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Impulsivity trait effects on the cognitive control of actions

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OVERVIEW



The flexible regulation of behavior is a fundamental feature of human cognition and requires efficient cognitive control mechanisms (Braver et al., 2009; Haggard et al., 2008). Cognitive control refers to the ability to regulate and adapt actions and thoughts in accordance to internal goals and environmental changes (Braver, 2012). In studying cognitive control ability, it is of high importance to consider the inter-individual variability (Kanai & Rees, 2011). Indeed, understanding variations due to personality traits have also potential clinical implications. This is a particularly important issue for impulsivity, which is a personality trait highly related to the operation of cognitive control processes, in particular regarding cognitive control of actions and response inhibition (Bari & Robbins, 2013; Franken & Muris, 2006). Despite this, the relationship between impulsivity and cognitive control is still largely unknown (Huang et al., 2017).

The relevance of studying impulsive behavior derives from its negative impact on the lives of individuals and society and for its association with several behavioral disorders and psychiatric conditions (Bari & Robbins, 2013; Fuster, 2008). Deficient control of behavior is in fact a key aspect of impulsivity, which is generally attributed to an impairment of the executive functions (Bari & Robbins, 2013). A typical feature of impulsive behavior is a predisposition toward rapid and unplanned reactions to internal or external stimuli, often resulting in the implementation of premature and

inappropriate actions (Durana & Barnes 1993; Evenden 1999; Moeller et al., 2001; Voon & Dalley, 2016). Trait impulsivity is therefore associated to maladaptive behaviors, as aggression, an increased propensity to engage in risky behaviors and a higher risk of homicide and suicide (Gansler et al. 2009; Moeller et al. 2001; Monahan et al. 2000). Notably, impulsivity is also a core feature of several psychiatric conditions as attention deficit/hyperactivity disorder (ADHD), schizophrenia, drug addiction, and impulse control disorders (e.g. pathological gambling, compulsive eating) (Bari & Robbins, 2013; Gut-Fayand et al., 2001; Jentsch & Taylor, 1999; Nigg, 2001). Investigating cognitive control abilities in healthy individuals with trait impulsivity turns out to be a very relevant issue since it allows to deeper understand mechanisms responsible for the deficient regulation of behavior characteristic of impulsive people, which could also have potential clinical implications.

The aim of the present research was to investigate trait impulsivity effects on the cognitive control of intentional and stimulus-driven actions, analyzing preparatory mechanisms.

A series of three experiments was included. The first two experiments investigated the timing component of intentional actions, analyzing the process between the decision to move and action execution, with behavioral and electrophysiological measures. Instead, the third experiment aims to enriches previous results exploring neural mechanisms involved in the preparation of a stimulus-driven action, with functional Magnetic Resonance Imaging (fMRI) technique.

The aim of the first experiment was to evaluate the relationship between behavioral measures of impulsivity and the awareness of a voluntary action. Seventy-four healthy volunteers underwent an impulsivity trait assessment using the Barratt

Impulsiveness Scale (BIS-11; Patton et al., 1995), performed a go/no-go task (Fillmore et al., 2009) and a behavioral task based on the Libet's clock paradigm (Libet et al., 1983). In particular, the Libet's clock task requires subjects to report the time of a self-initiated movement (M-judgement) and the time they first feel their intention to move (W-judgement). What we found was a positive relationship between the W-judgement and impulsivity measures, that is the higher was the score in the attentional and motor impulsivity subscales of the BIS-11 and the number of inhibitory failure responses in the go/no-go task, the lower was the difference between the W-judgement and the actual movement (i.e. the awareness of intention to move was closer to the voluntary movement execution). In contrast, no relationship emerged with M-judgement. The present findings suggest that impulsivity is related to a delayed awareness of voluntary action. We hypothesize that in impulse control disorders, the short interval between conscious intention and actual movement may interfere with processes underlying the conscious 'veto' of the impending action.

The aim of second experiment was to shed light on the relationship between impulsive personality trait and the timing component of intentional actions, investigating the dynamics of brain potentials related to motor preparation. Indeed, individual differences in the perception of volition and in the 'veto' interval might be related to differences in the Readiness Potential (RP) components. To investigate this hypothesis, 19 healthy participants performed a task based on the Libet's clock paradigm (Libet et al., 1983), during the EEG recording, and underwent an impulsivity trait assessment using the BIS-11 questionnaire (Patton et al., 1995). We observed a positive relationship between impulsive personality trait and motor system excitability during the preparation of self-initiated movements. In particular, the RP showed an

earlier negative rising phase and a greater amplitude, with the increasing of BIS-11 scores. Based on present results, we conclude hypothesizing that trait impulsivity might be characterized by a less effective preparatory inhibition mechanisms, which have a fundamental role in the control of behavior.

The third experiment aimed to deeper understand preparatory top-down control mechanisms in relation to trait impulsivity, analyzing the preparation to a stimulus-driven action. To this purpose, we focused on motor impulsivity component. Compared to the other factors of BIS-11 (Patton et al., 1995), motor impulsivity seems to be more highly related to the efficiency of cognitive control mechanisms in the context of stimulus-driven actions, because of its close relationship to response inhibition, action restraint and premature responding (Bari & Robbins, 2013; Franken & Muris, 2006; Gorlyn et al., 2005; Huang et al., 2017; Keilp et al., 2005; Spinella, 2004). Therefore, twenty-six young healthy adults were administered the BIS-11 questionnaire for the assessment of motor impulsivity trait (Patton et al., 1995) and underwent fMRI acquisition during the execution of an event-related go/no-go task. In order to investigate motor preparation processes, we analyze the ‘readiness’ period, in which subjects were waiting and preparing for the upcoming stimulus (go or no-go). We found no correlation between motor impulsivity scores and the go/no-go behavioral performance, probably because of the specific task design. Conversely, we observed one cluster of significant positive associations, composed by the left postcentral gyrus (PCG), the left precentral gyrus (PRG), the left superior parietal lobule (SPL), the anterior and posterior division of the left supramarginal gyrus (SMG) and the left angular gyrus (AG). The greater sensorimotor activation found in the present study is in line with previous electrophysiological data. We can hypothesize

that this greater sensorimotor activation lateralized to the left hemisphere could be driven by subthreshold right-hand motor responses, as a consequence of a disinhibition of the motor system during the preparation of a movement. Furthermore, the greater activation found in left inferior and superior parietal lobule, might be related to a more effortful proactive control implementation, probably reflecting a compensatory mechanism implemented by participants with higher degree of motor impulsivity trait to reach a correct inhibition. Current findings provide a rationale for further studies aiming to better understand proactive control functioning in healthy impulsive people and in clinical populations.

CHAPTER 1



INTRODUCTION

The flexible regulation of behavior is a fundamental feature of human cognition and requires motor and cognitive control processes (Braver et al., 2009; Haggard et al., 2008). In particular, the ability to adapt our behavior is based on the prediction of potential outcomes, the subsequent comparison between predicted and actual effects and the decision about the need to adapt responses (Haggard et al., 2008). Motor and cognitive control processes are difficult to disentangle (Haggard et al., 2008). When we talk about motor control, we don't refer to the neural and functional 'motoric' mechanisms directly involved in the coordination and implementation of movements (Haggard et al., 2008). Instead, we refer to the 'cognitive' ability to plan and select motor programs on the basis of internal goals and intentions or in a stimulus-driven way (Haggard et al., 2008). For this reason, motor control is strictly related to cognitive control, which is the more general ability to adjust thoughts and actions according to behavioral goals (Braver, 2012). Cognitive and motor control are in turn closely related to executive functions, described as top-down functions involved in the control of behavior, emotion and cognition, which become necessary when going on 'automatic pilot' or acting relying exclusively on instinct or intuition becomes maladaptive, insufficient or impossible (Diamond, 2013; Nigg, 2017).

The majority of studies on cognitive control of actions has focused on bottom-up stimulus-driven processes (Aron, 2011; Di Russo et al., 2016). Only in recent years, has been demonstrated the crucial role of top-down endogenous processes, with which we refer to preparatory mechanisms occurring before acting and showing tight connections with cognitive processing (Aron, 2011; Di Russo et al., 2016; Liebrand et al., 2017). Preparatory activity is a complex process, formed not only by the mere motor preparation mechanism but also by many cognitive processes, which depend on the aspects of the action and its consequences (Aron, 2011; Di Russo et al., 2016).

For this reason, action preparation is not only guided by motor areas, but involved other regions as the prefrontal, parietal and sensory cortices, which are activated in order to adjust responses, relying on the prediction of future events and on the anticipation and prevention of interferences (Aron, 2011; Di Russo et al., 2016). Premotor top-down mechanisms involved in the control of behavior are present both before the implementation of voluntary goal-directed actions, in the form of the so called preparatory inhibition mechanism, and before the execution of stimulus-driven actions, in the form of the proactive inhibitory control mechanism (Duque et al., 2017). Based on recent evidences we can argue that these preparatory and proactive control mechanisms represent the core of cognitive control (Di Russo et al., 2016).

In studying cognitive control of actions, it is of high importance to consider that this cognitive function varies from person to person. Investigating and exploiting individual differences is a common research tradition within psychology (Kanai & Rees, 2011). Using an individual differences approach can indeed provide valuable information that complements and extends findings from group-mean studies, which instead compute an average of behavioral and neural responses across individuals,

treating the inter-individual variation as a source of ‘noise’ (Kanai & Rees, 2011). Furthermore, in measuring and interpreting results about cognitive control abilities we cannot fail to consider the variability due to the impulsive personality trait, given its close relationship with cognitive control process efficiency. Indeed, impulsive personality trait is generally attributed to an impairment of the executive functions, regarding in particular motor control and inhibitory processes (Bari & Robbins, 2013; Franken & Muris, 2006). The presence of an impulsive personality trait can negatively affect the lives of healthy individuals, allowing the execution of purposeless and unproductive actions, which interfere with career goals and social relationships (Bari & Robbins, 2013; Fuster, 2008). Furthermore, impulsive personality trait is associated with aggression, an increased propensity to engage in risky behaviors, a higher risk of homicide and suicide (Gansler et al. 2009; Moeller et al. 2001; Monahan et al. 2000) and is a core feature of several psychiatric conditions as attention deficit/hyperactivity disorder (ADHD), schizophrenia, drug addiction, and impulse control disorders (e.g. pathological gambling, compulsive eating) (Bari & Robbins, 2013; Gut-Fayand et al., 2001; Jentsch & Taylor, 1999; Nigg, 2001). For these reasons, investigating cognitive control abilities in healthy subjects with impulsivity trait turns out to be a very relevant issue since it allows to deeper understand mechanisms responsible for the deficient regulation of behavior characteristic of impulsive people, which could also have potential clinical implications.

CHAPTER 2



COGNITIVE CONTROL OF INTENTIONAL ACTIONS

Motor responses lie on a continuum between voluntary actions and simple reflexes at the extremities (Haggard, 2008). While reflexes are defined as immediate motor responses, voluntary actions are characterized by a ‘freedom from immediacy’ and involve two subjective experiences, which are absent in reflexes (Shadlen & Gold, 2004). These experiences are the ‘intention’, which refers to the condition of planning or being about to do something and the ‘sense of agency’, that is the feeling of having the control over one’s own behavior (Haggard, 2008). Hence, a movement is perceived as voluntary when is preceded and motivated by a conscious experience of intending to act and when is associated with a vivid sense of control over it (Haggard, 2008). An internal event that causes a movement could be an inner impulse or urge, described also as a “pre-conceptual movement of the mind” (Jo et al., 2015; Figure 1). This impulse might be considered the first step of the gradual phenomenon of consciousness observed during the preparation of a voluntary movement (Jo et al., 2015). If this urge is subtle, it may be difficult to experience it or it may not enter awareness (Jo et al., 2015). Sometimes, instead, this inner impulse is so strong that subjects have difficulty in restrain from action execution (i.e. addictive behaviors, impulse control disorders, autonomic behaviors to avoid imminent danger to life) (Jo et al., 2015). When this pre-conceptual impulse is combined with a personal goal, it forms an *intention* (conceptual

level) (Jo et al., 2015). Whether to commit this intention is then determined by the latest *decision* process, also known as the ‘late whether decision’ of the Haggard model about volition (2008), discussed below (Haggard, 2008). Thus, realizing to stand for a voluntary movement might start when we become aware of the inner impulse (Jo et al., 2015).

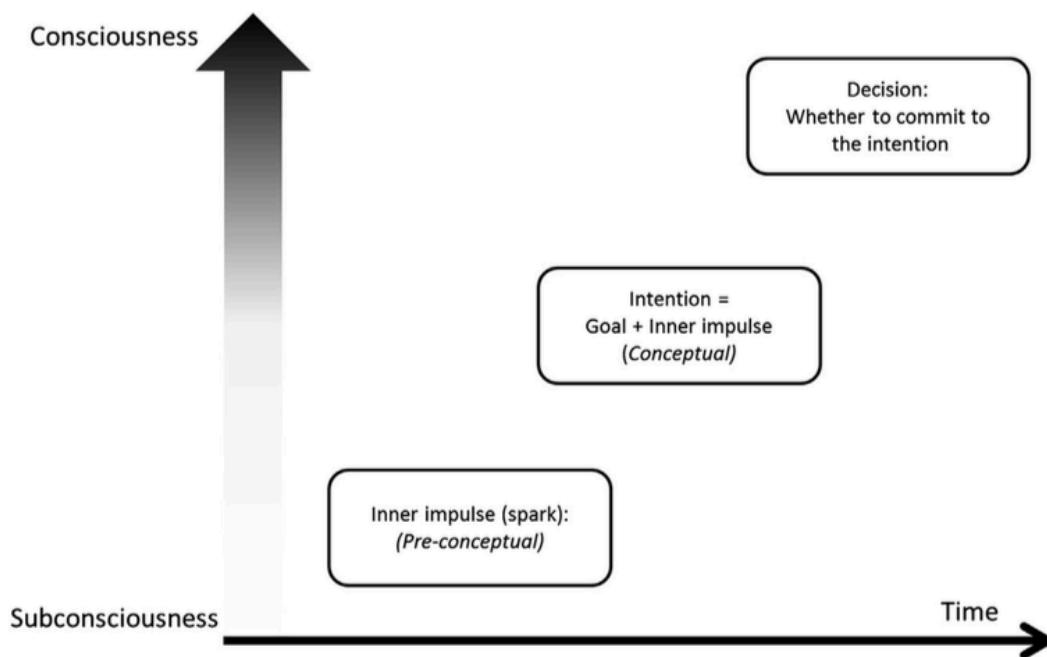


Figure 1. A graphic representation of the gradual phenomenon of consciousness during the preparation of a voluntary movement (Jo et al., 2015).

2.1 The ‘www-model’ of intentional actions

Beyond the decision about whether to execute an intended action, the process of implementing a voluntary action is made up of the decision about when to act and what action to perform (Brass & Haggard, 2008; Haggard, 2008). For this reason, it is considered a form of decision making (Haggard, 2008). These three decisions, each of

which specifies different details about the action, are the three components of the ‘What, When, and Whether model’, or simply ‘www-model’, of intentionality, first proposed by Jahanshahi in 1998, and then implemented by Brass & Haggard in 2008 (Figure 2).

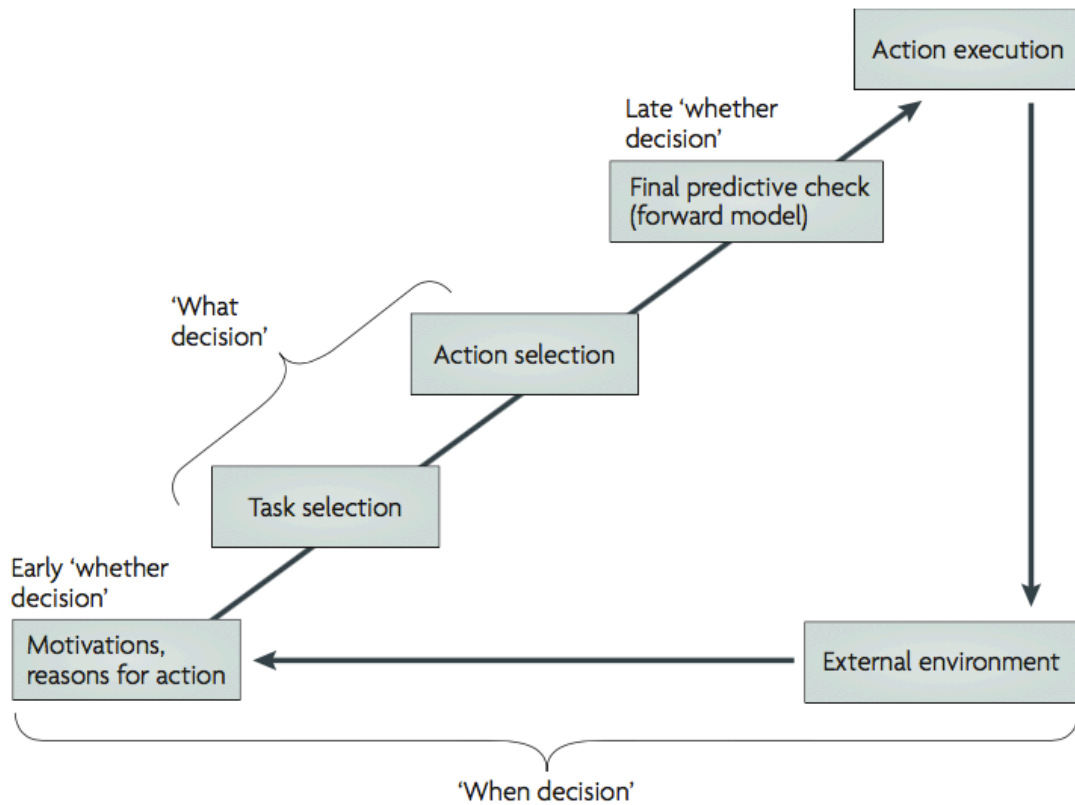


Figure 2. A graphic representation of the ‘www-model’ of intentionality (Haggard, 2008).

In particular, the *What* component of intentionality refers to the content of an action, that is the decision about which action to perform (Brass & Haggard, 2008). This component is composed by two forms of decision, that is the earlier ‘goal selection’ and the later ‘movement selection’ (Haggard, 2008). The first refers to the choice between different goals (or tasks) and the second to the choice between different possible actions to perform in order to achieve the goals (Haggard, 2008).

The *When* component of intentionality refers to the timing of intentional actions, that is the decision about when to perform the selected action (Brass & Haggard, 2008). In everyday life, the decision about when to perform an action usually depends on the combination between internal motivations and external circumstances and on the coordination with other actions and routine processes (Haggard, 2008). In the laboratory context, the *When* decision has become an important experimental tool (Haggard, 2008). Experimenters usually compare conditions in which participants decide when to perform a voluntary action and conditions in which they perform the action at a fixed time, that is in response of a stimulus (stimulus-driven actions) (Haggard, 2008).

The *Whether* component of intentionality refers to the choice between the action execution and the intentional inhibition of the action itself (Brass & Haggard, 2008). According to the model of Haggard (2008), this decision has an early and a late component. The early component reflects the first decision to make any action at all, based on needs, desires or other motivations for action (Haggard, 2008). The late component exerts its role after the action selection process (*What* decision) and before the action execution (Haggard, 2008). This late component reflects a ‘final predictive check’ before the commitment of the motor system (Haggard, 2008). In particular, the *What* decision send information which activate motor outputs (Haggard, 2008). This detailed information about the oncoming voluntary action were not available at the time of the early *Whether* decision. The function of the late *Whether* decision is to make a check on these information in order to verify if the upcoming selected action is still suitable to achieve the selected goal (Haggard, 2008; Miall & Wolpert, 1996). This process is of fundamental importance since the selected action might turn out to

have too high costs, or it might not be appropriate to achieve the goal because of a change in the environment or in the task. If the selected action turns out not to be suitable to achieve the goal, the checking process correct it or cancel it, exerting a ‘veto’ (Haggard, 2008). This decision might have a critical role in the control of behavior.

For what concern the neural underpinnings of intentionality, Jahanshahi in 1998 proposed a ‘unitary’ neural system behind all different components of intentionality. This system comprised the pre-frontal cortex (PFC), the anterior cingulate cortex (ACC) and the supplementary motor area (SMA), receiving inputs from the striatum, through the thalamus (Jahanshahi, 1998). Instead, according to the vision of Brass & Haggard (2008) the components of intentional actions are partially independent both at a cognitive and a neural level. Authors identified a distributed meso-frontal system, which is activated differentially for the content, the timing and the possibility of generating an intentional action (Brass & Haggard, 2008). Recently, Zapparoli and colleagues (2017) in their meta-analytical review, corroborate the existence of a multi-component neural model of intentionality, which expands the www-model of Brass & Haggard (2008) going beyond the mesial wall of the frontal lobe. In particular, authors identified a ‘rostro-caudal gradient’ within the medial prefrontal cortex, with more anterior regions involved in the *Whether* decisions and more posterior regions involved in the *What* and *When* components of intentionality (Zapparoli et al., 2017). In particular, for what concern the *What* component they found activations in the middle part of the right cingulum, a region typically involved in conflict processing and monitoring (Botvinick et al., 2004; Carter & van Veen, 2007; Zapparoli et al., 2017). Regarding the *When* component, they found a cluster in the right SMA (Zapparoli et

al., 2017). This result is supported by studies on Parkinson's disease (PD), which is characterized by a deficit in the timing of intentional action and in the awareness of the intention to move (Brass & Haggard, 2008; Tabu et al., 2015). With regard to the *Whether* component, instead, they identified a cluster in the anterior part of the right cingulum (Zapparoli et al., 2017). Beyond this meso-frontal system, Zapparoli and colleagues (2017) identified other regions which are differently activated for the three components of intentional actions. For the content of actions, they found clusters in the right supramarginal gyrus, a result corroborated also by the previous findings about the role of the inferior parietal lobule in the representations of actions and intentions and in the motor awareness (Desmurget et al., 2009; Gallivan et al., 2011; Tunick et al., 2007; Zapparoli et al., 2017). The timing component of intentionality is instead related to the activation of the pallidum, a structure involved in the regulation of voluntary movements, the frontal operculum, implicated in the synchronization of intentional movements, the lenticular nuclei and the thalamus (Graybiel, 1998; Thaut, 2003; Zapparoli et al., 2017). For what concern the probability to generate an action, data clustered at the level of the thalamus, the putamen and the right anterior insula (Zapparoli et al., 2017). The basal ganglia, in general, are known to be involved in action selection and inhibition (Humphries & Gurney, 2002; Humphries et al., 2006) and a dysfunction of these structures are present in pathologies characterized by movement disorders, as Gilles de la Tourette Syndrome and obsessive-compulsive disorder (OCD) (Bandelow et al., 2016; Felling & Singer, 2011; Ganos et al., 2013; Leckman et al., 2010; Mink, 2006; Zapparoli et al., 2015). Instead, anterior insula has been previously associated to response inhibition, concentration and cognitive effort (Allen et al., 2007; Wager et al., 2005).

2.2 Free will and sense of agency

A movement is perceived as voluntary or ‘freely willed’ when is preceded and motivated by a conscious intention or *will* and when is associated with a vivid sense of control, or agency, over it (Haggard, 2008). The concept of free will is, therefore, hard to define and is a matter of study and debate for many disciplines (Batthyany, 2009; Deutschländer et al., 2017; Haggard, 2008; Kane, 2005; Lavazza, 2016; Libet et al., 1983; Mele, 2009; Wegner, 2002). Indeed, until half a century ago the debate around this topic was confined in the field of philosophy, becoming later a matter of study also for neuroscientists, first in time and by relevance Benjamin Libet, which first questioned the existence of free will (Lavazza, 2016). The term *will* is a synonymous of intention, choice or decision, and it can be experienced consciously or unconsciously (Klemm, 2010). The term *free*, instead, implies a conscious causation, that is a condition in which an intention, choice, or decision is made among alternatives without external or internal constraints (Klemm, 2010). The awareness of the *will* give rise to the conscious experience of having control over one’s behavior.

Another way to define free will is considering the presence of three conditions (Walter, 2001). The first condition is the “ability to do otherwise”, which define an individual as free when he has the possibility to choose between at least two alternatives of action (Lavazza, 2016; Walter, 2001). According to the second condition, that is “responsiveness to reasons”, an individual is considered free when he makes decisions on the base of a rational motivation, and not as consequence of a random choice (Lavazza, 2016; Walter, 2001). The third condition, named “control over one’s choices”, refers to the sense of agency (Lavazza, 2016; Walter, 2001).

According to this condition, an individual is free when he is the author of his choices and his behavior, without the interference of external factors (Lavazza, 2016; Walter, 2001). In this sense, sense of agency refers to the feeling of being the owner of one's decisions and actions and, for this reason, has a crucial role in our social behavior (Chambon et al., 2014; Chambon & Haggard, 2012; Haggard, 2017; Haggard & Tsakiris, 2009). Our society depends on the idea that individuals are responsible for their own actions and for their consequences, that is they consciously intend particular outcomes, and that their actions reflect those intentions (Haggard, 2017; Lavazza, 2016; Lavazza & Inglese, 2015). For this reason, agency is a fundamental component of conscious free will: our belief in free will arises because we strongly feel that we control our own behavior (Frith, 2013). We tend to attribute free will to all humans as a default condition, since we believe in the theory that people have the ability to decide freely and, therefore, that they are responsible for their actions (Lavazza, 2016; Nahmias et al., 2007). Failures in the experience of agency, which undermine our belief in free will, have relevant repercussions on our society: if I cannot be considered 'free' to act, then I cannot even be held responsible for what I do (Lavazza, 2016). Abnormal sense of agency is recognized as one key symptom of some mental disorders (e.g. schizophrenia) but also in healthy people sense of agency can be easily fooled, in that it can be over- or under-estimated, producing aberrant and unwanted actions and leading people to incorrectly think about their control capabilities (Haggard, 2017; Saito et al., 2015).

The experience of control we normally feel about our everyday actions results from a balanced mixture of prospective and retrospective mechanisms within the intention-action-outcome chain (Chambon et al., 2014; Chambon & Haggard, 2012;

Sidarus & Haggard, 2016). Both prospective and retrospective mechanisms involve the monitoring of action related signals and their comparison with other relevant information for consistency (Moore et al., 2009). The connection between intention and action outcome is the basis of our experience of agency (Sidarus & Haggard, 2016). The encoding of mismatches between intentions and action outcomes is fundamental to prevent aberrant and unwanted actions. Agency can be inferred retrospectively, after an action has been performed, by matching predicted and actually experienced consequences of the action (Chambon et al., 2014; Chambon & Haggard, 2012; Sidarus & Haggard, 2016). In this framework, agency depends on how predictable the consequences of one's action are, getting stronger when the match between the predicted and the experienced consequences of an action gets closer (Chambon et al., 2014). Agency relies also on real-time, prospective signals arising from internal circuits of action preparation (Chambon et al., 2014; Chambon & Haggard, 2012; Sidarus & Haggard, 2016; Wenke et al., 2010). In this framework, an unconscious subjective sensation of control is generated in advance of the action itself, within the action selection process in which intentions are transformed into specific actions to achieve desired effects (Chambon et al., 2014). This mechanism continuously monitors the action selection process, matching action intentions with ongoing action related signals and checking the compatibility relying on the process fluency (Chambon et al., 2014). Signals sent by this monitoring mechanism could serve as advance predictors of successful actions (Chambon & Haggard, 2012) and may provide the subject with an important 'on-line' marker of control as the action is unfolding and, therefore, a marker of volition (Chambon et al., 2013; Chambon et al., 2014). This sensation of control is achieved without the need to wait until sensory

feedback becomes available and may protect against aberrant experiences of agency and xenopathic experiences, like loss of control over one's actions and thoughts (Chambon et al., 2014). Prospective signals could therefore prevent delusions of volition arising from excessive reliance on post hoc judgments of action-effect associations (as occurs in schizophrenic 'delusions of control') (Voss et al., 2010). At the same time, an excessive reliance on these prospective signals may produce the opposite delusion of omnipotence, in which the mere decision to act is incorrectly assumed to produce successful action outcomes (Chambon et al., 2014). Neuroimaging studies investigating the prospective sense of agency show the critical role of the angular gyrus (AG) in prospective and retrospective sense of agency (Chambon et al., 2013; Wenke et al., 2010). Ventral AG seems to be involved in retrospective comparison between predicted and actual consequences of actions (Farrer et al., 2008), while dorsal AG seems to be involved in detecting mismatch between intention and action, independent of action outcomes (Chambon et al., 2012). Prospective sense of agency is accounted for by exchange of signals across a prefrontal-parietal network: AG monitor fluency or dysfluency action signals coming from the DLPFC to construct an experience of agency prior to actions and their outcomes, providing the subject with an on-line, subjective marker of volition (Chambon et al., 2012; Chambon et al., 2013; Frith et al., 1991; Wenke et al., 2010).

2.3 Measuring volition

In the laboratory context, voluntary actions are usually contrasted with stimulus-driven actions (Haggard, 2008). Intentional actions are independent from stimulus, a

characteristic that makes them difficult to study, since experimental studies are generally based on the release of a known input or stimulus and the measurement of the system's response. To overcome this problem, in studies measuring volition, subject performance is only partially determined by the stimulus or by the instructions, while one of the component of intentional actions remain 'free': the participant can decide *when* to perform a fixed action (Libet et al., 1983); at a fixed time, the participant can choose which action to perform ('*what*') between at least two different possibilities (Frith et al., 1991; Haggard & Eimer, 1999; Shadlen & Gold, 2004); the participant can decide *whether* or not to perform a fixed action (Brass & Haggard, 2007; Libet et al., 1983). The timing component of intentional actions ('*when*') was first studied by Benjamin Libet and colleagues in 1983. With his well-known paradigm, Libet measured for the first time the relationship between the onset of the neural activity related to the preparation of a voluntary movement and the timing of the conscious intention to move. Participants had to watch a rotating clock and make self-paced finger movements during EEG recording. After each movement, participants had to report the clock hand position at the time at which they first felt the *conscious awareness of wanting* to move (Libet et al., 1983). Libet found that the onset of the neural activity related to the preparation of voluntary movements preceded the awareness of the intention to move by 350 ms and the actual movement by 500 ms on average, opening the debate about the existence of free will. The fact that our conscious intention or decision to make a voluntary movement resulted to follow the onset of the brain activity related to the movement, led to the hypothesis that our decisions and, therefore, our freedom, are illusory (Lavazza, 2016).

Libet studies had a great impact on our concepts of volition, freedom and responsibility, and represent one of the main arguments against the existence of free will (Guggisberg & Mottaz, 2013; Lavazza, 2016). We have the conviction that our actions are a consequence of our intentions and desires and we take it for granted that our decisions and actions are influenced by the content of our consciousness (Guggisberg & Mottaz, 2013). Instead, according to Libet studies our actions are determined by unconscious neural processes while consciousness represents only a late secondary effect of neural processing, with no influence on our decisions and actions (Guggisberg & Mottaz, 2013). On the other hand, Libet himself (2009) suggested the presence of a ‘free won’t’, that is after becoming aware of the intention to act, the upcoming action can be ‘freely’ and intentionally inhibited before its implementation. Indeed, the interval between the conscious intention and the movement onset seems to be sufficient to allow a conscious ‘veto’ of the impending action (Brass & Haggard, 2007; Kühn et al., 2009; Matsushashi & Hallett, 2008; Walsh et al., 2010). Recently, it was found that this vetoing can be exerted until a ‘point of no return’, after which the initiation of an action cannot be cancelled (Schultze-Kraft et al., 2016). This ‘free won’t’ process ‘saves’, in a way, the concept of moral responsibility, though the issue about conscious veto and free won’t is as problematic as the one about conscious intention and free will, since even the veto could be a consequence of unconscious neural processes (Haggard, 2008; Velmans, 2007).

2.4 The Readiness Potential as a marker for the onset of neural movement preparation

The neural activity observed before the preparation of a voluntary movement is referred as Readiness Potential (RP; Vaughan et al., 1968) and was first reported by Kornhuber and Deecke in 1965 as the *Bereitschaftspotential* (Deecke, 2014; Deecke & Kornhuber, 1978; Deecke et al., 1969; Deecke et al., 1976; Libet et al., 1983; Cui et al., 1999). The RP represents the earliest component of the motor-related cortical potential (MRCP), and is defined as a slow negative build-up of scalp electrical potential originating in frontal-central areas up to 2 seconds before the onset of spontaneous self-initiated movements. This early component of MRCP reflects a slow increasing in excitability over supplementary motor areas and has been associated with a preconscious readiness for the upcoming action. The latest component of the MRCP, named NS or late RP, starts from 400-500 ms before the movement onset and is defined as a more rapidly increase in excitability of premotor and motor areas, reflecting in a steeper negative slope. This latest RP component is often associated to the moment of the motor preparation in which the conscious decision to move occurs. At the time of movement onset, electrocortical activity performs a negative peak, named motor potential (MP) component, originating in the primary motor cortex (M1). After this negative peak, neural activity rapidly forms a positive peak, called re-afferent potential (RAP), at around 200-300 ms after movement onset. This positive potential is associated to afferent somatosensory inputs and is produced by the activity in the primary somatosensorial area (S1).

The original interpretation refers to the RP as the “electro-physiological sign of planning, preparation, and initiation of volitional acts” (Kornhuber & Deecke, 1965) and as a preconscious readiness for the upcoming action (Kornhuber & Deecke, 1965). Therefore, the observation of Libet and colleagues that RP related brain areas activated before the awareness of the movement onset has been interpreted as a “deflation of freedom” (Lavazza, 2016; Soon et al., 2008), concluding that free will is just an illusion.

New interpretations about the nature of the RP are arising in recent years (for a review see Schmidt et al., 2016). The main one is the Selective Action-Related Slow Cortical Potential Sampling Hypothesis, or just SCP Sampling Hypothesis (Schmidt et al., 2016), which consider the RP reflecting the ebb and flow of the background neuronal noise. According to this hypothesis, fluctuations of Slow Cortical Potentials (SCPs) are of fundamental importance in the stimulation of spontaneous voluntary movements, because they unconsciously modulate the reactivity threshold and influence the time at which the neural decision threshold is exceeded (Schmidt et al., 2016). Indeed, actions are more likely to be carried out in the negativity phase of SCPs, that is in the rising and in the negative crest phase of the potential, with respect to the falling phase and the positive through (Jo et al., 2013). For this reason, fluctuations of SCPs show the specific RP pattern when recorded time-locked to movement onset (Birbaumer et al., 1990; Schmidt et al., 2016). Moreover, the negativity phase of SCPs is experienced with a subjective sensation of an ‘urge to move now’ (Schmidt et al., 2016). The presence of a sub-threshold inappropriate ‘urge to move’ intention or impulse does not always turn into a behavioral inappropriate response. Indeed, in 15-25% of trials with correct overt responses there are ‘partial errors’ that remain under

threshold (van den Wildenberg et al., 2010). In this case, these covert errors are expression of impulses but they do not turn into overt errors. The supplementary motor complex (SMC), and in particular the pre-SMA, has a key role in this control mechanism, in that it suppresses on-line the sub-threshold activated responses, preventing it from turning into overt errors (Spieser et al., 2015).

2.5 Preparatory inhibition mechanism

Motor preparation involves the recruitment of excitatory and inhibitory neural mechanisms (Greenhouse et al., 2015). Inhibition processes are, therefore, implemented not only when a movement needs to be cancelled after a stop signal ('reactive inhibition'), but also during the preparation of voluntary or stimulus-driven movements (Duque et al., 2017). Specifically, when inhibition of the motor system occurs in anticipation of a stop signal and, therefore, in the context of stimulus-driven actions, we refer to 'proactive inhibition'. Instead, the suppression of corticospinal excitability occurring during the preparation of a voluntary movement is called 'preparatory inhibition' (Davranche et al., 2007; Duque & Ivry, 2009; Duque et al., 2010, 2012, 2017; Elswijk et al., 2007; Greenhouse et al., 2015; Hasbroucq et al., 1997, 1999a, b; Soto et al., 2010; Touge et al., 1998; van Sinclair & Hammond, 2009). However, this differentiation is not present in all studies. Probably because proactive inhibition is an emerging theme in the inhibitory control research, are not yet well specified commonality and differences in the functional role and in neural mechanisms between proactive and preparatory inhibition.

Focusing on literature about preparatory inhibition, the suppression of corticospinal excitability found before the initiation of a movement has led to several hypotheses regarding its functional role during action preparation (Duque et al., 2017).

One hypothesis suggest that preparatory inhibition serves to assist action selection (Bestmann & Duque, 2016). A variant of this idea is the ‘competition resolution’ model, according to which the role of preparatory inhibition is to assist action selection through a competitive process, which suppresses competing response representations, facilitating response selection and assisting in determining which response to make (Coles et al., 1985; Duque et al., 2010, 2017; Usher & McClelland, 2001, 2004). Therefore, according to this model, the implementation of the selected response relies on the suppression of the non-selected action representation (Tandonnet et al., 2011; van der Wildenberg et al., 2010). Instead, another variant of the action selection hypothesis, named ‘impulse control’ model, suggests a global suppression of motor representations in order to prevent the selection of inappropriate action representations (Duque & Ivry, 2009; Duque et al., 2017).

A second hypothesis have focused on the regulation of action initiation, suggesting that preparatory inhibition serves to prevent selected muscles from becoming prematurely active (Duque et al., 2010; Labruna et al., 2014).

According to a third, hybrid hypothesis, the role of preparatory inhibition might be to modulate the gain of the motor system, allowing to increase the signal-to-noise ratio associate with a selected action, decreasing background activity and increasing neuronal sensitivity to excitatory drive (Chance et al., 2002; Churchland et al., 2006; Greenhouse et al., 2015; Hasbroucq et al., 1997).

Relevant signs of inhibition have been observed from investigations of corticospinal excitability during motor behavior (Duque et al., 2017). TMS studies have found the presence of inhibitory interactions between M1 in the two hemispheres and inhibitory projections from several frontal regions and from the cerebellum to M1 (Celnik, 2015; Neubert et al., 2010; Wischniewski et al., 2016). Furthermore, a role in the corticospinal inhibition associated to the preparation of voluntary movements might be played by the subthalamic nucleus (STN), which has a relevant role in the inhibition related to action stopping, since it has been found to generate motor inhibition to set the threshold for action selection (Aron et al., 2016; Duque et al., 2017; Herz et al., 2016).

The functional role of preparatory inhibition, however, is still matter of debate and the source of the corticospinal inhibition is not yet clearly identified. Furthermore, future studies are required to better understand the relationship between preparatory and proactive motor inhibition in terms of functional role and neural substrates.

CHAPTER 3



IMPULSIVITY TRAIT EFFECTS ON THE COGNITIVE CONTROL OF INTENTIONAL ACTIONS

In studying motor control ability, it is of high importance to consider the inter-individual variability. Understanding variations in the cognitive control of actions due to personality traits have also potential clinical implications. A personality trait closely related to the operation of cognitive control processes is the impulsive personality trait, which is generally attributed to an impairment of the executive functions, regarding in particular motor control and the inhibitory processes (Bari & Robbins, 2013; Franken & Muris, 2006). However, the relationship between impulsivity and cognitive control is still largely unknown (Huang et al., 2017).

Impulsive personality trait is defined as a predisposition toward rapid and unplanned reactions to internal or external stimuli, without adequate forethought, often resulting in inappropriate and premature actions (Durana & Barnes 1993; Evenden 1999; Moeller et al., 2001; Voon & Dalley, 2016). Trait impulsivity represents a multidimensional construct, mediated by distinct psychological and neural mechanisms (Aichert et al., 2012; Barratt et al., 1987; Buss & Plomin, 1975; Dalley & Robbins, 2017; Eysenck & Eysenck, 1977; Gerbing et al., 1987; Pietrzak et al., 2008).

We can broadly divide trait impulsivity in ‘motor’ and ‘decisional’ subtypes (Voon & Dalley, 2016).

Motor impulsivity reflects a failure in response inhibition and includes ‘waiting impulsivity’, which is related to action restraint prior to movement initiation, and ‘stopping impulsivity’, which refers to the reactive inhibition of a prepotent response after movement initiation (Dalley & Robbins, 2017). Motoric forms of impulsivity can be assessed using tasks like the go/no-go (GNG) and the stop-signal task (SST) (Dalley & Robbins, 2017). The GNG typically measure premature responding (waiting impulsivity), whereas the SST measure the ability to stop an already started action (stopping impulsivity) (Dalley & Robbins, 2017).

Decisional impulsivity, instead, includes ‘reflection impulsivity’ or ‘impulsive choice’, which refers to the tendency to make rapid decisions without adequate forethought, and ‘delay discounting’, which is related to the tendency to select smaller-sooner rewards over larger-later rewards, because of a discount or devalue of future long-term outcomes (Dalley & Robbins, 2017). Decisional impulsivity is therefore related to difficulties in delaying gratification or exerting self-control, reflecting an impaired goal-oriented behavior, and is measured behaviorally with the delay-discounting task (Dalley & Robbins, 2017).

In addition to the objective measures, the heterogeneity of impulsivity is also captured by self-report inventories. The most used questionnaire for assessing impulsivity is the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995). The BIS-11 measures also three sub-components of impulsivity, named ‘motor impulsivity’, that is the tendency to act without thinking, ‘attentional impulsivity’, referring to the readiness to make quick cognitive decisions and ‘non-planning impulsivity’, which

refers to the degree of focus on only the present (Patton et al., 1995). In particular, subjects are asked to respond to a list of statements selecting the most appropriate answer from: “rarely/never”; “occasionally”; “often”; “almost always/always”. For example, motor impulsivity may be evaluated using responses to sentences as “I do things without thinking”; “I act on impulse”; “I make up my mind quickly”; or “I am happy-go-lucky”. Attentional impulsivity is assessed using items as “I ‘squirm’ at plays and lectures”; “I don’t pay attention”; or “I often have extraneous thoughts when thinking”. In addition, non-planning impulsivity can be evaluated using responses to sentences as “I plan tasks carefully”; “I am self-controlled”; “I save regularly”; or “I am more interested in the present than in the future”.

Although some of these dimensions of impulsivity are related to each other, suggesting overlapping neural mechanisms, often instead they do not inter-correlate or even they are dissociated, pointing to a possible relative independence of a part of these underlying neural mechanisms (Dalley & Robbins, 2017; Green & Myerson, 2013). Indeed, impulsive behavior seems to be mediated by dynamic networks. Striatal interactions with the prefrontal cortex (PFC) and the hippocampus, with neuromodulation by the ascending monoamine system, appears to be central to impulsivity (Dalley & Robbins, 2017; Dalley et al., 2011). In particular, the striatum operates within a complex network, which includes basal ganglia and ‘top-down’ influences from limbic structures and the neocortex, including PFC, and ‘bottom-up’ modulation from monoamine systems comprising the dopaminergic system (Dalley & Robbins, 2017; Dalley et al., 2011).

The relevance of studying impulsive behavior derives from its impact on the lives of individuals and society. Indeed, the presence of an impulsivity trait can

negatively affect the lives of healthy individuals, allowing the execution of purposeless and unproductive actions, which interfere with career goals and social relationships (Bari & Robbins, 2013; Fuster, 2008). Furthermore, impulsive personality trait is associated with aggression, an increased propensity to engage in risky behaviors, a higher risk of homicide and suicide (Gansler et al. 2009; Moeller et al. 2001; Monahan et al. 2000), and is a core feature of several psychiatric conditions as attention deficit/hyperactivity disorder (ADHD), schizophrenia, drug addiction, and impulse control disorders (e.g. pathological gambling, compulsive eating) (Bari & Robbins, 2013; Gut-Fayand et al., 2001; Jentsch & Taylor, 1999; Nigg, 2001).

3.1 Experiment 1 - Relationship between impulsivity traits and awareness of motor intention

3.1.1 Introduction

Electrophysiological and neuroimaging studies suggest that our actions are initiated by unconscious mental processes long before awareness of intention to act (Haggard, 2008; Hallett, 2007, 2016; Libet et al., 1983; Soon et al., 2008). However, the interval between conscious intention and movement onset seems to be sufficient to allow a conscious ‘veto’ of the impending action (Brass & Haggard, 2007; Kühn et al., 2009; Matsushashi & Hallett, 2008; Walsh et al., 2010). It has been hypothesized that such an inhibition process may occur after the intention to perform an action has become conscious (Libet, 2009). This vetoing can be exerted until a ‘point of no

return', after which the initiation of an action cannot be cancelled (Schultze-Kraft et al., 2016).

The term 'intentional inhibition' refers to the ability to voluntarily suspend or inhibit an action and has been proposed as a core process of self-control (Filevich et al., 2012). Although the neural substrate of intentional inhibition is still under investigation (Filevich et al., 2012), a brain network including at cortical level the pre-supplementary motor area (preSMA) and the dorsal fronto-median cortex (dFMC) has been reported to be involved when subjects had to intentionally stop an impulsive response (Brass & Haggard, 2007; Kühn et al., 2009).

Deficient voluntary control of action and intentional inhibition are key aspects of impulsive behavior. Impulsivity represents a broad concept that includes the inability to inhibit or control actions regardless the consequences, the abnormality in decision making, and an increased propensity to engage in risky behaviors (Bari & Robbins, 2013). Impulsivity traits, along with lack of self-control and behavioral inhibition, characterize a number of psychiatric conditions such as attention deficit/hyperactivity disorder, drug addiction, schizophrenia, and impulse control disorders (e.g. pathological gambling, hypersexuality, compulsive eating and shopping) (Bari & Robbins, 2013).

In this framework, the time in which awareness of the intention to act occurs may represent a crucial aspect for an efficient intentional inhibition process at the individual level. The objective of the present study was to evaluate the relationship between impulsive personality traits and the awareness of the intention to move. To this aim, 74 healthy participants performed a behavioral task based on the Libet's clock paradigm and underwent an impulsivity traits and inhibitory control assessment. We

hypothesized that impulsivity could be related to a delayed awareness of voluntary action, i.e. conscious intention to move closer to the actual execution of a self-initiated movement.

3.1.2 Materials and methods

Participants

Seventy-four healthy volunteers (54 women; mean age 24.8 years, range 19–48) with no history of neurological and psychiatric disease or drug abuse, normal hearing and normal or corrected-to-normal vision were included in the study. Participants were mainly recruited from the Psychology students community of the University of Florence.

All participants gave their written informed consent to the procedure and the processing of personal data. All data were collected and processed anonymously. Prior to the evaluation, each subject was blind to the purpose of the study, which was carefully explained after the completion of the evaluation. Approval of the ethical aspects was provided by an internal Committee of the Psychology section of the Department of Neuroscience, Psychology, Drug Research, Child Health of the University of Florence.

Impulsivity and inhibitory control assessment

All participants completed the Barratt Impulsiveness Scale (BIS-11), a 30-item self-report questionnaire widely used to measure impulsive personality traits (Patton et al., 1995). Each item is measured on a 4-point Likert scale, with higher values

indicating greater impulsivity (Patton et al., 1995). The BIS includes three subscales: (1) readiness to make quick cognitive decisions (attentional impulsivity), (2) tendency to act without thinking (motor impulsivity), and (3) degree of focus on only the present (non-planning impulsivity).

The inhibitory control was measured by the visual cued go/no-go task (Fillmore et al., 2009) (see also www.impulsivity.org). The participant sat at a distance of approximately 50 cm from the center of a computer screen. Visual stimuli consisted of rectangles (7.5 x 2.5 cm). Subjects were instructed to push a button on the keyboard (spacebar) with the index finger of the dominant hand, as soon as a 'go' target (green rectangle) appeared and to suppress the response when a no-go target (blue rectangle) was presented. The task consisted of 250 trials. In each trial, the preliminary 'go' or 'no-go' cues (white vertical or horizontal rectangle respectively) were displayed immediately before the actual 'go' or 'no-go' target stimuli. The cues provided information on the probability that a 'go' or 'no-go' target was presented. Namely, in the 'go' cue condition 'no-go' target was 20% (25 trials), whereas in the 'no-go' condition 'no-go' target was 80% (100 trials).

Cue stimuli were displayed with a random duration between 100 and 500 ms and were preceded by a fixation point for 800 ms. The duration of the target stimuli was 1000 ms. Software E-PRIME 1.2 (Psychology Software Tools, Inc., Sharpsburg, PA, USA) was used for stimuli presentation and response recording. The proportion of inhibitory failures (i.e. percentage of response after a 'no-go' target) and the reaction times in the 'go' target were used as measures of inhibitory control.

Libet's clock task

The task was based on the original clock paradigm created by Libet et al. (1983) (Figure 3). Participants sat in front of a computer screen with the index finger of their dominant hand on a keyboard. An analogical clock (diameter 4 cm, marked with conventional intervals from 0 to 55 in steps of five units) with a hand rotating clockwise with a revolution period of 2560 ms was displayed on the center of the screen. At each trial, the initial clock hand position was random.

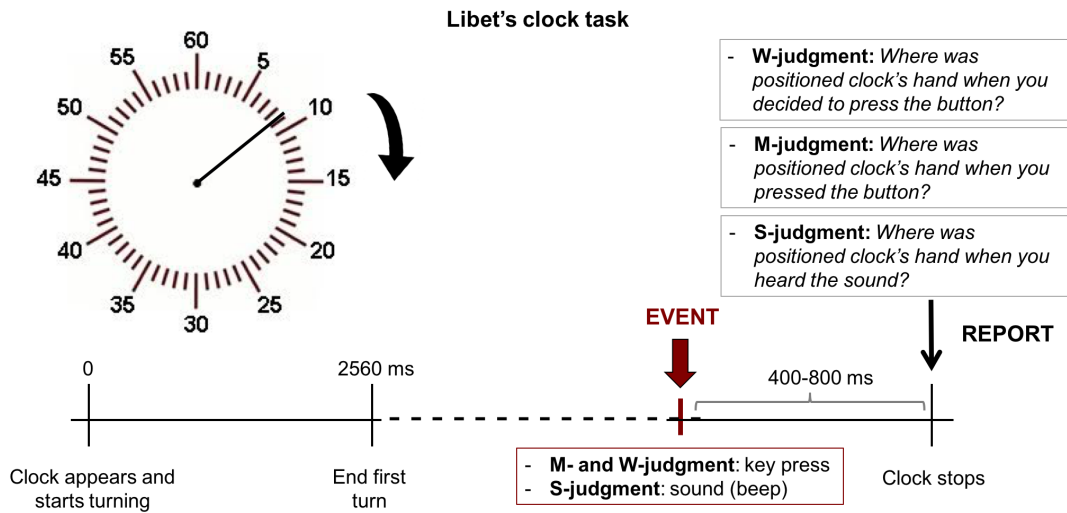


Figure 3. Schematic representation of the Libet's clock task used in our study

The task consisted of three experimental conditions performed in separate blocks: movement (M), 'wanting to move' (W), and stimulus (S) judgement. In the M and W judgement conditions participants were instructed to focus their attention on the actual onset of a movement or to their intentional decision to move. Namely they were requested to press the key by their index finger whenever they want. They were instructed to avoid planned or pre-decided responses and not to push the button before the clock hand completed the first round. After each trial, subjects had to report as

accurately as possible, the position of the clock's hand at the time they perform the actual key press (M-judgement) and the time they first feel (become aware) their intention to move (W-judgement). As a control condition to assess the ability to estimate time events, subjects were asked to report the clock's hand position when an acoustic tone was randomly delivered by headphones (S-judgement). After each event (key press or tone presentation), the clock hand stopped the rotation at a random interval between 400 and 800 ms. Each block consisted of 30 trials. The experimental phase was preceded by a practice session. The order of the three experimental blocks was randomized and counterbalanced across subjects.

3.1.3 Data analysis

The measure used to quantify the behavioral performance in the Libet's clock task was the differences between the time in which subjects reported the movement execution (M-judgement) or the intention to move (W-judgement) and the time in which they performed the actual key press.

Separately for each individual, M-judgement and W-judgement values were normalized to control condition (S-judgement) and expressed as z-scores using the formula: $z = (A - B)/SD_s$, where A and B are the individual time values in the experimental (M-judgement or W-judgement) and control (S-judgement) conditions, respectively, while SD_s is the individual standard deviation of the control condition. For example, in the case of the mean time in which a subject reported the intention to move (W-judgement) with respect to the actual key press was -239.4 ms, and the mean (\pm SD) time in which he reported the S-judgement was 7.7 ± 47.7 ms, therefore the

individual z-score was -5.18 as calculated by the formula $[(-239.4) - 7.7]/47.7$. Such normalization was performed in order to 'correct' M and W values on the basis of the individual general ability to estimate time events. The relationship between individual z-scores values and the score obtained in the BIS-11 total score and subscores was tested by calculating the Pearson's correlation coefficients separately for M-judgement and W-judgement. The response inhibition was evaluated by measuring how many times (expressed as percentage) participants failed to inhibit responses to no-go targets. All tests were two-tailed and significance was set at $P < 0.05$. Analyses were performed using the software IBM SPSS 20.0 (SPSS, Chicago, IL, USA).

3.1.4 Results

The mean (\pm SD) difference between the time in which subjects reported the movement execution (M-judgement) and the time in which they performed the actual key press was -36.6 ± 40.5 ms. As expected, the intention to move (W-judgement) was reported more in advance of the actual movement execution (-146.3 ± 126.4) and of the M-judgement. In the control condition, subjects were accurate in estimating the time of the acoustic tone (-15.1 ± 55.1) (Figure 4).

A positive relationship between the time in which subjects reported the intention to move (W-judgement) and BIS-11 total score emerged from our data, but such a trend was not significant ($r = 0.183$, $P = 0.118$; Figure 5a). However, when specific dimensions of impulsivity (evaluated by subscores of BIS-11 scale) were considered, significant correlations emerged. Namely, the higher was the score in the attentional ($r = 0.233$, $P = 0.046$; Figure 5b) and motor ($r = 0.261$, $P = 0.024$; Figure 5c)

impulsivity subscales, the lower was the difference between the W-judgement and the actual key press (i.e. the awareness of intention to move was closer to the voluntary movement execution). In contrast, no relationship emerged between the W-judgement and the non-planning impulsivity sub-score ($r = 0.011$, $P = 0.925$; Figure 5d).

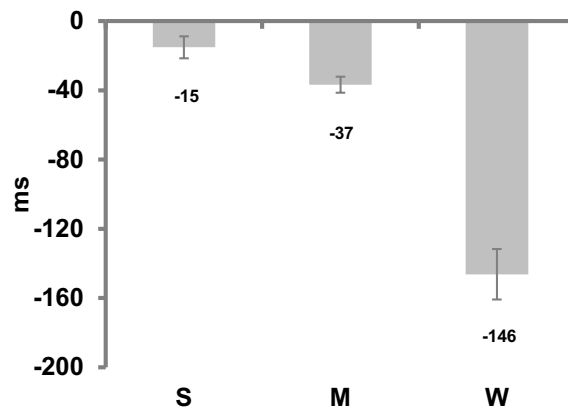


Figure 4. Behavioral data (mean±SE) for the movement (M), ‘wanting to move’ (W), and stimulus (S) judgement conditions of the Libet’s clock task.

In addition, a significant positive correlation emerged between W-judgement and failure inhibition expressed as percentage of response for ‘no-go’ stimuli ($r = 0.254$, $P = 0.029$; Figure 6), i.e. the higher the number of inhibitory failure responses in the go/no-go task, the lower was the difference between the W-judgement and the actual key press.

No significant correlations were seen between the M-judgement measure and BIS-11 total score or sub-scores (BIS-11 total score; $r = 0.169$, $P = 0.149$; attentional impulsivity: $r = 0.129$, $P = 0.272$; motor impulsivity: $r = 0.174$, $P = 0.137$; non-planning impulsivity: $r = 0.116$, $P = 0.324$). We compared all variables (i.e. BIS-11 total and sub-scores; M, and W-judgements z-scores; and percentage of inhibition failures in the go/no-go task) by independent sample t-tests, in order to evaluate gender differences. No significant differences between females and males emerged in either

BIS-11 total (females mean \pm SD: 59.3 ± 9.9 , male: 60.0 ± 11.1 ; $t = -0.257$, $P = 0.798$) and attention (females: 15.7 ± 3.5 , male: 17.0 ± 3.8 ; $t = -1.375$, $P = 0.173$), motor (females mean \pm SD: 19.5 ± 3.9 , male: 19.7 ± 3.0 ; $t = -0.236$, $P = 0.814$), and non-planning (females mean \pm SD: 24.0 ± 5.1 , male: 23.2 ± 5.5 ; $t = 0.574$, $P = 0.568$) sub-scores. Such data are consistent with US and Italian BIS-11 normative data (Fossati et al., 2001; Patton et al., 1995) in which females and males mean scores did not differ. Moreover, no gender differences emerged for M ($t = 1.433$, $P = 0.156$), and W-judgements ($t = 0.643$, $P = 0.523$) z-scores, and for percentage of inhibition failures in the go/no-go task ($t = -0.074$, $P = 0.941$).

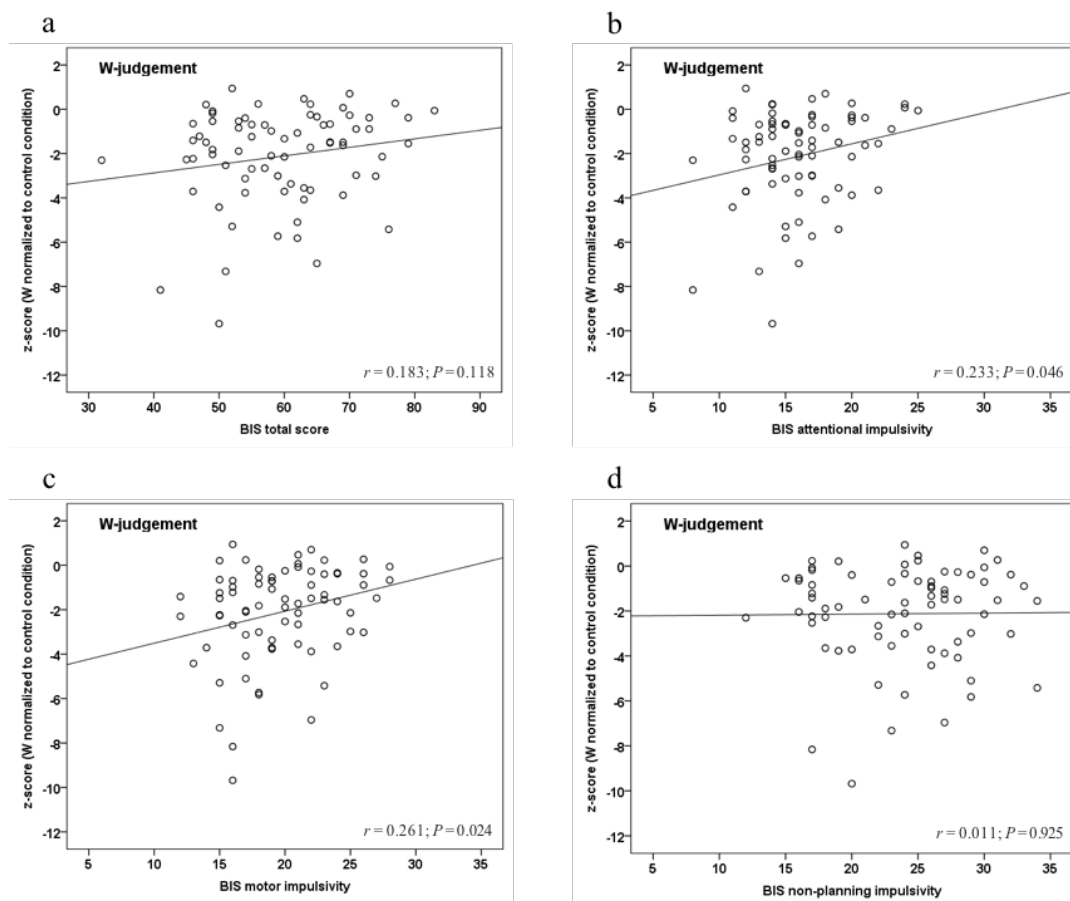


Figure 5. Relationship (linear fit) between the time in which subjects reported the intention to move (W-judgement) and BIS-11 total score (a) and sub-scores: attentional impulsivity (b); motor impulsivity (c), non-planning impulsivity (d).

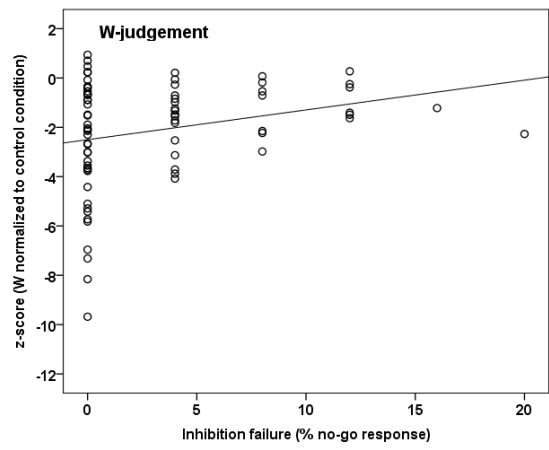


Figure 6. Relationship (linear fit) between the time in which subjects reported the intention to move (W-judgement) and failure inhibition expressed as percentage of response for ‘no-go’ stimuli.

3.1.5 Discussion

The main result of the current study is that, in healthy humans, the time elapse between the conscious intention to move (W-judgement) and the execution of a self-initiated movement is related to impulsive personality traits. Namely, the closer was the awareness of intention to move to the movement onset, the higher were the score in the attentional and motor impulsivity subscales of BIS-11 and the number of inhibitory failure responses in the go/no-go task. This finding is quite specific because no significant relationship emerged between the W-judgement and the non-planning impulsivity sub- score of BIS, or between the awareness of actual movement execution (W-judgement) and BIS-11 total score or sub-scores.

The ability to voluntarily inhibit an action has been proposed as a core process of self-control and is related to impulsive behavior (Filevich et al., 2012). A delay in conscious intention to act has been reported in patients with parietal lesions (Sirigu et al., 2004), psychogenic tremor (Edwards et al., 2011) and Gilles de la Tourette

syndrome (Moretto et al., 2011). Interestingly, a recent study in patients with the Gilles de la Tourette syndrome, despite not replicating the delayed W-judgement finding, reported a specific relationship between perception of volition and voluntary self-control (Ganos et al., 2015). Namely, participants who were able to suppress their tics reported an earlier intention to act compared to those who did not (Ganos et al., 2015). Our data extended findings in neurological conditions characterized by disorders of volition (Kranick & Hallett, 2013), suggesting that a relationship between delayed awareness of the intention to act may be related to personality traits. We argued that in healthy individuals with higher impulsivity traits, such delayed perception of volition can more likely exceed the ‘point of no return’, after which the initiation of an action cannot be cancelled (Schultze-Kraft et al., 2016), causing failed voluntary inhibition.

The protocol from Libet and coworkers was tailored to characterize the time profile of the unconscious mental processes preceding a voluntary motor act (Libet et al., 1983). In order to obtain objective measures, the subject was asked to perform a standardized, self-paced movement. This represents a different condition with respect to the ecologic, spontaneous motor actions directly related to impulsive behaviors. Interestingly, the current data show that the timing of the motor intention to move (W-judgement) reflects impulsivity traits notwithstanding this lab oversimplification of the motor act. We speculate that in clinical conditions, such as impulse control disorders, reaching conscious intention close to the actual movement may interfere with processes underlying conscious ‘veto’ of the impending action, representing a basis for impulsive behaviors.

At this stage of research, our goal was to verify whether a behavioral measure of the perceived timing of motor intention as tested by this simplified Libet's protocol was related to impulsivity traits. EEG recordings as well as focal interference with cerebral activity by noninvasive brain stimulation techniques (Parkin et al., 2015) will represent valuable tools for future investigation aiming to shed light on the neural basis of this relationship.

These data in healthy volunteers have further potential clinical implications. First, further investigation comparing W-judgement in ICD patients and healthy individuals is worth verifying the relevance of the correlation between conscious intention to move and impulsivity demonstrated in the present study. Second, ICDs can be observed in patients with Parkinson's disease (PD) and represent a critical issue for clinical management (Weintraub et al., 2010). ICDs are more frequent during dopamine agonist treatment. It has been hypothesized that dopaminergic therapy might trigger ICDs in individuals with specific impulsivity traits (Isaias et al., 2008). However, the relationship between therapy and individual predisposing factors is still debated and neurobiological markers for an early identification of PD patients at risk to develop ICDs are lacking. Recently, using the Libet's clock paradigm, a delayed awareness of motor intention has been found in a group of treated PD patients (Tabu et al., 2015). However, these authors have not investigated a possible relationship between the perceived timing of motor intention and impulsivity traits in PD patients (Tabu et al., 2015). The current findings provide a rationale for further studies aiming to clarify whether awareness of motor intention may help to identify PD patients at risk of developing ICD during dopaminergic treatment.

3.2 Experiment 2 - Electrophysiological activity prior to self-initiated movements is related to impulsive personality traits

3.2.1 Introduction

Conscious voluntary control of actions is a crucial aspect of our existence. In our everyday life, we are constantly faced with the decision whether to execute or inhibit an action, to choose the appropriate action to perform and the right timing (Di Russo et al., 2016). The timing component of the sense of will during intentional actions was first investigated by Libet and colleagues in 1983. With his ‘clock paradigm’, Libet found that the onset of the neural activity related to the preparation of voluntary actions preceded the awareness of the intention to move. This pre-movement neural activity, referred as Readiness Potential (RP), was first reported by Kornhuber and Deecke in 1965 as the *Bereitschaftspotential*. The RP is a slow negative build-up of scalp electrical potential originating in pre-motor and supplementary motor areas up to 2 seconds before the onset of spontaneous self-initiated movements (Shibasaki & Hallett, 2006).

Libet’s experimental approach and subsequent interpretations have been criticized (see Guggisberg & Mottaz, 2013), particularly in the debate on the existence of ‘*free will*’. However, Libet's findings suggesting that the brain processes underlying movement initiation starts long before the subjective sense of willing the movement, have been extensively replicated (Haggard, 2008; Hallett, 2016).

The timing of the sense of will related to intentional actions has been reported to be affected by different neurological and psychiatric conditions. Namely, a delay in

conscious intention to act has been reported in patients with parietal lesions (Sirigu et al., 2004), psychogenic tremor (Edwards et al., 2011), Gilles de la Tourette syndrome (Ganos et al., 2015; Moretto et al., 2011), and in Parkinson's disease (Tabu et al., 2015). Moreover, the timing of will can be experimentally manipulated by non-invasive brain stimulation techniques as transcranial magnetic and transcranial direct current stimulation (Douglas et al., 2015; Lau et al., 2007). An intriguing hypothesis is that, in healthy humans, the variability in the timing in which awareness of the intention to act occur, may be related to personality traits. Recent studies (Caspar & Cleeremans, 2015; Giovannelli et al., 2016), revealed a relationship between the timing component of intentional actions and individual differences in impulsivity trait. Namely, in the study of our research group (Giovannelli et al., 2016) the higher was the level of attentional and motor trait impulsivity, the closer was the awareness of the intention to move to the action onset, i.e. the smaller was the interval between the conscious decision to move and the movement onset. We speculated that in individual with traits of impulsivity the delayed awareness of the intention to move could exceed the 'point of no return' more frequently, determining a deficit in the intentional inhibition process (Giovannelli et al., 2016).

Impulsivity represents a multidimensional and non-unitary trait mainly characterized by the tendency to act without thinking (Patton et al., 1995), a failure in planning (Buss & Plomin, 1975; Eysenck & Eysenck, 1977; Patton et al., 1995) and a lack of perseverance/persistence (Buss & Plomin, 1975; Gerbing et al., 1987). Moreover, impulsivity is associated with an increased propensity to engage in risky behaviours, and is a core feature of several psychiatric conditions such as attention deficit/hyperactivity disorder, schizophrenia, substance abuse, and impulse control

disorders (e.g. pathological gambling, compulsive eating) (Bari & Robbins, 2013; Gut-Fayand et al., 2001; Jentsch & Taylor, 1999; Nigg, 2001). Recent models identify different key dimensions of impulsivity (see Dalley & Robbins, 2017 for a review). Motoric forms of impulsivity that reflects an overall failure in response inhibition and includes ‘waiting impulsivity’, related to action restraint prior to movement initiation, and ‘stopping impulsivity’, which refers to the reactive inhibition of a prepotent response after movement initiation (Dalley & Robbins, 2017). Decisional impulsivity, includes ‘reflection impulsivity’ or ‘impulsive choice’, which refers to the tendency to make rapid decisions without adequate forethought, and ‘delay discounting’, which is related to the tendency to select smaller-sooner rewards over larger-later rewards, because of a discount or devalue of future long-term outcomes (Dalley & Robbins, 2017). The multidimensional nature of the impulsivity is also reflected in questionnaires used to assess this personality traits. The Barratt Impulsiveness Scale (BIS-11), is one of the most used questionnaire to assess impulsivity and includes three subscales: attention, motor, and non-planning impulsiveness.

Based on our previous behavioral findings (Giovannelli et al., 2016), it is conceivable that motor dimensions of impulsivity may be particularly relevant for studying mechanisms underlying voluntary control of actions. The RP has been classically interpreted as reflecting movement preparation (Shibasaki & Hallett, 2006), however, studies investigating how this cortical potential is influenced by impulsivity traits are lacking. The aim of the present study was to extend our previous behavioral findings to evaluate the relationship between impulsive personality trait and the dynamics of brain potentials related to motor preparation as reflected by RP. To this

end, nineteen healthy participants performed a task based on the Libet's clock paradigm, during the EEG recording, and underwent an impulsivity trait assessment.

3.2.2 Experimental Procedures

Participants

Nineteen healthy participants (14 women; mean age = 24.26, SD = 6.37; range 19-42) were included in the study. They were right-handed and had normal or corrected-to-normal vision. All participants were volunteers recruited among degree or PhD students from the University of Florence and were requested to fill a semi-structured questionnaire during the informed consent procedures, in order to collect demographic and anamnestic information. They reported taking no medication and had no history of neurological or psychiatric disease, and drug abuse. Informed consent to the procedure and the processing of personal data was obtained from all subjects, with the option to withdraw without consequences. All data were collected and processed anonymously. Written informed consent was obtained from each participant, in conformity with the Helsinki Declaration. An internal Committee of the Psychology section of the Department of Neuroscience, Psychology, Drug Research, Child Health of the University of Florence approved the experimental protocol.

All participants completed the BIS-11, a 30-item self-report questionnaire widely used to measure impulsive personality traits (Patton et al., 1995). Each item is measured on a 4-point Likert scale, with higher values indicating greater impulsivity. The BIS includes three subscales: (1) readiness to make quick cognitive decisions (attentional impulsivity), (2) tendency to act without thinking (motor impulsivity), and

(3) degree of focus on only the present (non-planning impulsivity). BIS-11 scores ranged between 41 and 83.

Experimental paradigm

During the EEG recording, participants sat in a comfortable room facing a computer monitor at 57 cm of distance with the index finger of their dominant hand on a keyboard. They performed a Libet's clock task based on the original clock paradigm created by Libet et al. (1983). After filling out an informed consent form, the electrode cap was mounted and participants were given task instructions and practice trials. They were asked to minimize blinking during task performance and to maintain visual fixation on a small point in the centre of the analogical clock, placed in turn at the centre of the monitor. The clock had a diameter of 4 cm (marked with conventional intervals from 0 to 55 in steps of five units, with a hand rotating clockwise and a revolution period of 2560 ms. At each trial, the initial clock hand position was random. The task consisted of three experimental conditions performed in separate blocks: movement (M), 'wanting to move' (W), and sound (S) judgement. In the M and W judgement conditions participants were requested to press a key with their right index finger whenever they want, focusing their attention on the actual onset of their self-initiated movement (M-judgement) or to their decision to move (W-judgement). They were instructed to avoid planned or pre-decided responses and not to push the key before the clock hand completed the first round. In the S-judgement condition an acoustic tone was randomly delivered by headphones and participants were asked to focus their attention on the actual onset of the tone. After each event (key press or tone presentation), the clock's hand stopped its rotation at a random

interval between 400 and 800 ms, and the ‘judgement screen’ appeared. In this ‘judgement screen’ participants were asked to report as accurately as possible, the position of the clock’s hand related to the time they performed the actual key press (M-judgement block), to the time they first became aware of their intention to move (W-judgement block), and to the time they heard the tone (S-judgement block). The S-judgement condition was performed as a control condition to assess the ability to estimate time events. Each block consisted of 40 trials. The order of the three experimental blocks was randomized and counterbalanced across subjects.

EEG data acquisition

Recordings were performed by a 32-channel Neuroscan system using SynAmp amplifiers (Compumedics, Charlotte, North Carolina, USA). EEG activity was continuously recorded from active electrodes mounted on an elastic cap (ActiCap, Brain Products, Munich, Germany) according to the extended International 10–20 System. The scalp locations were: FP1, FP2, F7, F3, FZ, F4, F8, FC5, FC3, FC4, FC6, T7, C3, CZ, C4, T8, CP5, CP1, CP2, CP6, P7, P3, PZ, P4, P8, O1, OZ, O2. Two additional electrodes placed at the right and left mastoids, served as references. Vertical and horizontal electro-oculographic (EOG) activity was recorded with additional electrodes located above and below the left eye and outside the outer canthi of both eyes. For all electrodes, the impedance was kept less than 5 K Ω . Electrical activity was amplified with a bandpass of 0.05–100 Hz and a sampling rate of 1000 Hz.

Trials were discarded if the voltage exceeded $\pm 100 \mu\text{V}$. Moreover, epochs with eye movement and muscular artifacts were discarded after visual inspection. The mean number of artifact-free epochs included in the analysis was 34 (range 19-40).

3.2.3 Behavioral data analysis

To quantify the behavioral performance in the Libet's clock task we measured the difference between the time in which subjects reported the movement execution (M-judgement) or the intention to move (W-judgement) and the time in which they performed the actual key press. Separately for each participant, M-judgement and W-judgement values were normalized to control condition (S-judgement). M-judgement and W-judgement values were therefore transformed in z-scores, using the formula: $z = (A-B)/\text{SDS}$, in which A represents the individual time values in the experimental conditions (M-judgement or W-judgement), B represents the individual time values in the control condition (S-judgement), while SDS represents the individual standard deviation of the control condition. This normalization was performed to "correct" M-judgement and W-judgement values based on the individual ability to estimate time events (Giovannelli et al., 2016).

3.2.4 EEG data analysis

In the offline analysis, separately for M-judgement and W-judgement conditions, epochs were time-locked on the event (participants key press) with a time window from 2500 ms prior to 1000 ms after the event, using the interval from -2600

ms to -2500 ms as baseline correction. All epochs with ocular artifacts larger than 40 μV were rejected. The epochs were then low-pass filtered at 20 Hz (12 dB) and averaged separately for each condition.

To explore the RP, data were analysed on Cz electrode (Haggard & Eimer, 1999). The relationship between individual onset and mean amplitude of the RP, and the BIS-11 total and subscales score was tested by calculating the Pearson's correlation coefficients separately for M-judgement and W-judgement conditions. The onset of the RP was identified using the 'criterion-based methods' (Mordkoff & Gianaros, 2000; Osman & Moore, 1993; Smulders et al., 1996). Specifically, we used the 'relative-criterion method', which defines the onset of the RP as the first point in time that the potential exceeds an arbitrary value (the 30% of the height of the peak). To calculate the mean amplitude of the RP we considered the interval between -2500 ms and the motor event (key press).

All tests were two-tailed and significance was set at $P < 0.05$ and adjusted by Bonferroni-correction (Bonferroni-corrected alpha levels are reported in the Results). Analyses were performed using the software IBM SPSS 20.0 (SPSS, Chicago, IL, USA).

3.2.5 Results

Behavioral results

The mean (\pm SD) of the BIS-11 total score was 57 ± 13 (range 41-83), 16 ± 5 (range 8-27) for the attentional impulsivity subscale, 18 ± 4 (range 14-28) for the motor

impulsivity subscale, and 23 ± 5 (range 16-34) for the non-planning impulsivity subscale.

Participants were accurate in estimating the time of movement execution (M-judgement) and the time of the acoustic tone (S-judgement) in the Libet's clock task. The mean (\pm SD) difference between the time in which participants reported the movement execution (M-judgement) and the time in which they performed the actual key press was -42.1 ± 34.8 ms. In the S-judgement condition, the difference between the time in which participants reported that they have heard the sound and the time in which the sound is presented was -39.3 ± 49.4 ms. In line with previous studies, the intention to move (W-judgement) was reported more in advance with respect to the actual movement execution and the M-judgement. Indeed, the mean difference between the time in which participants reported the intention to move and the time in which they performed the actual key press was -212.5 ± 66.1 ms.

No significant correlations were seen between W- and M-judgement values (normalized to control S condition) and BIS-11 total score or subscores (W-judgement: BIS-11 total score, $r = -0.006$; $P = 0.981$; attentional impulsivity, $r = -0.010$; $P = 0.968$; motor impulsivity, $r = 0.000$; $P = 1.000$; and non-planning impulsivity $r = -0.005$; $P = 0.984$; M-judgement: BIS-11 total score, $r = -0.082$; $P = 0.739$; attentional impulsivity, $r = -0.107$; $P = 0.664$; motor impulsivity, $r = 0.026$; $P = 0.915$; and non-planning impulsivity $r = -0.124$; $P = 0.613$). Similar non-significant results emerged also when non-normalized data for M-judgement and W-judgement were considered.

EEG results

Significant or close to significance correlations (Bonferroni-corrected alpha level for eight [RP onset and mean amplitude x BIS total and subscores] correlations $0.05/8 = 0.006$) were found between BIS-11 total score and the RP onset ($r = -0.579$, $P = 0.009$; Figure 7A, Table 1) and between BIS-11 total score and the RP mean amplitude ($r = -0.663$, $P = 0.002$; Figure 7B, Table 1), in the W-judgement condition. That is, the higher was the score in the BIS-11, the earlier was the onset of the RP and the greater was its mean amplitude. Grand-averaged waveforms of the readiness potentials recorded during the Libet's clock task in subjects with high and low impulsivity trait (9 and 9 subjects, respectively) defined on the basis of a median split of the BIS-11 total score (median score = 57) is given in the Figure 8. Similarly, when specific dimensions of impulsivity (evaluated by subscores of BIS-11 scale) were considered, significant or close to significance correlations with both RP measures were found (Table 1). In contrast, no significant correlation emerged between BIS-11 total score or subscores and either RP onset and mean amplitude evaluated in the M-judgement condition (Table 1).

In the W-judgment condition no correlation was found between aspects of the RP and behavioral W measure, both for normalized data (RP onset: $r = 0.132$; $P = 0.589$; RP amplitude: $r = 0.105$; $P = 0.668$) and non-normalized data (RP onset: $r = 0.253$; $P = 0.296$; RP amplitude: $r = 0.225$; $P = 0.354$). Similarly, in the M-judgment condition no correlation emerged between RP and behavioral M measures, both for normalized data (RP onset: $r = -0.076$; $P = 0.757$; RP amplitude: $r = -0.117$; $P = 0.634$) and non-normalized data (RP onset: $r = -0.050$; $P = 0.840$; RP amplitude: $r = -0.234$; $P = 0.334$).

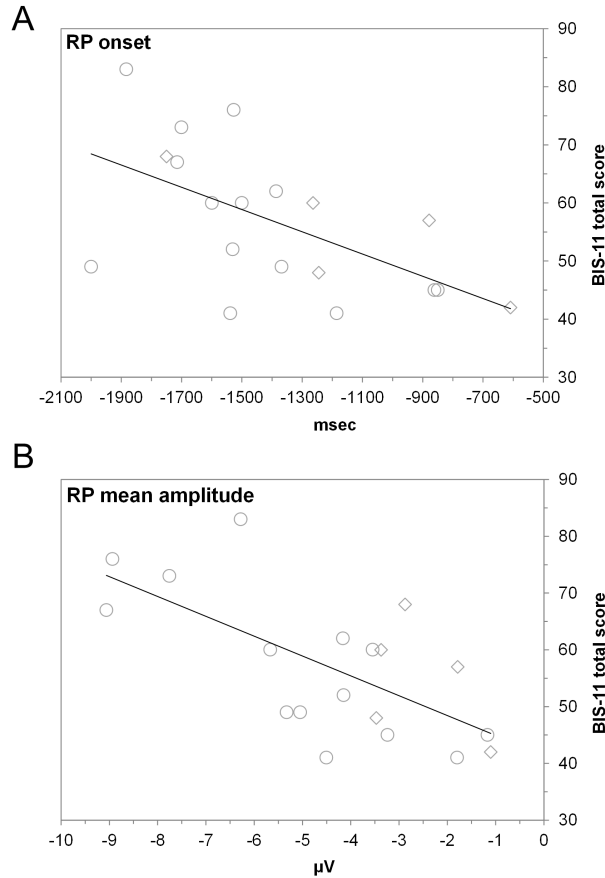


Figure 7. Relationship (linear fit) between BIS-11 total score and (A) the RP onset ($r = -0.579$, $P = 0.009$); and (B) the RP mean amplitude ($r = -0.663$, $P = 0.002$). Circles and diamonds indicate female and male participants, respectively.

		BIS-11			
		Total score	Attentional impulsivity subscale	Motor impulsivity subscale	Non-planning impulsivity subscale
<i>W-judgement condition</i>	Onset	$r = -0.579$, $P = 0.009$	$r = -0.592$, $P = 0.008$	$r = -0.507$, $P = 0.027$	$r = -0.455$, $P = 0.051$
	Mean amplitude	$r = -0.663$, $P = 0.002$	$r = -0.476$, $P = 0.040$	$r = -0.639$, $P = 0.003$	$r = -0.692$, $P = 0.001$
<i>M-judgement condition</i>	Onset	$r = -0.296$; $P = 0.219$	$r = -0.254$; $P = 0.295$	$r = -0.251$; $P = 0.300$	$r = -0.292$; $P = 0.224$
	Mean amplitude	$r = -0.320$; $P = 0.181$	$r = -0.201$; $P = 0.408$	$r = -0.226$; $P = 0.351$	$r = -0.438$; $P = 0.061$

Table 1. Pearson's correlation coefficients and P values of the relationship between onset and mean amplitude of the RP and the BIS-11 total and subscales score for M-judgement and W-judgement conditions of the clock task.

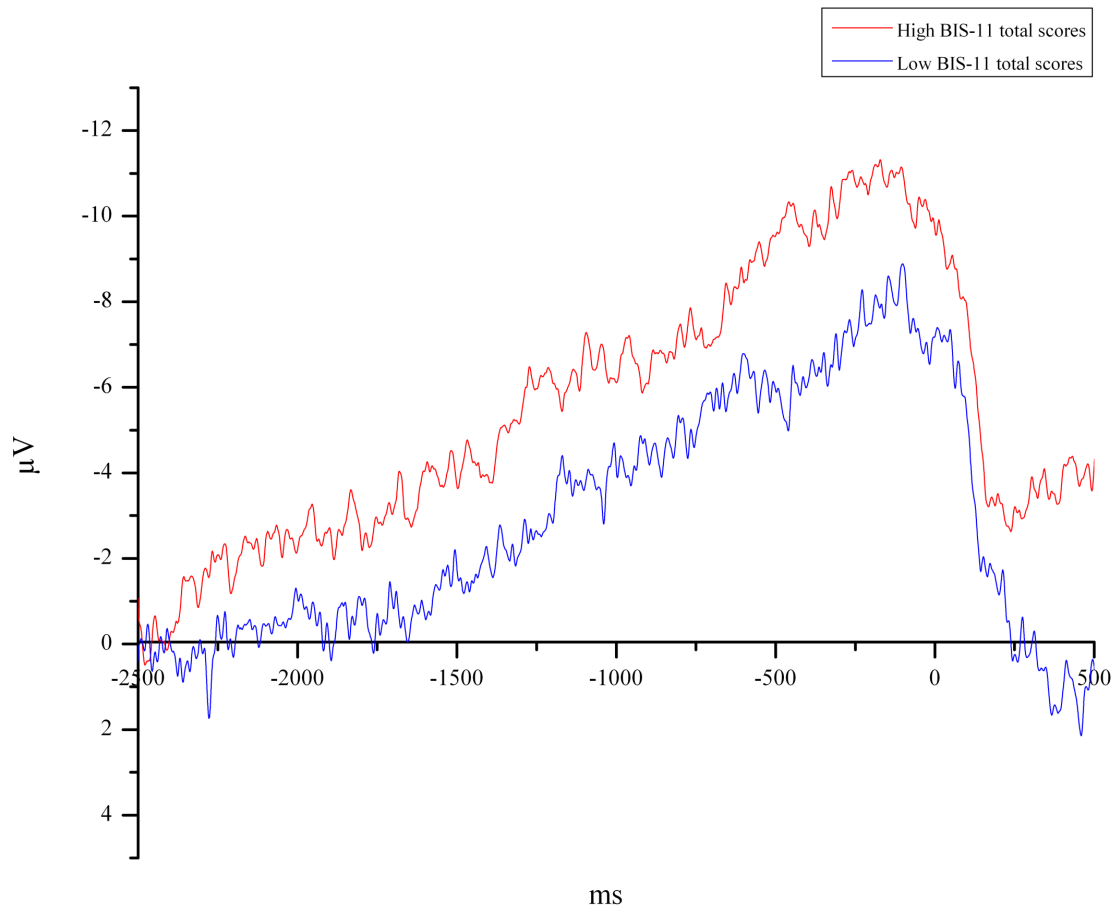


Figure 8. Grand-average (Cz electrode) of the RP recorded during the W-judgment condition of the Libet's clock task in subjects with high (red) and low (blue) impulsivity trait (9 and 9 subjects, respectively), defined on the basis of a median split of the BIS-11 total score (median score = 57).

3.2.6 Discussion

The main finding of the present study is the relationship between impulsive personality traits and pre-movements electrophysiological activity as revealed by the RP. Namely, the RP shows an earlier negative rising phase and a greater amplitude during the preparation of self-initiated movements in subjects with higher BIS-11 score. Interestingly, this relationship has been specifically observed for the experimental condition in which subjects were requested to pay attention to the

intention (i.e. W-judgement condition) while was not present in the condition when attention was focused to the movement (i.e. M-judgement condition).

The readiness potential has been classically interpreted as reflecting movement preparation mechanisms related to increasing excitability of premotor and motor circuits (Shibasaki & Hallett, 2006). The earlier negative rising phase and the greater amplitude of the RP observed in individuals with impulsive personality trait in the W-judgement condition, may reflect differences in motor system excitability during motor preparation. In this framework, we might hypothesize less effective preparatory inhibition mechanisms, which have a fundamental role in the control of behaviour. During the preparation of voluntary movements motor system excitability is transiently suppressed (Davranche et al., 2007; Duque & Ivry, 2009; Duque et al., 2010, 2012, 2017; Greenhouse et al., 2015; Hasbroucq et al., 1997, 1999a, 1999b; Sinclair & Hammond, 2009; Soto et al., 2010; Touge et al., 1998; van Elswijk et al., 2007). This preparatory inhibition process seems to reflect an automatic gain modulation mechanism that allows to increase the signal-to-noise ratio associate with a selected action, decreasing background activity and increasing neuronal sensitivity to excitatory drive (Chance et al., 2002; Churchland et al., 2006; Greenhouse et al., 2015; Hasbroucq et al., 1997). Recently, Spieser and colleagues (2015) have provided evidence that a hyperpolarization of the motor system induced by transcranial direct current stimulation (tDCS) reduces the sensitivity to neural noise, increasing motor system efficiency. Then, preparatory inhibition permits to improve motor behavioral performance allowing to avoid a premature implementation of an action and to prevent selection of inappropriate responses. Therefore, we speculate that in impulsive individuals the presence of a greater motor system excitability during the preparation

of voluntary movements, might determine a reduction in the operation of this gain modulation mechanism and, accordingly, a diminished motor system efficiency.

The lack of correlation between the moment of the awareness of motor intention (W) and the onset of the potential is in keeping with previous studies (e.g. Haggard & Eimer, 1999) challenging the hypothesis of a causal relation between the RP and time of the conscious intention to move. Recent interpretations on the nature of the RP have been proposed (Schmidt et al., 2016). The main one is the Selective Action-Related Slow Cortical Potential Sampling Hypothesis (SCP Sampling Hypothesis, Schmidt et al., 2016), which consider the RP reflecting the ebb and flow of the background neuronal noise. According to this hypothesis, fluctuations of SCPs are of fundamental importance in the stimulation of spontaneous voluntary movements, as they unconsciously modulate the reactivity threshold and influence the time at which the neural decision threshold is exceeded. Indeed, actions are more likely to be carried out in the negativity phase of SCPs, that is in the rising and in the negative crest phase of the potential, with respect to the falling phase and the positive trough (Jo et al., 2013). For this reason, fluctuations of SCPs show the specific RP pattern when recorded time-locked to movement onset. Moreover, the negativity phase of SCPs is experienced with a subjective sensation of an ‘urge to move now’. The presence of a sub-threshold inappropriate ‘urge to move’ intention or impulse does not always turn into a behavioral inappropriate response. Indeed, in 15-25% of trials with correct overt responses there are ‘partial errors’ that remain under threshold (van den Wildenberg et al., 2010). In this case, these covert errors are expression of impulses but they do not turn into overt errors. The supplementary motor complex (SMC), and in particular the pre-SMA, has a key role in this control mechanism, in that it suppresses on-line

the sub-threshold activated responses, preventing it from turning into overt errors (Spieser et al., 2015). We may speculate that this control mechanism might be less efficient in impulsive people, leading to an insufficient control of the sub-threshold inappropriate ‘urge to move’ intentions.

Finally, the correlation between impulsivity traits and awareness of motor intention, as revealed by time of the W-judgement, did not reach the significance level. This was likely due to the small sample size that constitutes a limitation of the present study. However, such relationship has been previously observed by two independent research groups in larger samples (Caspar & Cleeremans, 2015; Giovannelli et al., 2016).

The greater amplitude of the RP observed may be affected by other factors, such as a greater intentional engagement in the execution of the movement and a greater motivation in successfully completing the task (Kornhuber & Deecke, 1965, 2016; Schmidt et al., 2017a,b). Further studies should investigate the role of these potentially influencing variables, along with other factors such as metacognition. Moreover, it will be interesting to evaluate the relationship between impulsivity dimensions, readiness potential, and awareness of motor intention in clinical and non-clinical populations characterized by high level of impulsivity such as adolescents.

CHAPTER 4



COGNITIVE CONTROL OF STIMULUS-DRIVEN ACTIONS

Stimulus-driven actions lie at an intermediate level in the between voluntary actions and simple reflexes (Haggard, 2008). Responses to external stimuli are characterized by features belonging to both voluntary and reflexes actions, and they are usually contrasted with voluntary actions in the experimental context (Haggard, 2008).

The majority of studies on cognitive control of actions has focused on bottom-up stimulus-driven processes (Aron, 2011; Di Russo et al., 2016). Only in recent years, has been demonstrated the crucial role of top-down endogenous processes, with which we refer to preparatory mechanisms occurring before acting and showing tight connections with cognitive processing (Aron, 2011; Di Russo et al., 2016; Liebrand et al., 2017). As in the case for intentional actions, even for stimulus-driven actions premotor top-down mechanisms play a fundamental role in the control of behavior (Duque et al., 2017). Standard models of cognitive control of stimulus-driven actions assume that motor control and motor inhibition processes are reactive and, therefore, triggered by the external stimuli in a bottom-up manner (Criaud et al., 2017). In recent years, instead, it has been highlighted the crucial role of the top-down proactive control

mechanism, which activates cognitive control in an anticipated manner and is responsible for a top-down form of inhibition (Braver, 2012; Criaud et al., 2017; Nigg, 2017). This ‘proactive’ form of inhibition is particularly relevant in daily life situations in which the required outcome is unknown and, therefore, we have to move with greater caution, withholding fast automatic responses to any upcoming stimuli.

4.1 Proactive and reactive control mechanisms

According to the ‘dual mechanisms of control’ (DMC) theory, there are two main control mechanisms, which are the already mentioned ‘proactive’ and ‘reactive’ control processes (Braver, 2012; Braver et al., 2009). These two processes differed in the time at which cognitive control is activated. Proactive control refers to a top-down endogenous process, which activates cognitive control in an anticipated and goal-oriented manner (Braver, 2012; Criaud et al., 2017; Nigg, 2017). Instead, when cognitive control is activated in a bottom-up manner, after the detection of an external signal reporting the presence of a change or a conflict in current events, we refer to a reactive control mechanism (Braver, 2012; Criaud et al., 2017; Nigg, 2017). Proactive and reactive control mechanisms differently interact with inhibitory control in the regulation of behavior (Aron, 2011). In particular, proactive control is responsible for a top-down form of inhibition, called ‘proactive inhibition’, while reactive control is strictly related to a bottom-up form of inhibition, that is ‘reactive inhibition’ or ‘behavioral inhibition’ (Nigg, 2017).

Motor inhibition related to action stopping refers to a condition in which a planned behavior needs to be cancelled because it becomes inappropriate relating to a stop-signal, a changing of intent or a changing in the environment (Duque et al., 2017).

Classical models of response inhibition assumed that motor inhibition processes were reactive and, therefore, triggered by external stimuli (Criaud et al., 2017). Response inhibition has usually been defined as a volitional, reactive and selective process (Criaud et al., 2017). This classical interpretation is questioned by new researches, which suggest a multidimensional nature of inhibition, paying particular attention on its reflexive, non-selective and proactive component (Criaud et al., 2017). Indeed, in addition to the reactive form of motor inhibition, we have to consider a proactive form of response inhibition, which plays a fundamental role in the control of behavior (Duque et al., 2017; Liebrand et al., 2017).

Reactive inhibitory control represents a ‘late correction’ process, which activates cognitive control after the detection of an external ‘stop signal’, in a bottom-up and interference sensitive manner, withholding or stopping the upcoming movement (Braver, 2012; Duque et al., 2017; Jacoby et al., 1999). The right inferior frontal cortex (rIFC) and the pre-supplementary motor area (pre-SMA) seems to play an important role in reactive control, as they process stop-signal sensory information, sending the inhibition command to the basal ganglia, in particular to the subthalamic nucleus (STN), in order to stop the motor response execution (Alegre et al., 2013; Aron & Poldrack, 2006; Eagle et al., 2007; Isoda & Hikosaka, 2008; Li et al., 2008; Meyer & Bucci, 2016; Ray et al., 2012; Schmidt et al., 2013).

Proactive inhibitory control is, instead, a top-down endogenous process, which refers to the anticipated and expectancy-based activation of cognitive control prior to

a conflict or challenge (Nigg, 2017). The use of proactive control is related to the ability to estimate the cost-benefit ratio and, therefore, the ability to evaluate the consequences of the employed control strategy, in order to achieve the goals (Braver, 2012). While reactive inhibitory control acts as a ‘late selection’ process, proactive inhibitory control operates as an ‘early selection’ process, which provides for sustained and anticipated active maintenance of goal representations, biasing in advance attention, perception and motor systems in a goal-oriented manner (Braver, 2012; Jacoby et al., 1999). This top-down control mechanism is crucial in daily life situations in which the required outcome is unknown and, therefore, we have to move with greater caution.

The implementation mechanism underlying proactive inhibitory control is not clear (Criaud et al., 2012). According to the standard view, proactive control consists in the temporary application of inhibition when necessary (Criaud et al., 2012). That is, when the context becomes uncertain or conflicting, the brain sets up a ‘no-go’ mode, anticipating stimulus onset. The functional significance of setting up a proactive inhibitory ‘no-go’ mode seems to be to avoid false alarms and inappropriate responses, having more time available to integrate perceptual information and, therefore, to select the appropriate response (Frank et al., 2007). According to the standard view, proactive inhibition seems to reflect the operation of two concurrent inhibitory mechanisms (Duque et al., 2010, 2012). One mechanism, labeled ‘competition resolution’, suppresses competing response representations facilitating response selection and assisting in determining which response to make (Coles et al., 1985; Duque et al., 2010; Usher & McClelland, 2001, 2004). The other mechanism, called ‘impulse control’, decreases the activation of the selected response in order to prevent

a premature execution (Duque et al., 2010). This latter inhibition mechanism acts like a ‘brake’ that transiently suppresses the motor output without stopping it completely (Jahfari et al., 2010; Meyer & Bucci, 2016): if the attended stimulus requires an action it release the response, setting the system in a ‘go’ mode; if the attended stimulus requires an inhibition of the response it maintains the system in the ‘no-go’ mode, without the need of additional inhibition (Di Russo et al., 2016). This proactive inhibition mechanism seems to be mainly regulated by the prefrontal cortex (PFC) (Bogacz et al., 2010; Di Russo et al., 2016; Jaffard et al., 2008). In particular, the dorsomedial frontal cortex (dmFC) has been identified as the source of the neural ‘brake’ mechanism (Criaud et al., 2017). Another crucial area is the pars opercularis of the iFg, which seems to exert a cognitive preparation, setting the system on the ‘no-go’ mode, regardless of whether the following impeding stimulus requires inhibition (‘no-go’) or a motor response (‘go’) (Di Russo et al., 2016).

In addition to the standard view regarding the implementation of the proactive control, we have to consider another view, which represents the proactive inhibition mode as the default state of the executive system (Criaud et al., 2012). According to this, “top-down control of sensorimotor reactivity would consist of releasing temporarily proactive inhibitory control” (Criaud et al., 2012). That is, when the context is no longer uncertain, control mechanisms generates a top-down signal that unlocks neural processes responsible for movements execution. The occasionally releasing of cognitive control is seen as a mechanism with reduced energy costs, given that setting up a ‘no-go’ mode whenever the everyday context becomes uncertain and potentially stimulating, would be inefficient and effortful (Criaud et al., 2012). The view according to which proactive control represents the default state of executive

control is also supported by some brain imaging studies, which found overlaps between the ‘default mode network’ of brain function and regions involved in proactive inhibitory control (Criaud et al., 2012; Jaffard et al., 2008).

The functional anatomy of motor inhibition processes is still a hot matter of debate, mainly because of the difficulty in distinguish the respective effects of proactive and reactive inhibition. A widely supported hypothesis is that proactive control activates and potentiates in advance the reactive inhibition network, thus allowing a faster and accurate stopping (Aron, 2011; Castro-Meneses et al., 2015; Chikazoe et al., 2008; Jahfari et al., 2010; Meyer & Bucci, 2016; Swann et al., 2012; van Gaal et al., 2008; Vink et al., 2005; Wessel et al., 2013; Zandbelt et al., 2013). This pre-activation of the inhibitory network has been associated with a reduced activity in areas related to reactive inhibition during the behavioral stopping (Chikazoe et al., 2009; Verbruggen & Logan, 2009). Proactive and reactive inhibition engage the rIFC, the dmFC, in particular the pre-SMA, the STN, the striatum (Aron, 2011; Ballanger et al., 2009; Jahfari et al., 2010; Vink et al., 2005; Zandbelt & Vink, 2010;), the supplementary motor area (SMA) and the inferior parietal cortex (IPC) (Boy et al., 2010a,b; Chen et al., 2010; Jaffard et al., 2008; Menon et al., 2001; Rubia et al., 2001; Swick et al., 2011; Wardak, 2011), with downstream effects on the primary motor cortex (M1) excitability (Claffey et al., 2010; Duque & Ivry, 2009; Sinclair & Hammond, 2009; Stinear et al., 2009;). The network involved in reactive inhibition seems, therefore, ‘prepared’ in advance by the proactive control, that is recruited during the decision-making process.

A different view is that of the DMC theory (Braver, 2012; Braver et al., 2009), according to which proactive and reactive control have distinct neural correlates. This

theory sustains that there are three networks, which are implicated in motor control, that is the PFC for cognitive control, the sensorimotor cortex for the execution of motor actions and the visuo-attention network (Liebrand et al., 2017). In this framework, proactive control has found to be associated with the sustained activation of the lateral PFC (IPFC) for the maintenance of task goals (Liebrand et al., 2017). Instead, reactive control has found to be related to the transiently activation of the IPFC, in reaction to external signals, and to the engagement of the anterior cingulate cortex (ACC), the posterior cortical, and medial temporal lobe regions (Huang et al., 2017; Liebrand et al., 2017).

Recently, Criaud and colleagues (2017) bring data in support of a new view according to which proactive and reactive processes interact in order to switch between action restraint and automatic reactivity. Indeed, they found only little overlap between regions activated by proactive and reactive inhibition, assuming that they rely on neighboring but different neural correlates and hypothesizing that the modulation operated by proactive control would not be properly related to the pre-activation of the reactive network. In particular, results show that proactive inhibition activates some of the areas involved in the reactive inhibition process, such as the SMA, the temporoparietal junction (TPJ) and the insula. However, authors found that proactive control seems to rely more on the pre-SMA activation, while reactive control mainly engage the SMA-proper. Furthermore, proactive inhibition seems to be related to the activation of a posterior part of the insula and a more anterior part of the TPJ, while reactive inhibition seems to rely on the middle/ventral portion of the insula and a more posterior part of the TPJ.

The difficulty in identifying a neural network for proactive and reactive inhibition is also due to the method of study. Motor inhibition related to action stopping is usually investigated with the ‘stop-signal task’ (SST) and the ‘go/no-go task’ (GNG), which are the two most popular paradigms used to study inhibitory control abilities (Aron et al., 2016; Bari & Robbins, 2013; Chambers et al., 2009; Chikazoe, 2010; Logan & Cowan, 1984; Schall & Godlove, 2012; Verbruggen & Logan, 2008). Neural circuits mediating performance in the SST and the GNG include the ACC, the lateral rIFC, the premotor cortex (PM), the pre-SMA, the striatum and the STN (Aron & Poldrack, 2006; Aron et al., 2014, 2016; Jahanshahi et al., 2015; Li et al., 2008; Schimdt et al., 2013; Swick et al., 2011; Watanabe et al., 2015; Wiecki & Frank, 2013; Zanbelt & Vink, 2010).

In the classical SST subjects are required to make a rapid response to a cue, occasionally interrupted by an unexpected ‘stop signal’ (~33% of trials), which indicates that subjects should inhibit the upcoming action (Logan & Cowan, 1984; Verbruggen & Logan, 2008). Similar is the GNG, in which two kinds of cues are presented in a random way and with variable percentages across studies: the ‘go’ cue requires subjects to make an action (usually a key press); the ‘no-go’ cue requires to inhibit the action (Aron et al., 2016; Criaud & Boulinguez, 2013). The number of false alarms, that is the number of errors committed in the ‘no-go’ trials, are usually take as a behavioral index of inhibitory control (Criaud & Boulinguez, 2013). As mentioned before, the standard models of these two response inhibition tasks assume that motor inhibition processes are reactive and, therefore, triggered by the external stimuli (Criaud et al., 2017). However, the nature of inhibition processes is multidimensional and the GNG seems more suitable to investigate proactive inhibition processes, since

it directs more emphasis on action restraint, with respect to the SST (Criaud et al., 2017). Therefore, inhibition measured with the GNG might be related to different mechanisms compared to that measured with the SST (Bari & Robbins, 2013; Criaud et al., 2017). In the GNG the critical inhibitory control process is non-selective and proactive, rather than selective and reactive (Criaud & Boulinguez, 2013; Criaud et al., 2017). While subjects are waiting for the stimulus, they don't have the certainty about the event to come and, therefore, they need to withhold fast automatic responses to any upcoming stimuli ('go' or 'no-go') through a proactive inhibition process. For this reason, the standard function ('no-go>go') usually used in GNG experiments to identify brain activity related to inhibitory control and related to reactive inhibition mechanisms, is present in all trials ('go' and 'no-go') and is not sufficient to fully investigate inhibitory control mechanisms (Criaud & Boulinguez, 2013). In addition, brain activity related to reactive inhibition is necessarily conditioned by the proactive inhibition brain activity that precedes the stimulus ('go' or 'no-go'). In order to properly investigate proactive inhibitory mechanisms with GNG, we need to analyze pre-stimulus activity and implement the standard task, adding a control condition, in which the context is no longer uncertain but predictable, that is a condition in which there is no need to refrain from reacting (Albares et al., 2014; Criaud et al., 2017).

4.2 Phasic alertness

Our wakefulness state is a flow, constantly changing, in which attention and consciousness undergo continuous fluctuations (Lin & Lu, 2016). This condition is due to a temporal attentional filter, named alertness, which operates rapidly mobilizing

resources when they are needed (Lin & Lu, 2016). Alertness can be divided in phasic and intrinsic (Raz & Buhle, 2006; Sturm & Willmes, 2001; Sturm et al., 1999; Yanaka et al., 2010). Intrinsic alertness, or arousal, refers to a state of general wakefulness (Yanaka et al., 2010). Indeed, phasic alertness is considered a fundamental form of attention, defined as “the ability to increase and maintain response readiness in preparation for an impending stimulus” (Raz & Buhle, 2006; Sturm & Willmes, 2001; Sturm et al., 1999; Yanaka et al., 2010). In particular, phasic alertness is triggered by the presentation of a cue stimulus, named ‘warning signal’ (WS), prior to the presentation of a response stimulus (‘go’ or ‘no-go’) (Di Russo et al., 2016; Yanaka et al., 2010). WS determine an event called ‘warning effect’, that is a reduction in reaction times (RTs) to the response stimulus (Yanaka et al., 2010). The ‘warning effect’, usually considered the behavioral measure of phasic alertness (Coull et al., 2001; Sturm et al., 1999), is the result of the pre-potentiation of the motor system, implemented by the top-down attentional system (Yoshida et al., 2013). Phasic alertness, indeed, acts as a counteracting force against inhibition processes, triggering motor preparation processing, reducing action threshold and, then, facilitating the preparation of motor responses (Callejas et al., 2004, 2005; Mannarelli et al., 2015; Weinbach & Henik, 2011). Therefore, phasic alertness inhibits cognitive control, reducing the time needed to encode stimuli and enhancing global processing (Lin & Lu, 2016; Weinbach & Henik, 2011). This condition may result in allocating attention to irrelevant stimuli and in the release of automatic, premature motor responses (Weinbach & Henik, 2011). For this reason, the facilitation of movement elicited by phasic alertness during motor preparation needs to be temporarily inhibited by the

proactive control, which has the function of adjusting the level of motor readiness (Criaud et al., 2012).

The presence of the WS seems to determine the activation of the ‘anterior alerting system’ (Sturm & Willmes, 2001), which is the network associated with vigilance and intrinsic alertness, and areas involved in the early stages of motor preparation (Yanaka et al., 2010). In particular, with ‘anterior alerting system’ we refer to the ACC, the thalamus and the midbrain (Sturm & Willmes, 2001). Other areas activated by WS are the dorsal premotor area (PMd), the insula and the pre-SMA (Yanaka et al., 2010). The alerting system, along with the PMd and the insula, seems to act as prime on the pre-SMA, triggering action selection and action preparation processes and determining the facilitation on motor processing (Yanaka et al., 2010). In particular, WS potentiates the pre-SMA for action implementation or inhibition, through the thalamic gating of the alerting system, which is controlled by the ACC, involved in attentional processes (Yanaka et al., 2010). A crucial role in the production and maintenance of alertness is also covered by the dorsolateral prefrontal cortex (DLPFC; Mannarelli et al., 2015).

4.3 Motor impulsivity

In studying motor control ability, it is of high importance to consider the inter-individual variability. Impulsivity is a personality trait highly related to the operation of cognitive control processes, in particular motor control and response inhibition (Bari & Robbins, 2013; Franken & Muris, 2006). Indeed, key characteristic of people with high impulsivity is just the difficulty in implementing cognitive control (Bari &

Robbins, 2013). Despite this, the relationship between impulsivity and cognitive control is still largely unknown (Huang et al., 2017). Some studies found correlations between impulsivity and cognitive control measurements (Keilp et al., 2005; Li et al., 2005; Pietrzak et al., 2008) while others have not (Horn et al., 2003; Reynolds et al., 2006). These discrepancies might be due to the heterogeneous nature of impulsivity.

Trait impulsivity represents a multidimensional construct, mediated by distinct psychological and neural mechanisms (Aichert et al., 2012; Barratt et al., 1987; Buss & Plomin, 1975; Dalley & Robbins, 2017; Eysenck & Eysenck, 1977; Gerbing et al., 1987; Pietrzak et al., 2008), and defined as a predisposition toward rapid and unplanned reactions to internal or external stimuli, without adequate forethought, often resulting in inappropriate and premature actions (Durana & Barnes, 1993; Evenden, 1999; Moeller et al., 2001; Voon & Dalley, 2016).

We can broadly divide trait impulsivity in ‘motor’ and ‘decisional’ subtypes (Voon & Dalley, 2016). Decisional impulsivity refers to the tendency to make rapid decisions without adequate forethought and is related to difficulties in delaying gratification or exerting self-control, reflecting an impaired goal-oriented behavior (Dalley & Robbins, 2017). Motor impulsivity, instead, reflects a failure in response inhibition and is related to difficulties in action restraint prior to movement initiation, and in the reactive inhibition of a prepotent response after movement initiation (Dalley & Robbins, 2017). Motoric forms of impulsivity can be assessed using tasks like GNG and the SST (Dalley & Robbins, 2017). The GNG typically measure premature responding, whereas the SST measure the ability to stop an already started action (Dalley & Robbins, 2017).

In addition to the objective measures, the heterogeneity of impulsivity is also captured by the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995), which measures three sub-components of impulsivity, named ‘motor impulsivity’, that is the tendency to act without thinking, ‘attentional impulsivity’, referring to the readiness to make quick cognitive decisions and ‘non-planning impulsivity’, which refers to the degree of focus on only the present (Patton et al., 1995).

The presence of several dimensions of impulsivity make it difficult to analyze the correlation with cognitive control, which includes in turn a set of complex mental processes (Huang et al., 2017). Therefore, only some studies found correlations between impulsivity and cognitive control measurements (Huang et al., 2017; Keilp et al., 2005; Li et al., 2005; Pietrzak et al., 2008). Furthermore, regarding BIS-11 dimensions, motor impulsivity appears to be the component more highly correlated with cognitive control, using cognitive control paradigms as the GNG, the SST and the Trail Making B (Gorlyn et al., 2005; Keilp et al., 2005; Spinella, 2004). In general, the BIS-11 factors seem to be differentially correlates with cognitive control processes (Huang et al., 2017).

Regarding the cognitive control of stimulus-driven actions, we know that proactive and reactive control mechanisms have different neural basis, with proactive control related specifically to PFC activation and reactive control associated to the activation of ACC, posterior cortical and medial temporal lobe regions (Braver et al., 2009; Huang et al., 2017). These two cognitive control mechanisms may differently contribute to impulsivity traits. In particular, the motor component of impulsivity, because of its close relationship to response inhibition, action restraint and premature responding, seems to be the impulsivity dimension more highly related to the

efficiency of cognitive control mechanisms in the context of stimulus-driven actions (Gorlyn et al., 2005; Huang et al., 2017; Keilp et al., 2005; Spinella, 2004).

4.4 Experiment 3 - Motor impulsivity trait and proactive control: an fMRI study

4.4.1 Introduction

The ability to flexibly control our behavior in relation to internal or external feedback requires suppressing inappropriate action tendencies or urges. Many daily-life situations require to refrain from acting in an automatic manner, braking internal desires which interfere with long-term plans, or interrupting ongoing actions which are no longer appropriate. Therefore, response inhibition, which refers to the ability to inhibit planned or ongoing motor actions, represents a crucial subcomponent of cognitive control (Mayer et al., 2016). Research on inhibitory control has been predominately based on studies investigating reactive mechanisms, that is the late-acting inhibition of prepotent motor responses following stimulus presentation (Aron, 2011; Criaud et al., 2017; Di Russo et al., 2016). These reactive mechanisms appear to depend on the operation of top-down endogenous processes, responsible for a proactive form of inhibition, which represents a critical component of the response inhibition system (Criaud et al., 2012). Indeed, the motor output pathway also shows inhibitory modulations during action preparation, even during the planning of simple movements (Duque et al., 2012, 2013, 2017; Greenhouse et al., 2015; Labruna et al., 2014; Lebon et al., 2015; van Campen et al., 2014). Therefore, the motor system is

inhibited not only when a movement needs to be aborted after an internal or external ‘no-go’ signal, but also when it is in the process of selection of a future action (Duque et al., 2017). The fundamental role of proactive inhibition processes emerges particularly in daily life situations in which the required outcome is unknown. In the laboratory context, this condition can be studied by the ‘go/no-go’ task (GNG) (Criaud et al., 2017). While subjects are waiting for the stimulus, they don’t have the certainty about the event to come and, therefore, they need to withhold fast automatic responses to any upcoming stimuli (‘Go’ or ‘Nogo’) through a proactive inhibition process. In this framework, proactive mechanisms activate cognitive control in an anticipated manner, biasing in advance attention, perception and motor systems (Braver, 2012; Criaud et al., 2017; Jacoby et al., 1999; Nigg, 2017). Proactive inhibition seems to reflect the operation of two concurrent inhibitory mechanisms (Duque et al., 2010, 2012). One mechanism, named competition resolution, suppresses competing response representations facilitating response selection and assisting in determining which response to make (Coles et al., 1985; Duque et al., 2010; Usher & McClelland, 2001, 2004). The other mechanism, called impulse control, decreases the activation of the selected response in order to prevent its premature execution (Duque et al., 2010). This latter inhibition mechanism acts like a ‘brake’ that transiently suppresses the motor output without stopping it completely (Jahfari et al., 2010; Meyer & Bucci, 2016): if the attended stimulus requires an action it release the response, setting the system in a ‘go’ mode; if the attended stimulus requires an inhibition of the response it maintains the system in the ‘no-go’ mode, without the need of additional inhibition (Di Russo et al., 2016). These two inhibition mechanisms involve independent prefrontal cortical projections to primary motor cortex (M1) (Greenhouse et al., 2015).

Indeed, the prefrontal cortex (PFC) and the inferior parietal cortex (IPC) seems to be responsible for proactive inhibition, and M1, the supplementary motor cortex (SMA), and the putamen likely represent the target sites of this inhibition (Jaffard et al., 2008).

Therefore, while on the one hand preparation mechanisms permit to pre-activate sensory and motor cortices, in order to execute an appropriate response at the correct time, on the other hand inhibitory neural mechanisms transiently suppress this motor excitability in order to increase cognitive and behavioral efficiency, avoiding the premature release of the motor output (Funderud et al., 2012). Hence, a crucial role of proactive control is to adjust the level of motor readiness, which is increased and maintained by phasic alertness during the preparation of a movement (Criaud et al., 2012; Raz & Buhle, 2006; Sturm & Willmes, 2001; Sturm et al., 1999; Yanaka et al., 2010). In the laboratory context, phasic alertness is triggered by a cue stimulus, named 'warning signal' (WS), preceding the response stimulus (Di Russo et al., 2016; Yanaka et al., 2010). WS activates the 'anterior alerting system' (Sturm & Willmes, 2001), which is the network associated with vigilance and intrinsic alertness, and includes the anterior cingulate cortex (ACC), the thalamus and the midbrain (Yanaka et al., 2010). This 'anterior alerting system', along with the dorsal premotor area (PMd) and the insula, seems to act as prime on the pre-SMA, triggering action selection and action preparation processes and determining a facilitation on motor processing (Yanaka et al., 2010). Therefore, phasic alertness acts as a counteracting force against top-down inhibitory processes, since it triggers motor preparation processing, reducing action threshold and, then, facilitating the preparation of motor responses (Callejas et al., 2004, 2005; Mannarelli et al., 2015; Weinbach & Henik, 2011). This facilitation of movement elicited by phasic alertness during motor preparation needs to be

temporarily inhibited by the proactive control, in order to avoid the release of automatic, premature motor responses (Criaud et al., 2012; Weinbach & Henik, 2011). The balance between phasic alertness and proactive inhibition could be altered in people with impulsivity traits, determining the typical failure in the inhibition of prepotent motor responses.

Deficient control of behavior is a key aspect of impulsivity, which is generally attributed to an impairment of the executive functions (Bari & Robbins, 2013). Trait impulsivity represents a multidimensional construct, mediated by distinct psychological and neural mechanisms (Aichert et al., 2012; Barratt et al., 1987; Buss & Plomin, 1975; Dalley & Robbins, 2017; Eysenck & Eysenck, 1977; Gerbing et al., 1987; Pietrzak et al., 2008), and broadly defined as a predisposition toward rapid and unplanned reactions to internal or external stimuli, without adequate forethought, often resulting in inappropriate and premature actions (Durana & Barnes 1993; Evenden, 1999; Moeller et al., 2001; Voon & Dalley, 2016). Impulsivity, along with lack of self-control and behavioral inhibition, characterize a number of psychiatric conditions such as attention deficit/hyperactivity disorder, drug addiction, schizophrenia, and impulse control disorders (e.g. pathological gambling, hypersexuality, compulsive eating and shopping) (Bari & Robbins, 2013; Gut-Fayand et al., 2001; Jentsch & Taylor, 1999; Nigg, 2001).

The heterogeneity of impulsivity is well captured by the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995), which measures three factors, named ‘motor impulsivity’, that is the tendency to act without thinking, ‘attentional impulsivity’, referring to the readiness to make quick cognitive decisions and ‘non-planning impulsivity’, which refers to the degree of focus on only the present. The presence of

several dimensions of impulsivity make it difficult to analyze the correlation with cognitive control, which includes in turn a set of complex mental processes (Huang et al., 2017). The three BIS-11 factors seem to be differentially correlated with cognitive control processes and, moreover, motor impulsivity appears to be the component more highly correlated with measures of cognitive control, as the GNG (Gorlyn et al., 2005; Huang et al., 2017; Keilp et al., 2005; Spinella, 2004). Furthermore, because of its close relationship to response inhibition, action restraint and premature responding, motor impulsivity trait might be the impulsivity dimension more highly related to the efficiency of the proactive control mechanism (Gorlyn et al., 2005; Huang et al., 2017; Keilp et al., 2005; Spinella, 2004).

Recently, it has been shown a relationship between impulsive personality trait and pre-movements electrophysiological activity as revealed by the Readiness Potential (RP) (Rossi et al., 2018). In particular, during the preparation of self-initiated movements the RP shows an earlier negative rising phase and a greater amplitude in subjects with higher trait impulsivity scores. These differences in the RP dynamics seem to reflect differences in motor system excitability during the preparation of a movement. Indeed, the greater amplitude of the RP observed in individuals with higher impulsivity traits, may reflect a greater motor system excitability, which might determine a diminished reactivity threshold and an insufficient control over sub-threshold inappropriate urges. These data lead us to hypothesize a less effective preparatory inhibition mechanism. Based on these data and on recent studies suggesting that voluntary and stimulus-driven systems share the same central preparatory mechanisms (Hughes et al., 2011; Schurger et al., 2012), we might expect a less effective proactive inhibition process and a greater phasic alertness in impulsive

people during the preparation of stimulus-driven actions. To test this hypothesis, we administered the Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995) to twenty-six healthy subjects, in order to measure the motor impulsivity dimension. Then, subjects underwent fMRI acquisition during execution of an event-related GNG, in which the response stimulus (Go or Nogo) was preceded by a ‘warning signal’ (WS), to trigger phasic alertness. Analyzing the ‘readiness’ period, in which subjects are waiting and preparing for the upcoming stimulus, allows us to investigate the operation of proactive control and its regulatory action on the level of phasic alertness.

4.4.2 Material and Methods

Participants

Twenty-six young healthy adults took part in the experiment (male=11, female=15; mean age=29.5 years, standard deviation=6.0 years; mean education=17.3 years, standard deviation=3.6 years). All participants were blind to the purpose of the study, right-handed and had normal or corrected- to-normal vision. None had history of psychiatric or neurological diseases. Participants were screened to ensure that they satisfied MRI safety requirements and no structural brain abnormalities on MRI sequences obtained before the fMRI task. Written informed consent was obtained from each participant, in conformity with the Helsinki Declaration and approved by the local ethics committee. All participants completed the BIS-11 questionnaire. Raw scores for the motor impulsivity subscale of the BIS-11 ranged from 12 to 29 (mean = 19, standard deviation = 4.23) and were converted to a z-score.

Experimental paradigm

Participants viewed stimuli on a MRI-compatible display system (SensaVue fMRI, Invivo Corporation, Gainesville, FL, USA) by means of a mirror attached to the head coil. The protocol replicated entirely a previous study (Gavazzi et al., 2017) both for what concern the paradigm and the scanning time per condition and subjects. Participants were asked to press a button as quickly as possible with their right index finger when a 'go' stimulus was presented and not to respond when no-go stimulus was displayed. A descending series of asterisks was presented at the beginning of each trial to prepare participants to the proper GNG stimulus ('readiness' condition). Each trial started with five asterisks presented for 250 ms, followed by a blank screen displayed for 750 ms; then four asterisks were presented for 250 ms followed by 750 ms of blank screen. The countdown continued until a single asterisk was displayed for 250 ms and followed by a blank screen for 750 ms (Figure 9). After disappearance of the last asterisk, the Go or the Nogo stimulus was presented for a temporal interval of 250ms. The letter 'X' was the stimulus for Go trials and the letter 'A' was the stimulus for the Nogo trials. Participants had to press one button of a MRI-compatible response collection system (Lumina LP-400, Cedrus Corporation, San Pedro, CA, USA) as rapidly as possible after the presentation of the 'X' letter. Reaction times were calculated. Pressing the button after a period of 1500 ms after the Go stimulus was considered an error of omission, whereas responses within 1500 ms after a Nogo stimulus were considered an error of commission. At the end of each trial a blank screen of rest was presented for 6 seconds. The entire experiment was composed by 2 sessions. A training session and an experimental session. The training session was composed by a block of 12 trials to ensure understanding of the instructions. The

experimental session was composed by a total of 48 trials, equally balanced but randomized among conditions: 24 Go and 24 Nogo trials. This task design was chosen to reduce behavioral performance confounds (i.e., reduced accuracy) and to reduce the possibility that differences in cerebral activity between Go and Nogo trials can be due to an 'odd-ball' effect (Liddle et al., 2001; Zandbelt et al., 2013).

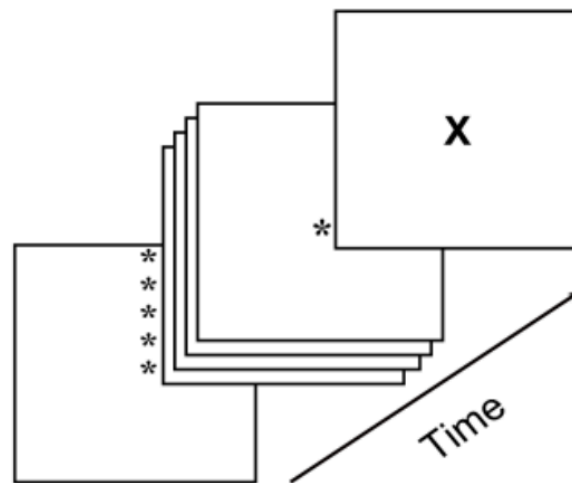


Figure 9. GNG procedure. Each trial started with a descending series of asterisks: five asterisks were presented for 250 ms, followed by a blank screen for 750 ms. Subsequently four asterisks were presented for 250 ms followed by 750 ms of blank screen. The countdown continued until a single asterisk was displayed for 250 ms and followed by a blank screen for 750 ms. Depending on the condition was displayed the Go ('X') or the Nogo ('A') stimulus for a temporal interval of 250ms. Subjects had to press a button as rapidly as possible after the presentation of the Go stimulus and to not answer to the Nogo stimulus.

MRI data acquisition

MRI acquisitions were performed on a 3T scanner (Ingenia, Philips Healthcare, The Netherlands) equipped with Omega HP gradients with maximum amplitude of 45 mT/m and slew rate of 200 T/m/s for each axis. All subjects underwent 3D T1-weighted imaging and fMRI, using a 32-phased-array-element head coil. T1-weighted MR images were acquired with a sagittal high resolution 3D sequence (repetition time [TR]/echo time [TE]/inversion time [TI] = 8/3.7/925.6 ms, flip angle [FA]=8°, slice thickness=1 mm, field of view [FOV]=240mm×240 mm, number of slices=191,

matrix size=352×352). For the fMRI experiment we employed a T2*-weighted echo-planar imaging (EPI) sequence (TR/TE = 3000/35 ms, FA=90°, slice thickness=4 mm, FOV=240 mm×240 mm, number of slices=39, matrix size=144×144). Two hundred and forty-five scans were acquired, for a total acquisition time of about 12 minutes, from which the first 5 scans were discarded to avoid T1-related relaxation effects.

4.4.3 MRI imaging analysis

Processing and analysis were conducted using FEAT (fMRI Expert Analysis Tool), version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Functional images of each individual participant were first corrected for motion using MCFLIRT (Jenkinson et al., 2002) and for slice-timing using custom parameters obtained from the manual of operation of the scanner. Temporal high-pass with cut-off at 50 s, and spatial smoothing using a 6 mm full width half maximum (FWHM) Gaussian kernel and grand-mean intensity normalization of the entire 4D data set by a single multiplicative factor were applied as filtering steps.

Co-registration of fMRI images to the individual high resolution T1- weighted image was carried out using 6 DOF registration (Jenkinson et al., 2002; Jenkinson & Smith, 2001). The individual high-resolution T1-weighted images were co-registered to the standard-space Montreal Neurological Institute (MNI) 152 brain, with an affine transformation followed by a non-linear transformation using FNIRT (Andersson et al., 2007a,b). Timepoints in the fMRI dataset corrupted by large motion (greater than 0.8 mm of the absolute mean displacement) were identified from motion correction parameters (MCFLIRT) and accounted for in a confound matrix at the subject level

analysis (Power et al., 2012). Stimuli affected by commission or omission errors to the task were censored including them in the confound matrix. The explanatory variable was convolved with a double gamma hemodynamic response function, whereas the temporal derivative was included and temporal filtering applied.

To establish within-group activity of Nogo-baseline condition, we investigated significant within-group positive and negative statistics using one-sample t-test and a mixed effects model using FLAME (FMRIB's local Analysis of Mixed Effects). The resulting Z (Gaussianized T/F) statistic images were thresholded using clusters determined by $Z > 4.0$ and a (corrected) cluster significance threshold of $p < 0.001$.

In revealing activity related to the motor preparation processes, a General Linear Model (GLM) for exploring activations associated to readiness condition was set at subject level analysis. The sequence of 'readiness' trials was comprised of volumes associated to asterisks presentation (two volumes per trial). In addition, to evaluate potential polarization due to Go or Nogo stimuli presented in the previous trial, a GLM for the ['Nogo readiness' – 'Go readiness'] contrast was set at subject level analysis. More precisely, the sequence of 'Go readiness' trials was comprised of volumes associated to the asterisks presentation when in the previous trial was presented a Go stimulus, whereas the sequence of 'Nogo readiness' trials was comprised of volumes associated to the asterisks presentation when in the previous trial was presented a Nogo stimulus. Since the experimental design involved randomized intervals stimuli we reduced autocorrelation in the data applying voxelwise prewhitening (Woolrich et al., 2001).

At the group level analysis, for the readiness condition we investigated significant within-group positive and negative regression statistics of BIS-11, motor

impulsivity subscale z-score, as the variable of interest, whereas gender, age and educational level were included in the model as nuisance covariates using a t-test and a mixed effects model using FLAME (FMRIB's local Analysis of Mixed Effects). For the ['Nogo readiness' – 'Go readiness'] contrast we investigated significant within-group positive and negative activations. The resulting Z (Gaussianized T/F) statistic images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $p < 0.05$.

4.4.4 Results

Behavioral data

The average percentage of correct responses was 99.8% for Go events (1 error of omission) and 96.2% for the Nogo events (24 errors of commission). Data containing commission or omission mistakes have been excluded by the reaction times analysis. Participants had an average reaction times of 364.8 ms and a standard deviation of 54.8 ms.

fMRI results

The Nogo-baseline condition analysis showed significant positive activations (Table 1). No significant negative activations were reported.

Analysis of BIS-11 motor impulsivity subscale regression with BOLD activations for the readiness condition revealed one cluster of significant positive association ($Z\text{-max} = 4.04$; $P = 0.0382$; $Z\text{-max-X} = -44\text{mm}$; $Z\text{-max-Y} = -24\text{mm}$; $Z\text{-max-Z} = 48\text{mm}$). According to the Harvard-Oxford Atlas (lateralized), the cluster

included the left postcentral gyrus (PCG), left precentral gyrus (PRG), left superior parietal lobule (SPL), anterior and posterior division of the left supramarginal gyrus (SMG), left angular gyrus (AG) (Figure 10). No significant cluster of positive or negative activation were found for the study of [‘no-go readiness’ – ‘go readiness’] contrast.

Region	Z-MAX	Z-MAX X (mm)	Z-MAX Y (mm)	Z-MAX Z (mm)	Voxels
Lateral Occipital Cortex R	7.12	38	-72	-18	8466
pre-SMA	5.99	0	10	48	4621
Insula/Putamen R	6.42	32	24	-6	4521
Lateral Occipital Cortex L	6.47	-38	-90	-2	3385
Middle Frontal/Precentral Gyrus R	6.06	54	6	38	1177
Cerebellum	5.64	-4	-78	-22	753
Superior Parietal Lobule L	5.39	-24	-56	44	624
Anterior Prefrontal Cortex L	5.52	-32	46	12	540
Superior Parietal Lobule L	5.55	-34	-44	60	527
Precuneus	5.29	0	-60	62	192
Middle Frontal/Precentral Gyrus L	4.74	-52	0	36	117

Table 1. Summary of the significant clusters of positive activation for the Nogo trials versus baseline condition (L = left; R = right). All coordinates are reported in MNI space. Note: p-value < 0.001

4.4.5 Discussion

Research on trait impulsivity is focused on the investigation of reactive inhibition processes. Proactive top-down inhibition is however a critical component of the response inhibition system, which has a relevant influence on reactive inhibition processes. Analyzing the readiness period, in which subjects are waiting and preparing for the upcoming stimulus, we investigated the operation of proactive control and its regulatory action on the level of phasic alertness. To this aim, participants were

administered the BIS-11 questionnaire for the assessment of motor impulsivity trait and underwent fMRI acquisition during the execution of an event-related GNG triggering phasic alertness.

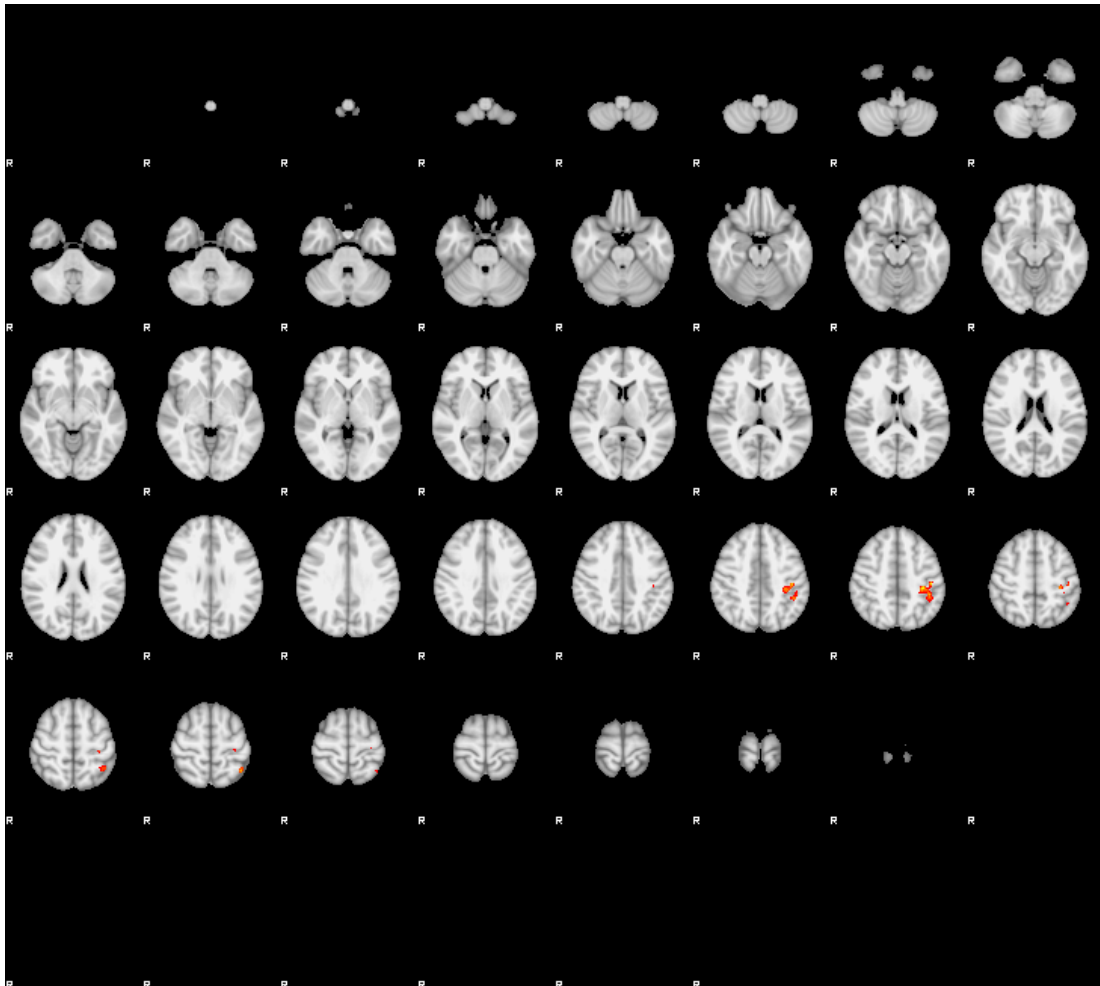


Figure 10. Cluster of significant positive associations (Z -max = 4.04; P = 0.0382; Z -max- X = -44mm; Z -max- Y = -24mm; Z -max- Z = 48mm) revealed by analysis of BIS-11 motor impulsivity subscale regression with BOLD activation during the ‘readiness’ period of the GNG task.

Behavioral errors were not highlighted by the specific task design employed here, where Go (50%) and Nogo (50%) stimuli were equally presented. This GNG task design allows to reduce behavioral performance confounds (i.e. reduced accuracy) typically observed in impulsive subjects during more difficult inhibitory control tasks.

In agreement with previous studies the Nogo-baseline condition analysis of fMRI data showed significant positive activation in right pre-SMA, bilateral occipital regions and the precuneus (Simmonds et al., 2008)

We found a positive association between motor impulsivity scores and the activation in left PCG, left PRG, left SPL, anterior and posterior division of the left SMG and left AG.

Our main result is the positive association found between motor impulsivity scores and the activation of left PCG and PRG, which are usually inhibited by prefrontal cortical projections during the preparation of motor responses (Greenhouse et al., 2015). Furthermore, these sensorimotor activations are lateralized to the left hemisphere and, therefore, concern the selected response (right-hand motor response). We can hypothesize that the greater sensorimotor activation observed with increased motor trait impulsivity could be driven by subthreshold right-hand motor responses. Indeed, impulsive errors entail both a motor system capture by an urge to act and a failed inhibition of that impulse (Spieser et al., 2015). However, an inappropriate urge does not always result in error, as it was found in our study because of the specific task design employed. During motor preparation, the presence of a greater amount of subthreshold motor responses in high impulsive people might involve a higher probability that these covert urges reach movement threshold and trigger a premature and undesired response. Furthermore, these data are in line with a previous electrophysiological study, which found a positive correlation between the amplitude of the RP and trait impulsivity scores during the preparation of self-initiated movements (Rossi et al., 2018). We cannot, however, exclude that the greater sensorimotor activation observed in the present study, can be due to an overt

movement of the right hand before the effective recorded movement. It is possible that, during the warning period, high impulsive subjects may have the tendency to make a greater amount of button touches, or even finger movements with the selected hand, which however do not lead to the complete pressure of the button. This condition might be due to an increased tension and a greater and persistent readiness to act. Further studies are needed to deeper investigate this aspect.

Another interesting result is the positive association between motor impulsivity scores and the activation in left inferior parietal lobule (IPL), that is the left AG and left SMG. This result is in line with a recent study, investigating cognitive control in trait impulsivity with a hybrid-designed Stroop task (Huang et al., 2017). Authors found a positive correlation between motor impulsiveness and proactive control in the left IPL. Activation in the IPL is usually associated with working memory, which has a fundamental role in proactive control (Yi et al., 2009; Yi & Friedman, 2011; Zhang et al., 2010). Furthermore, Jaffard and colleagues (2008) postulated that the IPL, together with the medial PFC (mPFC) seems to be responsible for proactive inhibition, and M1, the SMA, and the putamen likely represent the target sites of this inhibition. Authors hypothesized an active role of the IPL in top-down inhibitory control. Activation of the inferior parietal cortex has been already reported in inhibition tasks (e.g., Blasi et al., 2006; Garavan et al., 1999, 2002, 2006; Kelly et al., 2004; Rubia et al., 2003; van Veen et al., 2001) but its specific role remains unclear.

Another region involved in proactive control and positively associated with motor impulsivity in our study is the SPL. This region, together with bilateral PMd and left putamen, is part of a network, named ‘SPL network’, which is connected with M1 and specifically involved in proactive inhibition, reflecting a top-down influence

over motor control (Jang & Hong, 2012; Rizzolatti et al., 2001; Schmahmann et al., 2007; Van Belle et al., 2014; Yeterian & Pandya, 1993; Zandbelt et al., 2013).

Therefore, the greater activation in left IPL and SPL found in our study might be due to a greater difficulty in completing proactive control processes. Moreover, the lateralization to the left hemisphere suggests that these activations are related to movement initiation. Furthermore, this more effortful proactive control might be related to the greater sensorimotor activation, which seems to characterize impulsive people.

IPL and SPL are also regions classically activated in attention-related tasks (Corbetta et al., 1993, 1998, 2000; Culham et al., 2001; Hopfinger et al., 2000; Perry & Zeki, 2000; Wojciulik & Kanwisher, 1999). In particular, SPL has found to be implicated in top-down attentional control (Corbetta & Shulman, 2002). For this reason, activations found in IPL and SPL might be also due to a higher attentional demand.

Contrary to our expectations, we didn't find associations between motor impulsivity scores and the activation of the phasic alertness network (Yanaka et al., 2010). This result might be due to the GNG design, which has a definite and constant interval between WS and the response stimulus. Further studies, using different GNG task design, will be needed to clarify the role of phasic alertness in trait impulsivity.

In conclusion, in studying proactive top-down control processes, it is of high importance to consider the inter-individual variability in trait impulsivity, with particular attention to the motor dimension. During response preparation, the greater left sensorimotor activation observed with the increase of motor impulsivity scores, could be driven by subthreshold right-hand motor responses. This condition might

represent a disinhibition of the motor system, characterized by a diminished reactivity threshold and a reduction in the control over covert urges. The present finding is in line with previous electrophysiological data concerning a greater motor system excitability in subjects with higher trait impulsivity score, reflected by a greater amplitude of the RP during the preparation of self-initiated movements (Rossi et al., 2018). Furthermore, the greater sensorimotor activation in our fMRI study is accompanied by a greater activation in left inferior and superior parietal lobule, which might be related to a more effortful proactive control implementation.

The brief scanning time and the sample size could represent a limitation in the present study. Future studies are needed to better understand proactive control functioning in healthy impulsive people and in clinical populations.

GENERAL DISCUSSION



Cognitive control of actions is the core feature underlying the ability to flexibly regulate our behavior and is characterized by a relevant inter-individual variability (Braver et al., 2009; Haggard et al., 2008). Investigating this function in relation to individual differences becomes of considerable importance in the case of trait impulsivity, whose maladaptive behaviors have a great impact on the lives of individuals and society (Bari & Robbins, 2013; Fuster, 2008; Gansler et al. 2009). A better understanding of cognitive control functioning in impulsive behavior is also functional to the study of associated psychiatric conditions (Bari & Robbins, 2013; Nigg, 2001).

The aim of the present research was to investigate trait impulsivity effects on the cognitive control of intentional and stimulus-driven actions, analyzing preparatory action mechanisms.

Three experiments were discussed. The first two investigated the timing component of intentional actions, analyzing the process between the decision to move and action execution, with behavioral and electrophysiological measures. Instead, the third study aims to enrich previous results exploring neural mechanisms involved in the preparation of a stimulus-driven action, using fMRI technique.

Overall, findings suggest the presence of an abnormal operation of preparatory mechanisms in trait impulsive people, both for intentional and stimulus-driven actions.

Concerning the cognitive control of intentional actions, results showed that trait impulsivity seems to be related to a delayed awareness of voluntary action, which appears to be a possible determinant of voluntary inhibition failures typical of impulsive behavior (Giovannelli et al., 2016). A shorter interval between the conscious decision to move (W) and the action execution, might interfere with processes underlying the conscious ‘veto’ of the impending action. Our data extended findings in neurological conditions characterized by disorders of volition, such as patients with parietal lesions (Sirigu et al., 2004), psychogenic tremor (Edwards et al., 2011), Gilles de la Tourette syndrome (Moretto et al., 2011, Ganos et al., 2015), and Parkinson’s disease (Tabu et al., 2015), suggesting that a delayed awareness of the intention to act may also be related to personality traits. We argued that in healthy individuals with higher impulsivity traits, such delayed perception of volition can more likely exceed the ‘point of no return’, after which the initiation of an action cannot be cancelled, determining a failure in voluntary inhibition.

We, therefore, wondered if individual differences in the perception of volition and in the ‘veto’ interval observed in impulsive people might be related to differences in the dynamics of brain potentials related to motor preparation. Indeed, EEG recording represent a valuable tool to shed light on the neural basis of the relationship between trait impulsivity and the timing component of intentional actions. We, therefore, investigated this relationship analyzing the dynamics of the Readiness Potential (RP) during the preparation of intentional actions. What we found was the presence of irregularities in the neural activity prior to action execution in function of trait impulsivity (Rossi et al., 2018). In particular, with higher impulsivity scores the RP showed an earlier negative rising phase and a greater amplitude. Individual

differences in the RP dynamics seems to reflect differences in motor system excitability during the preparation of self-initiated movements. In particular, the earlier negative rising phase and the greater amplitude of the RP observed in high impulsive subjects, lead us to hypothesize the presence of a greater activation of the supplementary motor area (SMA) and the pre-supplementary motor area (pre-SMA) during motor preparation. We may speculate that this condition might determine a reduction in the operation of the preparatory inhibition mechanism and in the control over sub-threshold urges, resulting in a diminished motor system efficiency. Indeed, preparatory inhibition process seems to reflect an automatic gain modulation mechanism, which allows to improve motor behavioral performance allowing to avoid a premature implementation of an action and to prevent selection of inappropriate responses (Braver, 2012; Criaud et al., 2017; Di Russo et al., 2016). Furthermore, the supplementary motor complex (SMC), and in particular the pre-SMA, has a key role in the control of actions, in that it suppresses on-line the sub-threshold activated responses, preventing it from turning into overt errors.

Present findings expand previous data revealing that the interval between the conscious intention to move and the execution of a self-initiated movement is related to impulsive personality traits (Caspar & Cleeremans, 2015; Giovannelli et al., 2016). However, we did not find any correlation between W and RP measures. This result is in line with theories who claim that there cannot be a causal relationship between the onset of the RP and W (Haggard & Eimer, 1999), refuting the original interpretation of the RP which defines the onset of the potential as the starting point of volitional acts (Libet et al., 1983). The relationship between W and RP in function of trait impulsivity needs to be thorough with future studies using larger samples.

Based on recent studies, which suggest that voluntary and stimulus-driven systems share the same central preparatory mechanisms (Hughes et al., 2011; Schurger et al., 2012), we wondered if the greater motor activation observed in impulsive people when preparing for voluntary movements could be present also in the preparation of stimulus-driven actions. We, therefore, explored proactive control mechanisms in relation to motor impulsivity, analyzing the ‘readiness’ period of a go/no-go during fMRI acquisition. We didn’t find differences in the behavioral performance, probably because of the task design. However, we found a positive association between motor impulsivity scores and the activation of left post-central gyrus (PCG) and left pre-central gyrus (PRG), which are usually inhibited by prefrontal cortical projections during the preparation of motor responses. It is possible that this greater left sensorimotor activation may be driven by subthreshold right-hand motor responses. We might, therefore, hypothesized a disinhibition of the motor system, characterized by a diminished reactivity threshold and a reduction in the control over covert urges. The present finding is in line with previous electrophysiological results (Rossi et al., 2018). However, we cannot exclude that the greater sensorimotor activation observed in this fMRI study can be due to overt movements of the right hand before the effective recorded motor response. It is possible that, during the warning period, high impulsive subjects may have the tendency to make a greater amount of button touches, or even finger movements with the selected hand, which however do not lead to the complete pressure of the button. This condition might be due to an increased tension and a greater and persistent readiness to act. Further studies are needed to deeper investigate this aspect.

Finally, the greater sensorimotor activation in our fMRI study is accompanied by a greater activation in left inferior and superior parietal lobule, which might be related to a more effortful proactive control implementation. This could reflect a compensatory mechanism implemented by participants with higher degree of motor impulsivity trait to reach a correct inhibition.

Overall, these findings suggest the presence of an abnormal functioning of preparatory mechanisms, both for intentional and stimulus-driven actions. This condition might be responsible for the maladaptive behavior, which characterize impulsive people.

Research on this topic is only at the beginning and current findings provide a rationale for further studies aiming to better understand the operation of preparatory and proactive control mechanisms in healthy impulsive people and in clinical populations.

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