel et al., 2014). Imaging experiments however, are also difficult since it can be almost impossible to precisely time-lock the inhibition decision to the recorded data: although free-choice

stimuli can be presented, disentangling the intentional processes from the decision processes can be unlikely. This problem requires the implementation of a careful experimental design and appropriate control conditions.

1.3.2.2. Gaps in the study of intentional inhibition

The concept of intentional inhibition remains relatively unexplored. The main question regards whether intentional inhibition genuine cognitive function that should be studied on its own. For example it may be argued that intentional inhibition is simply a symmetrical response choice to action or that it may not be unique in comparison to stimulus-driven inhibition (Mostofsky & Simmonds, 2008). Otherwise, if intentional inhibition can be dissociated from other forms of inhibition, then its study could be extremely fruitful: by only focusing on stimulus-driven inhibition researchers may leave a large gap in how we make intentional decision to act and to inhibit, which can be very important for the understanding of everyday behaviour. Although the exploration of the behavioural and neural underpinnings of intentional inhibition has already begun, progresses are still necessary, in particular for the definition of the factors that ultimately modulate and determine our decision to inhibit actions.

1.3.3. Past research on intentional inhibition

Despite the significant challenges outlined above, several studies have attempted to circumvent these problems by means of specifically tailored experiments, in which participants were free to decide whether to execute or inhibit a particular behaviour (Kühn et al., 2009). Below is a description of some existing literature on intentional inhibition.

1.3.3.1. Behavioural investigations

Standard behavioural paradigms able to study intentional inhibition have been not designed yet. As previously reported one approach is to adapt existing stimulus-driven inhibition paradigms including a 'free-choice' condition. Parkinson and Haggard (2014) used a Go/Nogo paradigm in order to explore whether the proportions of free-choices to inhibit or to act can be modulated by the presentation of subliminal primes. Free-choice targets were included in addition to standard instructed go and nogo response target and the effect of two types of priming latencies were exploited: positive compatibility effect (PCE) in which compatible primes facilitate responding, and negative compatibility effect (NCE) in which compatible primes inhibit responding (Eimer & Schlaghecken, 2003). Results shown that go and nogo primes bias the probability that the behavioural response would be freely chosen according to the compatibility effect demonstrating that the unconscious mechanisms that concur to determine the free decision to inhibit the action can be unconsciously primed (Parkinson & Haggard, 2014).

Higher-level beliefs represent another important influence on free decisions to inhibit actions. Participants who have been exposed to anti-free will messages, and therefore have been induced to reject the concept of free will, are less likely to exert self-control and to inhibit actions when given the choice (Rigoni, Demanet, & Sartori, 2015; Rigoni, Kühn, Gaudino, Sartori, & Brass, 2012). Importantly, these influences on our free decisions to inhibit have only been apparent because intentional inhibition and stimulus striven inhibition have been studied as separate constructs.

1.3.3.2. The neural correlates of intentional inhibition

The neural correlates of intentional inhibition have been elucidated by means of fMRI studies. Although the activity related to intentional inhibition largely overlaps with the networks characterizing externally-driven inhibition (Schel et al., 2014), increased

activity within the dorsal part of the frontomedian cortex (dFMC) has also been reported (Brass & Haggard, 2007; Kühn, Haggard, et al., 2009; Lynn, Muhle-Karbe, & Brass, 2014; see Fig. 1.3).

Brass and Haggard (2007) adapted the Libet task to study intentional inhibition. Alike the standard Libet task (Libet, Gleason, Wright, & Pearl, 1983), participants produced self-paced responses while watching a rotating clock. After, the time on the clock at which the 'urge' to respond was perceived by the participants was reported. In this version of the task, at the last moment participants could also choose to inhibit their urge to respond right before executing the intended action. Significant activation in the dFMC was reported for the first time when the response was inhibited in contrast to executed (Brass & Haggard, 2007).

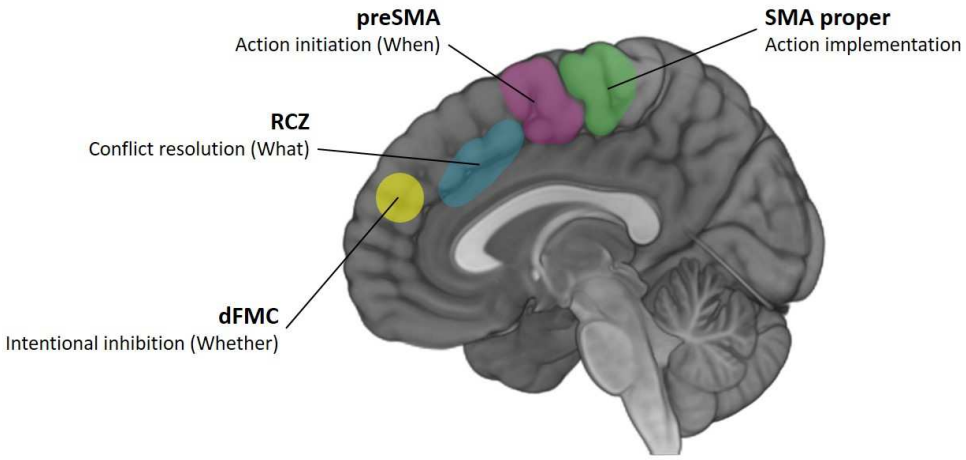

Figure 1.3: Schematic overview of brain regions in the frontomedian wall, along with their assumed functions within the 'WWW' model of intentional actions (Brass & Haggard, 2008). Image displayed in neurological convention. dFMC, dorsal frontomedian cortex; RCZ, rostral cingulate zone; preSMA, pre-supplementary motor area; SMA, supplementary motor area.

Subsequent studies have supported the involvement of the dFMC in intentional-inhibition. In the 'marble task' (Kühn et al., 2009), participants watch a marble rolling down a ramp.

An unpleasant sound was produced when the marble smashed at the bottom of the ramp. However, in some trials the marble turns from white to green and participants were requested to press a key as fast as possible to stop the marble and prevented from smashing it. When the marble remains white, participants were instructed to make a free decision whether to stop or not the marble from rolling down the ramp. Once again activation of the dFMC was reported when participants freely choose to stop rather than let the action to unfold (Kühn et al., 2009). Moreover increased effective connectivity was reported between the dFMC and the preSMA areas, when participants decide to inhibit rather than execute the action. Other studies using the same paradigm suggested intentional and stimulus-driven inhibition largely overlap in their brain activations, and the contribution of the dFMC depended on previous trial history. With a high number of preceding consecutive action trials, the dFMC was less recruited in subsequent intentional inhibition trials (Schel et al., 2014) suggesting that the greater the automaticity of action the less the contribution of the dFMC to free-choices. Interestingly, greater action automaticity also reduces the likelihood that participants chose to inhibit the response.

Initially thought of as a late 'veto area', with the ability to halt voluntary motor commands (Kühn, Haggard, et al., 2009), the dFMC has been recently indicated as a key region for self-control, allowing to disengage from strong impulses and intentions (Lynn et al., 2014). A point worth noting, however, is that whereas some studies failed to identify inhibition-related activity over the dFMC (Hartwell et al., 2011; Kühn & Brass, 2009), others found dFMC activation confined to externally-driven inhibition (Lynn et al., 2016; Severens et al., 2012). These inconsistencies make the role and underlying functioning of dFMC quite controversial.

CHAPTER 2

EXPERIMENTAL MANIPULATIONS OF FREE-CHOICES

On the basis of the theoretical framework and the empirical work introduced in the first chapter of this thesis, at least three general considerations concerning volition can be drawn:

i. Voluntary – free – choices to act and to inhibit can be dissociated from reflexed – stimulus driven – action and inhibition both at their behavioural and functional level.

ii. Far from depending exclusively on conscious decisional processing, free choice decisions origin from brain mechanisms that precede – and intuitively cause – intention awareness.

iii. Both the neural networks and the cognitive mechanisms that govern free choices can be experimentally manipulated.

With this in mind, the present chapter will introduce the experimental manipulations that I have adopted in my experimental work: subliminal priming and the modulation of the level of arousal. First I will propose a general overview of the two concepts and how they are conceptualized within the field of cognitive psychology and neuroscience. Next I will provide some examples of how these variables can be manipulated to achieve a deeper understanding for the generation of free choices.

2.1. Priming: an overview

The term 'priming' is used in cognitive psychology, social psychology, motivational research, emotion research and other related fields with different interpretations (for a review see Bermeitinger, 2016). In its broader sense 'priming' describes the process by

which a stimulus or event B (typically named target) is preceded by a stimulus or event A (the prime) which has an hypothesized effect on B. In cognitive psychology, the term 'priming' takes its narrowest interpretation and usually the effects of A on B lays in the time scale of milliseconds up to a maximum of few seconds. In sequential priming paradigms, participants are usually instructed to ignore the rapid presentation of the prime and must respond to targets, which appear in rapid successions. Although the precise response to the target may vary considerably depending on the subject of study (e.g., word choices, reaction times, actions choices, target classification, beliefs), primes modulates response options in a way that a condition is more likely to occur than another. For this effect to take place, primes and target generally share some common features (e.g., perceptual, semantic, conceptual) and this relation allows to infer the underlying cognitive process which is the dimension under investigation (Bermeitinger, 2016). One of the most employed priming paradigms is the 'response priming'. In response priming paradigms the relation between primes and targets is determined by the elicited motor responses. Since primes and targets 'call' for the same category of responses, the most common manipulation involves the set-up of conditions were prime and target elicit the same motor responses (compatible conditions) or opposite motor responses (incompatible conditions). The dependent variables collected in this task are typically error rates and reaction times: compatible conditions elicits faster reaction times and lower error rates when compared to incompatible conditions.

In response priming paradigms, albeit participants are not asked to make inferences about the content of the information provided by the prime, it cannot be always assumed that the effect of the latter does not play a role in participants' implicit evaluations. Many studies reduced such confounding artefacts by presenting primes below the threshold of conscious processing, thus inducing subliminal priming effects (Schmidt, 2008). To preclude conscious processing of primes researches employed paradigms where

primes' timing is reduced drastically or, more sophisticatedly, where a masking stimulus is presented immediately after the prime stimulus precluding its conscious visibility (Lingnau & Vorberg, 2005; see Fig. 2.1).

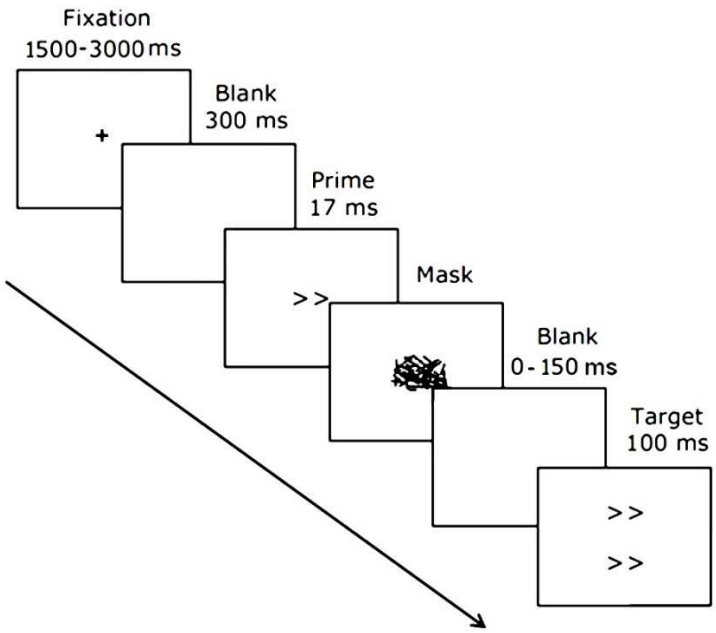

Figure 2.1: A schematic representation of a typical subliminal response priming paradigm (taken from D'Ostilio & Garraux, 2012)

Crucially it has been demonstrated that, unbeknownst to participants, subliminal primes can be used to influence free decisions (Bodner & Mulji, 2010; Eimer & Schlaghecken, 2003; Ocampo, 2015; Schlaghecken & Eimer, 2004). According to this literature, responses can be biased in the way that compatible prime-target response options are chosen more often than the incompatible ones. Recent interpretations suggest that the effects of primes in response priming paradigms arises from both motor and perceptual mechanisms (Krüger, Klapötke, Bode, & Mattler, 2013). For instance the *rapid chase theory* suggests that primes and targets elicit a race of activations of motor responses that move from visual to motor areas (Schmidt, Niehaus, & Nagel, 2006). In this race primes produce a pre-activation of a response option that is further affected by the activation produced later on by the target and

diverted accordingly. In this interpretation, simple feed-forward processing would govern the sequential activations of the motor responses elicited by the two types of stimuli. Activations related to subliminally presented primes can proceed undetected avoiding slower feedback processing from visual to motor areas (Schmidt et al., 2006).

2.1.1. Subliminal priming of free-choices

Recent evidence provided convincing support for the adoption of subliminal priming as a meaningful method to investigate the role of unconscious processes in human choice behaviour. In a typical implementation of this method subliminal primes are presented prior to free choice targets to investigate whether such priming has an influence upon which action is subsequently chosen. Here, the crucial question is whether unconscious information modulate the 'what' component of volitional control (Brass & Haggard, 2008). For example Schlaghecken and Eimer (2004) used a two-choice reaction time task in which some choices were instructed, since a visual stimulus (left or right pointing arrows) indicated which choice should be made (left or right button presses), whereas randomly interspersed 'free choice' targets (double headed pointing arrows) indicated that participants were free to choose either responses. Unbeknownst of the participants, targets were preceded by backward masked – subliminal – stimuli (left or right pointing arrows of the same shape of the targets) that created compatible and incompatible prime-target conditions which primed participants to choose one or the other response option. Results demonstrated that participants' responses followed the 'compatibility effects' induced by the priming manipulation. Interestingly in a subsequent experiment the authors introduced only free choice trials, thus eliminating the task demands related to the instructed trials. In this version of the task free choices were no longer modulated by the primes suggesting that the impact of subliminal information on behaviour is mediated by currently active intentions and not by the mere solicitation of primes at the motor level

(Schlaghecken & Eimer, 2004). This type priming research on free action alternatives has been carried out with relatively low-level constructs such as the priming of specific response options, like the abovementioned study, but also with implications at higher-level semantic representation (Gaillard et al., 2006; Ocampo, 2015) even generalizing to novel stimuli that therefore cannot trigger already acquired stimulus-response mappings (Ocampo, 2015).

A recent line of research demonstrated that also free choices to inhibit can be subliminally primed providing support for the presence of neural processes operating outside conscious awareness in intentional inhibition tasks (Filevich et al., 2013; Parkinson & Haggard, 2014). In a novel version of a Go/Nogo paradigm with intermixing free choice trials, Parkinson and colleagues (2017) manipulated free choice decisions of 'whether' to produce an action or not, by subliminally presenting neutral, angry, fearful and happy emotional faces before instructed and free choice target. Interestingly angry faces lead participant to inhibit responses in free choice trials more often if compared with other emotional faces. Crucially, since they collected EEG recordings of brain activity during the task, they identified a frontal-midline EEG component during intentional decisions that was modulated by subliminal angry faces only (Parkinson, Garfinkel, Critchley, Dienes, & Seth, 2017). The modulation of the brain activity within this area of the frontal lobe converge with previous research on volition (Brass et al., 2013; Libet et al., 1983). This suggests that intentional control processes such as intentional inhibition can be modulated outside conscious awareness even by complex (high-level) information in the environment.

To conclude priming has been proven to be a useful tool for the behavioural and neural investigation of free choices. Subliminal priming have been shown to avoid confounds related to participants' implicit evaluation on the purposes of the study. Moreover subliminal primes have the ability to modulate the activity in those brain areas that predict the unconscious generation of a 'free' choice suggesting a reconsideration of the importance of free will, and free won't.

2.2. Defining arousal

The arousal construct, as discussed in this section, is confined to those instances that are associated with physical exercise. I will focus primarily on exercise-induced arousal, choosing not to discuss the potential roles of other types of arousal states, though a similar rationale might be applicable to a wider range of cases, from emotional arousal to caffeine' consumption.

Ever since its earliest definition as a psychological construct, researchers referred to arousal as if it represents a broad range of physiological manifestations (Hanoch & Vitouch, 2004). Within this original conceptualization arousal typically implies a set of brain activations that affect the overall state of readiness to respond to any external or internal events (Hebb, 1955), which in turn cause energy mobilization within the organism (Duffy, 1962). Given the experimental evidence that similar physiological and psychological manifestations, also called stressors, (e.g., emotions, exercise, stress, caffeine) caused similar arousal states, it was assumed that arousal represented a unidimensional phenomenon, a continuum from 'low' to 'high' energy, from sleep to wakefulness (Duffy, 1962). Since the beginnings of experimental psychology it was also observed that arousal and performance share a peculiar relationship. For instance the 'Yerkes-Dodson law' (also named inverted-U theory) claimed that performance correlates with arousal following an inverted U-shaped function: at low level of arousal, performance will be poor but, as arousal rises to a moderate level, performance will become optimal. However, if arousal continues to rise, performance will return to decrease (Yerkes & Dodson, 1908). Since arousal was considered a by-product of stressors that provoked it, a similar inverted-U function for stressor-performance was observed, as seen for physical exercise (Davey, 1973). According to the unidimensional perspective, these associations were mediated by the allocation of attentional resources during performance at different arousal levels (Easterbrook, 1959). Importantly, this perspective assumes that all cognitive abilities are maintained by a non-

specific supply of energetic resources and the volume of available resources allocated to a specific task depends also on an individual's arousal level (Kahneman, 1973).

The perspective of a unidimensional arousal representing all arousal states has been criticised and empirical data did not give full support for the hypothesis that performance is an inverted-U function of exercise intensity (Chang, Labban, Gapin, & Etnier, 2012; McMorris & Graydon, 2000). First because it has been demonstrated that different measures of arousal are poorly correlated (Thayer, 1989). Second because neurophysiological evidence revealed that the thalamus and the ascending reticular formation, although known to play a critical role in the regulation of arousal since the earliest definitions (Moruzzi & Magoun, 1949), are not a uniform system but, rather, consist of several – interconnected – arousal systems, differentiated by specific neurotransmitters (Robbins, 1997; Robbins & Everitt, 1995). On the basis of these evidences several theoretical accounts of arousal considered a multidimensional approach as more appropriate for describing the interactions between stressors and task (Pribram & McGuinness, 1975; Sanders, 1983). For instance, Sanders (1983) drawing from the neuropsychological model proposed by Pribram and McGuinness (1975), claimed that different, but interactive, energetic systems take place in order to affect the diversity of cognitive processing stages that are required during performance. He argued that arousal should be divided into arousal, activation and effort. 'Arousal' was defined as the phasic energetic state at any particular time of the performance, which causes a general increase in alertness and attention. Task-related 'activation' was seen as the tonic readiness to respond that causes a change in arousal state from baseline. Finally, the third mechanism, 'effort', receives information from both 'arousal' and 'activation' states in order to coordinate performance outcome (Pribram & McGuinness, 1975; Sanders, 1983). What seems to be crucial here is that these models predicts that two modes of attentional and motor control sub-serves different aspect of the performance: an involuntary control mode accounts for the effects of arousal and

activation, while a voluntary control mode is driven by effort (Pribram & McGuinness, 1975). Effort disentangles the effects of arousal and activation to avoid undesirable reactions. Without a control system "behaving organisms would be constantly aroused by their movements and moved by arousing inputs" (Pribram & McGuinness, 1975, p. 439).

In conclusion, task' performance is assumed to be dependent on the allocation of energetic resources to specific cognitive processes. The volume of the energetic pool is determined by individual' arousal and activation levels while the precise allocation is supervised by the effort. As physical exercise can be assumed to be a stressor (Davey, 1973), then exercise-induced arousal should be capable of affecting cognition likewise other stressors. As I will discuss in the next section, the distinction of voluntary-involuntary, or explicit-implicit, mechanisms laid the foundations for the understanding of how exercise and cognitive performance interact, both at the neural and behavioural level.

2.2.1. Effects of exercise-induced arousal on cognition

The effects of exercise on cognitive functions have been widely documented, demonstrating both positive and negative effects depending on the precise cognitive mechanism assessed, the timing and the intensity of the exercise selected and the variety of methodologies used to collect participants' arousal levels. A number of studies have focused on measuring the effects of acute exercise on cognition employing study designs that required a single – relatively short – bout of exercise (Chang et al., 2012; Lambourne & Tomporowski, 2010). These studies have typically assessed predictions inherited from 'arousal' theories under the common assumption that cognitive performance is dependent on the allocation of limited energetic and metabolic resources (Hockey, 1997; Kahneman, 1973; Sanders, 1983; Yerkes & Dodson, 1908). Although individual studies generate inconsistent results, there is a general consensus that acute exercise would have a positive – thought small – effect on cognition for performances that stress information processing

at perceptual, decisional and motor stages. However cognitive tasks that recruit executive processing would be negatively affected. Accordingly, bottom-up, automatic and conscious processes would be improved while top-down, effortful and unconscious processes would be impaired (Audiffren, 2009; Tomporowski, 2003). This idea of a bidirectional continuum (e.g. automatic-effortful) is not new and closely resembles the previously descripted models of voluntary-involuntary allocations of energetic or attentional resources during information processing (Pribram & McGuinness, 1975). However Sanders' model (1983) predicted positive effects of exercise in both bottom-up and top-down processes assuming that a better performance is associated with increased conscious effort allocated to the task, failing to recognize the negative effects observed for top-down processing. Since more recent empirical evidence gave support to the existence of opposing effects of exercise on cognition, new theoretical models have been put forward.

At the basis of these new interpretations is the key notion that the brain utilizes two functionally distinct though interacting systems to manipulate and represent information. The content of the explicit system is rule-based, can be verbally expressed and it is tied to conscious awareness. In contrast, the content of the implicit system is devoted to experience, it cannot be verbalized (it can only be investigated through task performance) and it is unconscious (Dienes & Perner, 1999; Dietrich, 2006). The explicit system is sub-served by prefrontal activity which is linked to higher order – conscious – representation of knowledge. The implicit system is mediated by basal ganglia and the cortical-subcortical connections to the motor cortex. This system does not hold higher-order representations but is fundamental for allocation of procedural knowledge. From an evolutionary perspective of motor control the coexistence of two systems has many implications. The main advantage of the implicit system is its efficiency and speed: since movements must be controlled 'online' the procedural knowledge of the implicit system can be accessed automatically without the need of further abstraction. The main advantage of the explicit

system is flexibility and coordination but it performs better 'offline' and it is slow (Sun, 2006): when the execution of a movement is a matter of time, the implicit system must be handle it, deactivating the explicit system in a flexibility/efficiency trade-off, in order to perform smooth sensorimotor integrations of the kind that distinguish sport and exercise (Dienes & Perner, 1999; Dietrich, 2006; Dietrich & Audiffren, 2011). These sorts of interactions are real-life experience when the execution of a complex movement is transferred from the implicit to the explicit domain, leading to an inevitable detriment of the performance.

But how does acute exercise manipulate the activity of the two systems while performing a cognitive task? Since the two systems appear modulating the activity on similar neural mechanism as those involved in the production of voluntary actions (explicit system) as opposed to stimulus-driven actions (implicit system), the answer to this question is crucial to the purposes of the present thesis.

2.2.2. The reticular-activating hypofrontality model

An integrative, neurocognitive model has been recently put forward to account for the detrimental and facilitating effects observed during acute exercise at moderate intensity. The reticular-activating hypofrontality (RAH) model (Dietrich & Audiffren, 2011) is based on the consideration that brain activity is fuelled by a constant but limited supply of metabolic resources. Since brain processes occurs in a competitive basis, increases in the activation of some brain areas must correspond to a concomitant deactivation of other areas (Dietrich, 2006). For instance, the RAH model recognizes the occurrence of two neurophysiological mechanisms during exercise: the activation of the arousal systems in the brainstem (the reticular-activating process) and the deactivation of neural structures that are not critically needed to maintain exercise (the hypofrontality process).

The reticular-activating process is composed of distinct thalamic and brainstem neurochemical circuits (Robbins & Everitt, 1995). More precisely three main systems of neuromodulators have been identified to influence cortical arousal: the noradrenergic, the dopaminergic and the serotoninergic systems. The activity of the noradrenergic axons mediates alertness, enhancing attention and the sensory processing of environmental challenges including novel stimuli (Aston-Jones, Chiang, & Alexinsky, 1991) maintaining discriminations processes under a high level of arousal. This system also innervates the prefrontal cortex helping detecting sensory signals reducing signal-to-noise ratio at the cortical level producing a modulatory influence on executive functions such as the inhibition of the processing of irrelevant stimuli (Ramos & Arnsten, 2007; Robbins & Everitt, 2007). The dopaminergic system affects behaviour accounting for the strength and frequency of behavioural outputs (Robbins & Everitt, 2007). The serotoninergic system moderate the effects the preceding systems promoting behavioural inhibition and cortical deactivation. Although for classical 'cognitive energetic' models (Kahneman, 1973; Sanders, 1983) the activity of the ascending reticular activating system has been the only neural substrate called into question to account for the effects of exercise on cognition, the sole action of the three systems cannot justify every reported effects, especially those on the explicit system. The effect of this group of arousal mechanism is mostly restricted to the facilitation of implicit bottom-up processes, speeding up response times and improving detection accuracy (Dietrich & Audiffren, 2011; McMorris, 2016).

As opposed to the reticular activating process, the hypofrontality process has been proven to be a solid account for the description of the inverse effects reported for the explicit system. The idea behind the hypofrontality process arises from the direct evidence that during exercise the brain is forced to a shift in the allocation of resources between regions required for emotional, cognitive, sensory and motor control (Ide & Secher, 2000). Since activation in some regions in the brain comes at the expense of other regions in the brain

(Miller & Cohen, 2001), during exercise the enormous demands of motor, sensory and autonomic structures (activated by the reticular-activating process) results in a diminished availability of resources for those cognitive and emotional processes that are not crucial for the implementation and maintenance of physical activity such as the frontal lobes (Dietrich, 2003, 2006).

The RAH model has proven to explain some inconsistencies within the interpretation of previous literature, thus stimulating future research on the effect of exercise on cognition. Rather surprisingly, to my knowledge no studies have tested the effect of acute exercise on the generation of free choices to act and to inhibit. Since the hypofrontality process is tied with the generation and modulation of consciousness, that in turn is the aspect defining voluntary motor control, the RAH model represent a fertile theoretical and neuropsychological ground for the investigation of the unconscious mechanisms that precedes and intuitively causes free-choices.

PART II

THE EXPERIMENTS

CHAPTER 3

SUBLIMINAL PRIMING OF FREE-CHOICES TO ACT AND TO INHIBIT

3.1. Introduction

Response inhibition is a fundamental component of humans' executive functions and refers to the ability of stopping the generation of unwanted behaviour up until the very last moment (Logan & Cowan, 1984), even when a motor plan have been already partially implemented (Logan, Cowan, & Davis, 1984; Schultze-Kraft et al., 2016). Although this component has been widely studied by means of Go/Nogo and SSTs (Logan, 1994), it has been recently proposed that such tasks cannot fully capture the complexity and the flexibility of humans' behavioural inhibition. Since in daily life, 'stop' or 'nogo' signals are quite rare, most of the time people must generate and implement internal commands to halt ongoing responses (Filevich et al., 2012). As introduced in the first chapter of the thesis, the 'WWW' model of voluntary actions (Brass & Haggard, 2008), proposes that 'intentional inhibition' and 'stimulus-driven inhibition' can be functionally dissociated with the latter representing the intentional – free – choice between executing or inhibiting a particular behaviour (Kühn, Gevers, & Brass, 2009). To date, the extent to which free-choices are a by-product of a conscious form of voluntary self-control is still a matter of debate (Baumeister, 2008; Frith et al., 1991; Haggard & Lau, 2013; Schurger & Uithol, 2015).In this respect, by means of two-alternative forced choice paradigms, it has been demonstrated that stimuli presented below the threshold of awareness can systematically bias response decisions even when such choices appear to be internally generated and free (Ocampo, 2015; Schlaghecken & Eimer, 2004; Teuchies et al., 2016). As a matter of fact, intentional decisions to act might not be taken as freely as one might think: to what extent intentional decisions to inhibit are necessarily based on a deliberate choice remains an open question (Parkinson & Haggard, 2014). For instance, Filevich and colleagues (2013) convincingly demonstrated

that free-choices to inhibit an action are anticipated by a specific pattern of neural activity that precedes the conscious decisional processes (Filevich et al., 2013) as demonstrated for free action choices (Libet et al., 1983; Soon et al., 2008). Their experimental manipulation permitted to differentiate the precursor activity related to free-decision to inhibit from the activity involved in the free-decision to act with the former producing significantly smaller pre-stimulus ERP amplitudes (Filevich et al., 2013). Arguably, the unconscious state of the brain that precede the decision appears to influence the outcome of the subsequent conscious decision, rather than vice versa, arguing against Libet's (1983) dualistic notion of a 'free won't'. In summary, the concept of intentional inhibition is still poorly understood and further investigations are needed for the clear definition of an independent psychological construct. As suggested by previous studies exploring its relationship with conscious and unconscious mechanisms would add valuable information on how everyday 'free' decision to stop behaviour are implemented.

Therefore, the present study aims to explore whether intentional decisions can be unconsciously biased. I capitalized on a paradigm which has the ability to reveal whether the cognitive mechanisms concerned with both free-choices to act and free-choices to inhibit can be modulated by masked – subliminal – primes (Parkinson & Haggard, 2014). In particular, the paradigm is a modified version of the Go/Nogo task implemented by Lingnau and Vorberg (2005). Participants were required to respond to three possible target stimuli (arrows) in three different conditions: (i) *cued action condition,* in which the choice to act is indicated by a cue (cued go targets); (ii) a *cued inhibition condition,* in which the choice not to act is indicated by a cue (cued nogo targets); or (iii) a *free-choice condition,* in which participants were free to choose whether to act or not (free-choice targets). The targets were preceded by masked primes (arrows), whose orientation could be congruent or incongruent with the 'go' and the 'nogo' targets (i.e., pointing at the same or at the opposite direction), or be 'neutral' (i.e., a double arrow without direction). In line with this

interpretation, I expect reaction times (RTs) to action trials to be speeded up by congruent primes and slowed down by incongruent primes. Furthermore I predict accuracy to be reduced by incongruent, when compared to congruent, prime-target associations within cued conditions. By effect of the subliminal prime presented before the target, a comparable pattern of results should characterize response choices in the free-choice condition. More in detail, I expect 'go' primes to increase the proportion of choices to act, and 'nogo' primes to increase the proportion of choices to inhibit the action, when compared to neutral primes.

3.2. Methods

3.2.1. Participants

A total of twenty-seven healthy volunteers participated in the study (16 female, M = 24.13 years, SD = 3.55), after giving oral and written consent. Data of one participant were discarded because of an excessive tendency to prefer action in free-choice trials (98.9% > 2.5 SD from sample mean). All analyses were conducted on the remaining twenty-six participants, whose mean age was 24.6 years (15 female, age range = 19-29 years). All participants had normal or correct-to-normal vision and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). None of the participants had a history of neurological or psychiatric disorder. The study was approved by the University of Padova Ethics Committee and carried out in accordance with the Declaration of Helsinki.

3.2.2. Stimuli

The paradigm was composed of three distinct prime stimuli and three distinct target stimuli (Fig. 3.1). Prime stimuli were small white arrows either pointing up, down or being neutral (overlapping up and down primes). The target stimuli followed the primes and were formed by the contour of either upward, downward or double headed pointing arrows.

Targets surrounded a metacontrast mask that superimposing the primes obstructed their visibility. Primes subtended a visual angle of 0.6° × 1.8°, targets of 1.4° × 3.8° and the mask of 1° × 2.2°. The stimuli were presented over a black background and always appeared aligned to the fixation cross in the middle of the screen. Stimuli shapes and dimensions are shown in Figure 3.1.

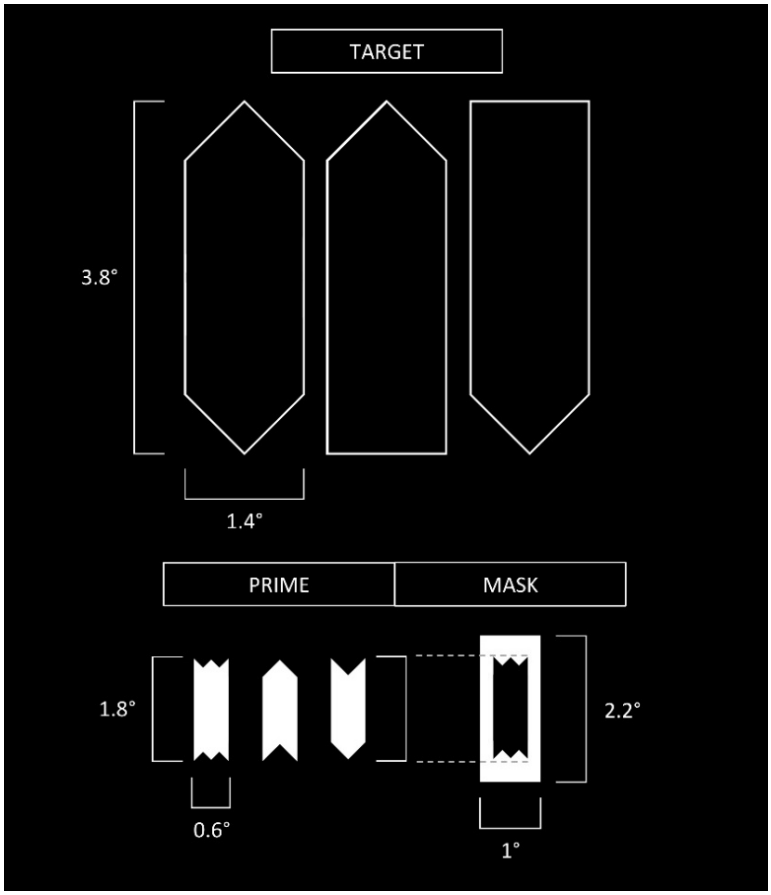

Figure 3.1: A schematic representation of the stimuli used in the paradigm. Values indicate the visual angle subtended.

3.2.3. Procedure

Participants were seated in a dimly lit room at a distance of 60 cm from a PC-driven CRT monitor (resolution 1280 × 1024; 75 Hz refresh rate) positioned in front of them, with their eyes at a height corresponding to the center of the screen. Responses were given with

the index finger of the right (dominant) hand using the spacebar of the keyboard positioned along the body midline of the participant. All trials started with a fixation cross (subtending 0.3°) that appeared in the center of the screen for 534 ms and was followed by a masked prime stimulus (from now on defined as 'prime') presented for 13 ms (1 frame at 75Hz ≈ 13.3 ms). Following the presentation of the prime, a fixation cross of 39 ms duration and subsequently the target surrounding a meta-contrast mask appeared. Both the target and the mask lasted for 120 ms. (see Fig. 3.2 for the sequence of events).

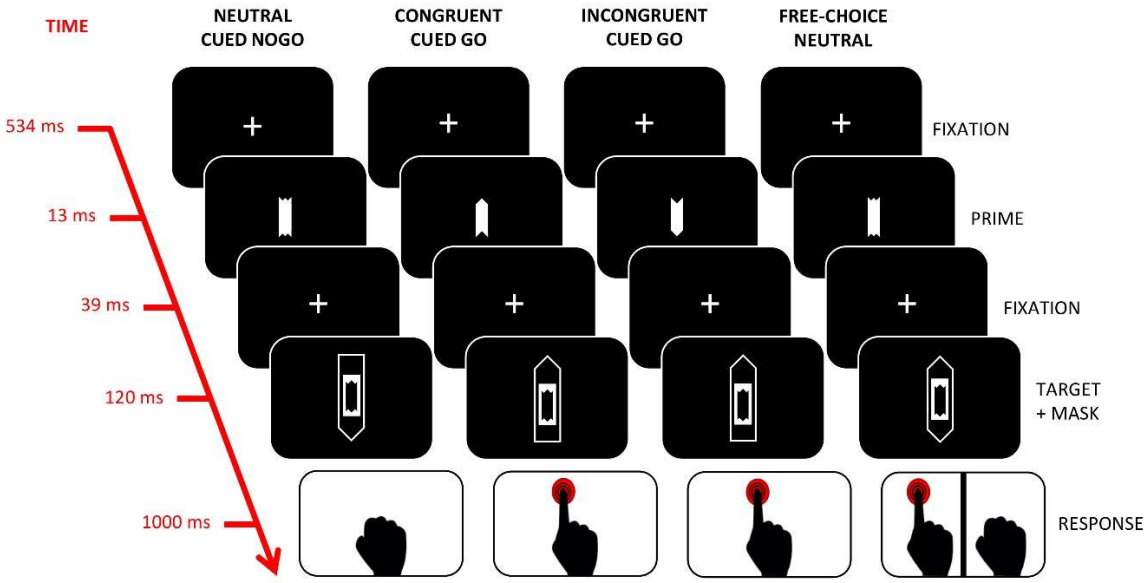

Figure 3.2: Stimulus sequence and timings in four examples of the possible masked prime/target combinations.

Having the same luminance as the prime, this backward stimulus sequence has been shown to effectively obstruct the visibility of the prime stimulus (Lingnau & Vorberg, 2005). Between trials a fixation cross was continuously displayed and interrupted only by a blank screen lasting the duration of a refresh of the monitor that signaled the beginning of the new trial. In contrast to previous studies (Parkinson & Haggard, 2014), I decided to use upward/downward pointing arrows and right hand responses in right-handed participants

to control for the possibility that go primes and targets might, in principle, produce spatial incompatibility effects of the Simon type (Simon, 1969). According to the orientation of the target stimuli, the trials of each block consisted in: cued go, cued nogo and free-choice trials. Prior to the beginning of each experimental block, participants received instructions about the identity of the go target (upward or downward pointing arrow) and they were requested to respond as quickly and accurate as possible by pressing the response button. In the same block, the nogo target consisted of an arrow having the opposite orientation of the go target. At the sight of the nogo target, participants were required to refrain from responding. The labeling of go and nogo targets according to arrow's orientation was counterbalanced between blocks and participants. Furthermore, they were told that a double-headed target arrow always represented a free-choice target to which they had to freely decide whether to answer or inhibit their response. They were asked to avoid the use of strategies (e.g., alternating between action and inhibition), differentiating their decision throughout the whole experiment. Since speed was stressed to lead participants preparing the action at the beginning of every trial, they had to decide at the very last moment whether to carry out their response or not. The response window was set at 1000 ms, starting from the appearance of the target. With regard to the prime stimuli, they were categorized in accordance with the orientation of the target stimuli. In particular, go primes had the same orientation of the go targets, nogo primes had the same orientation of nogo targets and neutral primes (overlapping up and down primes) served as control conditions. Task presentation and response registration were controlled using E-prime 2.0 experimental software (http://pstnet.com/eprime.cfm). Each experimental sessions was split in 4 blocks lasting approximately 6 min each, for a total of about 25 min. A total of 384 trials (96 trials per block) was administered, divided into: 25% go targets, 25% nogo targets and 50% free-choice targets. Each target was preceded by go, nogo or neutral primes, with equal probability (33.3%). A higher proportion of cued go trials with respect to cued nogo or free-

choice trials would have produced a tendency toward choosing to act in free-choice trials that would have been indistinguishable by the effect of the primes. Since there are also studies reporting inhibitory activity using equal probabilities for go and nogo stimuli consistent with studies using lower probability inhibitory cues (Konishi, 1999; Roth et al., 2007), I opted to use the same frequency for go and nogo trials. Moreover an equal number of go and nogo stimuli has been adopted to avoid the 'oddball' effect of nogo stimuli (Stevens, Skudlarski, Gatenby, & Gore, 2000). The inter-trial-interval (ITI) was randomized and included duration between 2000 and 2500 ms. After the last experimental session was completed, participants were informed regarding the presence of the masked primes, and were then asked to take part in a short testing phase to verify primes discriminability. A total of 30 testing trials was administered (10 repetitions for each of the three prime stimuli): testing trials were identical to free-choice trials but participants were asked to focus on prime appearance and ignore the target, trying to decide whether the prime was pointing up, down, or was neutral, by making unspeeded but forced choices. The shape and the position of the prime were described to the participants prior to the beginning of the discrimination task. Participants did not receive feedback regarding their success or failure of detecting the prime. In case of uncertainty, they were instructed to simply guess. Participants were trained to familiarize with the task instructions during a training session prior to the beginning of the experimental session.

3.2.4. Statistical analyses

Statistical analyses on the effects of interest were computed by means of linear mixed-effects (LME) models for RTs, and generalized mixed-effects (GLME) models with a binomial link function for free-choice behavior and error rates (Pinheiro & Bates, 2000). As compared to traditional repeated-measures ANOVA approach, LME and GLME provide greater statistical power for the analysis of repeated observations and provide a robust

method of dealing with unbalanced data such as in the present experiments (Baayen, Davidson, & Bates, 2008). LME and GLME models allow to consider simultaneously the standard fixed-effects factors controlled by the experimenter and the random-effects factors. For the LME and GLME models used in this study, random effects consisted of participants, experimental block and gender. Models were fitted using restricted maximum likelihood (REML). For the computation of the models, R (R Core Team, 2017), lme4 (Bates, Mächler, Bolker, & Walker, 2015), nlme (Pinheiro, Bates, DebRoy, Sarkar, & R Core Team, 2017), and lmerTest (Kuznetsova, Brockhoff, & Christensen, 2014) were used. Likelihood ratio tests of the full model with the effect in question against the model without the effect in question allowed to estimate *p*-values. The strength of evidence in favor of one model over the other is reported as the relative likelihood based on the models' Akaike information criterion (AIC) computed as $AIC_{RL} = e^{x}\,[(AIC_{m1} - AIC_{m2})\,/\,2]$ where AIC_{RL} represent the relative likelihood of the model with the effect in question, and the two models, AIC_{m1} and AIC_{m2}, being compared (Akaike, 1987; Burnham & Anderson, 2010; Wagenmakers & Farrell, 2004). As preliminary analysis, to guarantee that unconscious perception of the prime was preserved for all participants, the results from the prime discrimination test were calculated as the mean percentage of primes correctly discriminated compared against the chance level of 33.3% accuracy. For the main analyses, RTs were obtained from participants' correct responses to go targets (cued go trials) and to free-choice targets when participants choose to press the button to answer (free-choice go trials). For RTs an LME model was computed with Prime (Go, Nogo, Neutral) and Target (Cued go, Free-choice go) as fixed effects. RTs outliers were removed following a two-steps procedure (Baayen & Milin, 2015): first, extremely shorts (< 200 ms) and extremely long (> 1000 ms) RTs were removed (less than 1% of the data). Second, after the standardized residuals of the full LME model have been computed, trials with absolute standardized residuals exceeding $\pm$ 2.5 *SD* were discarded (about 2.6% of the data). Free-choice trials were

analyzed in order to uncover how masked priming influenced participants' choice to execute or inhibit the actions in both low and high arousal conditions. The number of choices to act or to inhibit as a function of subliminal primes was computed by fitting a GLME model with Prime (Go, Nogo, Neutral) as fixed effect. Since participants were asked to avoid the use of strategies (e.g., alternating between action and inhibition), free-choice trials have been further explored by looking at sequential dependencies between trials in both low and high arousal conditions. Responses in the current free-choice trial (trial *n*) with those in the previous trial (trial $n-1$, which could either be a cued trial or another free-choice trial) were compared to see whether participants had a tendency to systematically respond the same (action - action; inhibition - inhibition) or the opposite (action - inhibition; inhibition - action) in trial n as in trial $n-1$. A GLME model was computed with Previous choice (Action, Inhibition) as fixed effect and the choice at trial n as dependent variable. In conclusion, error rates within each cued condition (omissions in cued action trials and false alarms in cued inhibition trials) were computed for each session as function of the subliminal prime by fitting GLME model with Prime (Go, Nogo, Neutral) as fixed effect. For both GLME and LME models, post-hoc analyses were performed on the effects of interests by means of planned pair-wise comparisons (t-tests) and the α level was set at 0.05 prior to Bonferroni correction. For all analyses the complete set of computed post-hoc t-test are reported. Cohen's *d* indices are reported as measure of effect sizes (Cohen, 1988).

3.3. Results

3.3.1. Prime discrimination

The results of the prime discrimination test show that primes were not consciously detected, $t(25) = 0.54$, $p = .472$, tested against the 33.3% chance level (mean % correct: $M = 31.32$, $SD = 3.83$). As measure of discriminability, *d'* was computed for each

prime/participant. The obtained d' values were not significantly different from '0' (no discrimination possible), $t(25) = 0.82$, $p = .962$ (d' values: $M = 0.23$, $SD = 0.09$).

3.3.2. Reaction times

The analysis on RTs yielded a significant main effect of Prime, $\chi^2(2) = 506.09$, $p < .001$, $AIC_{RL} > 100$ and Target, $\chi^2(1) = 251.01$, $p < .001$, $AIC_{RL} > 100$. The main effect of prime indicates that response timing were faster if preceded by go primes when compared to neutral, $t(25) = 9.28$, $p < .001$, $d = .26$, or nogo, $t(25) = 19.02$, $p < .001$, $d = .53$, primes. Conversely, nogo primes slowed down the response if compared to neutral primes, $t(25) = 9.76$, $p < .001$, $d = .27$. Following, the significant main effect of target indicates that responses to cued go targets were faster compared to the free-choice go targets overall, $t(25) = 9.79$, $p < .001$, $d = .27$. The interaction Prime × Target was significant, $\chi^2(2) = 6.35$, $p = .041$, $AIC_{RL} = 2.35$, indicating that the effect induced by go primes was stronger in the cued condition but the effect induced by nogo primes was stronger in the free-choice condition. In order to explore the interaction effect specific post-hoc comparisons were performed: *cued neutral prime – cued go prime* (mean difference: $M = 40$ ms), $t(25) = 8.88$, $p < .001$, $d = .36$; *free-choice neutral prime – free-choice go prime* ($M = 31$ ms), $t(25) = 5.53$, $p < .001$, $d = .21$; *cued nogo prime – cued neutral prime* ($M = 36$ ms), $t(23) = 8.07$, $p < .001$, $d = .33$; *free-choice nogo prime – free-choice neutral prime* ($M = 41$ ms), $t(25) = 6.68$, $p < .001$, $d = .26$. Figure 3.3 summarizes the mean RTs for each type of target and prime.

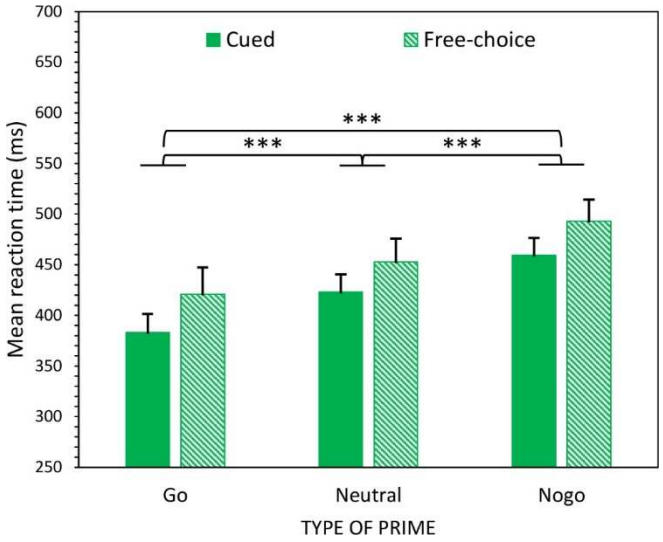

Figure 3.3: Sample mean of response times (cued go and free-choice go trials). Error bars show standard error of mean. ***p < .001; **p < .01; *p < .05.

3.3.3. Free-choice behavior

For the free-choice condition the analysis looked at how the primes biased the choices made by the participants. The response bias was defined as the percentage of free-choice trials in which each participant choose to respond as a function of the preceding masked prime. The analysis showed a main effect of Prime, $\chi^2(2) = 56.28$, $p < .001$, $AIC_{RL} > 100$, indicating that subliminal primes were biasing participants' free-choices. Participants choose to respond after a go prime more often when compared to neutral primes: *go – neutral* (mean difference: $M = 7\%$), $t(25) = 3.70$, $p < .001$, $d = .10$; or when compared to nogo primes: *go – nogo* ($M = 13\%$), $t(25) = 7.19$, $p < .001$, $d = .20$; and choose more often to inhibit the response after a nogo prime if compared to neutral prime: *neutral – nogo* ($M = 6\%$), $t(25) = 3.49$, $p = .001$, $d = .10$ (Fig. 3.4a). Looking at the sequential dependencies in free-choice trials, the Previous choice regressor was significant, $\chi^2(1) = 28.96$, $p < .001$, $AIC_{RL} > 100$ (Fig. 3.4b). Participants choose to respond action (*n*) after an action trial (*n – 1*) about 58% of the times, and choose to respond inhibition (*n*) after an inhibition trial (*n – 1*) about 50% of the

times. The significant effect indicates that the response to trial *n – 1* was slightly biasing the response at trial *n* by inducing a repetition of the same response (action).

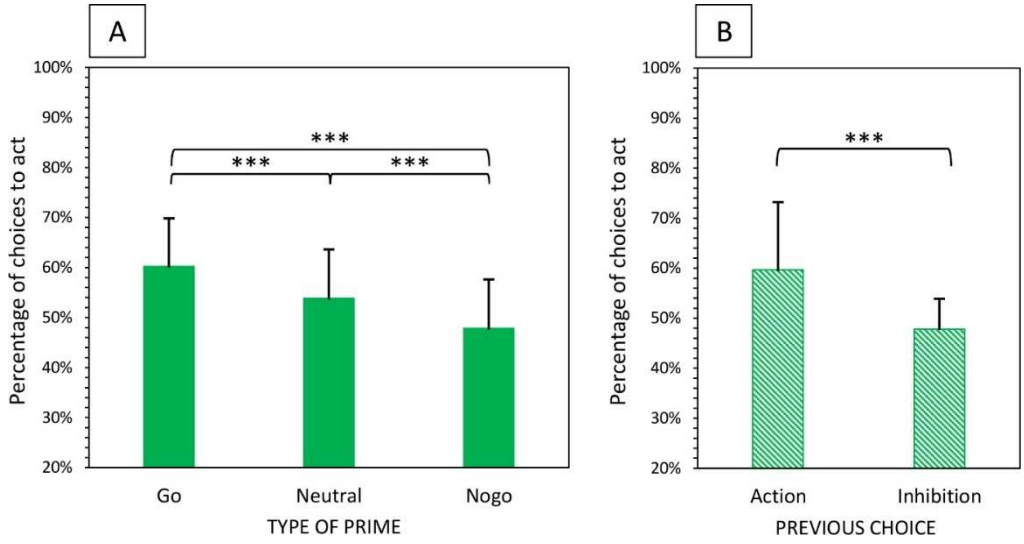

Figure 3.4: Mean percentage of free-choice trials in which participants chose to act rather than inhibit responses, as modulated by type of primes (go, nogo and neutral – panel A). Mean percentage of free-choice trials in which participants chose to act as a function of the preceding trial (panel B). Error bars show standard error of mean. *** p < .001; ** p < .01; * p < .05.

3.3.4. Error rates

Errors in cued trials were generally few (see Fig. 3.5). Within cued inhibition trials the mean rate of false alarms was 8.7%. The GLME model on false alarms yielded a significant main effect of Prime, $\chi^2(2) = 95.05$, $p < .001$, $AIC_{RL} > 100$ that indicates that false alarms were more numerous after a go prime was presented (15.8.%) if compared to neutral (7.1%) or nogo primes (3.3%) intuitively reflecting the incompatibility between the response suggested by the prime (go) and the response required by the target (nogo – Fig. 3.5b). Within cued action trials participants were more accurate and the mean rate of omissions was 1.3%. The GLME model on omissions yielded a significant main effect of Prime, $\chi^2(2) = 6.20$, $p = .045$, $AIC_{RL} = 3.01$, indicating that also in cued action trials the incompatibility

between primes and target was affecting the general level of accuracy: omissions were more numerous after a nogo prime was presented (2.1.%) if compared to neutral (0.9%) or go primes (0.9% – Fig. 3.5a). Mean values for each condition, percentage of errors in cued trials and percentage of responses in free-choice trials are reported in Table 3.1.

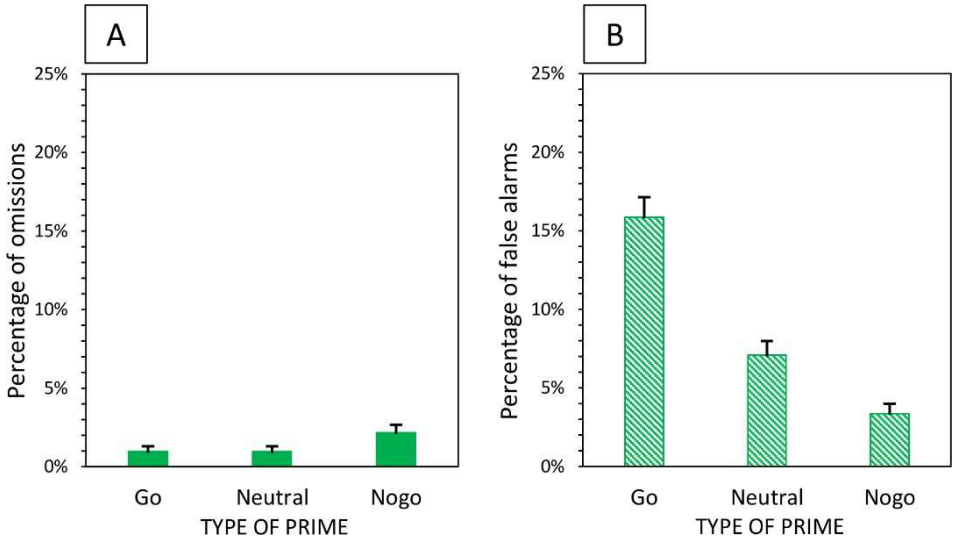

Figure 3.5: Mean percentage of omissions (panel A) and false alarms (panel B) as modulated by type of primes (go, nogo and neutral). Error bars show standard error of mean.

Table 3.1: Reaction time (RT) and standard deviation (SD) in milliseconds of both free-choice and cued trials, percentage of errors in cued go and cued nogo conditions, percentage of responses in free-choice condition, split for each prime (upper part), and collapsed across primes (lower part).

PRIME	TARGET	RTs (±SD)	% Errors	% Go responses
Go	Cued go	383.2 (±16.5)	0.96	
Neutral	Cued go	423.4 (±10.9)	0.96	
No	Cued go	459.4 (±13.3)	2.16	
Go	Cued nogo		15.8	
Neutral	Cued nogo		7.09	
No	Cued nogo		3.36	
Go	Free-choice go	421.1 (±26.1)		60.2
Neutral	Free-choice go	452.6 (±23.2)		53.8
No	Free-choice go	493.1 (±20.1)		47.8
Cued go trials		421.8 (±8.6)	5.60	
Cued nogo trials			1.36	
Free-choice go trials		452.9 (±11.2)		53.9

3.4. Discussion

The present study sought to investigate whether stimuli presented under the threshold of conscious awareness might produce a bias within participants' voluntary decision processes. More in detail, participants were asked to respond to cued and free-choice targets following the presentation of three varieties of masked primes that could elicit congruent or incongruent prime-response conflicts. Intentional action and inhibition responses were compared with stimulus-driven responses. Since voluntary actions and intentional inhibition might better describe everyday life situations, where no specific signals to stop are provided (Brass & Haggard, 2007; Filevich et al., 2012), defining its precise function is of utmost importance.

In line with the hypotheses and previous findings (Parkinson & Haggard, 2014), go primes had the ability to shorten RTs when compared to neutral primes. On the opposite, nogo primes determined longer RTs when compared to neutral primes. The effect of go

(congruent) primes was more pronounced in the cued condition compared to the free-choice condition, but the effect of nogo (incongruent) primes was more pronounced in the free-choice condition, as revealed by the interaction effect between primes and targets. As opposed to free-choice trials, in cued trials the response option (action) is automatically triggered by the appearance of the cued go target. The retention of the information at the low-level of direct motor execution leaves less space for higher-level attentional control to compensate for the bias induced by the subliminal primes boosting the execution of the response. In free-choice (go) trials instead, the (high-level) decisional processes involved (highlighted by the longer RTs for the free-choice go conditions in comparison to those for the cued go conditions) might mediate the effect of congruent primes but be more affected by incongruent information. This support the idea that primes were affecting free-choices at the decisional level and not merely modulating the motor threshold (Schlaghecken & Eimer, 2004). Accordingly incongruent primes produced more errors in both cued go and cued nogo conditions (omissions and false alarms) when compared to congruent or neutral primes.

The primary goal of the study was to test whether it was possible to bias the free decision to withhold the response as demonstrated for free actions (Demanet, De Baene, Arrington, & Brass, 2013; Schlaghecken & Eimer, 2004; Teuchies et al., 2016). Results showed that masked primes were able to induce the free decision process, both toward a significant increase of choices to act in action-congruent conditions, and toward an increase of choices to inhibit in inhibition-congruent conditions. Although go and nogo targets with equal probabilities were presented, the finding that the overall rate of false alarms was higher than the overall rate of omission suggests that the experimental design was successful in inducing a robust urge toward the action. This also implies that the experimental manipulation proposed might be suited for the study of intentional inhibition. One of the major difficulties in the study of intentional inhibition is selecting a

paradigm that gives enough time to make a free-choice to inhibit under a strong impulse to act (Lynn et al., 2014): in the present paradigm participants were free to choose between the two response options. Moreover they were provided with enough time (1 second window) to decide whether to act or to inhibit but, importantly, such time-window was not too long for the participants to post-decide. In addition participants were previously instructed to be always ready to act at the appearance of each target and eventually inhibit the response.

Although participants were requested to respond in a balanced and random way (to the best of their possibilities) their responses deviate from chance level, which does not represents pure randomness. Unexpectedly, results showed that participants were more prone of choosing to act in free-choice trials (trial *n*) when the preceding trial (*n-1*) was an action trial too (cued go or free-choice go). These trial-to-trial dependencies, albeit relatively small in their effects, have been commonly reported in voluntary actions studies (Lages & Jaworska, 2012). Previous research dealing with the production of random response sequences showed that naïve participants have difficulties to produce random sequences and sequential dependencies across trials are commonly observed in binary decisions. These dependencies may indicate an involvement of memory and possibly executive control (Lages, 2002; Lages & Jaworska, 2012). Moreover stimulus-driven inhibition studies reported that the ability of inhibiting actions depends on the preceding context (Durston et al., 2002). Similarly, a recent study of Schel and colleagues (2014) found that the volume of activity on the areas devoted to intentional inhibition processing (i.e., dFMC) depended strongly on the preceding context. Along the same lines of the present results, intentional inhibition responses were less likely to occur when there were more preceding action trials (Schel et al., 2014). These effects, albeit small, might represent a possible confounding effect and a-major limitation of the present study.

To sum up, as speculated by previous research, intentional decision to inhibit may be taken not as 'voluntary' as one might expect. In line with my hypotheses the present

findings shows that voluntary – free – choices to act and to inhibit might partially depend on the unconscious neural processes that precede and possibly determine the outcome of the decision. Since behavioural studies can provide only a limited and undirected description of the processes involved in intentional inhibition (no behavioural output is observable and the decisional process is not under the control of the experimenter) previous studies in this field of research typically make use of neuroimaging techniques. The experiment presented in Chapter 4 utilize fMRI providing further information on how the brain compute such decisions and how subliminal stimuli are processed within the network of brain areas involved in free-choices.

CHAPTER 4

MODULATING THE FREE-CHOICE NETWORK:

EFFECTS OF INTENTIONALITY AND SUBLIMINAL INFORMATION[1]

4.1. Introduction

The neural mechanisms involved in intentional inhibition have been tested by means of specifically tailored experiments, in which participants were free to decide whether to execute or inhibit a particular behaviour (Kühn, Haggard, et al., 2009). A peculiarity of these experiments relies on the fact that such tasks do not result in any overt behavioural response to be explored (since the action has been inhibited) and, more importantly, there is no external imperative signal that time-locks the voluntary decision to a precise moment. Due to these factors, intentional inhibition has been widely investigated through neuroimaging techniques with the aim to define whether intentional and stimulus-driven inhibition rely on the same neural substrates and mechanisms or not (Schel et al., 2014). Stimulus-driven inhibition has been commonly associated with increased activity in the fronto-basal ganglia network including the dPFC, the IFG (mostly in the right hemisphere), the preSMA and the basal ganglia (most prominently the dorsal striatum and the STN – Aron, 2011; Bari & Robbins, 2013). Although the activity related to intentional inhibition largely overlaps with the networks characterizing externally-driven inhibition (Schel et al., 2014), increased activity within the dFMC has also been reported (Brass & Haggard, 2007; Kühn, Haggard, et al., 2009; Lynn et al., 2014). Initially thought of as a late '*veto area*', with the ability to halt voluntary motor commands (Kühn, Haggard, et

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al., 2009), the dFMC has been recently indicated as a key region for self-control, allowing to disengage from strong impulses and intentions (Lynn et al., 2014). A point worth noting, however, is that whereas some studies failed to identify inhibition-related activity over the dFMC (Hartwell et al., 2011; Kühn & Brass, 2009), others found dFMC activation confined to externally-driven inhibition (Lynn et al., 2016; Severens et al., 2012). These inconsistencies make the role and underlying functioning of dFMC quite controversial. In summary, since the concept of intentional inhibition is still poorly understood, further research is needed to investigate the role of specialized functional areas, such as the dFMC, in modulating these processes.

Despite the specific neuroanatomical correlates, the extent to which free-choices are linked with a conscious form of voluntary self-control is still a matter of debate. For instance, free-choice action decisions made by patients with preSMA lesions show anomalous susceptibility to subliminal primes. Typically, healthy participants' free-choice RTs are increased in congruent prime-target combinations when presented at NCE latencies (Eimer & Schlaghecken, 2003; Parkinson & Haggard, 2014). By contrast, patients with a preSMA lesion, shows faster RTs in the same condition (Sumner, 2007) suggesting that a normal function of the preSMA is to suppress involuntary responding to subliminal stimulation, and patients with preSMA lesions are therefore hyper-responsive. Patients did not consciously perceive the primes, which however influenced their free behaviour. A recent study of Teuchies and colleagues (2016) utilized masked arrows as subliminal primes, showing that the activity over some areas of the 'free-choice network', specifically the RCZ, the left anterior insula (AI), the DLPFC and the supramarginal gyrus (SG), was modulated according to the congruency between the prime and the response. The study suggests an involvement of these areas in solving the conflict between the external unconscious information and the free response selection (Teuchies et al., 2016). These evidences suggest that testing whether subliminal clues in the environment are able to

modulate neural activity in areas such as the dFMC or regions of the choice network would add invaluable information on the mechanisms by which we make intentional decisions to inhibit or to act.

To this aim in the present study I capitalize on the paradigm proposed in Chapter 3 to explore whether the brain areas involved in making free-choices are elicited by participants' responses to free-choice trials and whether the same neural activity is modulated by the presentation of congruent or incongruent subliminal primes. At the behavioural level, I expect that primes would affect participants' responses as highlighted by the results of the previous experiment: RTs to action trials to be speeded up by congruent primes and slowed down by incongruent primes. Furthermore I predict accuracy to be reduced by incongruent, when compared to congruent, prime-target associations within cued conditions. By effect of the subliminal prime presented before the target, a comparable pattern of results should characterize response choices in the free-choice condition. The present study, however, allows to make further inferences on how subliminal primes are processed within these brain networks, untangling whether primes would affect the response at motor level or at the decisional level. Within the 'decision making' literature choice performances for this type of tasks are commonly described by race or diffusion models (Gold & Shadlen, 2007; Leuthold & Kopp, 1998). These models assume that participants accumulate independent evidence to support one decision versus another (in this case action or inhibition) until a decision threshold is reached (Hanes & Schall, 1996). Since the rate at which cortical activity grew toward that threshold is determined in part by ongoing stochastic fluctuations of neural activity (Schurger et al., 2012), subliminal primes could influence the responses to go and nogo stimuli in different ways: on the one hand primes could enhance the excitability of post-decisional motor pathways, having a direct impact in the actual implementation of the action and thus modulating RTs to go trials (Smith, 2000). On the other hand, primes might also bias the

actual neural "free decision" in favour of initiating or inhibiting the action: by managing the noise level within action decision circuits, primes would change the level at which the threshold is reached. Accordingly, while still modulating RTs to go trials, subliminal primes would operate also on choices suggesting that the brain incorporates whatever information is available, even subliminal, into its decisions about whether to initiate an action or not. This interpretation is consistent with previous studies showing that the influences of subliminal primes at (low-level) automatic stages of motor processing are mediated by (high-level) current intentions and task set, or rather the set of stimulus-response mappings imposed by task instructions (Schlaghecken & Eimer, 2004).

Since I predict the present paradigm to be able to disentangle between forced and free components of response inhibition in relation to subliminal processing, I focused on a network of brain regions described by previous studies dealing with the generation of free-choices (Kühn & Brass, 2009; Kühn, Haggard, et al., 2009; Teuchies et al., 2016). I expect that areas linked to the 'free-choice network', specifically the RCZ, that is the part of the medial frontal cortex extending posteriorly and dorsally from the ACC, the DLPFC, the inferior parietal lobule (IPL) and the AI to be more involved in intentional rather than in cued conditions, in both action and inhibition trials (Forstmann, Brass, Koch, & von Cramon, 2006). Furthermore, to clarify the role of the dFMC – the '*veto area*' – in voluntary choices to inhibit a response, I conducted a ROI analysis focused on this region, directly comparing brain activity related to inhibition trials. To conclude, I conducted another set of ROI analyses to test whether information provided by subliminal information conveyed by the prime might modulate the activity in the same set of regions of the network. Based on the aforementioned findings for intentional actions (Teuchies et al., 2016), I hypothesize that the RCZ, the DLPFC, the IPL and the AI would be affected by the priming manipulation: I expect these areas to be more involved in incongruent rather than congruent prime-response mappings, given their specific role in overcoming inconsistent sources of

information (Teuchies et al., 2016). With regard to the specific involvement of the dFMC I conducted a ROI analysis focused on this region, as did for the first set of ROI analyses comparing free-choice inhibition trials only, among the three levels of congruency.

4.2. Methods

Concerning the behavioural component of the present experiment the methods, the procedures and the data analysis were identical to those described in Chapter 3 with the following exceptions.

4.2.1. Participants

A total of twenty-eight healthy volunteers participated in the study (17 female, mean age: M = 23.53 years, SD = 2.86), after giving oral and written consent. Data of four participants were discarded: one participant was discarded because of an excessive tendency to prefer inhibition in free-choice trials (3.64%, < 2.5 standard deviations from sample mean), and three participants for head motion exceeded tolerance (> 3.5 mm in translation, and 3.5 degrees in rotation). All analyses were conducted on the remaining twenty-four participants, whose mean age was 23.8 years (16 female, age range = 19-30 years).

4.2.2. Procedure

During stimuli presentation, participants were lying down in the scanner and wore MR-compatible LCD video goggles (VisuaStim XGA, Resonance Technology Inc.) with a resolution of 800 × 600 and 60 Hz refresh rate. Responses were given with the index finger of the right (dominant) hand using an MR-compatible response box (Evoke Response Pad, Resonance Technology Inc.) positioned along the body midline of the participant. Every trial started with a small fixation cross in the center of the screen for 560 ms followed by a

masked prime stimulus presented for 17 ms (1 frame at 60Hz ≈ 16.7 ms). The prime was immediately succeeded by a fixation cross of 35 ms duration, followed by the target surrounding a meta-contrast mask. Both the target and the mask lasted for 136 ms.

4.2.3. Design

An event-related design was adopted and the entire task was split in 4 scanning runs, each of them lasting approximately 9 min and 40 s. ITI was jittered including duration from 3000 to 9000 ms, and the software Optseq2 (http://surfer.nmr.mgh.harvard.edu/optseq) was used to optimally randomize the order and spacing between stimuli in order to ensure orthogonality of the stimulus conditions. ITI duration was independently randomized within each single experimental run. During the prime discrimination task the scanner acquired images, with the purpose of reproducing the same experimental conditions of the experimental session (images were not analyzed).

4.2.4. MRI data acquisition and preprocessing

Data were acquired with a 1.5 T Siemens Avanto whole body MRI scanner (Siemens Medical Systems, Erlangen, Germany) equipped with a standard Siemens eight channels coils. Participants were positioned headfirst and supine in the magnet bore. The head was held in place with clamps to avoid head motion. Functional images were acquired with a gradient-echo, echo-planar (EPI) T2*-weighted sequence in order to measure blood oxygenation level-dependent (BOLD) contrast throughout the whole brain (37 contiguous axial slices acquired with ascending interleaved sequence, matrix size = 56 × 64 voxels, 3.5 mm × 3.5 mm × 4.0 mm resolution, FOV = 196 × 224 mm, flip angle = 90°, TE = 49 ms). Volumes were acquired continuously for each run with a repetition time (TR) of 3 s; 196 volumes were collected in each single scanning run, resulting in 4 functional runs of 9 min and 48 s duration (39 min and 12 s of acquisition time in total). High-resolution anatomical

images were then acquired for each subject using a T1-weighted 3D magnetization prepared rapid acquisition gradient echo (MPRAGE) sequence (176 axial slices with no interslice gap, data matrix = 256 × 256, 1 mm isotropic voxels, TR = 1900 ms, TE = 2.91 ms, flip angle = 15°). Data were preprocessed and analysed using statistical parametric mapping (SMP12 – Wellcome Trust Centre for Neuroimaging, London, UK) working in Matlab environment (MathWorks, Natick, MA, USA). The first three scans of each individual time series were removed because of the non-equilibrium state of the magnetization in order to allow for stabilization. The ArtRepair toolbox for SPM12 was used to detect slices corrupted by motion artifacts and/or signal spikes (Mazaika, Whitfield-Gabrieli, & Reiss, 2007). Then the data was slice time corrected taking the central slice as reference, realigned to the mean image by rigid body transformation, coregistered with the image of the gray matter obtained from the structural image segmentation, normalised to the montreal neurological institute (MNI) template, and smoothed using a 7 mm × 7 mm × 8 mm full-width-at half-maximum (FWHM) Gaussian Kernel. Finally, the ArtRepair toolbox was applied again to detect outlier volumes concerning global intensity or large scan-to-scan movement (Mazaika et al., 2007).

4.2.5. fMRI analyses

For first-level analyses, the preprocessed images were analyzed with a general linear model (GLM – Friston, Holmes, et al., 1994) for each subject. Trials were modeled according to the combination of prime Congruency (Congruent, Incongruent, Neutral) and the response to the Target (Cued action, Cued inhibition, Free-choice action, Free-choice inhibition), producing 12 different regressors of interests. Trials on which an error was made (omissions in cued go trials and false-alarms in cued nogo trials) were included as an additional nuisance variable (≈ 3.5% of all trials) and realignment parameters were modeled as regressors of no interest to account for motion artifact in the data. For each

participant, the four runs were modeled as separate session in the GLM. The fMRI time series were then analyzed by convolving a canonical hemodynamic response function (HRF) to the onset of the target and the duration of the events in the GLM was set to 0 s. One-sample t-tests were performed in order to produce images for each single condition for each participant. First, a whole brain analysis has been conducted, to explore the specific role of intentionality on the response or in response inhibition. For this analysis primes were collapsed and the resulting matrix is a 2 × 2 factorial design with Response (Action, Inhibition) and Intentionality (Free-choice, Cued) as factors. Images for each of the four conditions were entered into a second level random effect analysis (RFX). First, at the whole brain level, cued vs free-choice trials were compared in order to reveal whether the 'free-choices network' was significantly involved in the present task. As a second step, a ROI analysis was implemented in those areas commonly reported to be involved during voluntary choices. ROI analysis were performed using the MARSBAR toolbox (http://marsbar.sourceforge.net; Brett, Anton, Valabregue, & Poline, 2002) considering the following anatomical ROIs: RCZ, bilateral AI, bilateral IPL and bilateral DLPFC (Brodmann area 46 – BA46) as key areas of the network (Forstmann et al., 2006; Teuchies et al., 2016). In this analysis I first compared free-choice action and inhibition trials with cued action and inhibition trials respectively. Then the two free-choice conditions were mutually compared. For the definition of the RCZ, given no anatomical map is available, the average of coordinates reported in other studies comparing free-choices to cued choices was considered (Demanet et al., 2013; Forstmann et al., 2006; Kühn, Haggard, et al., 2009; Lynn et al., 2016; Mueller et al., 2007; Teuchies et al., 2016; Wisniewski, Goschke, & Haynes, 2016). A 10-mm radius sphere was built around the resulting coordinates according to the MNI stereotaxic space (MNI *x, y, z*: 0 27 38). In addition, in order to test whether the task elicited intentional inhibition mechanisms as reported in previous work (Kühn, Haggard, et al., 2009), a ROI analysis focusing on the dFMC was conducted comparing cued and free

choice inhibition trials. To this extent I created a spherical ROI with 10 mm radius around the MNI coordinates for dFMC taken from on Kühn, Haggard, et al., (2009; MNI *x, y, z*: -7 42 21). Finally, to verify how masked priming should influence free-choices, the four ROIs related to the 'free-choice network' (RCZ, AI, DLPFC and the IPL) and the dFMC were entered in a 3 × 4 factorial design with factors: Congruency (Congruent, Incongruent, Neutral) and Target (Cued action, Cued inhibition, Free-choice action, Free-choice inhibition). The congruence between primes and the response given to each different target produced twelve different conditions. For the dFMC analysis I focused on the effect of primes on free-choice inhibition trials only. I hypothesized that a go prime presented before a free-choice trial would produce an even stronger action tendency. In particular, this increase would require the activation of the neural mechanisms specifically related to intentional inhibition (i.e., dFMC) in those trials that were effectively inhibited (incongruent free-choice inhibition trials). Finally, to disentangle the possible mechanisms by which priming would affect choices and not just the motor state of responses, I conducted an exploratory ROI analysis on primary motor cortex (M1). If primes operate affecting participants' responses by increasing preparatory activity of the motor neurons involved in producing the action, one would expect to find significant differential activity for incongruent vs congruent trials even in absence of an actual motor response. Alternatively if primes affect the activity of the neural representations of choices but not directly the motor processes one could predicts no differences within motor cortices. To this purpose I contrasted congruent versus neutral versus incongruent nogo trials (cued and free-choice) within primary motor cortex. For the definition of the ROI I computed the contrasts 'action > inhibition' at the whole brain level in conjunction with Brodmann area 4 (BA4) as defined by the brain atlas automated anatomical labeling (AAL) (Tzourio-Mazoyer et al., 2002). For all ROI analyses, planned contrasts were performed using paired sample t-tests in order to test for the effect of interests, adopting a significant level of $\alpha = 0.05$ prior

to Bonferroni correction. For whole brain analysis all reported effects were thresholded at $p < 0.05$, family-wise error (FWE) corrected with cluster-extent based thresholding method with a low cluster-defining primary threshold, $p_{uncorrected} < 0.001$ (Woo, Krishnan, & Wager, 2014). Cluster-extent threshold was estimated by gaussian random field theory (RFT) method (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994) implemented in SPM12.

4.3. Results

4.3.1. Behavioral results

4.3.1.1. Prime discrimination

A prime discrimination test was performed by computing the mean percentage of trials correctly discriminated, and comparing this value against the chance-level using single sample t-tests. Results show that primes were not consciously detected (mean % correct: $M = 32.08$, $SD = 9.26$), $t(23) = 0.48$, $p = .632$ tested against the 33.3% chance level. As measure of discriminability, d' was computed for each prime/participant. The obtained d' values were not significantly different from '0' (no discrimination possible), $t(23) = 0.48$, $p = .632$ (d' values: $M = 0.32$, $SD = 0.09$)

4.3.1.2. Reaction times

Outliers were removed following a two-steps procedure (Baayen & Milin, 2015): first, extremely shorts (< 200 ms) and extremely long (> 1000 ms) RTs were removed (less than 1% of the data). Second, after the standardized residuals of the full LME model have been computed, trials with absolute standardized residuals exceeding $\pm$ 2.5 SD were discarded (about 2.4% of the data). The analysis on RTs yielded a significant main effect of Prime, $\chi^2(2) = 248.47$, $p < .001$, $AIC_{RL} > 100$ and Target, $\chi^2(1) = 61.25$, $p < .001$, $AIC_{RL} > 100$ but not a significant interaction Prime $\times$ Target, $\chi^2(2) = 2.28$, $p < .319$, $AIC_{RL} = 2.35$. Since the interaction between factors was not significant I looked at the post-hoc comparisons for go

RTs (cued go, free-choice go combined) comparing go and nogo primes conditions with the neutral prime condition. The main effect of prime indicates that response timing was faster if preceded by go primes when compared to neutral, $t(23) = 5.88$, $p < .001$, $d = .17$, (neutral – go ≈ 26 ms), or nogo, $t(25) = 12.66$, $p < .001$, $d = .38$, (nogo – go ≈ 57 ms), primes. Conversely, nogo primes slowed down the response if compared to neutral primes, $t(23) = 6.76$, $p < .001$, $d = .20$, (nogo – neutral ≈ 31 ms). Following, the significant main effect of target indicates that responses to cued go targets were faster compared to the free-choice go targets overall, $t(23) = 5.32$, $p < .001$, (cued – free-choice ≈ 20 ms). Figure 4.1 summarizes the mean RTs for each type of prime.

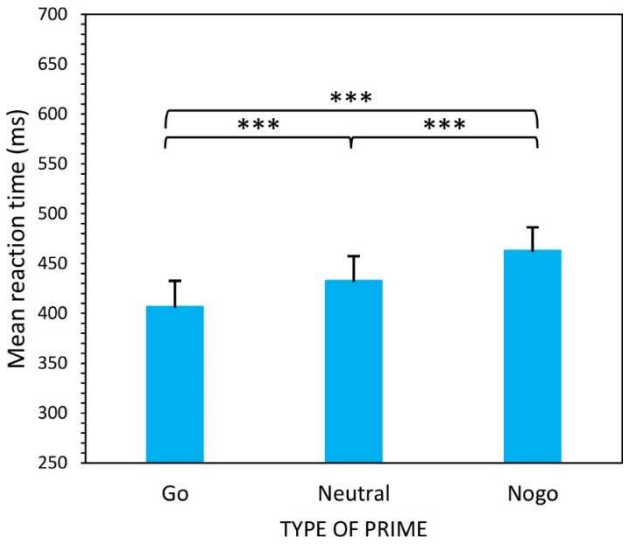

Figure 4.1: Mean reaction time in milliseconds (ms) for Go trials (cued and free-choice trials combined). Error bars show standard error of mean. *** p < .001; ** p < .01; * p < .05.

4.3.1.2. Free-choice behaviour

For the free-choice condition the analysis looked at how the primes biased the choices made by the participants. The response bias was defined as the percentage of free-choice trials in which each participant choose to respond as a function of the congruency with the preceding masked prime. The total proportion of actions in free-choice trials was

51%. Unlike the results reported for the study described in Chapter 3, the results show that in free-choice trials the response was not influenced by the presentation of the prime $\chi^2(2) = 4.69$, $p = .095$, $AIC_{RL} = 1.41$. Participants did not choose to act significantly more often after a go prime ($M = 53\%$; $SD = 11$; congruent trials), neither when compared to neutral, $t(23) = 1.973$, $p = .061$ nor as expected by chance $t(23) = 1.329$, $p = .197$. Similarly, participants did not show a significant reduction in the proportion of free-choice responses after a Nogo prime ($M = 49\%$, $SD = 14$; incongruent trials) when compared to neutral trials, $t(23) = .171$, $p = .865$, or to chance level, $t(23) = .181$, $p = .858$ (Fig. 4.2a). Looking at the sequential dependencies in free-choice trials, the Previous choice regressor was not significant, $\chi^2(1) = 1.03$, $p = .31$, $AIC_{RL} = 1.21$. Participants choose to respond action (*n*) after an action trial (*n-1*) ~ 52% of the times, and choose to respond inhibition (*n*) after an inhibition trial (*n-1*) ~ 49% of the times. The lack of significance indicates that the response to trial *n-1* was not biasing the response to trial *n* neither by inducing an increase of switches nor by systematically repeating the same response. This result supports the conclusion that participants have been responding in a balanced and random way to the best of their possibilities as requested by the experimenter (see Fig. 4.2b).

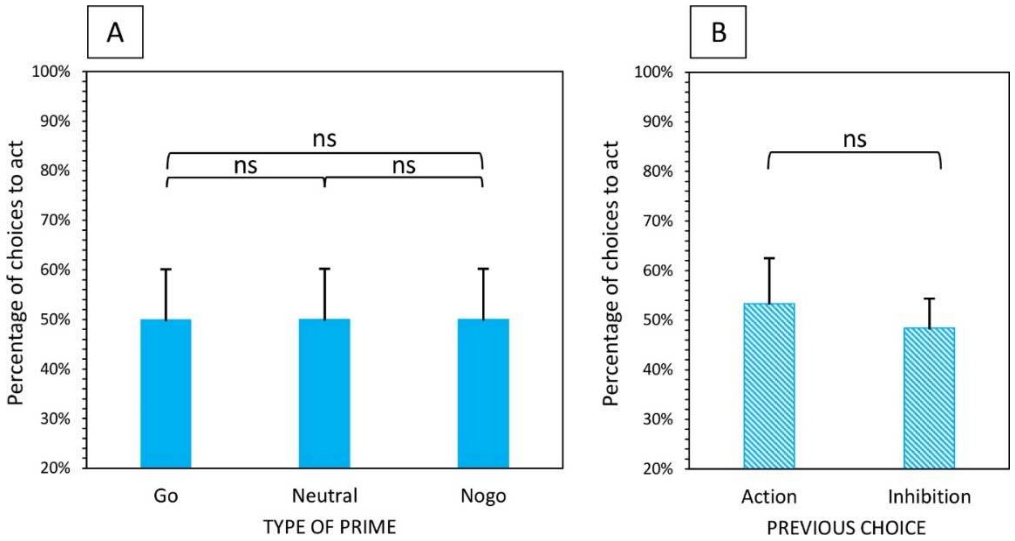

Figure 4.2: Mean percentage of free-choice trials in which participants chose to act rather than inhibit responses, as modulated by type of primes (go, nogo and neutral – panel A). Mean percentage of free-choice trials in which participants chose to act as a function of the preceding trial (panel B) Error bars show standard error of mean. ns = non-significant.

4.3.1.3. Error rates

Within cued inhibition trials the mean rate of false alarms was 8.6% (Fig. 4.3b). The GLME model on false alarms yielded a significant main effect of Prime, $\chi^2(2) = 14.259$, $p < .001$, $AIC_{RL} > 100$, indicating that false alarms were more numerous after a go prime was presented (12.8.%) if compared to neutral (8.1%) or nogo primes (7.9%) intuitively reflecting the incongruence between the response suggested by the prime (go) and the response required by the target (nogo). Within cued action trials participants were more accurate (mean rate of omissions 5.6% – see Fig. 4.3a) and the GLME model on omissions did not yield a significant main effect of Prime, $\chi^2(2) = 0.454$, $p = .796$, $AIC_{RL} = .16$, indicating that in cued action trials the incompatibility between primes and target did not affect the general level of accuracy.

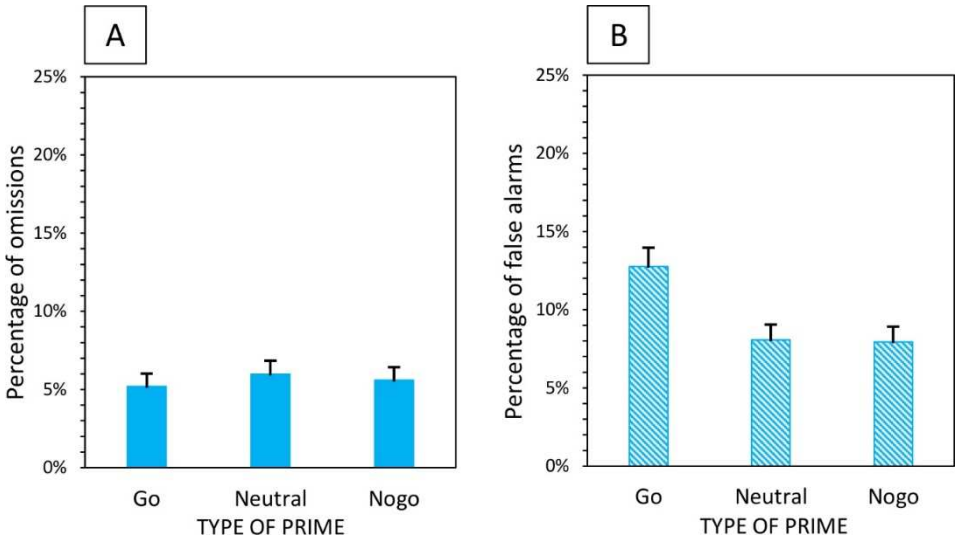

Figure 4.3: Mean percentage of omissions (panel A) and false alarms (panel B) as modulated by type of primes (go, nogo and neutral). Error bars show standard error of mean.

In summary, congruent primes have the ability to shorten RTs when compared to neutral primes. The incongruent, when compared to neutral primes, determined longer RTs. Overall, RTs for the cued go conditions were shorter than those for the free-choice go conditions, reflecting the possible underlying decisional processing. In addition to this, incongruent prime-target associations produced more errors (false alarms) in the cued inhibition condition. In contrast to my hypotheses and differently from the previous study (Chapter 3), subliminal priming was unable to bias the participants' choices towards either acting or inhibiting the response. Mean values for each condition, percentage of errors in cued trials and percentage of responses in free-choice trials are reported in Table 4.1.

Table 4.1: Reaction times (RTs) and standard deviation (SD) in milliseconds of both free-choice and cued trials, percentage of errors in cued go and cued nogo conditions, percentage of responses in free-choice condition, split for each prime (upper part), and collapsed across primes (lower part).

PRIME	TARGET	RTs (±SD)	% Errors	% Go responses
Go	Cued go	410.6 (±17.5)	5.21	
Neutral	Cued go	425.9 (±15.9)	5.99	
No	Cued go	453.8 (±14.5)	5.60	
Go	Cued nogo		12.8	
Neutral	Cued nogo		8.07	
No	Cued nogo		7.94	
Go	Free-choice go	422.6 (±23.1)		53.9
Neutral	Free-choice go	451.1 (±21.3)		49.9
No	Free-choice go	476.8 (±19.1)		49.5
Cued go trials		430.1 (±9.42)	5.60	
Cued nogo trials			9.49	
Free-choice go trials		450.2 (±12.3)		50.8

4.3.2. fMRI results

4.3.2.1. Whole brain activation of the choice network

At the whole brain level I looked at the brain regions that showed significant activity when contrasting free-choice and cued trials (see Fig. 4.4 and Table 4.2 for all main contrasts). Concerning the main effect of Intentionality, the direct comparison 'free-choice > cued' highlighted activity within the 'free-choice network' (Fig. 4.4a and Table 4.2a), including the bilateral IPL, a large cluster extending from the preSMA to the ACC (defining the RCZ), the left AI, the superior frontal gyrus (SFG) and the bilateral DLPFC (minimum k > 69, height threshold t = 3.119). These activations closely resemble previous findings in which free-choices and cued choices were contrasted (Demanet et al., 2013; Lynn et al., 2016). The opposite contrast (cued > free-choice) returned activity on the P and Angular gyri bilaterally (minimum k > 109, height threshold t = 3.119 – see Table 4.2b). The effects of response' type (action, inhibition) were also computed to reveal the activation related to

action and inhibition trials. We observed significant activity for the contrast 'action > inhibition' in the bilateral cerebellum, the bilateral primary and secondary somatosensory cortices, the AI and the ACC. In addition, significant activity was also detected in the left thalamus and in the left putamen (see Fig. 4.4b and Table 4.2c). The opposite comparison (inhibition > action) did not reveal any significant results.

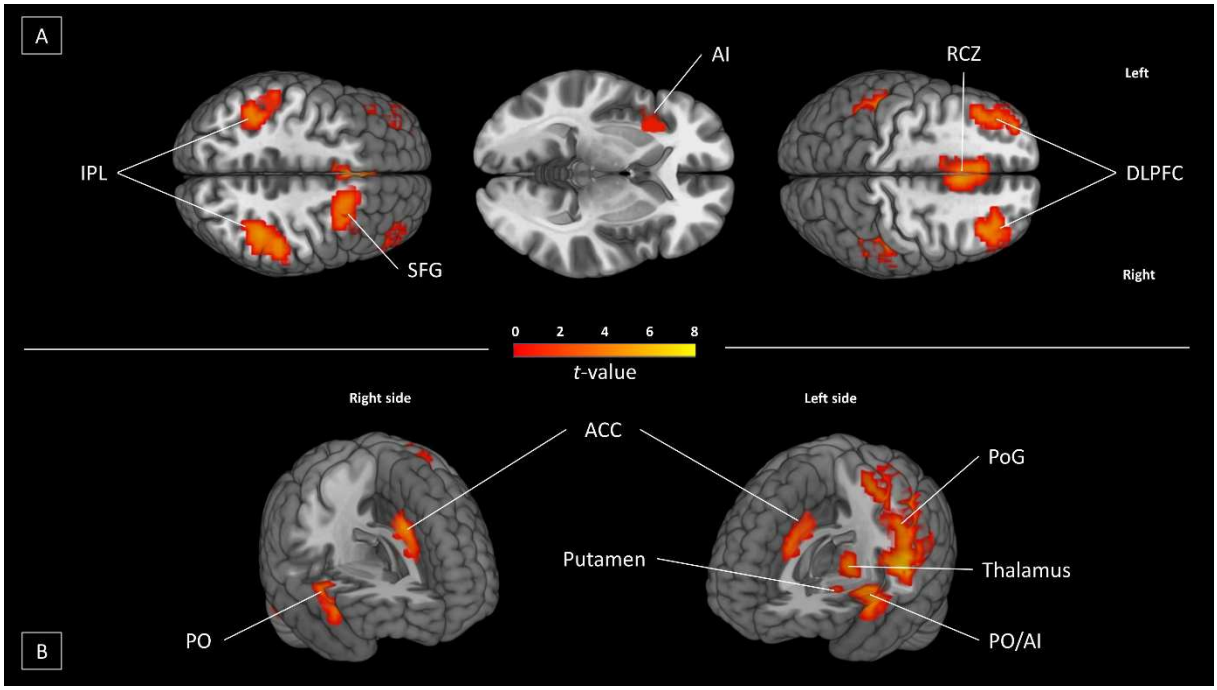

Figure 4.4: Renderings of the whole-brain contrasts, comparing free-choice versus cued trials (panel A) and comparing action versus inhibition trials (cued and free-choice collapsed). The contrast inhibition > action did not determine significant activation at the whole brain level. Activation maps were thresholded at $p < .05$, family-wise error rate (FWE) corrected with cluster-extent based thresholding method with a low cluster-defining primary threshold, $p < .001$. The colour bar represents t values. Images are displayed in neurological convention. IPL: Inferior Parietal Lobule; SFG: Superior Frontal Gyrus; AI: Anterior Insula; RCZ: Rostral Cingulate Zone; DLPFC: Dorsolateral Prefrontal Cortex; PO: Parietal Operculum; ACC: Anterior Cingulate Cortex; PoG: Postecentral Gyrus.

Table 4.2: Results of the whole-brain analysis for free-choice > cued trials (Table 4.2a); cued > free-choice trials (Table 4.2b), action > inhibition (Table 4.2c) and free-choice action > free-choice inhibition trials (Table 4.2c). *p* value < .05, corrected for multiple comparisons (FWE; Family Wise Error). Side: L: Left, R: right; k: cluster extent; MNI: Montréal Neurological Institute. Adopted cluster extent varies according to the reported comparison.

Region	*Side*	*Cluster level*		*Peak level*	*MNI*		
		p(FWE)	*k*	*t-value*	*X*	*Y*	*Z*
Table 4.2a – Free-choice > Cued (k > 69)							
Rostral Cingulate Zone (RCZ)	R	0.000	173	6.36	1	18	42
Anterior Cingulate Cortex (ACC)	L			5.13	-6	32	22
Superior Frontal Gyrus (SFG)	R	0.000	81	5.78	19	14	62
Superior Frontal Gyrus (SFG)	R			4.27	29	11	54
Inferior Parietal Lobe (IPL)	R	0.000	116	5.40	43	-46	46
Supramarginal Gyrus (SG)	R			5.10	54	-32	46
Dorsolateral Prefrontal Cortex (DLPFC)	R	0.000	98	5.30	36	32	26
Middle Frontal Gyrus (MFG)	R			4.64	33	42	18
Middle Frontal Gyrus (MFG)	R			4.23	47	42	18
Anterior Insula (AI)	L	0.000	77	5.03	-48	14	-6
Anterior Insula (AI)	L			4.78	-34	14	2
Dorsolateral Prefrontal Cortex (DLPFC)	L	0.000	114	4.90	-38	49	6
Middle Frontal Gyrus (MFG)	L			4.46	-41	32	30
Middle Frontal Gyrus (MFG)	L			4.38	-41	39	18
Inferior Parietal Lobe (IPL)	L	0.000	69	4.74	-38	-49	46
Table 4.2b – Cued > Free-choice (k > 109)							
Angular Gyrus (AG)	L	0.000	175	5.32	-38	-77	30
Angular Gyrus (AG)	L			4.22	-41	-56	22
Precuneus (P)	L	0.000	139	5.31	-3	-63	22
Precuneus (P)	R			4.84	8	-60	22
Angular Gyrus (AG)	R	0.000	109	5.12	40	-63	14
Angular Gyrus (AG)	R			5.06	40	-77	26
Table 4.2c – Action > Inhibition (k > 31)							
Parietal Operculum (PO)	L	0.000	598	6.81	-59	-18	14
Anterior Insula (AI)	L			6.51	-41	-4	6
Postcentral Gyrus (PoG)	L			6.13	-48	-32	54
Cerebellum (I → IV Lobules)	R	0.000	427	6.75	26	-60	-22
Cerebellum	R			5.98	5	-67	-10
Cerebellum	R			4.72	47	-60	-30
Cerebellum	L	0.000	147	5.52	-20	-63	-22
Cerebellum	L			4.93	-31	-70	-26
Cerebellum	L			4.22	-38	-60	-26
Anterior Cingulate Cortex (ACC)	L	0.001	63	5.50	-3	11	34
Cerebellum (VIII → X Lobules)	R	0.000	104	5.45	12	-63	-46
Cerebellum	R			4.56	22	-53	-50
Cerebellum	R			3.83	5	-67	-34
Putamen	L	0.008	41	4.55	-24	0	-14
Thalamus	L	0.026	31	4.51	-13	-18	6
Parietal Operculum (PO)	R	0.014	36	4.38	54	18	-10
Table 4.2d – Free-choice Action > Free-choice Inhibition (k > 56)							
Parietal Operculum (PO)	L	0.000	234	5.93	-59	-18	14
Postcentral Gyrus (PoG)	L			5.49	-48	-32	54
Anterior Insula (AI)	L	0.000	99	5.70	-41	-4	6
Parietal Operculum (PO)	L			4.99	-55	7	10
Cerebellum (I → IV Lobules)	R	0.000	260	5.66	26	-60	-22
Cerebellum	R			4.48	8	-70	-14
Cerebellum (VIII → X Lobules)	R	0.001	56	4.52	12	-63	-50
Cerebellum	L	0.000	82	4.36	-38	-74	-22

4.3.2.2. Increased ROIs activity for free-choices

Since I was primarily interested in the activity related to the 'free-choice network', I looked at the specific comparisons between the levels of the two factors within the five ROIs selected on the basis of prior hypotheses: the RCZ, the AI, the IPL, the DLPFC and the dFMC. The main effect of Response (Action, Inhibition) was significant in the bilateral AI, left: $F(1,23) = 17.72$, $p < .00$, right: $F(1,23) = 4.83$, $p = .029$, and left IPL, $F(1,23) = 10.64$, $p = .001$, whereas the main effect of Intentionality (Free-Choice, Cued) highlighted significant results in the left AI, $F(1,23) = 5.07$, $p = .025$, the RCZ, $F(1,23) = 22.71$, $p < .001$, right IPL, $F(1,23) = 5.04$, $p = .026$, and the bilateral DLPFC, left: $F(1,23) = 5.07$, $p = .025$, right: $F(1,23) = 5.47$, $p = .020$. The interaction Response × Intentionality yielded no significant results in any of the considered ROIs. The post-hoc analysis concerning inhibition effects revealed that the RCZ, $t(23) = 4.52$, $p < .001$, the left AI, $t(23) = 2.68$, $p = .004$, the right IPL, $t(23) = 1.98$, $p = .024$ and the left DLPFC, $t(23) = 1.83$, $p = .041$, were significantly more engaged by free-choices inhibition trials (free-choice inhibition > cued inhibition; Fig. 4.5a). In general, the considered ROIs appeared to be more engaged in action than in inhibition trials: concerning the effect of intentionality, free-choice action trials appeared to elicit higher activity in respect to cued action trials (free-choice action > cued action; Fig. 4.5b) within the bilateral DLPFC, left: $t(23) = 1.72$, $p = .044$, right: $t(23) = 2.16$, $p = .016$, and the RCZ, $t(23) = 2.21$, $p = .014$. The comparison between free-choice trials (free-choice action > free-choice inhibition; Fig. 4.5c) highlighted significant increased activity within the bilateral AI, left: $t(23) = 2.61$, $p = .005$, right: $t(23) = 1.98$, $p = .037$, and left IPL, $t(23) = 2.78$, $p = .003$, however no further results were observed in the opposite contrast. The main findings of the ROI analysis are reported in Figure 4.5.

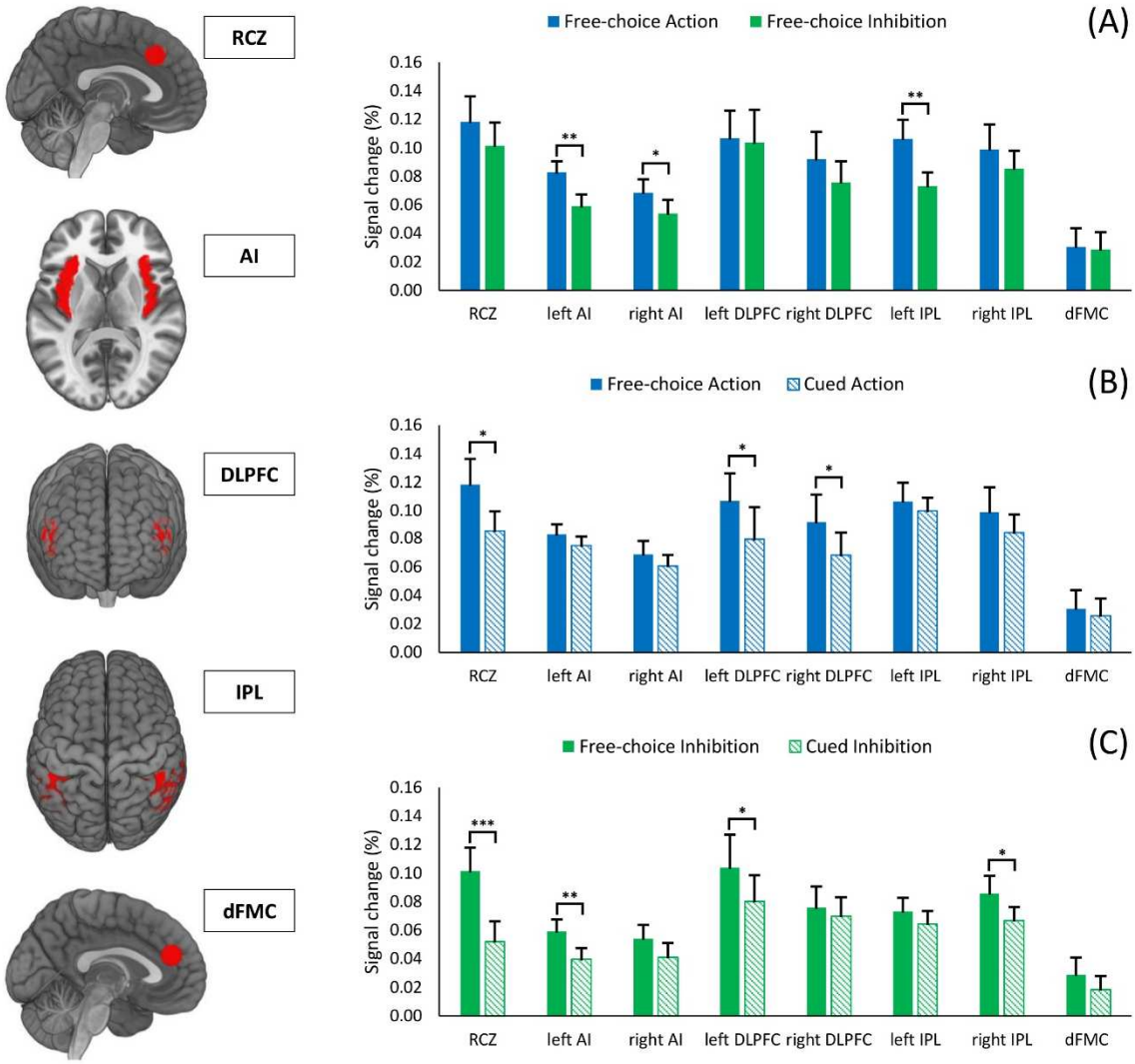

Figure 4.5: Comparison between free-choice and cued conditions within the considered ROIs: A) free-choice action > free-choice inhibition action; B) free-choice action > cued action; C) free-choice inhibition > cued inhibition. Images are displayed in neurological convention. RCZ: Rostral Cingulate Zone; AI: Anterior Insula; DLPFC: Dorsolateral Prefrontal Cortex; IPL: Inferior Parietal Lobule; dFMC: Dorsal Frontomedian Cortex. ROIs are mapped to an MNI render provided with the MRIcroGL software. Charts represent mean percent signal change. Error bars show standard error of mean. *** $p < .001$; ** $p < .01$; * $p < .05$.

In summary, free-choice conditions systematically produced activation on both the RCZ and the bilateral DLPFC. This pattern emerges more clearly when the two conditions are mutually compared (free-choice action vs. free-choice inhibition): both RCZ and DLPFC show a similar activation level for both conditions. This evidence was further supported

when the contrast 'free-choice action > free-choice inhibition' was conducted at the whole brain level: the analysis yielded activation of motor (bilateral cerebellum) and left somatosensory areas (parietal operculum extending to the postcentral gyrus and to the AI), as expected given the implementation of the response in free-choice action trials (minimum $k > 56$, height threshold $t = 3.119$), however no other decision-related clusters of activation survived. On these bases, the two free-choice conditions seem to rely on an overlapping network of activity. Notably, the ROI analysis over the dFMC did not reveal significant higher activity relative to free-choice inhibition trials when compared to cued inhibition trials (free-choice inhibition > cued inhibition; see Fig. 4.4c and Table 4.2d).

4.3.2.3. Primes did not modulate the choice network

To further examine the predictions on how the masked priming modulates the activity on the areas of interest during free-choices, I conducted a second set of ROI analyses. The regions related to the 'free-choice network' (RCZ, AI, DLPFC and the IPL) were submitted to a factorial design based on Congruency (Congruent; Incongruent; Neutral) and Targets (Cued action; Cued inhibition; Free-choice action; Free-choice inhibition). Neither the main effect of Congruency nor the interaction Congruency × Target revealed significant effects within any of the four ROIs, indicating that subliminal prime stimuli were unable to modulate the activity within this areas, neither by increasing the activity for incongruent trials nor reducing the activity for congruent trials. Furthermore, masked primes were unable to modulate the activity of the dFMC within free-choice inhibition trials. Incongruent primes (go prime) did not engaged dFMC more than congruent, $t(23) = 0.53$, $p = .701$ or neutral $t(23) = 1.33$, $p = .908$ primes. To conclude, the ROI analysis on the activity of M1 in nogo trials (cued and free-choice combined) did not reveal a significant increase of activity for incongruent (go) primes when compared to congruent (nogo), $t(23)$

= 0.28, $p = .390$, or neutral primes $t(23) = 0.82$, $p = .792$, neither when congruent primes are compared with incongruent, $t(23) = 0.28$, $p = .609$, or neutral primes, $t(23) = 1.04$, $p = .851$.

4.4. Discussion

Previous research suggested that activity of some neural structures in the frontomedian wall, such as the RCZ, might account for the voluntary choices of response alternatives (Kühn, Gevers, et al., 2009). Beyond the RCZ, making voluntary action choices involve a broader network including AI (Brass & Haggard, 2010; Droutman, Bechara, & Read, 2015), the IPL and the DLPFC (Forstmann et al., 2006; Mueller et al., 2007). Implementing the paradigm presented in Chapter 3, I compared intentional action and inhibition trials, with stimulus-driven trials. Since alike free actions, voluntarily inhibiting an action requires the explicit decision not to implement a pre-potent action (Lynn et al., 2014) I hypothesized that such a decision would trigger activity on the same network of areas plus those regions involved with intentional inhibition directly (dFMC; Brass & Haggard, 2008; Lynn et al., 2014). In this respect, when contrasting free-choice versus cued trials at the whole brain level, activity on a network including the RCZ, the bilateral IPL, the right SFG, the bilateral DLPFC and the left AI was detected. These activations closely match previous findings comparing free and cued choices (Forstmann et al., 2006; Lynn et al., 2014; Schel et al., 2014; Wisniewski et al., 2016).

4.4.1. Making voluntary choices

To further explore the findings obtained at the whole brain level and to better examine the neural pattern underlying intentional situations, I conducted a ROI analysis on the key areas identified in previous literature (Forstmann et al., 2006; Schel et al., 2014). I found that the level of intentionality had the ability to modulate their activity: specifically, when contrasting free-choice action trials with cued action trials significant activity in the

RCZ and bilateral DLPFC was observed, which was not detectable for the opposite comparison. The same ROIs, together with AI and right IPL, were significantly more activated by free-choice inhibition trials if compared with cued inhibition trials. Furthermore, when comparing free-choice actions with free-choice inhibition neither the RCZ nor the DLPFC showed an effect. Rather, bilateral AI and left IPL showed significant differential activity. A similar pattern emerged at the whole brain level. Altogether, these findings suggest that 'intentional' trials recruit RCZ and DLPFC, independently from the choice's outcome (action or inhibition).

The RCZ has been shown to support various cognitive processes such as response conflict (Orr & Banich, 2014) voluntary control of actions (Forstmann et al., 2006) and even decision-making (Lau, Rogers, Ramnani, et al., 2004). In all these studies RCZ activation arises when participants deal with uncertainty while voluntary deciding a plausible response. With respect to RCZ, the present findings are in agreement with the idea that intentionally deciding to inhibit the response is the functional synonymous of evaluating a response option. Therefore, this process might not require the support of a specialized functional area such as the dFMC (Kühn & Brass, 2009). Kühn and Brass (2009) employed a modified version of a SST adding a free-choice condition, to demonstrate that the activity of the 'free-choice network' was comparable for voluntary action and non-action decisions. Since in their paradigm participants took the decision in advance, such as an unbiased choice between responding or not, they preferred to dissociate between an *early whether* and *late whether* component in intentional inhibition (based on the 'WWW' model of Brass & Haggard, 2008). Here results demonstrate that RCZ is not solely involved when the decision to inhibit an action occurs in *early* stages (Kühn & Brass, 2009), but its contribution is crucial also during *late* inhibition processes.

Also other brain areas were more engaged by free-choice conditions, namely the DLPFC, the IPL and the AI. The activation of the DLPFC is thought to reflect attention and

working memory related processes due to random generation of button presses allowing to keep track of previous choices (Hadland, Rushworth, Passingham, Jahanshahi, & Rothwell, 2001; Jenkins et al., 2000). Since the task for the participants was to decide as freely as possible at the appearance of the free-choice target, and try to respond/inhibit the action 'in a random but balanced manner' this might have determined its involvement. This is further supported by behavioural results on sequential dependencies between trials that showed how, indeed, participants were responding randomly to the best of their possibilities. Nevertheless, DLPFC activity might equally reflect a general preparatory process like increased demands on conflict monitoring (Brass & Haggard, 2007; Lau et al., 2006). Teuchies et al. (2016) found activity in the DLPFC in free-choice trials, but the ROI did not show the conflict activation pattern found in other areas (i.e., RCZ and AI). This evidence supports the view that the DLPFC might be involved in attention to the selection of the response rather than in the actual response selection (Lau, Rogers, Ramnani, et al., 2004). It must be said, however, that divergent results might be partly due to the differences in tasks, stimuli and designs across studies.

The insular cortex, and more precisely the left AI, has been commonly reported in tasks requiring intentional demands (Brass & Haggard, 2007; Droutman et al., 2015; Mueller et al., 2007) and response inhibition studies (Aron, 2006; Swick, Ashley, & Turken, 2011). Despite its well-established role in interoceptive awareness (Craig, 2009) the description of the specific function elicited by various cognitive tasks is often explicitly neglected. In this study the bilateral activation of AI was involved in action trials, both free-choice and cued, when compared with inhibition trials, and in free-choice inhibition when compared with cued inhibition conditions. A recent perspective suggests that the AI may play a role in monitoring and evaluating action-outcomes by signalling whether an action was successful or not. The feedback information may reinforce action representations to make them more or less available in future occasions (Brass & Haggard, 2010). In this light,

it is possible that the AI evaluates the outcomes of the responses when performed, and identifies the consequences of not acting in intentional inhibition. Likewise AI, the same pattern of activation was observed for the IPL: the right IPL in particular, showed differential activity in free-choice inhibition trials when compared with cued inhibition conditions and the left IPL in both free-choice and cued action trials compared with inhibition trials. The activation of the left IPL in both free-choice and cued action trials is consistent with the evidence for a role of this region within the fronto-parietal action control network (Forstmann et al., 2006) and for the visuomotor processing required in action planning.

4.4.2. Masked priming of free-choices

The study presented in Chapter 3 suggested that alike for free actions, also intentional inhibition is subjected to non-conscious cognitive processes. The fact that the 'free-choice network' is shown to be sensitive to non-conscious information in the environment (Teuchies et al., 2016), raised the question of whether such decisions are truly voluntary or might be the result of neural preceding unconscious neural activity (Filevich et al., 2013). Driven by this curiosity the main goal of the study was to test whether it was possible to bias the free decision to withhold the response as demonstrated for free actions and whether such bias corresponded to a modulatory activity at the cortical level. Although results show that nogo primes slowed down RTs in both cued and free-choice action conditions and go primes induced more errors in cued inhibition condition, primes were unable to bias the free decision process, neither toward a significant increase of choices to act in action-congruent conditions, nor toward an increase of choices to inhibit in inhibition-congruent conditions. To test whether the lack of a behavioural result further extended to neural data, I conducted another set of ROI analysis including the congruency of the priming as effect of interest. In line with behavioural results the selected brain areas

appear not to be modulated by the congruency between prime and participants' responses (i.e., to press or not to press). The null effects elicited by the present subliminal priming manipulation (though of the exact nature of previously used paradigms) are in contrast with what has been reported by Teuchies et al. (2016). Though, it must be said, that the paradigm by Teuchies and colleagues (2016) requested a choice between action alternatives, and not the choice of whether acting or not. Speculatively, subliminal effects might produce weaker effects in a Go/Nogo task compared to a situation where a direct stimulus-response mapping is set and the direction of the response is primed.

4.4.3. The role of dFMC

Similar to studies failing to reveal an involvement of the dFMC in intentional inhibition tasks (Hartwell et al., 2011; Kühn & Brass, 2009) or to those observing dFMC activity in cued-choice trials (Lynn et al., 2016; Severens et al., 2012), the present findings did not collect evidence in favour of an activation of the dFMC in intentional inhibition trials. The interpretation of its function in the context of 'disengagement from strong impulses' (Lynn et al., 2014) may partially explain the lack of dFMC found here. Lynn et al. (2014) describes three critical determinants to engaging the dFMC in intentional inhibition paradigm. First, the response must be given under the circumstance of choice. Second, there must be enough time permitting to take the decision in order to avoid pre-decisions or post-decisions to inhibit the response. Third, the decision must be taken under a strong urge to act (Lynn et al., 2014). In the present study a balanced frequency of cued go and nogo trials might have produced a weaker response tendency if compared with previous paradigms that used a higher proportion of go trials with respect to nogo trials. Here however, participants were explicitly instructed to always prepare the response but eventually decide to withhold it by taking an in-the-moment decision and this was further stressed by giving a very short response window (1 sec) in order to avoid post-decisions.

Crucially, even if participants were instructed to avoid such behaviour, I did not control explicitly for the possibility that they took the decision before the start of the trial, thus producing pre-decisions. Nevertheless, RTs in the free-choice go trials were significantly slower than those in the cued go trials implying that the two conditions were elaborated differently, with free-choice go trials requiring further decisional processing. This suggests that participants decided whether to act or not at time of the appearance of the stimulus, not in advance. Moreover, the higher rate of errors in cued nogo compared to go trials indicate that this paradigm was successful to induce a robust urge toward the action. Taking into account these considerations, I cannot rule out that a lack of significant differential activity in the dFMC was necessarily produced by a weakened impulse toward action. Supported by the results of false alarms in cued inhibition trials, the second ROI analysis capitalized on the effect of incongruent primes to boost the urge toward acting in free-choice inhibition trials. Although I hypothesized that this manipulation would have produced additional activation of the dFMC this was not the case. These mixed findings point to the fact that at present no clear conclusions can be drawn on the validity of subliminal priming for the determination of the psychological mechanisms and neural substrates of intentional inhibition.

To sum up, the present fMRI study aimed at investigating the neural correlates of intentional choice between acting and inhibiting within the same behavioural paradigm. In agreement with previous studies the BOLD activity of brain areas concerned with voluntary decision processes was modulated by the degree of intentionality of the response (Lynn et al., 2016; Schel et al., 2014; Teuchies et al., 2016). The RCZ and the DLPFC in particular, were equally active in both voluntary conditions. This finding confirms the possible key role of both structures in making voluntary choices, suggesting that intentional inhibition and voluntary action might be considered two side of the same coin, or rather two possible outcomes of the same decisional process. In contrast with the

findings of the previous study however, present results did not give support for the efficacy of subliminal stimuli as possible modulators of the cognitive and neural mechanisms linked to volition. A reasonable explanation lies on the vulnerability of the effects usually reported in subliminal priming paradigms (Bermeitinger, 2016). To circumscribe this possibility, the study presented in the next chapter (Chapter 5) investigates the importance of arousal in enhancing the efficacy of subliminal stimuli and, in turn, to determine the origin of voluntary choices.

CHAPTER 5

THE EFFECT OF EXERCISE INTENSITY ON FREE-CHOICES TO ACT AND TO INHIBIT[2]

5.1. Introduction

It has been demonstrated that exercise-induced arousal has selective effects on cognitive functions. Exercise appears to facilitate certain aspects of processing such as response speed and accuracy and enhances the processes involved in problem-solving and goal-oriented actions (Chang et al., 2012; Tomporowski, 2003). One of the questions attracting considerable interest is whether modulating the level of arousal could influence higher-level cognitive functions such as response inhibition. For instance, Weinbach and colleagues (2015) included an alerting cue (i.e., an irrelevant stimulus) in a SST to increase participants' level of arousal for a short period of time. Interestingly, the increase of the arousal induced by the alerting cue RTs to go stimuli on one hand and shortened SSRT (which is a measure of efficacy of the inhibitory processes) on the other, indicating an improvement in response inhibition. In authors' perspective, the results highlight the role of basic, lower-level, mechanisms in modulating complex, higher-level, cognitive processes, such as inhibitory control, in order to produce high-coordinated action performances (Weinbach, Kalanthroff, Avnit, & Henik, 2015). Along the same lines, a study by Chu and colleagues (2015) tested the effects of acute exercise on the inhibitory aspect of executive function using behavioral and electrophysiological approaches. To examine the effects of exercise-induced arousal on motor response inhibition, college students

[2] *Published:* **Dall'Acqua, T.**, Li, C., Ceccarini, F., Grigoletto, D., Marcolin, G., Paoli, A., & Castiello, U. (2018). Exercise-induced arousal affects free-choices to inhibit. *Psychology of Sport and Exercise*, 35, 89–97.

underwent a stop-signal task following acute aerobic exercise. In this study the level of exercise was determined via the 'submaximal treadmill walking test' carried out prior to behavioral testing. A sedentary control session, that involved reading, was also included. The main findings from this study suggest that acute exercise results in a shorter SSRT, but does not alter the go RTs (Chu, Alderman, Wei, & Chang, 2015).

Overall, the aforementioned studies suggest that exercise-induced arousal have the ability to modulate cognitive functions just like response inhibition. Depending on the different moderators that are taken into account (e.g., type of cognitive performance, fitness level, task duration), mixed finding are reported for cognitive abilities tested during exercise. Much of the existing work examining the association of exercise and cognitive functions derives from 'arousal theories' (e.g., Hockey, 1997; Kahneman, 1973; Sanders, 1983; Yerkes & Dodson, 1908). However a more recent account has been proposed. The RAH model proposes that during exercise, higher-order computations of prefrontal cortices and the actual motor implementation compete for the allocation of limited metabolic resources (Dietrich, 2006; Dietrich & Audiffren, 2011). Since cognitive processing is set to a lower priority during exercise, available resources are drawn from the brain regions that are not essential to perform the exercise, provoking a decline in complex mental processing. On the other hand, cognitive performances that rely on more automatic brain processing (e.g., reaction times, response accuracy, stimuli detection) would be enhanced due to downregulation of the frontal cortex and consequent disinhibition of the arousal networks in the brainstem. It must be said however, that some results support the RAH model (Lambourne & Tomporowski, 2010) whereas others do not (Chang et al., 2012).

So far, the effects of arousal on response inhibition have been investigated with paradigms concerned with inhibition driven by external stimuli (Logan & Cowan, 1984; Verbruggen & Logan, 2008). However, the study presented in Chapter 4 proposed that intentional inhibition might rely on cortical mechanisms partially distinguishable from

those characterizing stimulus-driven inhibition (Kühn, Gevers, et al., 2009; Schel et al., 2014). Moreover, the results provided in Chapter 3 strongly suggest that the cognitive mechanisms responsible for generation of free-choices to act and to inhibit significantly depend on unconscious processing and can be modulated by subliminal stimuli accordingly. To my knowledge no studies have previously explored the role of arousal in determining the generation of free-choices. The present study capitalized on the very same paradigm to investigate whether arousal has the ability to modulate intentional inhibition as previously reported for external kind of inhibition (Chu et al., 2015; Weinbach et al., 2015). By asking participants to perform the task while pedaling on a cycle ergometer, the paradigm was administered at a different level of workload intensities with the specific purpose of eliciting different levels of exercise–induced arousal.

Although I hypothesize the main results to be in line with those of Chapter 3, the specific effects of the arousal manipulation are predicted to be twofold. On the one side arousal would modulate low-level processing enhancing RTs and accuracy. On the other side, according to the RAH model (Dietrich & Audiffren, 2011) free-choice performance should be disrupted by the arousal manipulation due to an impairment of high-level executive functions responsible for the decisional and attentional processing. Likewise, this is expected to boost the effect of subliminal primes. RTs of cued and free-choice trials would to be shortened in the high arousal condition when compared to the low arousal condition. Further, the pattern induced by subliminal priming is expected to be consistent between low and high arousal conditions, namely faster RTs after a go prime and slower RTs after a nogo prime. In line with previous evidence, an increase of arousal is predicted to improve response accuracy reducing the number of errors in cued conditions (omissions and false alarms). With respect to the proportion of choices to act or to inhibit in free-choice trials I predict a general increase of choices to act in high arousal condition, due to enhanced impulsiveness and disinhibition of brainstem circuits. Although I expect an

improvement in the accuracy for cued trials in the high arousal condition, when no specific control is required (i.e., in free-choice trials where no right or wrong response is given by the experimenter) priming might affect responses differently. The impulsiveness and disinhibition of attentional resources elicited by the heightened arousal would produce a stronger effect of subliminal priming on the proportion of free-choices: go primes would increase the proportion of actions and nogo primes would increase the proportion inhibition choices more in the high compared to the low arousal condition.

5.2. Methods

Methods of the present experiment were identical to those described in Chapter 3 with the following exceptions.

5.2.1. Participants

Given the absence of previous studies to rely on for the determination of the appropriate sample size, for this study a priori power analysis was conducted using a freely-available software (G*Power 3.1.9; Faul, Erdfelder, Lang, & Buchner, 2007). The effect-size calculation was based on a recent review on the effect of acute exercise on cognitive performances (Chang et al., 2012). The optimum sample size of 15 participants was calculated by fixing the probability of a type 1 error at an alpha of 0.05, to yield 0.80 power for an effect size of 0.23. Because of the possibility that a small number of participants would produce unreliable free-choice data within this kind of paradigms (Parkinson & Haggard, 2014) a total of 20 healthy volunteers participated in the study after giving oral and written consent. Data of one participant were discarded because of an excessive tendency to prefer inhibition in free-choice trials (2.34 %, < 2.5 *SD* from sample mean) which render free-choice data potentially unreliable. All analyses were conducted on the remaining nineteen participants (13 female, $M = 25.36$ years, $SD = 0.67$). All participants had normal or

correct-to-normal vision and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Despite the low-risk physical effort required by the test the following exclusion criteria were adopted to ensure the homogeneity of the sample: hypertension, diabetes, heart diseases and obesity (Body Mass Index, BMI > 30) or severe underweight (BMI < 16). This information was collected with a self-report questionnaire. Demographic and fitness data are presented in Table 5.1.

Table 5.1: Demographic and fitness characteristics of study participants (mean ± SD).

Variables	Female (N = 13)	Male (N = 6)	Total (N = 19)
Age (years)	24.92 (±3.15)	26.33 (±2.42)	25.36 (±2.95)
Height (cm)	162.85 (±5.96)	176.83 (±5.74)	167.26 (±8.80)
Weight (kg)	57.96 (±8.63)	73.33 (±11.52)	62.82 (±11.85)
BMI (kg/m^2)	21.84 (±2.96)	23.41 (±3.16)	22.33 (±3.03)
Handedness (Oldfield, 1971)	0.79 (±0.21)	0.87 (±0.15)	0.82 (±0.19)
HR_{max} (bpm)	195.07 (±3.14)	193.66 (±2.42)	194.63 (±2.94)
$Load_{max}$ (watt)	148.52 (±31.21)	200.21 (±24.67)	164.84 (±37.7)
30% of $Load_{max}$ (watt)	44.55 (±9.36)	60.06 (±7.40)	49.45 (±11.33)

5.2.2. Design

The study was divided into an *assessment* session and two experimental sessions: *baseline* and *physical-load*. In the *assessment* session the experimenter gave only a brief introduction to the study and participants filled the informed consent and exclusion criteria form. All participants that met the criteria underwent the 'sub-maximal workload test' during the same session. The *assessment* session was separated at least 24 hours from the other two sessions. During both the *baseline* and the *physical-load* sessions, participants completed the computer-based task while cycling the cycle-ergometer under two different workload conditions in order to elicit two different level of arousal. In the *baseline* session the experimenter put the heart rate monitor on participants' chest and ask them to start cycling at 60 rpm (rate per minute) with 25 watt load. While warming-up

participants read the instruction on the monitor in front of them. About 2 min of warm-up was ensured for each participant. After this time participants were allowed to start whenever they felt ready by simply pressing the response button. During the whole session participants needed to maintain the speed constant while the watt remained unchanged and the heart rate frequency was monitored throughout. At task completion they were asked to continuing pedaling for a cool-down phase at a lower work rate up until their heart rate significantly decreased and they felt ready to stop the exercise. The experimental setting and procedure for the *physical-load* session was the same as the *baseline* session, the only difference regarded the heightened watt load intensity which caused an increase of the exercise-induced arousal. Based on the performance on the 'sub-maximal workload test' a customized watt load was assigned to each participant for the *physical-load* session. Since they were asked to maintain the cadence of 60 rpm constant, the physical effort required in this session was considerably higher compared to the *baseline* session. During both experimental sessions the heart rate frequency was collected at the beginning of the task and at the end of each block. The sequence of the *baseline* and *physical-load* sessions was randomly assigned across participants on the second and third visit to eliminate possible biases based on order and learning effects. For all participants the two sessions occurred approximately one week apart.

5.2.3. Sub-maximal workload test

Since equivalent workload intensities might correspond to a different level of fatigue depending on participants' individual fitness level, personalized workload intensities were calculated corresponding to the 30% of the predicted maximal load ($Load_{max}$) for each participant. In order to determine this percentage of $Load_{max}$ participants underwent to the YMCA sub-maximal cycle ergometer test (Beekley et al., 2004; Pescatello & American College of Sports Medicine, 2014). This test allowed to determine the predicted

$Load_{max}$ at the age-predicted maximum heart rate (HR_{max}; e.g., 220 minus age). The protocol for this test consisted of four three-minute stages (12 min in total) with increasing workload intensities starting at 25 watt for the first stage. At the second stage, the workload intensity was raised to a specific value based on the stabilized heart rate frequency collected at the end of the first stage. If the heart rate frequency was lower than 90 bpm the second stage was set to 100 watt, if it was higher than 90 bpm but lower than 100 bpm it was set to 75 watt and if it was higher than 100 bpm to 50 watt. The third and the fourth stages consisted of increments of 25 watt each. Throughout the whole test participants were required to maintain a cadence of 60 rpm. Heart rate data were collected through a chest band (Polar, Kempele, Finland) and subjective experience of exertion throughout the test was recorded by means of a 6–20 Borg scale (Haile, Gallagher, & J. Robertson, 2015) at the end of each stage. Before the test, participants were asked to warm-up for two min pedaling at 25 watt gradually reaching the cadence of 60 rpm. At the end of the test a cool-down period was ensured consisting of a continuation of the exercise with watt load equivalent to that of the first stage of the test protocol gradually decreasing cadence. Heart rate was monitored for a surveillance period until stabilized.

5.2.4. Procedure

A representation of the experimental setup and an example of a trial sequence are shown in Figure 5.1. Participants were seated in a dimly lit room on a cycle ergometer (Ergoselect 200, Ergoline GmbH, Germany) at a distance of 60 cm from a PC-driven CRT monitor (resolution 1280 × 1024; 75 Hz refresh rate) positioned on a tripod, with their eyes at a height corresponding to the center of the screen. Responses were given with the index finger of the right (dominant) hand using a response button fixed on the handlebar of the cycle ergometer. During the prime discrimination task participants were asked to continue

cycling, with the purpose of reproducing the same experimental conditions of the experimental sessions.

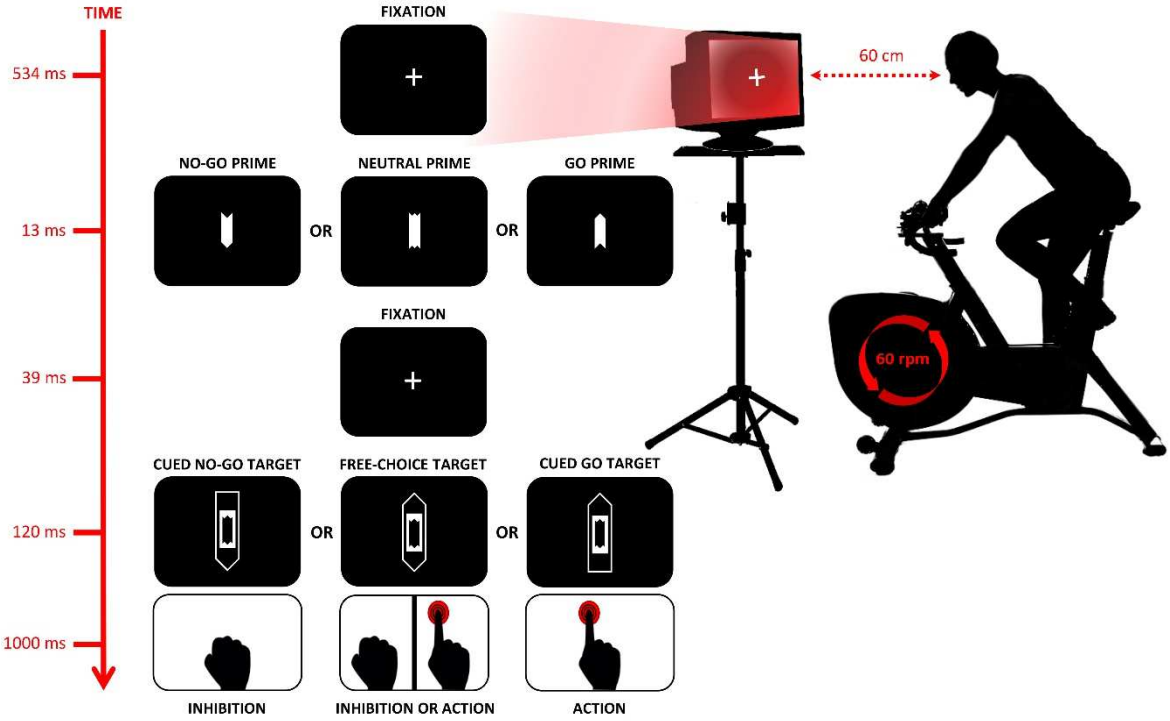

Figure 5.1: A schematic representation of the experimental setup and the stimulus schema including the timing and the masked prime/target combinations. In the proposed example the upward arrows indicate the cued go target; rpm: revolution per minute.

5.2.5. Statistical analyses

Statistical analyses on the effects of interest were computed by means of LME models (for RTs and heart rate variability) and GLME models with a binomial link function (for free-choice behavior and error rates; Pinheiro & Bates, 2000). As preliminary analysis, individual heart-rate variability within each experimental session was controlled to ensure that participants' heart rate frequency was kept constant throughout the blocks, indicating that a stable level of exercise-induced arousal was maintained during the whole session. Each level of the independent variable consisted of five time-points, one at the beginning

of the experiment and four at the end of each block. A LME model on heart rate frequency with Time (T1, T2, T3, T4, T5) and Session (Baseline, Physical load) as fixed effects was computed. For RTs an LME model was computed with Prime (Go, Nogo, Neutral), Target (Cued go, Free-choice go) and Session (Baseline, Physical load) as fixed effects. RTs outliers were removed following a two-steps procedure (Baayen & Milin, 2015): first, extremely shorts (< 200 ms) and extremely long (> 1000 ms) RTs were removed (less than 0.5% of the data). Second, after the standardized residuals of the full LME model have been computed, trials with absolute standardized residuals exceeding $\pm$ 2.5 *SD* were discarded (about 2.5% of the data). Free-choice trials were analyzed in order to uncover how masked priming influenced participants' choice to execute or inhibit the actions in both low and high arousal conditions. The number of choices to act or to inhibit as a function of subliminal primes was computed by fitting a GLME model with Prime (Go, Nogo, Neutral) and Session (Baseline, Physical load) as fixed effects. Since participants were asked to avoid the use of strategies (e.g., alternating between action and inhibition), free-choice trials have been further explored by looking at sequential dependencies between trials in both low and high arousal conditions. Responses in the current free-choice trial (trial *n*) with those in the previous trial (trial *n-1*, which could either be a cued trial or another free-choice trial) were compared to see whether participants had a tendency to systematically respond the same (action-action; inhibition-inhibition) or the opposite (action-inhibition; inhibition-action) in trial *n* as in trial *n-1*. A GLME model was computed with Previous choice (Action, Inhibition) and Session (Baseline, Physical load) as fixed effects and the choice at trial *n* as dependent variable. In conclusion, error rates within each cued condition (omissions in cued action trials and false alarms in cued inhibition trials) were computed for each session as function of the subliminal prime by fitting GLME model with Prime (Go, Nogo, Neutral) and Session (Baseline, Physical load) as fixed effects. For both GLME and LME models, post-hoc analyses were performed on effects of interests by means of planned pair-wise

comparisons (*t*-tests) and the α level was set at 0.05 prior to Bonferroni correction. For all analyses the complete set of computed post-hoc t-test are reported. Cohen's *d* indices are reported as measure of effect sizes (Cohen, 1988).

5.3. Results

5.3.1. Preliminary analyses and prime discrimination

As preliminary control measure, heart rate frequency collected during the sub-maximal workload test correlated positively with participants' responses to the Borg scale, $r(74) = 0.73$, $p < .001$. Regarding the experimental sessions, the preliminary analysis on heart rate variability revealed a statistical significant effect of Session, $\chi^2(1) = 149.63$, $p < .001$, $AIC_{RL} = 5.85$, but not of Time, $\chi^2(4) = 1.99$, $p = .737$, $AIC_{RL} = .05$, and neither the interaction Session × Time, $\chi^2(4) = 0.44$, $p = .978$, $AIC_{RL} = .02$. On average heart rate frequency was modulated by the low and the high arousal condition (baseline: $M = 100.42$, $SD = 12.1$; physical load: $M = 114.53$, $SD = 8.69$), but within each condition the frequency was maintained constant (see Fig. 5.2). The results of the prime discrimination test show that primes were not consciously detected, $t(18) = 0.66$, $p = .689$, tested against the 33.3% chance level (mean correct: $M = 30.6\%$, $SD = 5.23$). As measure of discriminability, *d'* was computed for each prime/participant. The obtained *d'* values were not significantly different from '0' (no discrimination possible), $t(18) = 0.57$, p = .722 (*d'* values : $M = 0.31$, $SD = 0.06$).

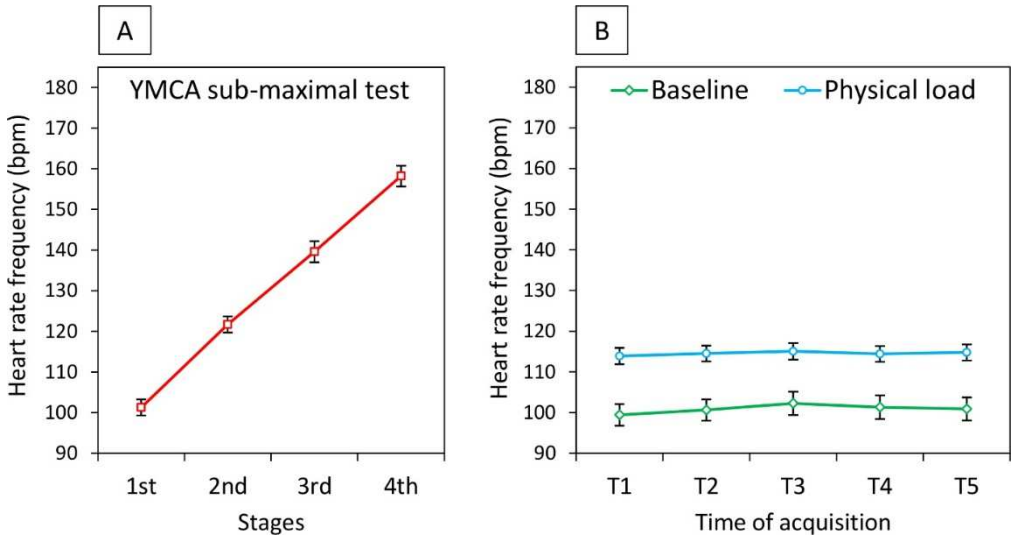

Figure 5.2: Mean participants' heart rate frequency acquired during the four stages of the YMCA sub-maximal test (panel A) and during both experimental sessions (panel B). Error bars show standard error of mean.

5.3.2. Reaction times

Figure 5.3 summarizes the mean RTs for each type of prime and for both experimental sessions. The analysis on RTs yielded a significant main effect of Prime, $\chi^2(2) = 392.79$, $p < .001$, $AIC_{RL} > 100$, Target, $\chi^2(1) = 398.03$, $p < .001$, $AIC_{RL} > 100$, and Session, $\chi^2(1) = 53.89$, $p < .001$, $AIC_{RL} > 100$. Although the main effect of Session indicates that in the high arousal condition (Physical load) the RTs were faster, $t(18) = 3.60$, $p < .001$, $d = .09$, the lack of the significant interactions Prime × Session, $\chi^2(2) = 3.06$, $p = .216$, $AIC_{RL} = .62$, and Target × Session, $\chi^2(1) = 1.66$, $p = .196$, $AIC_{RL} = .84$, indicates that primes and targets were elaborated in the two conditions by the participants similarly. The main effect of prime indicates that response timing were faster if preceded by go primes when compared to neutral, $t(18) = 7.72$, $p < .001$, $d = .21$, or nogo, $t(18) = 16.86$, $p < .001$, $d = .48$, primes. Conversely, nogo primes slowed down the response if compared to neutral primes, $t(18) = 9.02$, $p < .001$, $d = .28$. Following, the significant main effect of target indicates that responses to cued go targets were faster compared to the free-choice go targets overall, $t(18) = 14.38$, $p < .001$, $d =$

.34. The interaction Prime × Target was significant, $\chi^2(2) = 8.54$, $p = .013$, $AIC_{RL} = 9.69$, indicating that the effect induced by go primes was smaller in the cued condition but the effect induced by nogo primes was smaller in the free-choice condition: cued neutral prime – cued go prime (mean difference: $M = 26$ ms), $t(18) = 6.56$, $p < .001$, $d = .27$; free-choice neutral prime – free-choice go prime ($M = 28$ ms), $t(18) = 5.63$, $p < .001$, $d = .22$; cued nogo prime – cued neutral prime ($M = 36$ ms), $t(18) = 8.74$, $p < .001$, $d = .39$; free-choice nogo prime – free-choice neutral prime ($M = 26$ ms), $t(18) = 4.95$, $p < .001$, $d = .22$.

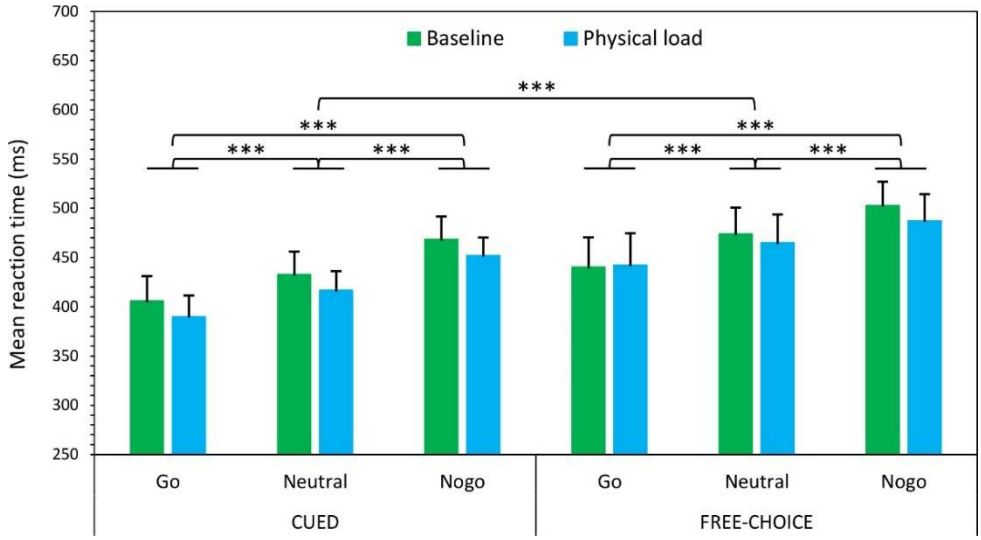

Figure 5.3: Mean RTs in milliseconds (ms) for go trials (cued and free-choice trials) split for each type of prime (go, no-go and neutral) in both experimental sessions (baseline and physical load). Error bars show standard error of mean. *** p < .001; ** p < .01; * p < .05.

5.3.3. Free-choice behavior

For the free-choice condition the analysis looked at how the primes biased the choices made by the participants. The response bias was defined as the percentage of free-choice trials in which each participant choose to respond as a function of the preceding masked prime. The analysis showed a main effect of Prime, $\chi^2(2) = 98.72$, $p < .001$, $AIC_{RL} > 100$ and a main effect of Session, $\chi^2(1) = 17.67$, $p < .001$, $AIC_{RL} > 100$, but not a significant

interaction Prime by Session, $\chi^2(2) = 3.29$, $p = .193$, $AIC_{RL} = .69$, indicating that once again the effect of priming, although present, was similar for both low and high arousal conditions (see Fig. 5.4a). Participants choose to respond after a go prime more often when compared to neutral primes: go minus neutral (mean difference: $M = 9\%$), $t(18) = 6.43$, $p < .001$, $d = .179$; or when compared to nogo primes: go minus nogo ($M = 13\%$), $t(18) = 9.22$, $p < .001$, $d = .261$; and choose more often to inhibit the response after a nogo prime if compared to neutral prime: neutral minus nogo ($M = 4\%$), $t(18) = 2.79$, $p = .015$, $d = .081$. Interestingly, overall participants were less prone to inhibit the response in the physical load condition when compared to the baseline condition: physical load minus baseline ($M = 5\%$), $t(18) = 4.10$, $p < .001$, $d = .098$. Looking at the sequential dependencies in free-choice trials, neither the Previous choice regressor, $\chi^2(1) = 3.20$, $p = .073$, $AIC_{RL} = .54$, nor the Previous choice by Session interaction, $\chi^2(1) = .23$, $p = .626$, $AIC_{RL} = .41$, were significant. Participants choose to respond action (*n*) after an action trial (*n-1*) 52% of the times, and choose to respond action (*n*) after an inhibition trial (*n-1*) 50% of the times (Fig. 5.4b). The lack of significance indicates that the response to trial *n-1* was not biasing the response to trial *n* neither by inducing an increase of switches nor by systematically repeating the same response. This result supports the conclusion that participants have been responding in a balanced and random way to the best of their possibilities as requested by the experimenter. The main effect of Session was significant $\chi^2(1) = 18.02$, $p < .001$, $AIC_{RL} > 100$, replicating the result of the previous analysis showing that participants choose to respond more in the physical load condition overall.

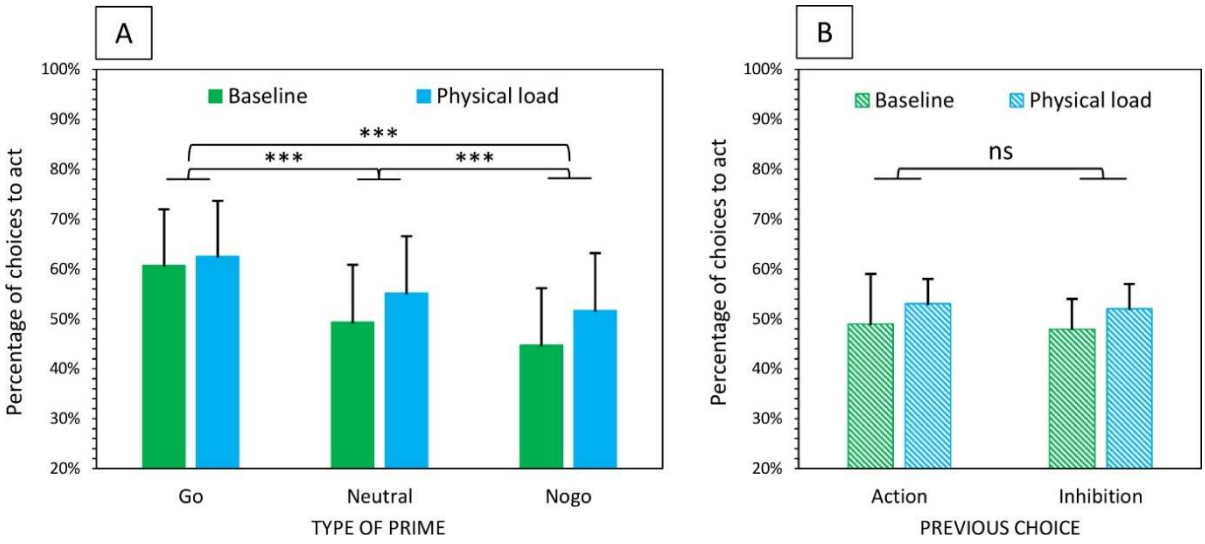

Figure 5.4: Mean percentage of free-choice trials in which participants chose to act rather than inhibit responses, as modulated by type of primes (go, nogo and neutral) and experimental sessions (baseline and physical load – panel A). Mean percentage of free-choice trials in which participants chose to act as a function of the preceding trial in both experimental sessions (panel B) Error bars show standard error of mean. *** p < .001; ** p < .01; * p < .05; ns = non-significant.

5.3.4. Error rates

Looking at both experimental sessions, errors in cued trials were generally few (see Fig. 5.5). Within cued inhibition trials the mean rate of false alarms was 8.6%. The GLME model on false alarms yielded a significant main effect of Prime, $\chi^2(2) = 47.80$, $p < .001$, $AIC_{RL} > 100$, but not of Session, $\chi^2(1) = 1.16$, $p = .279$, $AIC_{RL} = .66$, or the interaction Prime × Session, $\chi^2(2) = .77$, $p = .678$, $AIC_{RL} = .19$. The main effect of prime indicates that false alarms were more numerous after a go prime was presented (12.9%) if compared to neutral (7.3%) or nogo primes (5.7%) intuitively reflecting the incompatibility between the response suggested by the prime (go) and the response required by the target (nogo). Within cued action trials participants were more accurate and the mean rate of omissions was 4%. The GLME model on omissions yielded a significant main effect of Session, $\chi^2(1) = 4.27$, $p = .038$, $AIC_{RL} = 3.11$, but not of Prime, $\chi^2(2) = 2.50$, $p = .286$, $AIC_{RL} = .47$, or the interaction, $\chi^2(2) = .89$, $p = .638$, $AIC_{RL} = .21$. In cued action trials the incompatibility between primes and target did

not affect the general level of accuracy, however participants make significantly less errors in the physical load condition (3.4%) compared to the baseline condition (4.6%). Mean values for each condition, percentage of errors in cued trials and percentage of responses in free-choice trials are reported in Table 5.1.

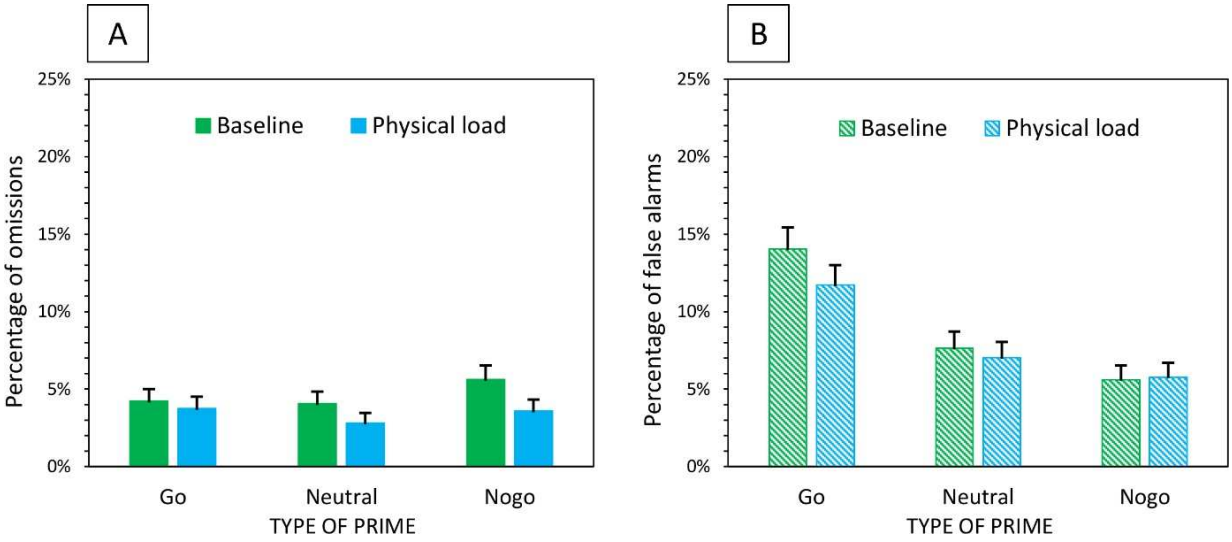

Figure 5.5: Mean percentage of omissions (panel A) and false alarms (panel B) as modulated by type of primes (go, nogo and neutral) and experimental session (baseline and physical load). Error bars show standard error of mean.

Table 5.2: RTs and Standard Deviation (SD) in milliseconds of both free-choice and cued trials, percentage of errors in cued conditions, percentage of responses in free-choice condition, split for each prime (upper part), and collapsed across primes (lower part). Data are presented for each session separately (central columns) and collapsed across sessions (right column).

		Baseline			Physical load			Baseline & Physical load		
PRIME	**TARGET**	**RTs (±*SD*)**	**% Errors**	**% Go responses**	**RTs (±*SD*)**	**% Errors**	**% Go responses**	**RTs (±*SD*)**	**% Errors**	**% Go responses**
Go	**Cued go**	406 (±109)	4.21		390 (±94)	3.75		398 (±102)	3.98	
Neutral	**Cued go**	432 (±101)	4.06		416 (±84)	2.81		424 (±93)	3.43	
Nogo	**Cued go**	468 (±101)	5.62		452 (±80)	3.59		460 (±91)	4.60	
Go	**Cued nogo**		14.06			11.71			12.89	
Neutral	**Cued nogo**		7.65			7.03			7.34	
Nogo	**Cued nogo**		5.62			5.78			5.70	
Go	**Free-choice go**	440 (±141)		60.7	442 (±132)		62.5	441 (±136)		61.6
Neutral	**Free-choice go**	474 (±126)		49.3	464 (±115)		55.1	469 (±120)		52.2
Nogo	**Free-choice go**	502 (±117)		44.7	487 (±105)		51.6	494 (±111)		48.2
Cued go		435 (±107)	4.63		419 (±89)	3.38		427 (±99)	4.01	
Cued nogo			9.11			8.17			8.64	
Free-choice go		470 (±132)		51.5	463 (±120)		56.4	466 (±125)		54.0
Cued & Free-choice go		453 (±121)			443 (±109)			448 (±115)		

5.4. Discussion

The present study sought to investigate whether performing or inhibiting responses depended on the physical exertion in a cycle ergometer test. More in detail the study explored whether cued and free-choices among alternatives outcomes (action or inhibition) are modulated differently by non-consciously perceived visual information in conditions of low and high exercise-induced arousal. While cycling, participants were asked to respond to cued and free-choice targets following the presentation of three varieties of masked primes that could elicit congruent or incongruent prime-response conflicts. Intentional action and inhibition responses were compared, with stimulus driven responses. To

introduce the arousal manipulation, personalized workload intensities were calculated according to participants' fitness level prior to the experiment. To my knowledge this is the first study attempting to explore the role of arousal as mediator in these processes.

In line with the hypotheses the behavioural results reported in Chapter 3 have been replicated: for both baseline and physical load conditions, go primes had the ability to shorten RTs when compared to neutral primes. On the opposite, nogo primes determined longer RTs when compared to neutral primes. This effect was more pronounced in the cued condition compared to the free-choice condition as revealed by the interaction effect between primes and targets. As opposed to free-choice trials, in cued trials the response option (action or inhibition) is automatically triggered by the appearance of the cued go target. The retention of the information at the low-level of direct motor execution, leaves less space for higher-level attentional control to compensate for the bias induced by the subliminal primes. This is further cleared up by the shorter RTs for the cued go conditions in comparison to those for the free-choice go conditions, intuitively reflecting the (high-level) decision processes involved in free-choices. Further, the study explored whether it was possible to bias the free decision to withhold the response as demonstrated for free actions (Demanet et al., 2013; Teuchies et al., 2016). Results shows that masked primes were able to induce the free decision process, both toward a significant increase of choices to act in action-congruent conditions, and toward an increase of choices to inhibit in inhibition-congruent conditions.

The primary interest of the present study was testing the impact of arousal on intentional action and inhibition, therefore the differences in participants' performances between the experimental sessions were investigated: RTs were shorter in the physical load session compared to the baseline session, for both cued and free-choice trials. Furthermore, the pattern evoked by each subliminal prime was consistent in the two arousal conditions. In line with previous literature indicating that exercise-induced arousal

benefits performance on cognitive tasks (Tomporowski, 2003; Weinbach et al., 2015), not only participants responded faster but also were more accurate as demonstrated by the analysis on error rates (at least for the omissions). It has been suggested that improvements in information processing during exercise are driven by alterations in brain neurotransmitter systems. A neuroendocrinological model has been put forward to explain how diverse cognitive functions might be either facilitated or obstructed by specific exercise conditions (McMorris, Tomporowski, & Audiffren, 2009). According to this model, the onset of physical activity triggers a chain of hormonal responses that gradually escalate as exercise increases in intensity. Norepinephrine and dopamine, in particular, are thought to influence pre-frontal lobe attentional systems by altering background neural noise relative to target saliency (Mesulam, 1990). An enhanced signal-to-noise ratio may improve stimulus encoding, decisional processes and response activation, and explain the reductions in participants' response times during exercise (Lambourne & Tomporowski, 2010).

Concerning free-choice behaviour results suggests that the number of choices to act or to inhibit were influenced differently by low or high arousal conditions. In particular participants made more 'action' choices in the physical load condition overall. This result is in accordance with the RAH model (Dietrich & Audiffren, 2011) suggesting that, during exercise, the physical effort drawn important metabolic resources from the cortical areas responsible for executive functioning, disinhibiting low-level motor impulses originating in the brainstem. Moreover the behavioral effects may be further strengthened by the disinhibition of the arousal systems in the brainstem fostering impulsiveness in the decisional process linked to free-choice trials. This is in line with the evidence for reciprocal enhancing effects between arousal and impulsiveness in perceptual decision making (Murphy, Vandekerckhove, & Nieuwenhuis, 2014), time perception (Wittmann & Paulus, 2008), economic decisions (Jahedi, Deck, & Ariely, 2017) and sexual behaviour (Ariely &

Loewenstein, 2006). In contrast with the hypotheses for free-choices, the lack of a significant interaction effect between prime and session, did not support the hypotheses of a strengthen effect of subliminal priming in the higher arousal condition. Although, an increase in arousal did not correspond to an increase in the magnitude of the priming effect, subliminal primes preserved their modulatory pattern in both conditions. A possible reason for this lack of effect may be found on the level of exercise intensity that was selected for the physical load condition. According to the 'ACSM guidelines for exercise testing and prescription' (Pescatello & American College of Sports Medicine, 2014) the 30% of $Load_{max}$ is considered a light exercise intensity. At this intensity, attentional resources may still preserve enough control on participants' free decisions as for the baseline condition, without being further disrupted by physical effort. Another possibility regards the moderate magnitude reported for subliminal priming' effects (Bermeitinger, 2016). A recent review on the effect of exercise on many cognitive domains indicated that acute exercise influenced participants' performance on some cognitive tests but not in others (Chang et al., 2012). Performance on tests that stressed information-processing speed and response speed was dependent on exercise demand, while tasks that required participants to make choice responses on the basis near-threshold perceptual discrimination were not (Chang et al., 2012). Accordingly, also the effects elicited by the subliminal manipulation may have not been robust enough to be dependent on exercise demands.

To sum up, in contrast with studies suggesting that an increase in arousal have the ability to improve the stopping of an already initiated response when driven by external stimulus (Chu et al., 2015; Weinbach et al., 2015), intentional inhibition did not benefit from the effect of arousal: the effect of subliminal primes was not reduced in the higher arousal condition as expected following an improvement of the executive control. On the contrary, arousal biased free-choices by increasing action choices overall, heightening impulsiveness and disinhibition of higher-order attentional control. In this circumstance

free decisions to inhibit seemed less voluntary determined if compared to the baseline condition. The effect of arousal on neurophysiological processes during exercise may account for the impact on basic bottom-up processes but have minimal or no effect on higher-level, top-down processes such as the control of the interference of subliminal irrelevant information. In light of this, I speculate that intentional inhibition and stimulus-driven inhibition might rely on partially distinct cognitive mechanism.

To conclude, the present study is the first to examine the effect of exercise–induced arousal on intentional action and inhibition. It extends previous literature by showing that not only externally driven processing benefit from an optimal exercise intensity. Under specific conditions exercise help individuals to perform the tasks rapidly and efficiently even when task' requirement are entirely internally driven. On the other hand, higher-order cognitive computations, such as making a free action or inhibition choices, might be impaired. When compared to previous experimentation (for review see: Chang et al., 2012; Lambourne & Tomporowski, 2010) the experimental setup adopted in the present study considers some novel features that allow to draw firm conclusions on the issues at stake here. First, instead of employing a pre- and post-exercise measurement design, the task is performed in concomitance of the physical effort under different workload intensities. Second, this study includes a test of maximal fatigue capacity and utilize intensities that are relative to each participant's maximum exercise workload. Third, the sample included a sufficient number of both male and female. It should be noted that females are widely underrepresented in this literature (Lambourne & Tomporowski, 2010). The present study, however, suffers from some technical limitations. In particular, an implicit limit of every study concerning free-choices lays in the instructions that are provided to the participants: there is a delicate balance between letting participants to truly choose freely and the experimental requirement of sampling enough data from all possible responses. Another limitation relates to the physiological recordings: arousal data were sampled only few times

for each participant to control for heart rate variability, but this aspect was no further analysed. Future studies should overcome at least this limitation by introducing a continuous recording of physiological data, allowing for a direct link between arousal intensity and the performance at the single trial.

CHAPTER 6

DECODING CONSCIOUS MOTOR PREPARATION IN PRIMARY MOTOR CORTEX[3]

6.1. Introduction

The concept of agency plays a profound role during voluntary decision making (Haggard, 2008; Haynes, 2011b) and has an impact on mental health (Haynes, 2011a; Ryan & Deci, 2000). Subjectively, performing a motor action is preceded by a conscious impulse that initiates the action (Hurley, 2002). The causal role of the conscious decision on simple motor actions was challenged by Libet et al. (1983) where the 'readiness potential' was recorded shortly before a formed a conscious decision to perform an action (see also Castiello & Jeannerod, 1991; Castiello, Paulignan, & Jeannerod, 1991). A controversy followed about how this observation relates to the causal role of consciousness for motor actions and the implications of free will (Breitmeyer, 1985; van de Grind, 2002). To investigate whether activity in decision related areas in the human brain predict the specific outcome of a choice beyond mere unspecific preparatory activation (Lau, Rogers, Haggard, et al., 2004), in two independent studies, Soon et al. (2008) and Bode et al. (2011) presented their participants a free-choice between pressing one of two buttons and asked them to indicate the time point when a decision for one action was consciously formed. fMRI activity was collected before, during and after the decision process showing that predictive patterns of brain activity in the precuneus and frontopolar cortex emerged up to 7 s prior to conscious decision to act, indicating that these brain areas encode information about

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[3] *In preparation:* Staib, M.*, **Dall'Acqua, T.***, Christophel, T., Haynes, J-D (2018). *Conscious motor preparation in primary motor cortex under uncertainty*.

** Shared first co-authorship*

upcoming decisions before they enter consciousness. Once the decision was made, preparatory motor activation was observed in primary and secondary motor areas (Bode et al., 2011; Soon et al., 2008; Toni, Schluter, Josephs, Friston, & Passingham, 1999), consistent with observed engagement of different motor areas during consecutive task stages (Bode & Haynes, 2009).

One conceptual limitation of any experimental design using volition is the lack of experimental distinction of neuronal processes that contribute to the behavioral outcome (Frith, 2013; Haggard, 2008) precluding an independent observation of conscious decision making and unconscious biases. For instance the studies described in the previous chapters (Chapters 3, 4 and 5) explored how the presentation of a prime affected the subsequent response to a target stimulus. These studies however cannot provide a direct evidence of the manner by which the information provided by the prime influences the subsequent elaboration of targets. Indeed these studies implicitly assumed that primes would modulate some non-specified decisional and/or motor processes that in order would influence the decisional and/or motor state of the response. Crucially, the experimental designs proposed so far, are not able to disentangle the neural preparatory mechanism that contribute to the behavioral outcome (action or inhibition in these studies) from the preparatory activity linked to intention. As a consequence an independent observation of the unconscious biases elicited by subliminal primes (that are the main interest of the present thesis) cannot be provided. For example in free-choice trials participants reported that they had not made a conscious decision before the presentation of the free-choice target (as required by the instruction of the experimenter). However the authenticity of this information is up to their subjective experience. It is possible, for example, that participants had already a conscious preference for one of the two alternative outcomes of the choice (action or inhibition), but this has not yet been evaluated as a decision up until the presentation of the free-choice target. Since the control of one's own conscious thoughts is

only conditional to the subject (Logan & Cowan, 1984), the possibility of spontaneous decision by participants, despite the instruction, must be taken into account. For example it cannot be ruled out that the activity related to intention at the moment of the choice could represent the even longer-term, or distant, intentions associated with the task (Haggard, 2008). In the same terms, the study by Soon et al. (2008) could not differentiate whether early activity patterns in frontopolar and parietal brain regions preceding the conscious decision truly reflect the unconscious formation of action intention or a general bias towards one of the possible motor outcomes. Given that is not possible to control all alternative interpretations simultaneously in a randomized experiment, the individual scenarios should be tested separately.

Here the possibility that these findings originate from a bias towards a specific motor action is eliminated by inducing a conscious tendency toward a one (of two) possible response outcomes. The (contractually formulated) argument of the present work is: if the decision to give a specific response, before the actual implementation of the latter, is conscious, then this mental event would have been identifiable by specific neural correlates. Since Soon et al. (2008) found that significant information about the specific motor outcome was collected only at the moment of participants' reported conscious intention and only in M1, then a significant activation of this region is predicted. This study sought to replicate these findings maximizing the comparability with Soons' results by using a similar experimental paradigm. Differently from Soon et al., (2008), the present study aims also to investigate how the motor preparation is carried on once a specific conscious tendency is experimentally set. To this end, participants observed the presentation of a cue stimulus that indicate which of two possible response options would be required 10 seconds later. The accuracy of the suggestion provided by the cue was varied and could diverge from the subsequent required response. The validity of the cue varied in blocks of 60%, 90% and 100% (deterministic) accuracy so that the predictive power of each

cue was previously determined. I applied MVPA to decode the content of the motor task in M1 in relation to the validity of the cue.

6.2. Methods

6.2.1. Participants

Ten healthy volunteers participated to the experiment (5 female: M = 24.6 years, SD = 3.8). All participants had normal or corrected-to-normal vision and were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). None of the participants had a history of neurological or psychiatric disorder and none of them had structural brain abnormalities. All participants gave written informed consent and were financially reimbursed for participation. The study was approved by the local ethics committee.

6.2.2. Stimuli and task procedure

Each participant completed a training session outside the MRI scanner and an experimental session in the MRI scanner. The two sessions took place on different days (see Fig. 6.1a). On day 1, participants received written instructions and filled the consent form. In the first training task ('target only'), participants familiarized with four abstract visual stimuli (Fig 6.1b) of which two indicated to press a button with the right index finger while the other two symbols indicated a button press with the left index finger, (the order was randomized across participants). For the creation of the stimuli, the focus was on (i) being as abstract as possible so that each participants could not consistently associate the target with other objects as verified by the experimenter in a debriefing session. During debriefing, participants reported no consistent associations with the abstract symbols. Moreover, in order to minimize systematic visual effects, (ii) stimuli were chosen to have similar physical features and to be equally complex: it was ensured that the color

distribution and complexity of the symbols were similar. Two visual symbols were associated to each possible response to ensure that the content of visual processing would have been dissociated from the content of motor preparation during the MVPA decoding. Training blocks were repeated until the participant pressed the correct button in 95% trials or more. As a second part of day 1, participants trained on the cueing tasks they would have performed in the MRI scanner on day 2. In the 'deterministic cueing task' (Fig. 6.1c), each trial started with a 2 s presentation of a circle containing one of the four symbols (cue), followed by a 0.5 s presentation of an empty square 6 s later (target) – i.e., 8 s of ISI. Participants were instructed to observe the cue, but withhold their response until the target appeared. The 'probabilistic cueing task' resembled the 'deterministic cueing task', except the target square now contained a symbol which could either prompt the same button press as the cue ('congruent') or the other button ('incongruent'). The chance of cue and target to indicate the same button ('cue validity') was displayed on the screen at the beginning of each block and could be low (60%) or high (90%). In the low validity condition, the target was congruent in 12 of 20 trials (60%) and incongruent in the remaining 8 trials (40%). In the high condition, 18 of 20 trials were congruent whereas 2 trials (10%) were incongruent. In half of the congruent trials, the visual symbol of cue and target were identical, and different in all other trials. All timings in the probabilistic cueing task were identical to the deterministic task. Training was repeated for four blocks per cue validity. The order of 60% and 90% validity blocks was randomized. Participants were instructed to respond as fast and accurately as possible. After 25% of all trials were presented, participants had to recall the cue symbol ('memory question') to ensure that the cue was not ignored. Between blocks, participants were encouraged to improve their reaction time to the target in the upcoming blocks, to motivate utilizing the cue during the task. On day 2, the participant was positioned in the MRI scanner and first repeated one training block of 20 trials displaying target symbols only. Next, 15 blocks of 20 trials of the main task were completed, with 5

blocks per cue validity (60%, 90% or deterministic). Each trial lasted 14 s on average. Similar to the training, participants were asked to utilize the cue as much as possible in order to improve response speed. Accuracy and RTs to the target stimulus were recorded for all trials.

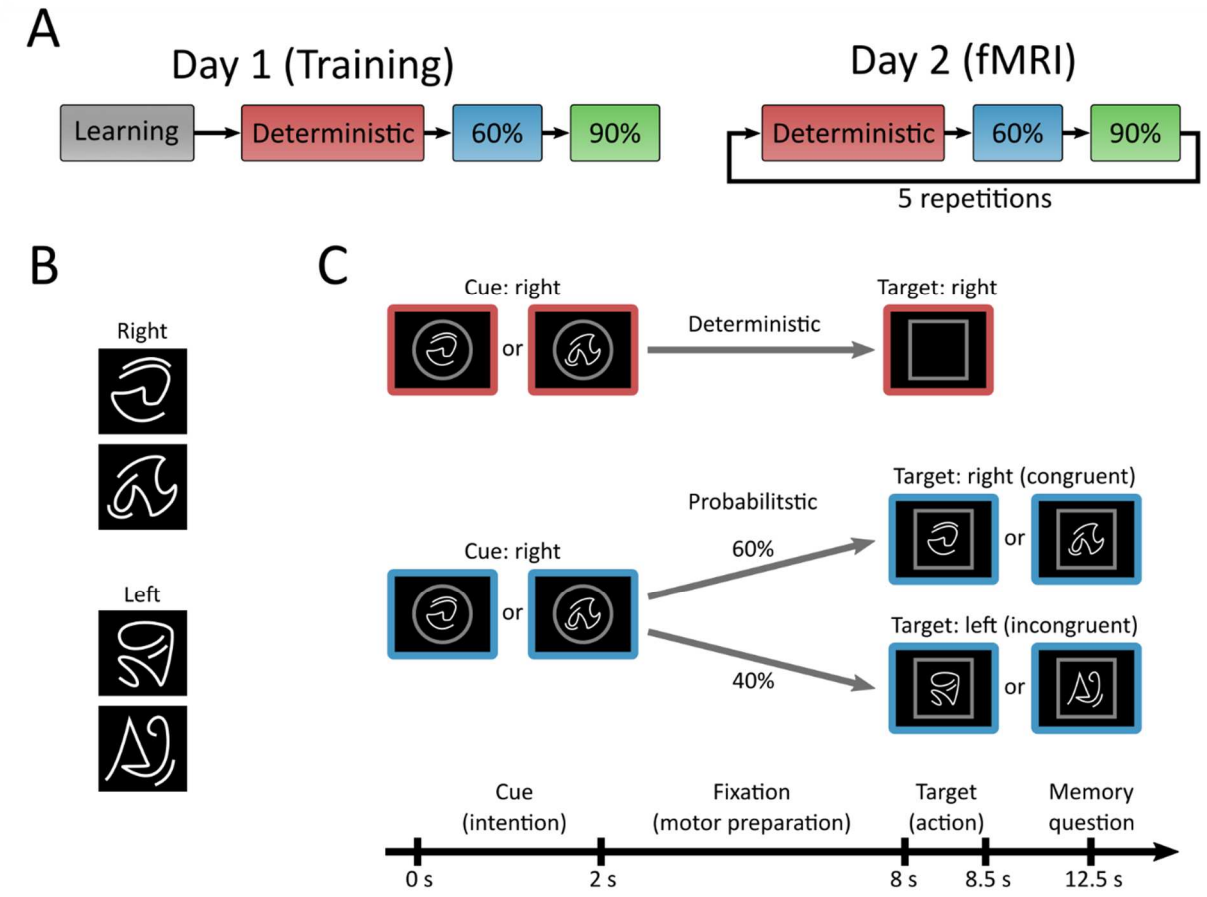

Figure 6.1: Stimuli and procedure of the cueing task. (A) Participants were introduced to the task outside the MRI scanner (day 1) and completed 5 blocks per cue validity (60%, 90% and deterministic) of 20 trials in the MRI scanner on day 2. (B) Abstract symbols were associated with a button press of the right or left index finger, randomized across participants. (C) In the deterministic cue paradigm (red), a cue symbol (circle) prepared the participant to press right or left when the target (square) appeared 6 seconds later. In the probabilistic cue paradigm, the target was either similar (congruent) or dissimilar (incongruent) to the cue. Cue validity was indicated at the beginning of each block to be 60% (blue) or 90% (green). Participants were asked to respond quickly and accurately to the target symbol. At the end of 25% of all trials, the participant was asked to recall the cue symbol in a memory question.

6.2.3. Behavioral data acquisition an analysis

To analyze how RTs and response error rate reflected information processing mechanisms for different cue validities, a drift diffusion model (DDM) was employed (Ratcliff, 1978). According to this model, during a two-alternative forced-choice task, sensory information of uncertain stimuli is assumed to be integrated over time and a decision is made when sufficient evidence for one option is accumulated. At the beginning of this integration process, an observer might initiate evidence accumulation with a bias towards one of the options. If, for example, prior knowledge exists that favors one option over the other, this bias is captured by the model as an unequal distance from the initial state (z_0) to the thresholds representing each option. In the paradigm used here, sensory uncertainty of the target stimulus is low, however, in each trial the cue introduces a bias towards a target direction, reducing the RTs and the error rate when cue and target are congruent. In turn, if cue and target are incongruent, the RTs and the error rate are increased. Cues with 90% validity were assumed to induce a stronger bias towards the congruent target direction. Here, using the DMA toolbox (Vandekerckhove and Tuerlinckx, 2007), this proposed effect was quantified by estimating how cue validity affects the initial bias (z_0) and its between-trial variability (sZ).

6.2.4. fMRI data acquisition

Data was acquired with a 12-channel 3 T Siemens Trio (Siemens Medical Systems, Erlangen, Germany) whole body MRI scanner. Participants were positioned headfirst and supine in the magnet bore. Functional images were acquired using a T2*-weighted EPI sequence (33 descending axial slices separated by a gap of 0.75 mm, matrix size = 64 × 64 voxels, 3 mm × 3 mm × 3.75 mm resolution, FOV = 192 × 192 mm, flip angle = 78°, TE = 30 ms, TR = 2 s) covering prefrontal, parietal, and most of temporal cortex. On average, ~140 volumes were collected in each single scanning run, resulting in 15 functional runs of 4 min

and 66 s duration (70 min of acquisition time in total). High-resolution anatomical images were then acquired for each subject using a T1-weighted MPRAGE sequence (192 axial slices with no interslice gap, data matrix = 256 × 256, 1 mm^3 isotropic voxels, TR = 1900 ms, TE = 2.52 ms, flip angle = 9°). For each participant, a whole brain magnetic field mapping sequence (3 mm slice thickness; 33 slices) was recorded to reduce image distortions during preprocessing.

6.2.5. fMRI data preprocessing

Preprocessing of EPI data was performed using standard procedures in SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). Images were corrected for geometric distortions caused by susceptibility induced field inhomogeneity (Cusack, Brett, & Osswald, 2003). A combined approach was used which corrects for both static distortions and changes in these distortions due to head (Andersson, Hutton, Ashburner, Turner, & Friston, 2001; Hutton et al., 2002). The static distortions were calculated for each subject from a B0 field map that was processed using the FieldMap toolbox as implemented in SPM12. Using these parameters, functional images were then realigned and unwarped, a procedure that allows the measured static distortions to be included in the estimation of distortion changes associated with head motion. Slice time correction was performed to correct for differences in acquisition time of individual brain slices (Sladky et al., 2011). No participant moved more than 4 mm in any direction during scanning. The motion-corrected images were then coregistered to the individual's anatomical T1 image using a 12-parameter affine transformation.

6.2.6. Definition of primary motor cortex

After pre-processing, BOLD responses to the target stimulus in the ‘deterministic cueing task’ was estimated for each voxel using a GLM. To do that, regressors was created

for left and right button presses per block by convolving the HRF with a stick function that is 1 at the time of an experimental event and 0 anywhere else, as implemented in SPM12. Cues were modelled as 2 s boxes, convolved with the HRF. Additionally, movement estimates and discrete cosine functions as regressors of no interest were added to reduce head motion induced artifacts and slow drifts from fMRI data. The linear contrasts *left minus right* and *right minus left* was computed for button presses in the deterministic paradigm only, to identify right and left M1, respectively. To exclude activation outside M1, the analysis was constrained to bilateral precentral gyrus (PG), as defined by the brain atlas AAL (Tzourio-Mazoyer et al., 2002) in conjunction with co-activation from "finger tapping" obtained from the online database Neurosynth (http://neurosynth.org). Thus, for each participant, masks for left and right primary motor cortices were created separately and forwarded to the MVPA.

6.2.7. Multivariate pattern analysis of individual time windows

In the MVPA the data from the probabilistic paradigm were analyzed, independent of the data used for defining the ROIs. First, for each voxel and block, BOLD responses were estimated for seven successive 2 s time windows (one per TR) starting 2 s before cue onset until 2 s after target onset. Definition of time windows was constrained to the 2 s TR of the fMRI scanning protocol. Analyzing individual time windows allows to assess time dependency of motor preparation relative to the cue presentation. A finite impulse response (FIR) model was evaluated in SPM, with one regressor per time point and target direction, separately for the cue validities 60% and 90%, summing up to 7 time points × 2 cue directions (left and right) × 2 cue validities (60% and 90%) conditions. Since all regressors included the same number of trials, confounding in decoding due to different sampling number was avoided (Ariani, Wurm, & Lingnau, 2015). Next, BOLD estimates in M1 for each condition were forwarded to MVPA, where each experimental block serves as

independent observation (i.e., 5 data points per condition). Support vector classification (Chang & Lin, 2011) was employed, as implemented in the Decoding Toolbox (Hebart, Görgen, & Haynes, 2015). The direction of the cue (left or right) was decoded for each validity and each time window separately using a leave-one-block-out cross-validation scheme. In this method, data from 4 out of 5 blocks was used to train the classifier, which was then tested on the remaining block, repeatedly for all 5 blocks as test data. Test accuracies were then forwarded to a repeated measurement ANOVA and directed one-sample t-tests against chance performance.

6.3. Results

6.3.1. Cue validity is retrieved from response behavior by a drift diffusion model

Consistent with the hypothesis, a main effect of congruency for reaction times, $F(1,35) = 39.5$, $p < .001$, and error rate, $F(1,35) = 49.9$, $p < .001$, was found in a congruency × cue validity repeated-measurement ANOVA, showing that participants responded faster and more accurately to the target if it was preceded by a valid cue, across cue validities (Fig. 6.2b). The benefit of a valid cue, as opposed to a cue signaling an opposing button press, was stronger for the 90% cue validity than for the 60% cue validity condition, as shown by a significant interaction of congruency and cue validity for reaction times, $F(1,35) = 16.5$, $p = .0032$, and error rate, $F(1,35) = 7.1$, $p = .0285$. RTs and error rate from congruent and incongruent trials (total number of trials with a response: 1981, from all participants) were included separately for the 60% and 90% cue validities into a DDM (Fig. 6.2). Trials in which no button was pressed were excluded from the analysis. The initial biases z_0 and their variance for each condition (60%; 90%) was estimated separately (see Table 6.1 for an overview of all parameters). Boundary separation a was modelled one per validity and constrains z_0 by $0 < z_0 < a$. The remaining parameters (drift rate and its within-trial and between-trial variability) describing the temporal evolution of the evidence accumulation

were assumed to be identical across conditions and therefore were estimated only once for all data. Per cue validity (60% or 90), the starting parameters by dividing $z_{0\ congruent}$ by $(z_{0\ congruent} + z_{0\ incongruent})$ were combined to calculate one bias that represents the bias induced by the cues. For the low validity (60%) condition, the computed bias (65.4%) slightly exceeds the expected bias of 60% by 5.4%, whereas for the high validity (90%) condition, the computed bias (82.3%) falls behind by 7.7%. These errors are within 1.6 times the standard deviations *sZ* for low validity cues and 1.2 times *sZ* for the high validity cues.

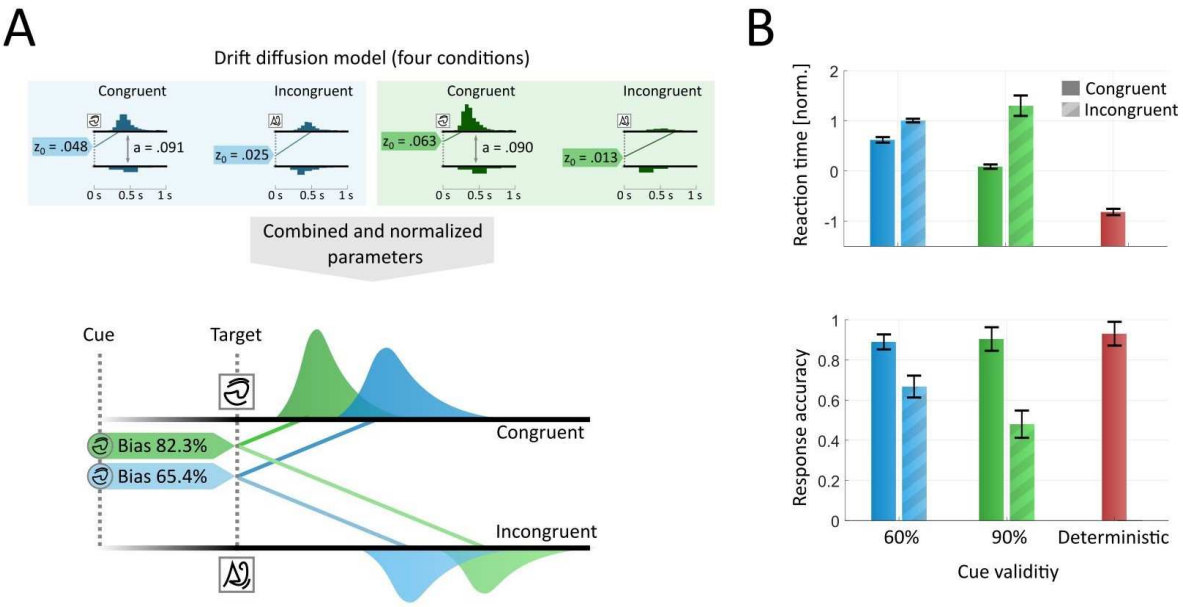

Figure 6.2: Reaction time and response accuracy. (A) A drift diffusion model (DDM) describes how information about the target direction is integrated over time and retrieves the initial biases induced by cues with 60% (blue) and 90% (green) validity for trials with congruent or incongruent targets. Upper panels: accuracy and reaction time of all participants from four conditions (cue validity × target congruency) was entered, and the initial bias z0 (and its variance sZ, not shown) was estimated for each condition. The histograms show reaction times for correct (top) and wrong (bottom) responses, respectively. Lower panel: z0 parameters from the congruent and incongruent condition are normalized for each cue validity, forming biases towards the congruent target. (B) Normalized reaction time and accuracy for 60% and 90% cue validities, and deterministic trials.

Table 6.1: Parameters of the drift diffusion model; z_0, initial bias; *sZ*, between-trial variability of z_0; *a*, boundary separation; *v*, within-trial variability in drift rate; *eta*, between-trial variability in drift rate; *Ter*, nondecision time; *st*, between-trial variability in nondecision time.

Parameter	60%, congruent	60%, incongruent	90%, congruent	90%, incongruent
z_0	0.0478	0.0252	0.0629	0.0135
sZ	0.0025	0.0026	0.0526	<0.0001
a	0.0909		0.0897	
v	0.2503			
eta	0.1322			
Ter	0.2986			
st	0.1491			

6.3.2. Early multivoxel patterns encode direction of motor preparation

A classifier was trained to predict cue direction (left or right) based on BOLD estimates from a FIR model, for 7 time windows starting 2 s before cue onset, separately for the 60% and 90% cues. The multivoxel analysis was spatially constrained to left and right M1 (Fig. 6.3a). To investigate how neurons in motor cortex engage in motor preparation before a button press, a Cue validity × Time window ANOVA was computed. For this analysis, time window 1 was excluded because was recorded before cue onset and thus does not contain any information about the cue direction of the current trial. In left M1, the ANOVA revealed a main effect of Time window $F(5,45) = 4.55$, $p = .001$, but no main effect of Validity, $F(1,9) = 0.12$, $p = .73$, or interaction between Time window and Validity, $F(5,45) = 1.47$, $p = .22$. Similarly, in right M1 a main effect of Time window was found, $F(5,45) = 3.32$, $p = .012$, Validity, $F(1,9) = 10.59$, $p = .01$, but no interaction, $F(5,45) = 1.37$, $p = .25$. One-sample t-tests for left or right M1 showed that for the 60% valid cue direction, above-chance accuracy was reached 10 s after cue onset, but never in right M1. For 90% valid cues, direction could be decoded after 6 s in left and right M1 (see Figure 6.5 for statistics). To investigate the spatial extent of action preparation across M1, the analysis was repeated including all voxels in left and right PG (Fig. 6.3b). A similar temporal pattern of decoding accuracies emerged where

above-chance was reached 6 s after cue onset in both hemispheres for 90% cues. In left PG the 60% cue was decoded 6 to 8 s after cue onset. For the PG, the direction for the deterministic cue was additionally decoded, because the atlas that defined the ROI is independent of the data used for MVPA. For the deterministic cue, decoding accuracy was above chance after 6 s in left and 4 s in right PG. Classification accuracies was then tested in four additional brain regions that were previously associated with voluntary and unconscious decision process (Bode et al., 2011; Soon et al., 2008b), i.e. the FP and the P in the left and right hemispheres, respectively. Although no above-chance classification in these regions during motor preparation was expected, above-chance accuracy 8 and 10 s after cue onset was found in FP and P. Figure 6.4 summarize all decoding accuracies for each considered ROI.

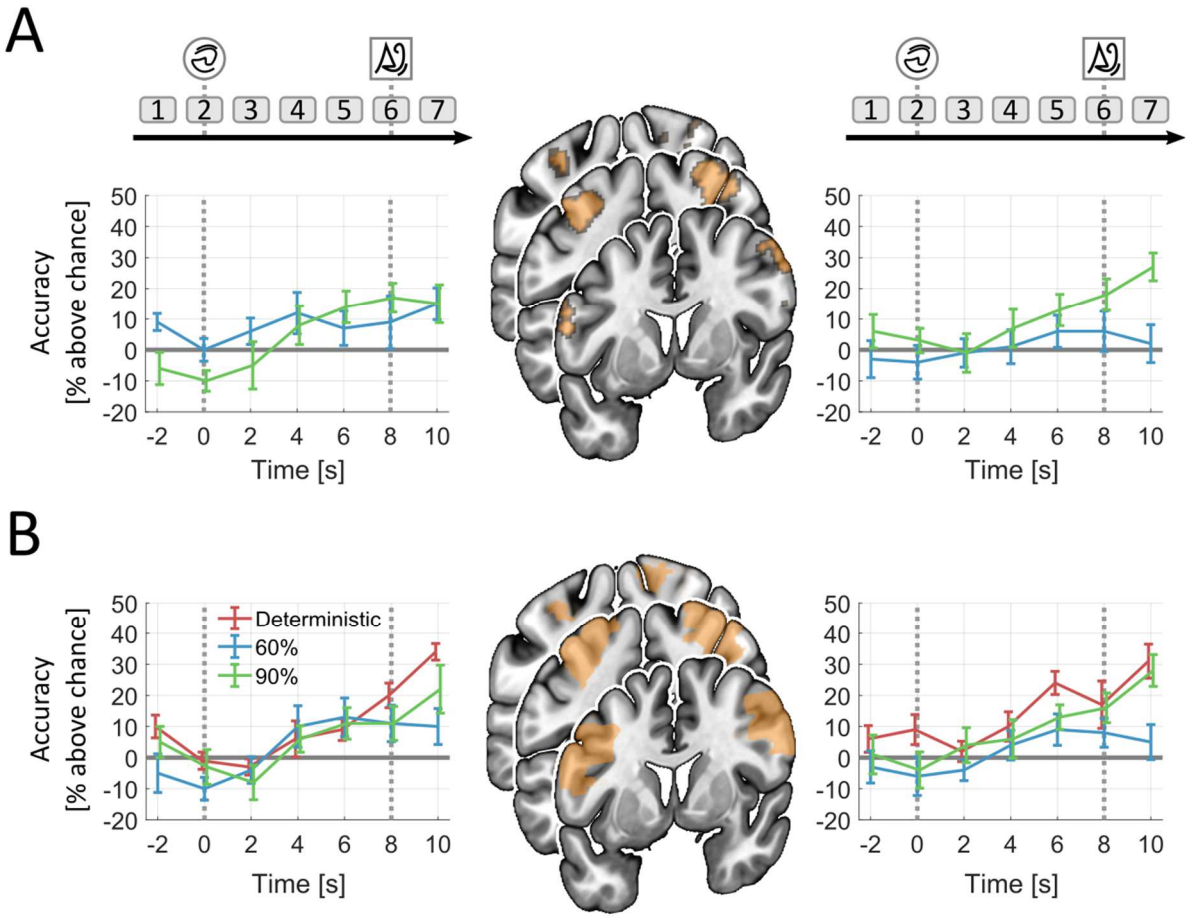

Figure 6.3: Decoding results for cue direction in seven time windows (left panels show results from left hemispheres and vice versa) with chance level at 50%. Vertical dashed lines indicate cue onset (0 s) and target (8 s). Multivariate classification was computed (A) in a functionally defined region within primary motor cortex (M1) and (B) in the precentral gyrus (PG). The analysis of PG included trials from the deterministic cue since this region was anatomically defined, independently from the target response. Note that for each cue direction, two different visual symbols could appear. Images are displayed in neurological convention.

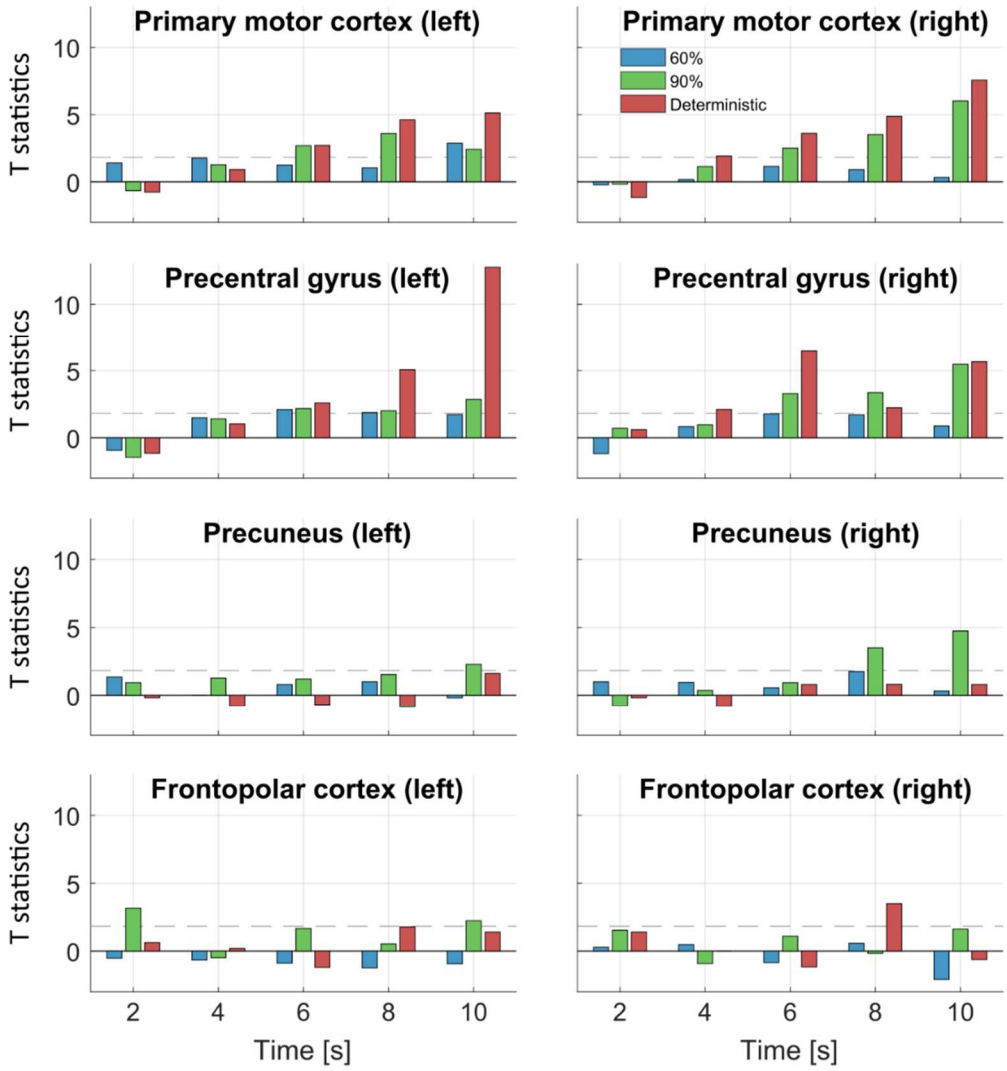

Figure 6.4: T-statistics from a directed one-sample t-test of decoding accuracies against chance level. Dashed line marks significance of p = .05.

To explore for further brain regions that are engaged in motor preparation, a searchlight analysis was performed on the whole brain of each participant in MNI space, and repeated a classification of cue direction for different time windows and cue validities. Classification accuracy maps for each participant were then smoothed and entered into a second level model. A one-sample t-test was performed separately for each time window and cue validity. Resulting statistical maps were thresholded at $p_{uncorrected} < .001$ and surviving clusters are reported if their cluster-level FWE-corrected p-value < .05 (Fig. 6.5). Notably, for this

exploratory analysis, the threshold for statistical significance was more conservative than for the previously reported ROI-based analyses. For the deterministic cue only, cluster of significant above-chance decoding accuracy was found in the SMA, at the MNI coordinates (MNI *x, y, z*: 8 -14 56). Additionally, significant classification performance in primary motor areas was confirmed as expected from the previous ROI based analyses. No above-chance decoding accuracy was found for 60% and 90% cue validities.

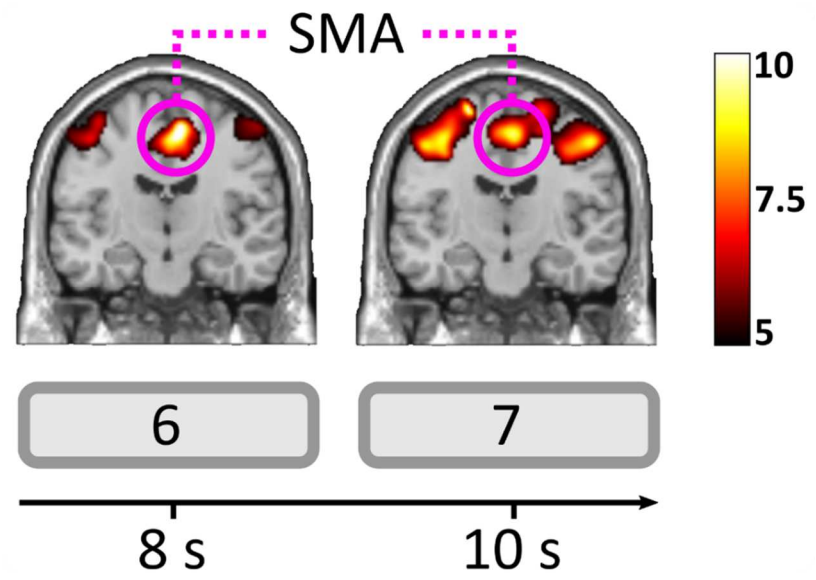

Figure 6.5: Searchlight analysis revealed above-chance accuracy in the supplementary motor area (SMA) across participants in time windows 6 and 7, i.e. 8 and 10 s after presentation of a deterministic cue. Lateral significant clusters show primary motor cortex (M1). Color bar indicates t-value. Images are displayed in neurological convention and thresholded at $p_{uncorrected} = .0001$ for visualization.

6.4. Discussion

In this study, I showed participants cues for a left or right button press that predicted a target button 8 s later, governed by varying validities. Each direction is indicated by one of two abstract visual symbols to separate responses to visual stimulation from motor preparation. In the experiment described here, low (60%), high (90%) and perfect

(deterministic) cue validities were employed to investigate the relation between motor certainty and pattern representations in primary motor cortex.

Motor preparation based on cue validity was reflected in overt behavior of participants. A DDM was used to retrieve the bias towards a target direction introduced by the cue. The DDM combines participant's response error and RT to model how information is integrated during visual presentation of the target, until a response is made. In this model, the starting bias was computed for each validity. The model could retrieve the impact of the highly valid cue on the tendency towards the predicted target, whereas the less predictive cue imposed a weaker bias. The strategy to prepare according to predictions from the highly valid cue (90%), but disregarding predictions from a low valid cue (60%) reflects an optimal strategy in a task where both response error and speed are relevant. Importantly, the gain in response accuracy and speed for targets following the highly valid cue is consistent with the assumption that the multivariate patterns representing cue direction emerge as a consequence of action preparation.

My main goal was to investigate how motor preparation is encoded in the left and right M1, P and FPC, which are all part of an extended motor network. To achieve that, I split the time interval between cue and target into individual time bins of 2 s each and used multivoxel classification to decode the cue direction for each time bin separately. I found that the direction of motor preparation after cue onset is encoded in M1 as temporally stabilizing multivoxel pattern. Classification accuracy increased steadily over the course of 11 s after cue presentation, following the slow temporal evolution of the BOLD signal (Grammont and Riehle 1999), with significant above-chance classification accuracies 7 s after cue onset for the highly valid and deterministic cue in left and right M1, and after 11 s for the low valid cue in left M1. In FP and P, I observed above-chance accuracy 9 and 11 s after cue onset. I then used a searchlight analysis to explore additional brain areas from

which preparatory signals can be decoded and was able to significantly decode the cue direction in bilateral SMA, consistent with earlier findings.

The present data identifies brain areas associated with conscious motor preparation towards a specific target. These results are put into perspective to the findings of Soon et al. (2008), where free decision making of an upcoming motor choice was associated with activity in FP and P even before the outcome entered consciousness, but not with activity in primary (Jeannerod, 1995; Schnitzler, Salenius, Salmelin, Jousmäki, & Hari, 1997) or supplementary motor areas (Ikeda, LüDers, Burgess, & Shibasaki, 1992). Instead, the authors found activity in M1 only after the motor action was performed. This is in keeping with the author's distinction of processes of unconscious decision making on the one hand, and conscious motor preparation on the other (Brass & Haggard, 2008; Castiello et al., 1991; Soon et al., 2008). The findings suggest that cued action preparation engages a motor network that is distinct from the network of unconscious free decision making (Assal, Schwartz, & Vuilleumier, 2007; Castiello & Jeannerod, 1991; Desmurget & Sirigu, 2009; Jahanshahi et al., 1995), and that both processes result in locally constrained, but spatially distributed patterns in M1, once a motor intention has entered consciousness.

CHAPTER 7

GENERAL DISCUSSION

As adult individuals we all experience a sense of voluntary control over most of our daily actions so that we perceive our actions as if 'we are deliberately choosing' to execute them. The experience of action as by product of conscious intention has always stimulated considerable scientific interest because of is explicit convergence with the concept of "free will" (Sinnott-Armstrong, 2014). As much as individuals' are capable of producing action based on internal set of criteria, it is also anecdotal evidence the capacity of "stopping oneself from doing something at the very last moment". This ability has been considered as form of volitional cognitive inhibitory control – or intentional inhibition – that allows for more flexible cognition and behaviour. Voluntary actions thus demonstrate a "freedom from immediacy" (Shadlen & Kiani, 2013). Related to this is the controversy regarding whether intentionally inhibiting an action requires conscious effort and control. Since Libet's (1983) well known experiment, several accounts have tried to replace the concept of "free will" with the capacity of a "free won't" proposing an implausible dualism, in which a form of conscious causation would provide an ultimate veto over action. This dualism however, is just as problematic as the idea of a conscious generation of action since could itself be a consequence of some preceding unconscious neural activity (Haggard, 2008). In this respect it has been recently proposed that also the intentional generation of a decision to inhibit is preceded by unconscious brain activity (Filevich et al., 2013) and, alike for voluntary actions (Schlaghecken & Eimer, 2004), also free decisions to inhibit can be biased outside conscious awareness (Parkinson & Haggard, 2014).

Starting from these evidences, the experimental work included in the present thesis aimed at extending what is known about the generation of voluntary action and inhibition choices. I defined voluntary – free – choices by contrasting them with stimulus-driven action and inhibition responses. This experimental approach allowed me to introduce two novel manipulations to examine the relative effects on voluntary processing: subliminal priming (Chapters 3, 4 and 5) and the modulation of the exercise-induced arousal (Chapter 5). While Chapter 3 and Chapter 5 investigate free-choices from a behavioural perspective, the study presented in Chapter 4 further looked at the neural circuits involved in making free-choices to act and to inhibit by means of fMRI. Chapter 6 was specifically tailored to explore the temporal dynamics of neural motor preparation and how they dissociate from those involved in response intentionality.

7.1. Unconscious determinant of a free-choice

What makes a voluntary act different from a reflexed action? Or, more ecologically: "*What is left over if I subtract the fact that my arm goes up from the fact that I raise my arm?*" (Wittgenstein, 1968; page 84). Whereas stimulus-driven actions and inhibition responses are determined by a precise form of stimulation, the occurrence and the timing of voluntary action and inhibition responses are not directly specified by any external stimulus which make them quite impenetrable to study experimentally. Although we feel voluntary actions as a product of our will, more convincingly their origin is determined by underlying unconscious decisional processing (Libet et al., 1983; Soon et al., 2008), upon which however, the experimenter has little or no control. To bypass the problem an ingenuous solution would be asking participants to produce responses following their, perceived, will but in the meantime implicitly manipulating the unconscious decisional processes that concur to produce the response. In this thesis, as in previous research (Parkinson & Haggard, 2014; Schlaghecken & Eimer, 2004; Teuchies et al., 2016), subliminal priming has

been used to modulate participants "free" response choices in order to infer the dynamics of the decisional processes that determined the choice, in this case whether to act or to inhibit. In Chapter 3 I designed and tested a paradigm that has demonstrated to be a suitable method for the purposes of my research question. The paradigm was a modified version of a Go/Nogo task that together with cued targets, also included a free-choice condition. Crucially, targets were preceded by a subliminal – masked – primes that were congruent or incongruent to the required response. As well as participants' reaction times and error rates also the number of free-choices to act or to inhibit were biased following primes suggestion. Finding that the mechanisms responsible for the choice to inhibit can be unconsciously biased suggested that the origin of the very same mechanisms might me partially unconscious to the individual, thus confirming that intentional inhibition cannot be identifiable as a "conscious veto" (Libet et al., 1983). These findings are in accordance with previous research reporting the unconscious neural underpinnings of free-choices to inhibit (Filevich et al., 2013).

A major limit in the study of voluntary action control must be specified however: instructions in experiment such as the one proposed in Chapter 3, typically tell participants to decide spontaneously but in a random and balanced manner (see methods section at page 56, Chapter 3). Although 'instructing spontaneity' is quite counterintuitive, this type of instructions are a necessary compromise to investigate free-choices. In particular, the tradition of linking volition to the capacity for randomness is based on the capacity of producing innovative behaviour (Haggard, 2008). The presence of embedded neural systems capable of unpredictable – random – behaviour makes great sense from an evolutionary perspective since they produce a clear survival advantage. Animal's survival depends both on the exploitation of known sources of food thought stereotyped behaviour and on the exploration of possible new resources through innovative actions, but also trough the capacity of inhibit the new action that results maladaptive. Since voluntary

actions are internally produced and independent by external stimuli they can be closely associated with exploratory processes rather than exploitation processes. It has been proposed that intrinsic neural noise may account for randomness in actions (Schurger et al., 2012), which in turn explain why response choice is chosen versus another (in this case action or inhibition). Theoretical models assume that participants accumulate independent evidence to support one decision versus another until a decision threshold is reached (Hanes & Schall, 1996). I proposed (page 70, Chapter 4) that subliminal primes, as presented within the paradigm used, could influence the responses to go and nogo stimuli in two different ways: or by enhancing the excitability of post-decisional motor pathways, or biasing the actual neural "free decision" in favour of initiating or inhibiting the action. There could be valid reasons to speculate that primes would induce their effect at a decisional level. First, Schlaghecken and Eimer (2004) showed that the effect of subliminal primes on free-choices are mediated by (high-level) current intentions and task set, or rather the set of stimulus-response mappings imposed by task instructions (Schlaghecken & Eimer, 2004). Although this clearly supports that primes cannot be effective solely by modulating the motor threshold of the response, the effects of the subliminal primes on free-choices can be attributed simply to visual congruency between prime and target stimuli, facilitating or inhibiting the appropriate response choice. Thus, the mechanism underlying those effects may not lie at high cognitive level. Second, Parkinson and colleagues (2017) avoided such confounding manipulating free-choices (to inhibit) with ecologically valid and socially relevant stimuli (i.e., emotional human faces) for which salience for volition cannot be accounted for in terms of low-level properties of congruence or incongruence (because the emotional face primes were not visually congruent with targets; Parkinson et al., 2017).

In the present thesis the behavioural study proposed in Chapter 3 could not directly assess whether primes were producing their effects in motor or decisional mechanisms.

However the study proposed in Chapter 4 measured the performance within the same paradigm (as described in Chapter 3) by means of fMRI. Therefore this study was more suited to address this question since it allowed to explore whether the effect or primes were detectable within motor or decisional areas of the brain. Neuroimaging techniques have been employed by the majority of studies that sought to investigate intentional inhibition, mainly because of two intrinsic limits in the investigation of the construct itself: (i) intentional inhibition does not results in any overt behaviour to explore, since the action has been inhibited; (ii) there are not external stimuli that time-locks precisely the related decisional processes, since intentional inhibition is stimulus-independent by definition. The aim of the study presented in Chapter 4 was threefold. First it intended dissociating the neural networks that are specifically engaged in making free-choices from those engaged in stimulus-driven responses: the whole-brain results revealed that a well-known "free-choice network" was crucially involved in free-choices both to act and to inhibit when contrasted with the cued counterparts. The network included the activation of the RCZ, the DLPFC, parietal cortices and AI. These areas closely match previous findings in studies contrasting free with cued choices (Forstmann et al., 2006; Lynn et al., 2016; Teuchies et al., 2016). Among this network of areas, the RCZ and the DLPFC were particularly related to the decision-making processes underpinned by free-choices, beyond the specific outcome that was then implemented (action or inhibition). Previous studies found these areas playing a similar evaluative role in free-choices between action alternatives (Demanet et al., 2013; Mueller et al., 2007; Teuchies et al., 2016). This suggests that the intentional inhibition or the intentional execution of an action might be evaluated as response alternatives by specialized areas as the RCZ and the DLPFC, at least for tasks as formulated in the present study. The second purpose of the study was to assessing whether intentional inhibition processes was supported by specialized areas such as the dFMC as previously reported (Kühn, Haggard, et al., 2009). Results did not support this notion by showing a lack of

differential activity in this area neither when contrasted with intentional action trials or cued inhibition trials, nor when evaluated looking at the congruency effects of primes. It must be noted however that priming effects on intentional inhibition were absent also in behavioural responses making the latter result less reliable. In general the RCZ and the DLPFC were better predictors of intentional inhibition processes suggesting that specialized mechanism might not be needed. The third, above-mentioned, aim of the study was to define whether primes would affect free-choices by modulating the activity within decisional areas, such as the "free-choice network", or by a direct influence on the motor pathways. This curiosity was driven by the evidence that in previous research subliminal priming effects were detectable in the modulation of activity within areas of the "free-choice network" (Teuchies et al., 2016). However, in these previous studies (Teuchies et al., 2016; Wenke et al., 2010), the task was to select between alternate actions. So, the differences between primes acting on decisions versus on motor processes were confounded, making it difficult to assess if the primes acted to modify choices rather than motor state (i.e., choice biases are due to interference between the alternate actions in primary motor areas). In contrast, the paradigm used in the current study actually cleanly allows these two alternative priming mechanisms to be distinguished in a better way than these prior studies. That is, the paradigm used seems better suited to pin down why primes are able to influence free-choices. However, in contrast to my hypotheses and to the findings reported in Chapter 3, the present study did not revealed a behavioural effect of priming in free-choices and this was reflected in the neural patterns accordingly. Although I proposed that this lack of an effect was produced by the instability of subliminal priming effects, in this study primes were able to bias the speed of responses in free-choice action trials and the rate of omissions. These results suggested that an evaluation of priming effects in M1 was still possible. Since also the motor activity in M1 was not modulated by primes, the

inconsistency of these result did not allowed to draw a firm conclusion leaving this question unsolved.

In this regard the study presented in Chapter 6 attempted to further deepening this interrogative by taking the opposite perspective. The study aimed to explore the neural underpinning of motor preparation in M1 when the decision to give a specific behavioral response is conscious. The study capitalized on a paradigm that was previously used to infer unconscious intentional preparation of a free-choice (Soon et al., 2008) to decouple the neural activity related to the choice from the neural activity related to motor preparation. Results showed that when the cue (i.e., the stimulus that informed about the upcoming required response) was almost at chance and highly invalid (60% condition; being almost uninformative) motor preparation in M1 was detectable only when the response was almost initiated and the target stimulus (signaling the actual required response) was already shown. In another condition the accuracy of the suggestion provided by the cue was increased (90% condition; being very informative) and motor preparation in M1 was detectable well before the presentation of the target stimulus, suggesting that automatic motor processing was triggered in advance. These findings allowed to conclude that cues (like primes) might have very different effects depending on whether task demands require internally selected motor choices or whether the required action is already specified.

I propose that future studies should address this question by looking at the effects of presenting cues under the threshold of conscious awareness in order to explore the temporal dynamics of unconscious motor preparation. Hypothetical results may provide meaningful insight on how free-choices are biased by unconscious perception.

7.2. The modulatory effect of physical exercise

Positive effects on cognition induced by moderate physical exercise are commonly reported in sport psychology's literature (Chang et al., 2012; Lambourne & Tomporowski,

2010). The majority of reported effects however, considered the beneficial effect of acute exercise in low-level motor processing such as the increase of reaction times or the improvement of signal detection and accuracy. Discussion of these findings usually capitalized on the dis-inhibitory effects that exercise-induced arousal would produce in the brain stem and the "arousal systems" (Robbins & Everitt, 1995). On the other hand the effects regarding high-level processing are more inconsistent reporting both slightly positive (Chang et al., 2012; Chu et al., 2015) but mostly negative (Dietrich, 2006; Lambourne & Tomporowski, 2010; Tomporowski, 2003) effects. This inconsistencies on the effects of exercise have been recently suggested to arise because together with the activation of the reticular-activating processes (the arousal systems), a downregulation of the frontal areas might concurrently occurs. Since brain processed compete for a limited number of metabolic resources those processes that are not directly involved in producing the motor act, such as executive functions, would be less fuelled by energetic resources (Dietrich & Audiffren, 2011).

Guided by this argumentation the study proposed in Chapter 5 aimed to uncover whether these double effects of exercise in cognition could be elicited my means of the paradigm described in Chapter 3. In particular, I was primarily interested in looking how exercise would affect voluntary actions and intentional inhibition processing. Crucially, to date no studies investigated these effect in the realm of volition. Since previous research enumerated voluntary motor control as one of the most unique human feature (Frith, 2013) clearly supported by neural processes located in the frontal cortex (e.g., see Chapter 4), defining the effect of arousal on these mechanisms is of utmost importance for everyday functioning. In the experiment I asked participants to perform the paradigm while pedalling on a cycle-ergometer at two level of workload intensities eliciting different level of arousal and fatigue accordingly. As primary result I was able to replicate the effects reported in Chapter 3 in both exercise conditions. Regarding the more interesting effects of

exercise in free-choice behaviour, results showed that the high arousal condition produced more action choices overall suggesting that intentional inhibitory mechanisms were overcame by the impulsivity induced by the exercise. Crucially also stimulus-driven inhibition mechanisms were not enhanced by the effect of exercise as demonstrated by the undifferentiated rate of false alarms between the two conditions. On the other side results reported also positive effects in low-level motor processing as demonstrated by the decrease of reaction times in both stimulus-driven and free-choice action conditions.

The double dissociation raised by these results has been recently conceptualized within a model – the RAH model – that accounts for both effects (Dietrich & Audiffren, 2011). In particular the model provides a clear description of downregulation of the frontal areas (hypofrontality process) and thus of the inverse effects reported for higher cognitive functioning. Importantly this downregulation is forcibly tied to the reduction of states of consciousness that commonly occurs during exercise, such as the 'experience of flow' (Dietrich, 2004). Moreover it is able to explain the positive (anxiolytic) effects on mood perceived during acute exercise due to a reduction in over-activity in frontal areas. The hypofrontality process predicts a downregulation of multiple brain areas that proceed in hierarchical fashion (Dietrich, 2003, 2006). Downregulation occurs in a five-stage hierarchy of consciousness: a the first stage higher-order processes are impaired by downregulation of the dorsolateral prefrontal cortex; at the second stage self-representation, sense of agency and emotional processes are impaired by downregulation of the ventromedial prefrontal cortex; at the third, memory, learning and basic emotions, supported by the limbic system, are impaired; at the fourth stage sensory processing in the thalamus are degraded; and at the end it occurs within arousal systems in the brainstem (Dietrich, 2006). Put in these terms even a subtle downregulation in the frontal cortex may be enough to impact top-down, explicit, responses and voluntary processing. A greater deregulation may

further limit the capacity of the frontal cortex to inhibit and coordinate the reticular activating process thus boosting bottom-up, implicit, activity (Dietrich & Audiffren, 2011).

Since the study proposed in Chapter 5 could only account for the behavioural effects of exercise on voluntary motor control, a direct evidence of the hypofrontality process can only be speculative. Future studies may overtake this limitations by using neuroimaging or electrophysiological techniques. As found in Chapter 4 free-choice behaviour appears being supported by a specialized network of brain areas. Would be of extreme interest to see whether the activity over this network can be gradually decreased while increasing exercise intensity thus giving direct support to the RAH model. By using the paradigm proposed in the present thesis it would be also possible to elucidate whether primes would works affecting free-choices at the motor or rather at the decisional level. As suggested by the RAH model if priming effects arises because of direct, low-level, visuo-motor congruency mechanisms, than an increase in exercise would increase the relative effect of congruent and incongruent primes. Since the ascending activating processes are particularly activated, on the one hand the motor threshold would be more easily reached with congruent primes, on the other hand incongruent primes would rapidly decrease pre-motor activation thus producing more choices to inhibit. Importantly all these effects would be reflected in the relative activity in primary motor cortices. However if priming effects arises because of congruency effects at the decisional level, then the hypofrontality produced by the increase in exercise would disrupt priming effects, and decrease the activity within the "free-choice network".

7.3. Concluding remarks

The experience of action as by product of conscious intention has always stimulated considerable scientific interest because of is explicit convergence with the concept of "free will" and moral responsibility (Sinnott-Armstrong, 2014). The capacity for voluntary action

is so fundamental to our existence that all known human cultures define individuals as an autonomous agents and thus responsible for what they do. Nevertheless defining how the conscious intention and the physical action interact, and how this would relate to normative and moral responsibility is as problematic as important. In particular, the decision *whether* to act or inhibit a misguided action is especially relevant for responsibility because of its concerns on the reasons that triggered the brain processes that produced the action and eventually, on the reason why other brain mechanisms did not intervene in withholding it. An effective balance between action and inhibition is a very important factor to prevent the execution of inappropriate motor plans and any of its causal external effects. In these circumstances a deeper understanding of the cognitive mechanisms that govern the capacity to inhibit urges and actions would be of utmost importance.

In this regard, the results provide by the experimental work I have conducted might have potentially interesting implications for self-control. Since individuals are not aware and cannot control many factors that unconsciously bias their free-choices to inhibit, should societies consider them responsible for their own failures to inhibit?

In this thesis subliminal priming of free decisions to inhibit have been evaluated within the restricted circumstances of the experimental setting and such type of effects are hardly generalizable to everyday motor control. Thus remains unclear whether the mechanisms involved are determinant for real life situations. Nevertheless the obtained results point out some intriguing considerations regarding team sports. Football athletes for example, continuously regulate their interactions with other players by both deciding on their own initiative 'the best athletic feat' for that specific game phase, but also through being able to inhibit the motor plan in reaction to an opponent's unexpected move. Concurrently, players are under great pressure caused by the physical exertion (the high level of arousal) and in that contingencies even a subtle change in the environment (like the prime) might be misinterpreted triggering an automatic but inappropriate move. Moreover

as proposed by the RAH model, the downregulation of frontal lobes is forcibly tied to the reduction of states of consciousness that commonly occurs during sport, such as the "experience of flow". Recalling the infamous bite of Luis Suarez proposed in the incipit of my thesis, I might now provide a clearer picture to understand why such "accidents" occasionally occurs: shall we consider him responsible for what he did?

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