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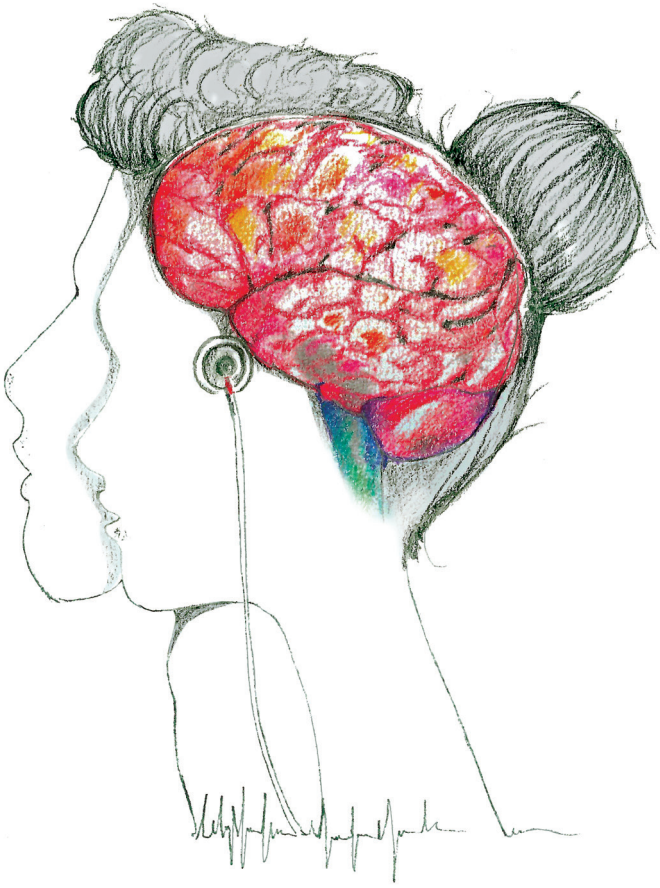
Getting ready to act

Neurocognitive aspects of action preparation

Rinaldo Livio Perri



University Press

Sapienza Università Editrice

Collana Studi e Ricerche 93

Medicina

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Rinaldo Livio Perri

SAPIENZA
UNIVERSITÀ EDITRICE
2020

Sapienza Università Editrice
Piazzale Aldo Moro 5 – 00185 Roma

www.editricesapienza.it
editrice.sapienza@uniroma1.it

Iscrizione Registro Operatori Comunicazione n. 11420

ISBN 978-88-9377-138-2

DOI 10.13133/9788893771382

Pubblicato a giugno 2020

Impaginazione/layout a cura di: Rinaldo Livio Perri

In copertina: Assunta Montanini, *Functional brain* (2020).

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1. General introduction

1.1. Motor control: the neurophysiology behind the voluntary action

Voluntary movements differ from reflex movements in several ways. The first important difference is that the voluntary movements are purposeful, so the direction, speed and nature of the movements depend on the goal of the motor behavior. Second, the performance of a voluntary movement might be influenced by practice and learning, such as in the case of training and sport activities. Finally, even if the voluntary movement may follow a sensory stimulus, this latter is not needed. In fact, the voluntary movement could be internally generated, differently from the reflexes, typically evoked by a stimulus. On the basis of the aforementioned characteristics one can already figure out the neurophysiological complexity behind the voluntary movement. For example, also a simple action such as reaching a bottle of water needs complex processes like the sensory identification and localization of the target, the planning of the movement, the action execution and monitoring; the information about the own body position and the external environment are also needed to prepare the limb movements and to correct the trajectory while reaching. All these functions are processed by different cortical and subcortical regions of the central motor system.

At cortical level, one of the more early and important discovery concerns the somatotopic organization of the motor areas. The pioneering studies of Gustav Fritsch and Eduard Hitzig (1870) demonstrated that the electrical stimulation of distinct areas of the

dogs' brain evoked movements in the contralateral side of the body. These results were immediately replicated by David Ferrier (1874), who extended them to the monkeys. Over the years, the animal and human studies in this field allowed to identify the extent and physiology of the cortical motor areas that are not limited to the primary motor cortex: in fact, as shown in Figure 1.1, they also include regions of the parietal and frontal cortex. The more anterior motor areas are part of the so called premotor areas, that is the supplementary motor area (SMA) and the premotor cortex. As we will see, there are also prefrontal cortex regions that can influence the movement, especially because of their role in the emotional and cognitive aspects such as the inhibitory control, motivation, working memory and attentional control. The main role of the cortical motor areas in the generation of a voluntary movement will be described below.

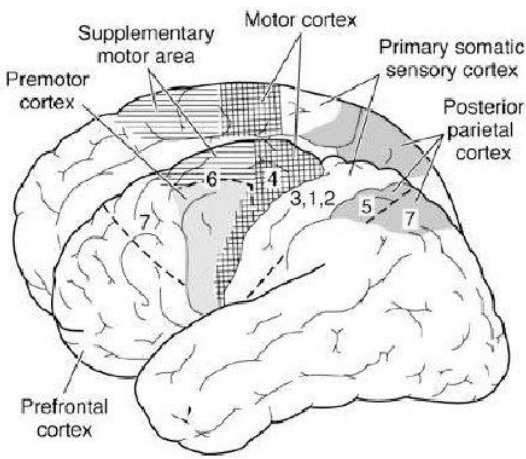

Fig. 1.1 Cortical motor areas.

1.1.1. The primary motor cortex

The primary motor cortex (also known as M1) is located in the Brodmann area (BA) 4, exactly in the posterior portion of the frontal lobe. As previously discussed, and as showed in Figure 1.2, the motor cortex contains a motor map of the body, with the face extending over the lateral surface, and the legs, arms, and trunk represented on the dorsal side.

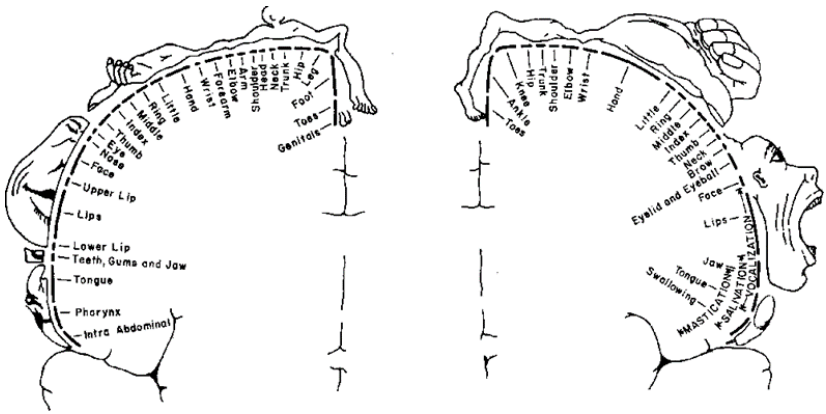

Fig. 1.2. Motor map of the primary motor cortex.

The body parts are not equally represented in the motor map; also, their cerebral proportions do not reflex the real body dimensions. In fact, muscles requiring precision and fine control, such as the hands, have larger representation on the cortex.

It is noteworthy that the somatotopic organization of the motor cortex is not fixed but can be modified as effect of motor learning and injury. This plasticity was demonstrated, for example, by Sanes et al. (1990) that denervated the whiskers area in the motor map of the rats; after that, they observed that the electrical stimulation of the same area evoked forelimb movements as effect of cortical reorganization. At the same time, a neuroimaging study of Karni et al. (2005) in human subjects showed the activation of larger areas of the motor cortex during the performance of trained motor sequences if compared to the untrained condition. The primary motor cortex is mainly involved in the execution of the intended movements. However, as summarized by Cheney (1985), three could be the functions of this area:

1) It receives motor instructions from other cortical areas and translates them into motor commands that specify the muscles to contract and relax, such as the force and timing of contraction.

2) Informs subcortical areas (cerebellum and basal ganglia) of the "intended" movement.

3) Participates in muscles stretch reflex and cutaneous grasp reflex. Summarizing, M1 is the last cortical area firing before the

execution of a voluntary movement: in a monkey study (Evarts et al., 1968) it was calculated that the neuronal populations of this area become active about 100 ms before the movement onset.

1.1.2. The premotor areas

The premotor areas are part of the BA 6, located just in front (anterior) to the primary motor cortex and extending on the lateral and medial surface of the cortex.

About 60 years after the first electrical stimulation studies of Fritsch, Penfield and Boldrey (1937) showed that the stimulation of the humans' premotor areas was able to produce movements as well. However, the intensity of the electrical stimulation had to be greater than that needed to evoke movements by the stimulation of the primary motor area. Moreover, different from the M1, the stimulation of these areas produced more complex movements involving multiple joints, such as reaching-like behaviors; also, the stimulation of the medial side of BA 6 produced bilateral movements, suggesting its role in coordinating the two sides of the body.

The lateral part of the BA 6 is defined as premotor cortex (see Fig. 1): specific functions of this area are difficult to identify, but it appears to be more involved in externally rather than internally cued movements. The premotor cortex receives strong cortical sensory inputs (Petrides and Pandya, 1984) and can affect movement by direct influence on M1, by major reentrance loops or by direct actions on brainstem influencing proximal and axial muscles (Wiesendanger, 1981; Cheney, 1985).

Otherwise, the medial part of the premotor areas is the SMA, in front of which is located a small area called pre-SMA. This latter region projects just to the SMA and has no a clear somatotopy. The pre-SMA is thought to be involved in the learning of a new motor sequence, because it is no more active during the execution of the same motor program after it has been learned (Krakauer and Ghez, 2000). At the same time, the pre-SMA becomes active when subjects have to discard a current plan and acquire a new plane for the future motor performance (Tanji, 1996), such as in case of task initiation and switching (Braver and Barch, 2006; Dosenbach et al., 2006).

One of the main cortical areas participating in the preparation of a voluntary movement is the SMA: the functions of this area were firstly

described by Roland and colleagues (1980) studying the local cerebral blood flow in human subjects. The SMA has reciprocal afferent and efferent connections with many cortical and subcortical areas like the basal ganglia, thalamus, cerebellum, M1, somatosensory cortex and posterior parietal association cortex (Jones et al., 1978; Tokuno et al., 1992). This area has been traditionally associated to the generation of internally guided movements, as demonstrated by the occurrence of "motor neglect" and lack of spontaneous activity on the contralateral side when SMA is lesioned (e.g. Laplane et al., 1977; Tanji et al., 1985). However, despite the selectivity for the internally guide behaviors, evidences about SMA activation in externally triggered movements suggest to overcome this strong definition (for a review see Tanji, 1994).

The SMA has also been demonstrated to be more active before the execution of complex and sequential movements instead of simple and repetitive ones: these motor behaviors seem to be sustained by the basal ganglia outputs to the SMA, as demonstrated by the deficits subsequent their impairment, such as in case of Parkinson's disease (for a review see Cunnington et al., 1996).

One of the most important aspect of the SMA is its activation long before the movement is executed. Over the years, such early activity led to the proposal that SMA is strongly involved in the preparation and programming of motor behaviors. In fact, electrophysiological studies in human subjects showed the contribution of the SMA already 1 or 2 sec. before the movement onset, that is, before the decision to act becomes conscious (for a detailed description, see below in this chapter).

1.1.3. The parietal cortex

There are different areas of the parietal cortex on both hemispheres involved in motor control. First of all, before moving people have to allocate their attention to the external environment, looking at the spatial relationship among objects and integrating different sensory inputs from their own body. There are evidence that BA 3 and 5 of the parietal cortex underlie these functions. Specifically, area 5 receives it main inputs from the somatensory cortex (BA 3, 2, 1), using them to guide the exploratory limb movements. The BA 5 receives also information from the vestibular system about the orientation of the

head in space, from the premotor areas about the motor programs and by the limbic regions about the motivational state (Ghez, 1991). This area projects anteriorly to the premotor areas and posteriorly to the BA 7, where the visual information are integrated with somatosensory inputs from area 5. BA 7 is involved in visual feedback of eye and limb movements, such as in the processing of visual information about position of the objects in space: it control movements by its projections to premotor areas and cerebellum. An important feature of some neurons of area 7 is their selectivity for motivationally salient objects, suggesting the involvement of this area in a more general process of visuo-spatial attentional. In fact, deficits to the BA 7 can conduct to several neuropsychological impairments such as: neglect syndrome in the contralateral visual field (especially the lesions to the right hemisphere), apraxia, astereognosis, and difficulties with accuracy and grasping movements (Cheney, 1985).

It is noteworthy that recent evidences suggest also the involvement of more posterior areas of the parietal cortex in the preparation of a voluntary movement. Specifically, there is a growing body of literature reporting the role of the inferior parietal lobule (IPL; BA 39, 40) in the "intention" to move (for a review see Desmurget and Sirigu, 2012). Specifically, if electrically stimulated, the IPL generates an endogenous and unspecific experience of "wanting to act", differently to what happen with the premotor areas stimulation that evokes the "urge" to produce a specific movement. These observations suggest the view of the IPL as the area processing the desire to move, long before a clear motor program is performed. Support to this hypothesis come also from clinical studies, showing that patients with lesioned IPL loss the conscious experience of "wanting to move" or show the alien hand syndrome.

Finally, the posterior areas of the parietal cortex (especially the BA 40) are also involved in the awareness stage of the motor error commission, electrophysiologically represented by the error positivity (Pe) component, emerging at 300 ms after the erroneous response (e.g. Gehring et al., 1993). In other words, if the subjects commit an error, such as in case of a decision making task, the posterior parietal cortices process the internal detection of error by identifying the discrepancy between the executed and the expected action, as evoked by the stimulus features (for a review see Desmurget and Grafton, 2000).

1.1.4. The prefrontal cortex

The prefrontal cortex (PFC) is the most rostral region of the brain. It underlines a large part of the higher cognitive functions of the human beings, like the attentional control, decision making, problem solving, emotional and cognitive appraisal, social behaviors, motor planning and control, behavioral inhibition and so on. Because of the high complexity of this brain region, the present description will be limited just to the basic functions of the PFC, especially as regard its role in motor preparation and control; conversely, the next sessions will be more focused on specific aspects of the relationship between PFC and behavioral performance.

Overall, different functions are attributed to the different areas of the PFC. The medial PFC (MPFC; also including the anterior cingulated cortex) is mainly involved in the processes of motility, attention and emotion, as showed by the loss of spontaneity and the difficulty in the movement initiation of the MPFC lesioned patients (Verfaellie and Heilman, 1987; Cummings, 1993).

The orbitofrontal cortex is mostly involved in aspects of personality and attentional control (e.g. Damasio et al., 1994). The orbitofrontal lesions typically induce changes of social behavior, impulsivity and executive disorders as, for example, the difficulty to focus the attention on the targets and to inhibit the distracters.

The lateral PFC (LPFC) has a key-role in the preparation and organization of movements, especially if they are novel and complex. The LPFC has not direct connections with M1, but it is interconnected with motor areas in the medial (SMA, pre-SMA) and lateral frontal lobe (premotor cortex), such as with cerebellum, superior colliculus, basal ganglia and parietal cortex (for a review see Miller and Cohen, 2011). Therefore, the LPFC does not directly process the movement, but exerts an indirect control on the behavior via the higher-order cognitive functions it sustains. Lesions to the LPFC get patients unable to plan and represent the sequence of the action, as firstly observed by Luria (1966) and then described in the so-called dysexecutive syndrome (Baddeley and Wilson, 1988). In other words, the LPFC is the main cortical region were the abstract representations of sequential actions, such as schemas, plans and concepts are processed (for a review see Fuster, 2001). Because it constitutes the neural substrates of the working memory (WM), it is also noteworthy the role of the LPFC

in the learning of a new motor sequence: in fact, neuroimaging studies showed that more automatic the movement is, less active the LPFC will be (Iacoboni et al., 1996; Petersen et al., 1998). The involvement of the LPFC in motor learning could also be explained by the necessity to mentally rehearse the new sequence: in fact, this area is more active when subjects imagine to move compared with when they really move (Stephan et al., 1995). However, neuropsychological data (Ferreira et al., 1998) suggested that patients with focal lesion to the PFC are still able to maintain visuo-spatial information in the short-term memory (STM), but they have difficulties to link these information to the organization of a forthcoming action. A neuroimaging study (Pochon et al., 2001) further confirmed this aspect, showing that the LPFC is part of a neural network mostly involved in the preparation of action based on information stored in WM rather than in the storage of sensory information in STM per se. At the same time, as showed in a monkey study of Saito and colleagues (2005), the preparatory activity of the LPFC does not represent the motor aspects of behavior, but it is related to the consequences of the movement, that is, the high-order motor control. From a neuropsychological point of view, the role of the LPFC in motor preparation could be defined as the temporal integration of information to guide the goal-oriented behavior. It is served by two temporally and complementary symmetric functions: working memory and preparatory set (Fuster, 2001).

Concluding, the PFC mainly supports three attentional systems participating in the motor control: the MPFC is involved in the motivation to perform the movement, the orbitofrontal cortex allows attention to be focused on the target, and the LPFC plans the action by temporally integrating the internal and external information received from wide neural connections. It is also noteworthy that the anterior attentional system is more engaged when subjects pay attention to the action, while the parietal cortices seem to be more active when subjects direct attention toward extrapersonal space or sensory events (see, e.g., Posner and Petersen, 1989). Finally, other than in the movement planning, the PFC has a key-role in the action monitoring as well. This function is reflected, for example, by the activation of some PFC regions (especially the medial and lateral areas) occurring after an erroneous motor behavior, such as in the case of the decision making tasks. Those activities reflect the processing of a conflict detection

system (Carter et al., 1998; Gehring and Knight, 2000) in which the PFC maintains online information for the appropriate response and the anterior cingulate cortex facilitates the implementation of the selected action (Paus et al., 1993). At electrophysiological level, this function is reflected by the error-related negativity (ERN) or error negativity (Ne) component, a frontal wave peaking at 50-100 ms after the erroneous response (e.g. Falkenstein et al., 1991). It was suggested that this component reflects both the response conflict processing (Yeung et al., 2004) and the mechanism of early mismatch between the intended and actual response (Falkenstein et al., 1991).

1.2. Motor preparation: neurocognitive aspects

The motor act represents one of the main behaviors by which human beings get in touch with the external environment. Because of this role, the movements are not just a peripheral response to the external events, but represent also the outcome of a series of neurocognitive processes acting long before the movement onset. In the last decades, the neuroscience research has repeatedly investigated how the high-order cognitive processes can influence the preparation of a movement, and its performance as well. Following, there will be described some of the most important cognitive activities that precede and influence the motor behavior, especially those that will be investigated in the studies of the next chapters.

1.2.1. Motor anticipation in the emotional context

Because of the role of the affective state in influencing the way how subjects interact with environment, emotions have also been studied as a state of action readiness (Frijda et al., 1989). In fact, recent evidences suggest that manipulating the emotional state before the movement execution influences the behavioral performance (e.g. Coombes et al., 2007, 2008).

The biphasic theory of emotion (Lang et al., 1998) is the main reference model of the psychophysiological studies in this field. Based on this theory, emotions are classified according to their valence (i.e., pleasant or unpleasant) and intensity (i.e., arousal level). Emotions are thought to activate the appetitive or defensive system, which influence the predisposition to act in different ways. Specifically, pleasant

emotions activate the appetitive system, that elicits approach behaviors and facilitates movements toward the body (e.g. food, sex; Marsh et al., 2005); at the opposite, unpleasant emotions (except for anger) activate the defensive system, that elicits withdraw behaviors and facilitates movements away from the body (e.g. danger, fear; Harmon-Jones et al., 2006). In other words, pleasant stimuli generally prime flexion movements, while the unpleasant ones are mainly associated to the extension movements (Chen and Bargh, 1999; Rotteveel and Phaf, 2004). Accordingly, response times (RTs) are usually faster when the emotional valence and the movement direction are compatible (Chen and Bargh, 1999). However, the notion that pleasant and unpleasant stimuli accelerate the flexion and extension movements, respectively, is still a matter of debate. For example, Marsh and colleagues (2005) observed that the exposure to threatening faces accounted for faster flexion than extension movements, suggesting a not rigid association between unpleasant context and extension. As suggested by Coombes and colleagues (2007), these contradicting results suggest that describing emotions and movements just in terms of matching between affective valence and movement direction may not be helpful. At the opposite, since the unpleasant context may elicit both approach (fight) and withdraw (flight) behaviors, it could be possible that the motor system is primed in a no direction-specific manner.

The relationship between emotions and movement was recently tested in the context of the forward gait initiation (Naugle et al., 2011): the results suggested that also a more complex movement, such as the gait initiation, might be influenced by the emotional context. Specifically, it was especially the anticipatory postural adjustments period to be affected by exposure to emotional stimuli. This last observation could be explained by the fact that the anticipatory postural adjustments are controlled by motor areas (i.e. SMA, premotor cortex, basal ganglia) tightly connected with limbic structures (Takakusaki et al., 2003), while stepping is under brain stem and spinal control, so less influenced by emotions. Because evidences of connections between emotions and brain motor areas, some studies employed the transcranial magnetic stimulation (TMS) to observe how the emotional states alter the corticospinal motor tract (CST) excitability (e.g. Baumgartner et al., 2007; Oathes et al., 2008). So far,

these studies generally suggest that the unpleasant emotional states increase the CTS excitability (Oliveri et al., 2003) and enhance the action preparation (Oathes et al., 2008). However, more recent studies showed that the CTS excitability (as index of motor preparation) is an arousal-driven process, while the emotional valence seems to act at movement speed and force production level (e.g. Coombes et al., 2009). In electrophysiological studies, the effect of the emotions on motor preparation has been studied throughout contingent negative variation (CNV) and stimulus preceding negativity (SPN) (e.g. Takeuochi et al., 2005; Mercado et al., 2007). The CNV and SPN are slow negative potentials emerging over the central brain areas and reflecting different anticipatory processes, such as the motor preparation and the orientation to the upcoming stimulus presentation. The modulation of these components is the typical target of paradigms investigating the motor preparation in cue-predicted tasks. The enhancement of the CNV and SPN potentials was described as arousal- dependent (e.g. Takeuochi et al., 2005), even if some authors observed an opposite emotion-dependent modulation, reporting a reduced CNV during the anticipation of unpleasant stimuli (e.g. Hart et al., 2012). The conflicting results reveal that the role of emotions in anticipatory processes is still a matter of debate. The inconsistent findings might be because the CNV and SPN are not unitary phenomena but represent a class of anticipatory processes, some of which are motivationally oriented, fear-related or subjectively relevance dependent.

1.2.2. Proactive inhibitory control

Psychologically, as suggested by Aron and colleagues (2004), the inhibition could be defined as "the suppression of inappropriate responses, stimulus-response mappings or task-sets when the context changes, and suppression of interfering memories during retrieval". In cognitive neuroscience research, the inhibition has usually been studied through motor tasks encompassing no action- or stop-stimuli paradigms, such as in the case of the stop signal and Go/No-go tasks. In the former, subjects are sometimes asked to stop an initiated movement after the presentation of the "stop-signal", while in the Go/No-go task the choice is between the action-stimuli vs. the to-be-inhibited ones. The inhibitory processes usually investigated in these

tasks are those taking place after the stimuli presentation, that is, the stage where subjects recognize the stimulus, compare its features with those stored in working memory and make a mapping before deciding if move or not (i.e. response inhibition). The process by which an initiated movement is stopped could be defined as reactive inhibition. Recently, a different form of inhibition has become a research topic in this field: the proactive inhibition (Jaffard et al., 2008). Differently to the reactive inhibition, the proactive inhibition reflects a set-process devoted to prevent the inappropriate emission of anticipated responses, and to prepare to suppress a particular response tendency (i.e. proactively and selectively). In other words, the proactive inhibition emerges in tasks requiring response selection, especially when there is uncertainty about the forthcoming stimuli to be categorized. In addition, the proactive inhibition represents a braking preparatory process emerging already before the stimulus presentation, differently to the reactive inhibition, emerging after the stimulus is categorized and just in case of inhibited trials. Because of these functions, the proactive inhibition leads to more accurate performance and to RTs slowdown, as typically observed when comparing simple vs. choice RT tasks (faster the former, slower the latter). The proactive inhibition is usually "removed" when the response decision has been reached.

Since the book of Ferrier (1886), the PFC has been identified as the main cortical areas processing the inhibitory control over behavior. Nowadays, there are growing evidences of the inferior frontal cortex (IFC), especially the right IFC (rIFC), as the main region underlying the motor inhibition (for a review see Aron et al., 2014). Specifically, the region involved in this function is that anterior to the precentralsulcus and inferior to the inferior frontal sulcus. It encompasses the pars triangularis, the pars opercularis and some of pars orbitalis (see Figure 1.3) (Aron, 2011).

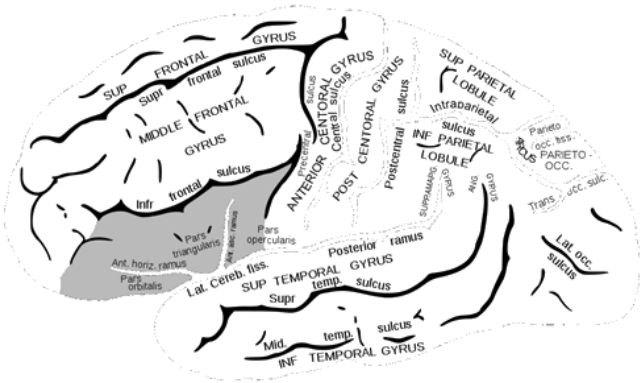

Fig. 1.3. The inferior frontal cortex (IFC).

The inhibitory role of the rIFC is exerted through a brain network composed by rIFC, basal ganglia and pre-SMA. Specifically, there are now converging evidences that the rIFC reduces the pre-SMA activity by suppressing the basal ganglia output via the subthalamic nucleus (STN, Aron et al., 2004, 2007).

The braking role of the rIFC acts during different kinds of inhibition, i.e., it can be turned on in both partially and tonically modes, and by different triggers, that is, externally, internally or automatically (for a review see Aron et al., 2014).

1.2.3. Preparatory brain activities and behavioral performance

As aforementioned, there are several cortical areas involved in the action preparation, especially as regard aspects like motivation, top-down attentional control, cognitive anticipation, motor preparation and proactive inhibition. A new challenge for the neuroscience research has become the understanding of how the preparatory brain activities can be linked to the performance of the subsequent motor behavior. In other words, there are evidence suggesting that very early activities can (partially or totally) predict the way in which the voluntary action will be performed.

Following, the main indexes of the behavioral performance will described, that is speed, accuracy and variability of the response. Each of them will be investigated in the studies of the next chapters.

1.2.3.1. Speed-Accuracy Tradeoff (SAT)

In the context of a perceptual discriminative task, decisions can be viewed as the result of continuous accumulation of sensory information from a baseline point until reaching a threshold (Ratcliff, 1978). Fast decisions are more error prone, while careful ones take longer (Wenzlaff et al., 2011): this phenomenon is known as the speed-accuracy tradeoff (SAT) (for a review see Bogacz et al., 2010).

Nowadays, different accumulator models have been proposed in this field, but the common assumption they share is that SAT is explained by the distance between the baseline activity and the response threshold. The accumulators, that is the activity of a population of neurons, are assumed to raise from a sensory input until the threshold is reached. If distance is small, decisions would be fast but error-prone; otherwise, if distance is large, decisions would be slower but accurate (see Figure 1.4).

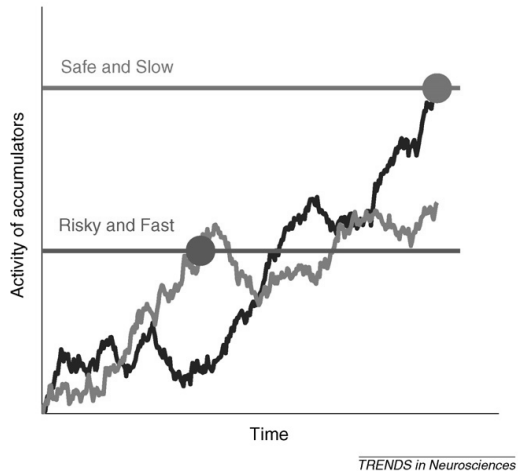

Fig. 1.4. An accumulator model of SAT in the context of a perceptual decision making task. The two noisy lines represent the raising of the accumulators from a baseline point (on the bottom). The horizontal lines represent two different response thresholds. Because of the distance from the baseline level, the higher threshold accounts for accurate and slow responses, the lower for inaccurate and fast responses (adapted from Bogacz et al., 2010).

From a theoretical point of view, both the baseline and the threshold can be modulated, but the mathematical models are not really focused on that: in fact, they state that a baseline increase would

be comparable to a threshold decrease, and vice versa. For this reason, the computational models claim that the behavioral performance cannot reveal which activity was modulated; at the opposite, the performance can just be explained by the baseline-to-threshold distance. Also, these models suggest that the neural changes related to the SAT should emerge in brain areas involved in decision making rather than in areas specialized in sensory and motor processing (Bogacz et al., 2010).

Despite the large amount of evidence supporting the mathematical models of decision-making, the neural mechanisms for adjusting the baseline-to-threshold distance are only partially understood (Kim and Lee, 2011).

In order to identify the brain regions associated to SAT, some studies employed tasks in which subjects were asked to emphasize the speed or the accuracy depending on the trials. Overall, fMRI studies found that fast decisions were associated to larger activity of the anterior striatum and pre-SMA (Forstmann et al., 2008), while others reported the activation of the premotor areas and the DLPFC as well (Ivanoff et al., 2008; van Veen et al., 2008). Consistently, EEG studies revealed larger activity of the lateralized readiness potential (LRP; i.e., the electrophysiological marker of the pre-SMA activity) in the time pressure condition (e.g. Sangals et al., 2002).

Even if there are convergent evidences about the pre-SMA engagement in processing the decision speed, much more controversial are the results regarding the neural areas subserving the accuracy domain. In addition, a still open question regards the presence of one or more speed and accuracy systems, such as the baseline and/or threshold modulation in that system. At the same time, because of some studies reported an association between SAT strategies and several trait dispositions (e.g. Flehmig et al., 2010), it is still not clear the effectiveness of tasks investigating the SAT by asking the subjects to emphasize speed over accuracy (or vice versa).

1.2.3.2. Response variability

The intra-individual variability (IIV), or intra-individual coefficient of variability (ICV), represents the individual dispersion of the behavioral responses among different trials of a response task. In other words, smaller the ICV, greater the consistency of the response.

A typical formula for calculating the variability is the following:

ICV = standard deviation of RT/mean of RT

Overall, the behavioral tasks tend to neglect the measures of variability in favor of more common indexes such as the mean RTs. However, the main problem is that when variability is high, the mean value represents an oversimplification and might lead to erroneous interferences (Nesselroade, 2002).

In healthy subjects, the response variability is typically influenced by age, showing a U shaped distribution across life span (Williams et al., 2005): in other words, it is large in the childhood, decreases in adolescence, stabilizes in adulthood and it increases in old age. An excessively large ICV is usually considered to be an index of cognitive deficits. For example, the response inconsistency is symptomatic of pathological conditions such as mild dementia, brain injuries, sleep deprivation, attention deficits hyperactive disorder, schizophrenia (e.g. Barkley et al., 1992; Hultschet et al., 2002). Also, the large response variability in adults has been associated to lesions of the microscopic white matter in the frontal cortex (e.g. Bunce et al., 2007).

Nowadays, there are convergent evidence about the role of the PFC, especially the DLPFC, in accounting for the response variability. However, some studies reported a greater DLPFC activation in subjects with high variability (e.g. Bellgrove et al., 2004), while others observed an association between the reduced DLPFC activity and the higher variability (Weissman et al., 2006). These contrasting results were respectively interpreted as a greater requirement of top-down attentional control (in case of higher activity), and as the occurrence of lapses in attention (in case of reduced activity) in subjects with large variability.

On the other hand, the electrophysiological studies in this field investigated the modulation of the attentional post-stimulus components (especially the P3; e.g., Saville et al., 2011), but no studies observed the preparatory activity of the PFC. Concluding, there are convergent evidence at both cognitive and neurophysiological level about the contribution of the PFC (especially the DLPFC) in the response variability, even if the degree of activation of this area is still a matter of debate.

1.3. Electroencephalographic studies of motor preparation and execution

Because of its high-temporal resolution, the electroencephalogram (EEG) has been largely employed in the study of the cortical motor processes. In fact, the EEG-based motor preparation has been investigated by clinical, cognitive, mirror neurons and brain-computer interface studies. In addition, the surface cortical localization of the motor areas (see previous sections) makes this technique very suitable for picking up the movement-related activities in the different stages of its processing. Two are the main approaches to the EEG signal analysis: the frequency and the event-related potentials (ERPs) domain. Each of them has advantages and limitations, depending on the goal of the study, such as on the timing and features of the paradigm. Both the frequency and the ERP approaches will be described below, paying particular attention to their role in the context of the motor preparation.

1.3.1. The frequency approach

Motor preparation in the frequency domain is mainly studied through the modulation of the sensorimotor rhythms (SMRs), that is the electrical oscillations recorded over the central sites of the EEG (i.e., over the posterior frontal and anterior parietal cortical areas). SMRs mainly fall into the mu (8-13 Hz) and beta (13-30 Hz) bands.

The decrease, or desynchronization, of the Rolandic wicket rhytm (i.e. the mu rhytm) during movement was firstly described by Chatrian et al. (1959). After that, a consistent literature showed the SMRs decrease during motor preparation and execution, also referred as event-related desynchronization (ERD; e.g., Pfurtscheller and Aranibar, 1979). ERDs are generally interpreted as an index of activated cortical networks, and the SMR ERD specifically emerges in case of execution of a voluntary movement (both externally and internally triggered). At the opposite, the increase of the SMR is defined as event-related synchronization (ERS), reflecting deactivated or inhibited cortical networks (Pfurtscheller, 1992). The SMR ERS typically emerges in association with sensorimotor events, like immediately after movement.

The mu ERD becomes evident over the contralateral Rolandic

region more than two seconds before the movement onset: it is bilaterally distributed during actual movement execution (Stancàk and Pfurtscheller, 1996). Overall, two types of mu ERD are distinguishable: the lower frequency (8-10 Hz) mu ERD reflects general motor preparation in any kind of movement, while higher frequency (10-13 Hz) mu ERD is more related to specific aspects of the task-performance. As aforementioned, also the beta rhythm shows a desynchronization during the motor preparation (even if less evident than mu ERD) and, more important, it exhibits the so-called beta rebound (e.g. Pfurtscheller, 1981), that is a post- movement ERS. See Figure 1.5 for an illustration of these effects.

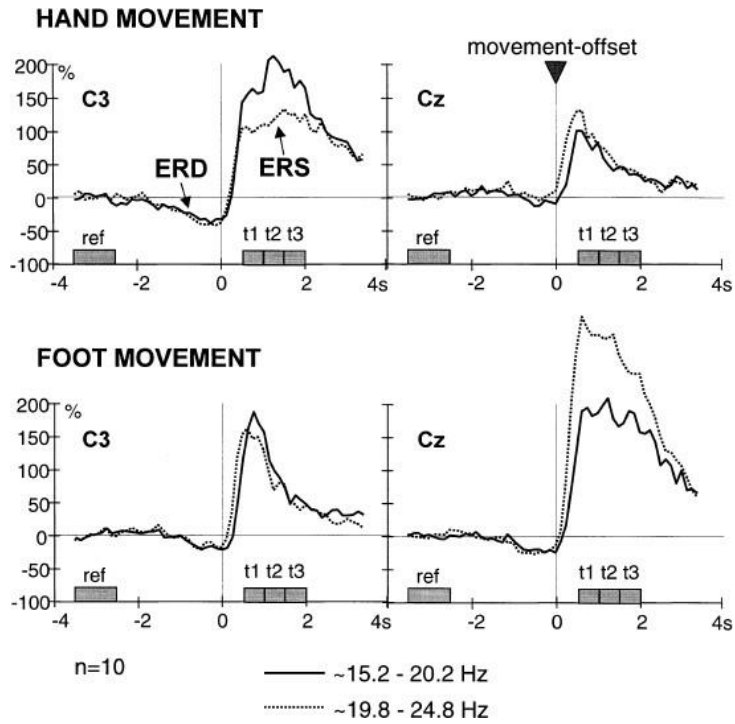

Fig. 1.5. Grand average beta ERD/ERS detected over the hand and foot areas. The vertical lines indicate the movement offset. Note the ERD prior to movement and the ERS after movement. (From Neuper and Pfurtscheller, 2001).

The mu ERD typically emerges with a simultaneous ERS in the neighboring cortical areas: this phenomenon is known as focal-ERD/surround-ERS. Finally, it is noteworthy that similar patterns

occur in case of imagined movements. This observation confirms the idea that the SMR patterns preceding the movement do not just reflect the movement preparation rather than a process of readiness to act, even if the movement is not actually emitted.

1.3.2. EEG analysis in the time domain: the event-related potentials (ERPs)

ERPs can be defined as brain responses evoked by specific sensory, cognitive or motor events. ERPs emerge as waveforms of different polarity (i.e., positive or negative), scalp distribution, onset and latency. The ERP amplitude is generally calculated as the voltage increase or decrease from a baseline point.

The following two sections will describe the pre-movement potentials and the typical post-stimulus ERPs affecting the behavioral performance. The formers are specifically related to the movement preparation stage, while the latter reflect the brain processing of the exogenous events (e.g., the visual stimulus).

1.3.2.1. Movement-related potentials: MRCPs

The movement-related cortical potentials (MRCPs) represent low-amplitude ERPs preceding or concomitant to the movement. The MRCPs can be detected by locking the EEG signal to the electromyographyc (EMG) onset activity, or to the trigger of an external device (e.g., the key press). The main MRCP is the Bereitschaftspotential (BP) that is a negative slow wave raising over the fronto-central derivations of the EEG: it was firstly described by Kornhuber and Deecke (1965). The BP emerges more than two seconds before the onset of a voluntary movement, and it represents the electrophysiological marker of the premotor areas excitability. About 300 ms after movement is executed, a positive wave called re-afferent potential (RAP) is typically observed over the contralateral somatosensory cortex.

The BP was also classified into two components that is the early BP and the late BP, also known as negative slope or NS' (Shibasaki and Hallett, 2006). The early BP begins about 2 sec before the movement onset: its amplitude represents the pre-SMA activity and it is bilaterally distributed over the scalp (i.e., there is no a clear

somatotopic organization). The NS' is referred to the amplitude increase of the BP at about 400 ms before the movement onset: this wave originates from the lateral premotor cortex and the contralateral M1 (i.e., it reflects a precise somatotopy). Concomitant to the movement execution, the motor potential (MP) is also observed: it emerges as the largest peak of the MRCPs, reflecting the maximum activity of the M1 area. See figure 1.6 for a representation of the main MRCPs taking place before and after the execution of a self-paced movement.

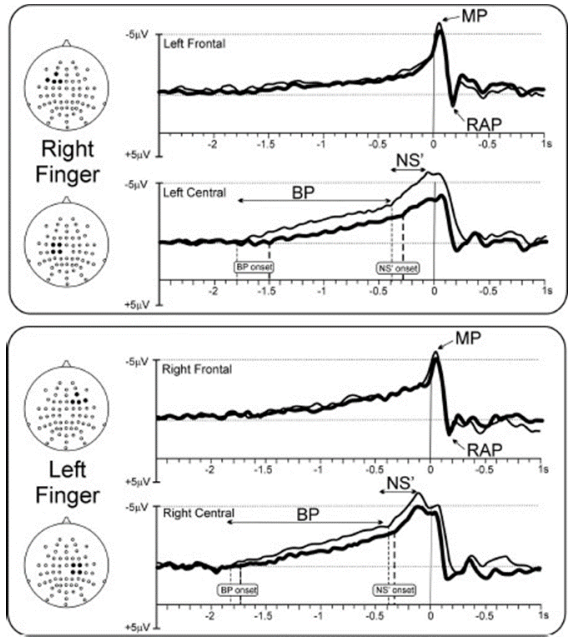

Fig. 1.6. Grand average MRCPs of two experimental groups (thick and thin lines) responding with the right (top) and left (bottom) index finger. (From Di Russo et al., 2005).

As aforementioned, the BP starts to raise long before the movement is executed and, also, long before it is consciously decided. In fact, since the famous study of Libet et al. (1983), it was demonstrated that the brain starts to process the movement long before we are aware of it. Nowadays, the early BP is considered as a "subconscious" phase of the action readiness, while the late BP or NS' reflects a stage of motor preparation associated with the conscious decision of movement (for

a review see Hallett, 2007). From a clinical point of view, the BP decrease is typically associated to neurological conditions, as revealed by studies reporting reduced BP amplitude in Parkinson's disease (e.g., Praamstra et al., 1998), frontal traumatic brain injury (e.g., Wiese et al., 2004) and SMA lesioned patients (e.g., Deecke et al., 1987). However, there are also cognitive and motivational factors influencing the BP modulation: for example, McAdam and Seales (1969) reported an increased BP in the monetary-reward trials if compared to the baseline (i.e., no reward) conditions. BP modulations were also observed as effect of sport (Di Russo et al., 2005) and motor skill practice (Wright et al., 2012), suggesting that the processes underlying this component are susceptible of modifications. Concluding, the MRCPs reflect the brain activities preceding the execution of a voluntary movement. MRCPs amplitude might be affected by several internal and external factors, such as motivation, cognitive skills, sport and neurological factors. The main MRCPs can be detected over the central areas of the scalp, even though Wiese and colleagues (2004) hypothesized that also the frontal regions can participate in the BP modulation via the SMA-PFC neural networks. This latter hypothesis was partly confirmed by a subdural electrodes study (Jahanshahi et al., 2001) showing the PFC contribution to the generation of MRCPs in the context of decision-making task. Anyhow, no specific frontal MRCPs have been reported in the EEG literature so far.

1.3.2.2. Stimulus-related potentials: an overview on the role and physiology of the main ERPs affecting the response execution

In this paragraph, it will be briefly described the ERPs whose activity can be directly or indirectly modulated as effect of the motor preparation and performance. Figure 1.7 shows the grand-average waveforms of the stimulus-locked ERPs preceding and following the presentation of a visual stimulus in the Go/No-go task presented in the next chapters. Each component will be separately described.

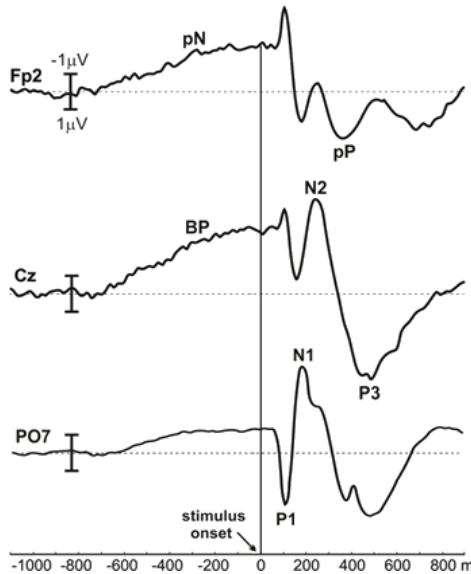

Fig. 1.7. Grand average waveforms of the main ERPs preceding and following the visual stimulus onset (time 0) in a behavioral decision making task. The activity over the prefrontal (top), central (middle) and parieto-occipital (bottom) sites is reported in a 2 sec time window.

The prefrontal negativity (pN) component

The prefrontal negativity (pN) is a slow wave emerging over the prefrontal sites. It starts about 800 ms before the stimulus onset in the Go/No-go paradigm presented in the next chapters. The inferior frontal gyrus has been described as the main source of this component, that is typically associated to the top-down control and the proactive inhibitory control devoted to the task (see next chapters for more details).

The P1 component

The visual P1 component is a positive wave emerging bilaterally over the occipital areas of the scalp. It peaks at 80-120 ms after the presentation of a visual stimulus.

The source of the P1 was identified in the ventral occipital cortex, specifically in the V4v area and the posterior fusiform gyrus. The P1 activity may be attributed to enhanced processing of the visual target information in the ventral areas specialized for pattern and object recognition (Martinez et al., 1999). The P1 amplitude is typically

considered to be affected by visual stimulus features (e.g., contrast, luminosity), such as by visuo-spatial attention. In fact, the P1 enhancement represents the facilitation at early sensory processing level for items presented at attended location (Di Russo et al., 2003). It was showed that also the top-down (i.e., no spatial) attentional processes can influence the modulation of this component (Taylor, 2002).

The N1 component

The visual N1 component is a negative wave emerging bilaterally over the occipital areas of the scalp. It peaks at 150-200 ms after the presentation of a visual stimulus. The N1 neural source was mainly located in the inferior occipital or occipito-temporal cortex, close to the border between BA 19 and 37 (Hopf et al., 2002). Spatial attention does not influence the N1 modulation; at the opposite, the N1 is larger in the discrimination tasks than in the simple detection tasks. This observation led to the proposal that this component reflects the discriminative processing within the focus of attention (Luck et al., 1990).

The N2 component

The N2 is a fronto-central distributed component peaking at 250-300 ms after the stimulus: its neural source was mainly localized in the anterior cingulate cortex (for a review see Folstein and Van Petten, 2008). There are two main cognitive accounts explaining the N2: according to the inhibitory control theory (e.g., Van Boxtel et al., 2001), the N2 reflects the inhibitory control to the no-response trials. On the other hand, according to the conflict monitoring theory (e.g., Nieuwenhuis et al., 2003), the N2 enhancement is associated to the higher conflict level: this latter would increase, for example, as effect of the low frequency condition. However, because of the complexity of this component, its function is still a matter of debate: in fact, it could be possible that the N2 reflects also different roles other than those suggested by the two main accounts. For example, Falkenstein et al. (1991, 2002) reported no N2 modulations in the auditory modality of the Go/No-go task: these evidences make difficult to explain the N2 just in terms of a general inhibitory control process. Further, it is also possible that the N2 represents an epiphenomenon related to the

frontal and parietal surface potentials summation, rather than the correlate of a specific cognitive process (for more details see Gajewski and Falkenstein, 2013, and chapter 5).

The prefrontal positivity (pP) component

The pP is a decision-making based component: in fact, it reflects the stimulus- response (S-R) mapping process. The anterior insular cortex has been described as the main source of the pP that reaches its maximum amplitude at about 300 ms after the stimulus presentation. The pP is typically larger after the target than non-target stimulus presentation. The pP was also labeled as Go-P2 (Gajewski and Falkenstein, 2013), anterior P2 (P2a; Potts et al., 2004), frontal selection positivity (FSP; Kenemans et al., 1993) and frontal P3 (P3f; Makeig et al., 1999). See next chapters for more information about this component.

The P3 component

The P3 is a prominent positive wave with a centro-parietal distribution. Its maximum activity emerges at 400-600 ms after the stimulus onset. From a cognitive point of view, the P3 represents a complex and multi-factorial component. In fact, there are several cognitive and physical factors influencing its modulation such as, for example, the arousal state, the exercise, the fatigue, the ageing and the stimulus frequency (for a review see Polich and Kok, 1995). Because of its complex nature, the neural sources of this component are still a matter of debate. Even if the scalp-recorded P3 mainly originates from cortical regions, it is reasonable that there are also other sources contributing to its generation, depending on the task and the cognitive processing (Polich and Kok, 1995

2. Getting ready for an emotion: specific premotor brain activities for self-administered emotional pictures

2.1. Introduction

The early identification of emotionally relevant information is critical for survival (Darwin, 1872), and anticipation of the future affective events is a crucial skill of the human brain, because it allows people to prepare the most adaptive response. Emotional expectancy entails multiple cognitive and motor processes, such as emotional regulation, retrieval of prior relevant events and preparation of the appropriate behavioral responses. In experimental neuroscience, it is important to distinguish anticipation from preparation. Anticipation consists in passively waiting for the stimulus and it is a perception-oriented stage of the expectancy process, while preparation is a more motor-related stage during which the motor system is getting ready for motor execution (Boxtel and Böcker, 2004).

Electroencephalographic (EEG) studies revealed three slow cortical potentials related to the expectancy and preparation processes: the Movement Related Cortical Potentials (MRCPs), the Contingent Negative Variation (CNV) and the Stimulus Preceding Negativity (SPN). The MRCPs are elicited by any voluntary movement and are interpreted as an index of the progressive cortical excitability necessary to prepare and execute movements. Among the MRCPs, one of the most studied is the Bereitschaftspotential (BP): a slow negative activity that, for self-paced movements, begins about 2-3 s before the movement onset and reflects the mere motor preparation (Shibasaki and Hallet, 2006) in premotor and motor brain areas, but also anticipation processes as stimulus timing evaluation (Berchicci et al.,

2012a, 2013, 2014; Di Russo et al., 2013a, b) and awareness of the consequences produced by the act (Di Russo et al., 2005a; Bozzacchi et al 2012a,b;), in prefrontal and posterior parietal areas. Conversely, the CNV and SPN are slow negative potentials reflecting the orientation to the upcoming stimulus presentation; thus, they can be related to the abovementioned perception-oriented process of the expectancy (for a review see Van Boxtel and Böcker, 2004). Few studies investigated the emotions throughout the CNV (e.g., Mercado et al., 2007) and SPN (e.g., Takeuchi et al., 2005) waves and they partially explained the neurophysiological mechanisms underlying expectancy of predictable emotions, but none of the available researches investigated the effect of the emotional expectancy by means of the MRCPs analysis.

The enhancement of the CNV and SPN potentials was described as arousal-dependent by pharmacological (Kopell et al., 1974), clinical (Wessa and Flor, 2007) and healthy subjects studies (Böcker et al., 2001; Takeuchi et al., 2005; Poli et al., 2007).

Nonetheless, other authors reported an opposite emotion-dependent modulation, showing a reduced CNV amplitude during the anticipation of unpleasant stimuli (Casement et al., 2008; Moser et al., 2009; Hart et al., 2012).

The conflicting results reveal that the role of emotions in anticipatory processes is still a matter of debate. The explanation for the inconsistent findings might be at least twofold: i) the SPN is not a unitary phenomenon, but a class of anticipatory responses, some of which are motivational-oriented, fear-related or subjectively relevance-dependent (Van Boxtel and Böcker, 2004); ii) the CNV-SPN paradigms did not control all of the methodological variables, such as the timing, the motor response after the stimulus or the presence of a feedback.

The modulation of emotional expectancy has also been investigated by means of functional magnetic resonance imaging (fMRI); in visual cued tasks, an increased activation was observed in left dorsolateral and medial prefrontal cortex during positive expectancy (Ueda et al., 2003), and in right dorsolateral prefrontal cortex (DLPFC), orbitofrontal and anterior cingulate cortices during negative respect to neutral expectancy (Davidson and Irwin, 1999; Nitschke et al., 2006). In addition, few works recording peripheral indexes demonstrated that also movement speed and force production varied as a function

of emotional valence (Coombes et al., 2009); in particular, the negative affective state activates the defensive circuitry (Coombes et al., 2005; Coombes et al., 2006), suggesting the involvement of motor-related central processes (Coombes et al., 2007).

Considering the low temporal resolution of fMRI and the before mentioned CNV-SPN methodological limitations, we sought to investigate the emotional expectancy by means of high-density EEG recording and MRCPs analysis. The main goal of this study is to elucidate the role of emotional expectancy in a self-paced paradigm that, unlike reaction time or triggered tasks, does not involve the perception of extra stimuli, such as cues, or additional cognitive processing, such as working memory or discrimination processes. In the current study, the subjects had neither to attend to the stimulus presentation nor to respond to it, but they were instructed to press a key in order to display an emotional picture on the screen. In other words, there was a temporal concurrence between anticipation and preparation processes, because the visual presentation of the stimulus was self-paced, indeed it coincided with the motor response. This methodological issue is very important, because it allows the subjects to self-initiate (and not just to passively receive) an affective experience, where the kind of emotions and their timing are clearly predictable. This situation is not rare in daily life because we do not just passively experience emotions produced by external events, but we can also deliberately decide to perceive something or not, that will affect ourselves emotionally. The use of the MRCPs analysis in an emotional expectancy paradigm might also allow us to shed light on the timing of the activity in the prefrontal cortex (PFC), which was reported to be active in the aforementioned fMRI studies. Indeed, recent studies showed that the PFC activity is detectable using the MRCPs overlapping in time the frontal BP component (Bozzacchi et al., 2012a,b; Berchicci et al., 2012a,b; Berchicci et al., 2013; Sanchez-Lopez et al., 2014). Furthermore, in order to investigate whether pictures processing is affected by expectancy, we adopted a large segmentation including both MRCPs and post-stimulus ERPs: indeed, we also studied the activity related to the processing of the emotional stimuli measuring the modulation of the P2 and N2 components, and the late positive potential (LPP), which is a slow stimulus-related activity reflecting sustained attention to affective contents (Schupp et

al., 2000, 2004). This methodological choice was based on the fact that the stimulus-triggered analysis with a baseline shortly before the stimulus onset could mask the pre-stimulus potentials, squeezing them on the 0 μV activity. Further, the latter method could not be useful to investigate the effects of the pre-stimulus neural adjustments on the modulation of the typical emotional ERPs.

Our hypothesis is that the expectancy of predictable emotions can modulate both MRCPs and post-stimulus brain processing. In particular, in the pre-motor phase we expect that the more arousing pictures (positive and negative) may modulate both the prefrontal activity and the BP component of the MRCPs more than neutral or scramble pictures. After the key-press and stimulus presentation, the negative stimuli may further modulate the P2 and N2 components, eliciting enhanced and reduced peak amplitude, respectively (Carretiè et al., 2004). At last, high arousing pictures may lead to larger LPP amplitude reflecting a sustained attention to emotional-relevant stimuli.

2.2. Material and methods

2.2.1. Participants

Fifteen healthy subjects (7 females; mean age=23.6, SD=4) were recruited from the student population at the University of Rome "Foro Italico". The volunteers received an extra credit on the psychology exam for their participation in the experiment. The participants had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders; all of the subjects were right-handed (Edinburgh handedness inventory; Oldfield, 1971). After explanations of the procedures, all of the participants provided written informed consent, approved by the local Ethical Committee.

2.2.2. Stimuli

Stimuli consisted of 320 affective pictures repeated twice in the course of the experiment for a total of 640 presented stimuli. Based on their valence and arousal ratings in the International Affective Picture System (IAPS; Lang et al., 1999), we first selected 240 images, equally divided into three emotional categories: positive, negative and neutral.

We adopted the following inclusion criteria: positive and negative pictures with a high arousal rating and a high and low valence rating, respectively. Instead, the neutral pictures were selected based on their medium valence and low arousal rating (see Table 2.1 for specific ratings of each category). However, in order to exclude any influence of semantic and autobiographical knowledge on the electrophysiological data, we worried to have a further control condition. For this reason, using CorelDraw™ software, we scrambled each neutral picture in order to have a scramble category. This approach, already adopted by several emotional studies (e.g. Schwaninger et al., 2006; McRae et al., 2012), allows the experimenters to keep the perceptual features unaltered removing the affective content of the pictures. Thus, a total of four emotional categories were employed in the experiment: positive, negative, neutral and scramble.

	Positive	Negative	Neutral
Valence: mean (SD)	7.13 (0.42)	2.18 (0.5)	5.03 (0.29)
Arousal: mean (SD)	6.1 (0.5)	6.4 (0.47)	2.87 (0.42)

Tab. 2.1: The affective ratings of the selected IAPS pictures for positive, negative and neutral categories.

2.2.3. Procedure

During the EEG recording, subjects were comfortably seated in front of a computer screen at a distance of 120 cm. A board was fixed on the armchair allowing the participants to freely push the button panel positioned on it. The fixation point was a yellow circle (0.15° x 0.15° of visual angle) in the center of the computer screen. The participants were asked to alternatively press two keys with the index and middle right fingers in a self-paced rating every 4-5 seconds (i.e. starting with the left key, they after had to press the right key and so still, without press twice the same) in order to display a picture on the screen: each key-press coincided with the stimulus onset. The experimenter communicated the key-category coupling before each block, so that the subjects always knew the affective valence of the stimuli associated with the key-press. The subjects performed 10 trials before starting the experiment, in order to familiarize with the key-presses speed; during the experimental session, the experimenter

always monitored the interval between stimuli providing the subject with feedback about his/her speed. Further, the inter-stimulus-interval (ISI) was subsequently calculated in order to exclude different distributions across blocks. The entire experiment consisted of four blocks, randomly presented and counterbalanced across participants, which were repeated twice. Each block contained 80 pictures, equally divided for each category (40 pictures per category) that was associated with a specific key side (see Table 2.2 for the key-category coupling and ISI values in the blocks). Each picture lasted 280 ms and each block approximately 6-7 minutes, automatically ending when all pictures were displayed; the whole experiment lasted 55-60 minutes.

Blocks	Key side		ISI
	Left	Right	mean (SD)
1	positive	negative	5.26 (0.83)
2	negative	neutral	5.23 (0.92)
3	neutral	positive	5.2 (1.02)
4	scramble	scramble	4.94 (1.06)

Tab. 2.2: Key-category coupling and inter-stimulus-interval (ISI) in the four experimental blocks. Left and right key sides correspond to the index and middle right finger, respectively. The ISI values are reported in seconds.

2.2.4. Electrophysiological recording and data analysis

EEG signals were recorded using BrainVision™ system (BrainProducts GmbH, Munich, Germany) with 64 electrodes mounted according to the 10-10 International System. All electrodes were referenced to the left mastoid. Horizontal and vertical electrooculogram (EOG) were also recorded using electrodes at the right external canthi and below the left eye, respectively. Electrode impedances were kept below 5KΩ. The EEG was digitized at 250 Hz, amplified (band-pass of 0.01-80 Hz including a 50 Hz notch-filter) and stored for offline averaging. Artifact rejection was performed prior to signal averaging to discard epochs contaminated by blinks, eye movements or other signals that were detected by an amplitude threshold of ± 100 μV. In order to investigate the effect of the emotional anticipation on both MRCPs and post-stimulus potentials, the artifact-free signals were segmented based on the key-press that triggered the onset of the visual stimulus, and then averaged in 3500

ms epochs (from 2500 ms before to 1000 ms after the stimulus/movement onset). To further reduce high frequency noise, the averaged signals were low pass filtered at 25 Hz (slope 24 dB/octave) and baseline corrected from -2500 to -2300 ms. All of the averaged epochs were stored into four emotional categories: positive, negative, neutral and scramble. For the MRCPs analysis, the mean amplitude of three 500 ms time windows before the key-press (-1500/-1000, -1000/-500 and -500/0 ms) was exported. Based on the scalp topography, we selected the electrodes where the signal was maximal and averaged them to obtain the following pools: left prefrontal (F9, FT9, Fp1), right prefrontal (F10, FT10, Fp2) and occipital (O1, Oz, O2) pool. According to the literature (e.g. Berchicci et al., 2012a), we considered the Cz site for the analysis of amplitude and onset of the BP. The BP amplitude was measured as the mean amplitude in the abovementioned time windows, and the onset latency was calculated as the first deflection larger than twice the absolute value of the baseline mean. For the statistical analysis, separate repeated-measures ANOVAs were performed on the three time windows, with Category and Pool as factors; only for the BP analysis, one-way ANOVAs were performed on the latency and amplitudes on the Cz site.

To investigate how the expectancy affects emotional processing, analyses on the post-stimulus event related potentials (ERPs) were also performed. For this purpose, and based on the scalp topographies, the occipital (O2, PO8) and frontal (Fz, FCz) sites were considered for the P2 and N2 components, respectively. The peak amplitudes and latencies of these components were measured for each subject with respect to the -2500/-2300 ms pre-stimulus baseline and submitted to separate one-way ANOVAs. Likewise, the late positive potential (LPP) was measured on all midline electrodes and divided in two time windows, according to the literature (e.g. Poli et al. 2007): the LPPa (mean amplitude from 400 to 700 ms after stimulus onset) and the LPPb (mean amplitude from 700 to 1000 ms after stimulus onset). For these components, a 4x2x8 ANOVA was computed, with Category (positive, negative, neutral and scramble), LPP (LPPa vs. LPPb) and Electrode (AFz, Fz, FCz, Cz, CPz, Pz, POz and Oz) as factors. Finally, in order to exclude different distributions of motor presses across blocks, the ISI values were compared by means of repeated measures ANOVA. For all of the mentioned ANOVAs, post-hoc comparisons

were conducted using *Fisher's* least significant difference (LSD) test. The overall alpha level was fixed at 0.05.

2.3. Results

Figure 2.1 illustrates motor/stimulus-related activities in four relevant sites (Fp2, Fz, C3, Oz). Time zero represents the movement onset and the simultaneous stimulus appearance. In all of the emotional categories, the brain potentials started about 2 s before the key-press over medial central sites and slowly rose showing the typical negative ramp of the BP. At the same time, a slow rising positivity was also present over prefrontal sites (prefrontal positivity, pP), but only in the two emotional categories (positive and negative). A sustained positive occipital activity started approximately 1500 ms before and lasted until the initiation of the movement in the negative emotional category only. Concomitantly to the key-press, the peak of the motor potential (MP) was prominent over the left central site contralateral to the used finger for all of the categories. The topographical distribution of the pre-motor components described above is shown in Figure 2.2. The stimulus onset produced a large P2 at 220 ms over occipital sites, and, concomitantly, a N2 over frontal areas, more evident in the negative and neutral category, respectively.

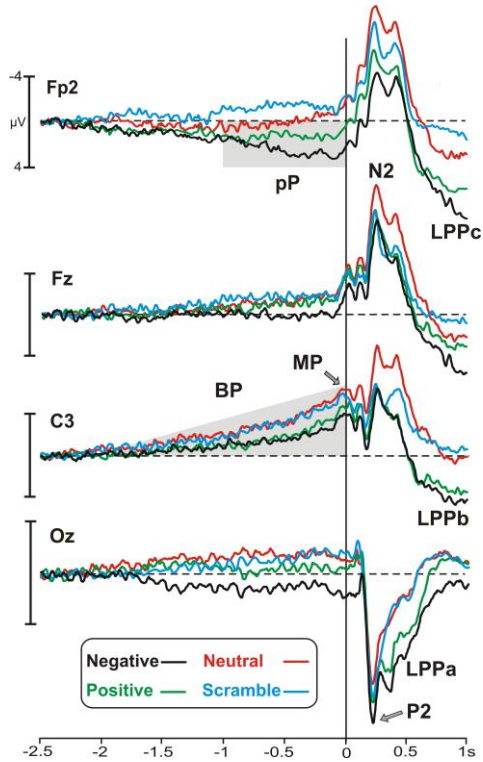

Fig. 2.1: Grand average waveforms of the emotional categories represented by different colors (specified in the legend) on the most relevant sites. Time 0 correspond to the key-press and the concomitant stimulus onset. pP: prefrontal-positivity; BP: Bereitschaftspotential; MP: motor potential; LPP: late positive potential.

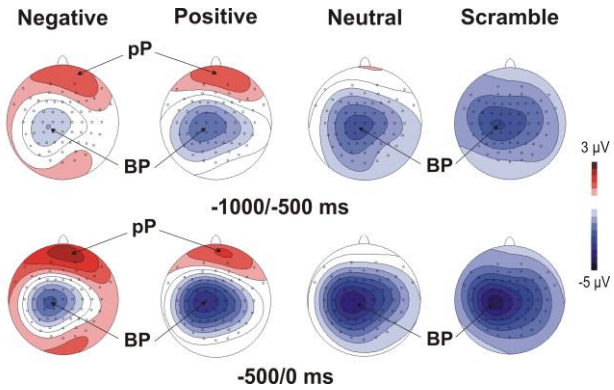

Fig. 2.2: Scalp topographies of the grand average of the MRCPs in the four categories. The maps display the mean amplitude on the scalp in two time windows before the key-press.

The late positivities were also present and started over medial parieto-occipital areas (LPPa) at about 300 ms and over medial central areas (LPPb) at about 400 ms, showing the stronger activity for high arousing categories. Moreover, starting from 500 ms a third positive activity was also observed on prefrontal areas. We called this potential LPPc, because, similarly to the LPPa and LPPb, it was larger for the more arousing categories. Both the LPPb and LPPc were small (but detectable) in the neutral category and absent in the scramble category. The topographical distribution of the LPPs is shown in Figure 2.3. a), while in Figure 2.3. b) the signal is restricted to a smaller time window in order to show the arousal effect by means of difference wave (high arousing minus low arousing pictures) in different sites.

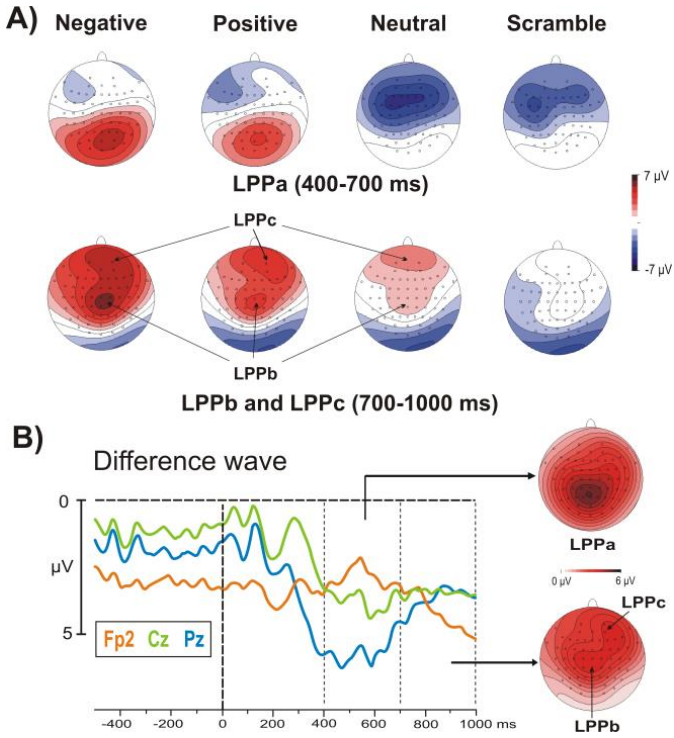

Fig. 2.3. a) Post-stimulus scalp topographical distribution of the LPPa, LPPb and LPPc in the four experimental categories. It can be observed that negative and positive stimuli elicit larger LPPs. Specifically, the LPPa, LPPb and LPPc show the maximum activity over posterior, frontal and prefrontal areas, respectively. **b)** High arousing (positive and negative) minus low arousing (neutral and scramble) categories: differential waves in three representative sites and topographical distribution of the LPPs.

Statistical analysis showed a Category main effect in both -1000/-500 ($F_{3,42}=3.38$, $p<0.05$) and -500/0 ($F_{3,42}=4.68$, $p<0.01$) time windows (Figure 2.4 a shows the respective statistical graphs). Post-hoc analysis revealed that, from 1000 to 500 ms before the key-press, occipital and bilateral prefrontal areas showed a larger positive activity during positive and negative expectancy compared to scramble ($p=0.01$ and $p=0.005$, respectively). Instead, in the -500/0 ms time window, the activity on the same electrode pools was greater during positive expectancy compared to scramble ($p=0.01$) and during expectancy of negative pictures compared to neutral ($p<0.05$) and scramble ($p<0.001$).

Neither Pool main effect nor Category x Pool interactions was significant; thus, the more arousing categories showed a large positivity in all of the considered Pools, and no laterality effect emerged on the prefrontal areas. The analyses on the BP mean amplitudes were not significant, while the ANOVA on the BP onset showed a significant effect ($F_{3,42}=2.87$, $p<0.05$): the onset of this potential progressively increased across categories from negative (mean=-1.39 s; SD=0.54) to positive (mean=-1.58 s; SD=0.51), to neutral (mean=-1.75 s; SD=0.5) and to scramble (mean=-1.9 s; SD=0.42). Nevertheless, post-hoc analysis revealed a significant difference only between negative and scramble categories ($p<0.01$). On the other hand, the analysis on the latency and amplitude of the P2 and N2 components did not show any significant effects, while ANOVA on the LPPs showed a significant Category main effect ($F_{3,42}=10.82$; $p<0.00001$), indicating a greater positivity for positive and negative categories as compared to neutral and scramble. Moreover, the LPP x Electrode interaction effect was also significant ($F_{7,98}=69.4$; $p<0.0001$), indicating that the positivity of the LPPa was more pronounced on parietal as compared to frontal and prefrontal sites, while the LPPb showed the opposite trend (see Figure 2.4 b).

No differences emerged between ISI values, so that the motor presses were uniformly distributed across the emotional categories; further, these data allowed us to exclude possible biases on EEG results.

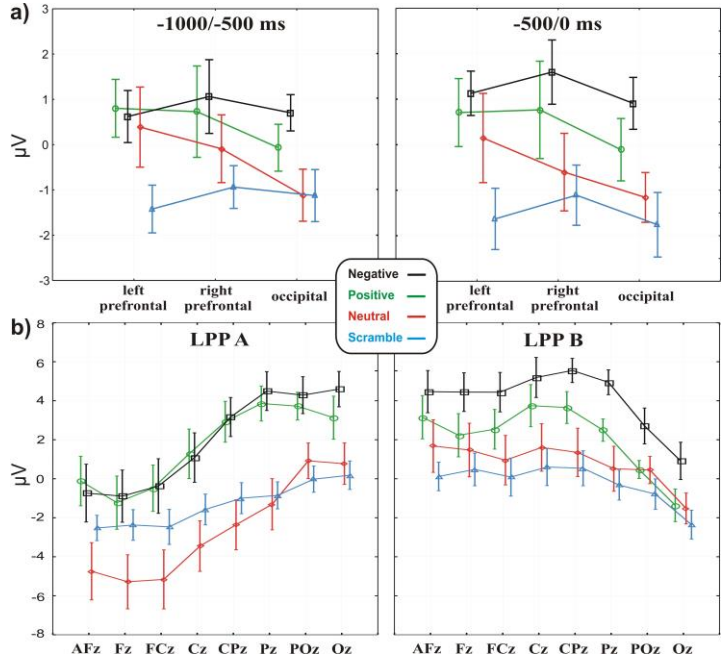

Fig. 2.4. a) Data (values are mean ± SEM) of the MRCP activities in the four emotional conditions, separately for the -1000/-500 and -500/0 time windows on the three electrode pools. **b)** Data (values are mean ± SEM) of the LPPa and LPPb activities in the four experimental conditions on the midline electrodes.

2.4. Discussion

The present study was designed to investigate how emotions modulate both premotor (MRCPs) and post-stimulus (ERPs) brain activities. In order to overcome some limitations of externally-triggered and reaction time paradigms (which introduce extra brain activity related to external stimuli before response initiation that overlaps and cancels-out the premotor activity), we adopted a self-paced paradigm. The results showed that the high arousing stimuli expectancy influences the motor preparation as showed by the larger MRCP activities over prefrontal and occipital areas with respect to the expectancy of neutral and scramble stimuli. The slow positive prefrontal activity started very early, at about 2 s before the key-press, together with the BP, and it was prominent during negative pictures expectancy. Present findings might appear conflicting with those in

which only an enhanced pre-stimulus negativity over central areas was found during negative expectancy (Takeuchi et al., 2005; Wessa and Flor, 2007; Poli et al., 2007). However, this inconsistency could be partly ascribed to the small number of recording electrodes (e.g., Wessa and Flor, 2007), the presence of anticipatory cues (e.g., Poli et al., 2007) or working memory demands (e.g., Carretiè et al., 2001) often employed in previous studies. Conversely, in the present study the subjects themselves created their emotional experience, displaying the pictures by means of key-press at self-paced ratings. Further, since the participants always knew the affective content of the forthcoming picture, they had to focus their attention only on the emotional expectancy and motor preparation. Finally, it is important to remind that the scrambled pictures allowed us to have a condition in which the subjects had merely to prepare a motor response in absence of any emotional expectancy.

To the best of our knowledge, a positive activity over prefrontal and occipital areas has never been found in EEG studies on emotional expectancy, but fMRI and lesion studies could partly explain our results. Indeed, some studies reported increased activation in prefrontal and orbitofrontal regions during expectancy of emotional stimuli (Davidson and Irwin, 1999; Ueda et al., 2003; Nitschke et al., 2006), and Bechara and colleagues (1994, 1996) repeatedly demonstrated that patients with bilateral lesions of the ventromedial PFC cannot anticipate future positive or negative consequences of their actions. It was also suggested that the PFC organizes anticipatory behavior in a top-down fashion by activating cortico-cortical and thalamo-cortical loops to sensory and motor areas (Brunia, 1999). Furthermore, the evidence that the perceptual encoding in the visual cortex is modulated by emotional significance of visual stimuli was reported by fMRI (Lang et al., 1998; Bradley et al., 2003) and ERP (see Olofsson et al., 2008, for a review) studies. Ueda and colleagues (2003) also observed that the expectancy, and not only the perception, of unpleasant stimuli produced a bilateral activation in the visual cortex as well as in prefrontal, amygdala and cingulate regions. Further, the intrinsic relationship between expectancy and motor preparation processes (which were overlapped in the present study) was posted by the work of Bermpohl and colleagues (2006a). They interpreted the emotional expectancy-related activation observed in the parieto-

occipital sulcus, supracallosal anterior cingulate cortex (SAC) and cingulated motor area (CMA) as a state of preparedness for action during the expectancy of motivationally relevant stimuli. In brief, they suggested a link between emotional expectancy and motor preparation, even in absence of movements.

It is also likely that the positive activity of the MRCPs over prefrontal and occipital areas reflects an enhanced pre-processing in the to-be-stimulated areas. Our hypothesis is in accord with studies on slow cortical potentials that assumed negative activities, such as the BP, are an index of progressive cortical excitability, reflecting a preparatory state for cerebral processing, whereas the positive activities indicate a decreased excitability, reflecting a greater allocation of perceptual processing resources (Rockstroh et al., 1989; Birbaumer et al., 1990; Schupp et al., 1994). Therefore, the prefrontal and occipital activities may reflect a state of pre-processing of affectively relevant material, anticipating or facilitating following motivated attentional processes, as reflected by the LPP. In line with the literature (Cuthbert et al., 2000; Schupp et al., 2000, 2003, 2004, 2006; Poli et al., 2007), this latter potential was larger following more arousing stimuli compared to less arousing stimuli, and it was mainly localized over parieto-occipital areas (LPPa). In addition, increased frontal and prefrontal positivity indexed by the LPPb and LPPc (from 700 to 1000 ms after the stimulus onset) was observed; the LPP anteriorization was also found in other studies (Diedrich et al., 1997; Gable and Harmon-Jones, 2010; Cunningham et al., 2005; Pastor et al., 2008), indicating sustained and enhanced attention to emotional stimuli by appetitive and defensive motivational system implication. Magnetoencefalographic (MEG) (Moratti et al., 2011) and fMRI (Sabatinelli et al., 2007; Liu et al., 2012) studies showed that the more arousing pictures modulate the LPP activating an extensive brain network composed of both cortical and subcortical structures like the amygdala, parieto-occipital and prefrontal cortex. These studies also suggested strong bidirectional influences between frontal and occipito-parietal cortices, leading to top-down and bottom-up processes interaction for emotional stimuli processing. Indeed, as suggested by other authors (Daffner et al., 2003; van de Laar et al., 2004), both prefrontal and parietal lobes contribute to attentional allocation to novel events, but playing different roles: emotional events

are more likely processed by prefrontal areas, while parietal lobes result to be mainly involved in the categorization of relevant stimuli. Even if a parietal and frontal LPP have been more or less frequently described in emotional processing investigation, no study reported a prefrontal LPP, as our work does: thus, it is reasonable to suggest that our paradigm increases the motivated attention to emotional pictures by pre-stimulus processing, as reflected by the pre-motor activities. It has been repeatedly demonstrated that the positive slow waves over frontal and parietal regions between 300 and 900 ms reflect the selective attention and working memory processing (Gevins et al., 1995, 1996; Rama et al., 1995) and, as suggested by fMRI studies (e.g. Dolcos et al., 2004), the enhanced PFC activity in emotional evaluation explains the better retention of affective stimuli. Further, as also demonstrated by Bermpohl and colleagues (2006b), the expectancy of emotional stimuli increased the neural response to the emotional (not neutral) pictures, especially in a emotional network including the medial prefrontal cortex (MPFC).

Our hypothesis on the affective modulation of the BP was not confirmed: the analyses on the BP have only revealed a later onset during the preparation to the negative compared to scramble pictures. A delayed BP onset has been previously reported in young people in comparison to elderly (Berchicci et al., 2012a) and in top-level shooters in comparison to controls (Di Russo et al., 2005a) reflecting less neuronal recruitment in the supplementary motor cortex (SMA). However, the BP amplitude was not different between emotional categories, probably because the prefrontal positivity had partially covered the BP activity, leading to a progressively delayed onset for more arousing conditions. In brief, based on these results, it is not possible to confirm a BP emotional modulation. At the same time, this study did not reveal affective modulation of the P2-N2 components, which showed the expected emotional modulation trend without reaching a statistical significance elsewhere reported (e.g., Carretiè et al., 2004). The reason may lie in the concomitant occurrence of the re-afferent positivity (RAP), which can partially modify the P2-N2 effect. The cortical generator of the RAP is the somatosensory cortex (Di Russo et al., 2005a, b), thus the cortical distribution of this component is similar to that of the frontal-central N2.

Finally, all of the considered cortical potentials showed the

strongest statistical significance in the negative category, especially in comparison to the scramble one. This finding suggests two main considerations: first, negative stimuli are probably perceived as more arousing in comparison to positive, regardless of IAPS normative ratings (e.g. Poli et al., 2007); second, scramble stimuli are very useful in emotional studies because of their totally lack of affective contents. Indeed, although neutral pictures are low arousing and theoretically not emotion-related, they contain faces, objects and other elements eliciting memories and cognitive evaluations that could be related to affective reactions. A limitation of this study is the absence of a self-report questionnaire on the affecting rating, such as the Self-Assessment Manikin (SAM) scale (Bradley and Lang, 1994). Indeed, data about subjective affective ratings could clarify whether the prefrontal and occipital activities during motor preparation are totally arousal-related irrespective of the valence, or if they are also affected by the negative valence. Unfortunately, it was impossible to use this approach in our protocol, because of the high number of stimuli employed. Another limitation of the present study regards the time window after the stimulus onset. Indeed, a longer time interval between each key-press could allow a larger segmentation of the signal; we have segmented until 1 s after stimulus onset in order to avoid the analysis of overlapped segments, but a better LPP modulation could be observed in a larger time window. Finally, since we investigated the MRCPs in a context of self-created emotional experience, the pre-motor and expectancy activities are obviously overlapped in this design: a paradigm with passive stimuli presentation will be needed to describe the activities more specifically related to the passive expectancy.

2.5. Conclusions

The results of this study show that both MRCPs and post-stimulus processing of high arousing pictures lead to larger slow positive potentials over anterior and posterior areas, reflecting a state of motivated attention to emotional relevant stimuli. After pictures presentation, the LPPs complex reflected this process, while in the MRCPs time window a positive potential was observed over prefrontal and occipital regions well before the key-press. These

expectancy activities in a context of motor preparation probably reflect enhanced pre-processing in the to-be-stimulated areas and a state of preparedness for action; we propose that both appetitive and defensive motivational systems could facilitate the forthcoming processing of survival-relevant contents, also before the stimulus presentation.

Considering both the emotional-modulation of perceptual encoding in the visual cortex and the role of the PFC in the motivational systems that process the behavioral responses to affective events (Rolls, 2002; LeDoux, 2003), it is likely that the reason why the emotional expectancy is able to modulate the premotor brain activity is to arrange in advance the approach-withdrawal responses to arousing experiences, increasing the probability to do the right thing and, in evolutionary terms, to survive. In conclusion, this study suggests that the response preparation to predictable events leads to specific anticipatory brain adjustments, allowing us to better cope with the subsequent affective experiences.

References

Bechara, A., Damasio, A. R., Damasio, H. and Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. Cognition 50, 7-15.

Bechara, A., Tranel, D., Damasio, H. and Damasio, A. R. (1996). Failure to respond autonomically to anticipated future outcomes following damage to prefrontal cortex. Cereb cortex 6, 215-225.

Berchicci, M., Lucci, G., Pesce, C., Spinelli, D. and Di Russo, F. (2012a). Prefrontal hyperactivity in older people during motor planning. Neuroimage 62, 1750-1760.

Berchicci, M., Stella, A., Pitzalis, S., Spinelli, D., and Di Russo, F. (2012b). Spatio-temporal mapping of motor preparation for self-paced saccades. Biol Psychol, 90, 10-17.

Berchicci, M., Menotti, F., Macaluso, A., and Di Russo, F. (2013). The neurophysiology of central and peripheral fatigue during sub-maximal lower limb isometric contractions. Front hum neurosci, 15, 7.

Berchicci, M., Lucci, G., Perri, R. L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. Front Aging Neurosci, 6, 48.

Bermpohl, F., Pascual-Leone, A., Amedi, A., Merabet, L. B., Fregni, F., Gaab, N., ... & Northoff, G. (2006a). Dissociable networks for the expectancy and

perception of emotional stimuli in the human brain. Neuroimage, 30(2), 588-600.

Bermpohl, F., Pascual Leone, A., Amedi, A., Merabet, L. B., Fregni, F., Gaab, N., ... & Northoff, G. (2006b). Attentional modulation of emotional stimulus processing: an fMRI study using emotional expectancy. Hum Brain Mapp, 27(8), 662-677.

Birbaumer, N., Elbert, T., Canavan, A., Rockstroh, B. (1990). Slow potentials of the cerebral cortex and behavior. Physiol Rev 70, 1–41.

Böcker, K.B.E., Baas, J.M.P., Kenemans, J.L. and Verbaten, M.N. (2001). Stimulus-preceding negativity induced by fear: a manifestation of affective anticipation. Int J Psychophysiol 43, 77-90.

Bozzacchi, C., Giusti, M. A., Pitzalis, S., Spinelli, D., and Di Russo, F. (2012a). Awareness affects motor planning for goal-oriented actions. Biol Psychol, 89, 503-514.

Bozzacchi, C., Giusti, M. A., Pitzalis, S., Spinelli, D., and Di Russo, F. (2012b). Similar cerebral motor plans for real and virtual actions. PloS one, 7, e47783.

Bradley, M. M., & Lang, P. J. (1994). Measuring emotion: the self-assessment manikin and the semantic differential. Journal of behavior therapy and experimental psychiatry, 25(1), 49-59.

Bradley, M. M., Sabatinelli, D., Lang, P. J., Fitzsimmons, J. R., King, W. and Desai, P. (2003). Activation of the visual cortex in motivated attention. Behav Neurosci 117, 369.

Brunia, C. H. M. (1999). Neural aspects of anticipatory behavior. Acta Psychol 101, 213-242.

Carretié, L., Martín-Loeches, M., Hinojosa, J. A. and Mercado, F. (2001). Emotion and attention interaction studied through event-related potentials. J Cognitive Neurosci,13, 1109-1128.

Carretié, L., Hinojosa, J. A., Martín-Loeches, M., Mercado, F. and Tapia, M. (2004). Automatic attention to emotional stimuli: neural correlates. Hum Brain Mapp 22, 290-299.

Casement, M. D., Shestyuk, A. Y., Best, J. L., Casas, B. R., Glezer, A., Segundo, M. A. and Deldin, P. J. (2008). Anticipation of affect in dysthymia: Behavioral and neurophysiological indicators. Biol Psychol 77, 197-204.

Coombes, S. A., Janelle, C. M. and Duley, A. R. (2005). Emotion and motor control: Movement attributes following affective picture processing. J Motor Behav 37, 425-436.

Coombes, S. A., Cauraugh, J. H. and Janelle, C. M. (2006). Emotion and movement: Activation of defensive circuitry alters the magnitude of a sustained muscle contraction. Neurosci Lett 396, 192-196.

Coombes, S. A., Cauraugh, J. H. and Janelle, C. M. (2007). Emotional state and initiating cue alter central and peripheral motor processes. Emotion 7, 275.

Coombes, S. A., Tandonnet, C., Fujiyama, H., Janelle, C. M., Cauraugh, J. H. and Summers, J. J. (2009). Emotion and motor preparation: A transcranial

magnetic stimulation study of corticospinal motor tract excitability. Cogn Affect Behav Neurosci 9, 380-388.

Cunningham, W. A., Espinet, S. D., DeYoung, C. G. and Zelazo, P. D. (2005). Attitudes to the right-and left: frontal ERP asymmetries associated with stimulus valence and processing goals. NeuroImage 28, 827-834.

Cuthbert, B. N., Schupp, H. T., Bradley, M. M., Birbaumer, N. and Lang, P. J. (2000). Brain potentials in affective picture processing: covariation with autonomic arousal and affective report. Biol psychol 52, 95-111.

Daffner, K. R., Scinto, L. F. M., Weitzman, A. M., Faust, R., Rentz, D. M., Budson, A. E. and Holcomb, P. J. (2003). Frontal and parietal components of a cerebral network mediating voluntary attention to novel events. J Cognitive Neurosci 15, 294-313.

Davidson, R. J. and Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. Trends cogn sci, 3, 11-21.

Darwin, C., (1872). The Expression of the Emotions in Man and Animals. J. Murray, London.

Di Russo, F., Pitzalis, S., Aprile, T. and Spinelli, D. (2005a). Effect of Practice on Brain Activity: An Investigation in Top-Level Rifle Shooters. Med Sci Sports Exerc 37, 1586-1593.

Di Russo, F., Incoccia, C., Formisano, R., Sabatini, U., and Zoccolotti, P. (2005b). Abnormal motor preparation in severe traumatic brain injury with good recovery. J Neurotrauma 22, 297-312.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013a). A passive exoskeleton can push your life up: Application on multiple sclerosis patients. PloS one, 8(10), e77348.

Di Russo, F., Lucci, G., Sulpizio, V., Berchicci, M., Spinelli, D., Pitzalis, S., Galati, G. (2013b). Spatiotemporal mapping of response inhibition in the prefrontal cortex. Neuropsychological Trends, 79. ISSN 1970-321X.

Diedrich, O., Naumann, E., Maier, S. and Becker, G. (1997). A frontal positive slow wave in the ERP associated with emotional slides. J Psychophysiol 11, 71-84.

Dolcos, F., LaBar, K. S. and Cabeza, R. (2004). Dissociable effects of arousal and valence on prefrontal activity indexing emotional evaluation and subsequent memory: an event-related fMRI study. Neuroimage 23, 64-74.

Gable, P. A., and Harmon-Jones, E. (2010). Late positive potential to appetitive stimuli and local attentional bias. Emotion 10, 441.

Gevins, A., Cutillo, B. and Smith, M. E. (1995). Regional modulation of high resolution evoked potentials during verbal and non-verbal matching tasks. Electroen Clini Neuro 94, 129-147.

Gevins, A., Smith, M. E., Le, J., Leong, H., Bennett, J., Martin, N., McEvoy, L., Du, R. and Whitfield, S. (1996). High resolution evoked potential imaging of the cortical dynamics of human working memory. Electroen Clin Neuro 98, 327-348.

Hart, S. J., Lucena, N., Cleary, K. M., Belger, A. and Donkers, F. C. (2012). Modulation of early and late event-related potentials by emotion. Frontiers in integrative neuroscience 6, 1-9.

Kopell, B.S., Wittner, W.K., Lunde, D.T., Wolcott, L.J. and Tinklenberg, J.R. (1974). The effects of methamphetamine and secobarbital on the contingent negative variation amplitude. Psychopharmacologia 34, 55-62.

Lang, P. J., Bradley, M. M., Fitzsimmons, J. R., Cuthbert, B. N., Scott, J. D., Moulder, B. and Nangia, V. (1998). Emotional arousal and activation of the visual cortex: an fMRI analysis. Psychophysiology 35, 199-210.

Lang, P.J., Bradley, M.M. and Cuthbert, B.N. (1999). International affective picture system (IAPS): Instruction manual and affective ratings. Technical Report A-4. Gainesville, FL: The Center for Research in Psychophysiology, University of Florida.

LeDoux, J. E. (2003). Synaptic self: How our brains become who we are. Penguin.

Liu, Y., Huang, H., McGinnis-Deweese, M., Keil, A., and Ding, M. (2012). Neural substrate of the late positive potential in emotional processing. J Neurosci 32, 14563-14572.

McRae, K., Misra, S., Prasad, A. K., Pereira, S. C. and Gross, J. J. (2012). Bottom-up and top-down emotion generation: implications for emotion regulation. Soc Cogn Affect Neurosci 7, 253-262.

Mercado, F., Hinojosa, J.A., Peñacoba, C. and Carretiè, L. (2007). The emotional S1-S2 Paradigm for Exploring Brain Mechanisms Underlying Affective Modulation of Expectancy. In L.N. Bakker (Ed.) Brain Mapping Research Developments. Hauppauge, NY: Nova Science Publishers. 197-209.

Moratti, S., Saugar, C., and Strange, B. A. (2011). Prefrontal-occipitoparietal coupling underlies late latency human neuronal responses to emotion. J Neurosci 31, 17278-17286.

Moser, J. S., Krompinger, J. W., Dietz, J. and Simons, R. F. (2009). Electrophysiological correlates of decreasing and increasing emotional responses to unpleasant pictures. Psychophysiology 46, 17-27.

Nitschke, J. B., Sarinopoulos, I., Mackiewicz, K. L., Schaefer, H. S. and Davidson, R. J. (2006). Functional neuroanatomy of aversion and its anticipation. Neuroimage 29, 106-116.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 104, 199-206.

Olofsson, J. K., Nordin, S., Sequeira, H. and Polich, J. (2008). Affective picture processing: an integrative review of ERP findings. Biol Psychol 77, 247-265.

Pastor, M. C., Bradley, M. M., Löw, A., Versace, F., Moltó, J. and Lang, P. J. (2008). Affective picture perception: Emotion, context, and the late positive potential. Brain res 1189, 145-151.

Poli, S., Sarlo, M., Bortoletto, M., Buodo, G. and Palomba, D. (2007). Stimulus-Preceding Negativity and heart rate changes in anticipation of affective pictures. Int J Psychophysiol 65, 32-39.

Rämä, P., Carlson, S., Kekoni, J. and Hämäläinen, H. (1995). A spatial oculomotor memory-task performance produces a task-related slow shift in human electroencephalography. Electroen Clin Neuro 94, 371-380.

Rockstroh, B., Elbert, T., Canavan, A., Lutzenberger, W. and Birbaumer, N. (1989). Slow Brain Potentials and Behaviour, 2nd edn. Urban and Schwarzenberg, Munich.

Rolls, E.T., (2000). Prècis of The brain and emotion. Behav and Brain Sci 23, 177–191.

Sabatinelli, D., Lang, P. J., Keil, A. and Bradley, M. M. (2007). Emotional perception: correlation of functional MRI and event-related potentials. Cereb Cortex, 17, 1085-1091.

Sanchez-Lopez, J., Fernandez, T., Silva-Pereyra, J., Mesa, J. A. M. and Di Russo, F. (2014). Differences in Visuo-Motor Control in Skilled vs. Novice Martial Arts Athletes during Sustained and Transient Attention Tasks: A Motor-Related Cortical Potential Study. PloS one, 9(3), e91112.

Schwaninger, A., Wallraven, C., Cunningham, D. W. and Chiller-Glaus, S. D. (2006). Processing of facial identity and expression: A psychophysical, physiological, and computational perspective. Prog Brain Res 156, 321-343.

Schupp, H.T., Lutzenberger,W., Rau, H., Birbaumer, N. (1994). Positive shifts of event-related potentials: a state of cortical disfacilitation as reflected by the startle reflex probe. Electroen Clin Neuro 90, 135–144.

Schupp, H.T., Cuthbert, B.N., Bradley, M.M., Cacioppo, J.T., Ito, T. and Lang, P.J. (2000). Affective picture processing: the late positive potential is modulated by motivational relevance. Psychophysiology 37, 257–261.

Schupp, H. T., Markus, J., Weike, A. I. and Hamm, A. O. (2003). Emotional facilitation of sensory processing in the visual cortex. Psychol Sci 14, 7-13.

Schupp, H.T., Cuthbert, B.N., Bradley, M.M., Hillman, C.H., Hamm, A.O. and Lang, P.J. (2004). Brain processes in emotional perception: motivated attention. Cogn Emot 18, 593–611.

Schupp, H. T., Flaisch, T., Stockburger, J. and Junghöfer, M. (2006). Emotion and attention: event-related brain potential studies. Prog brain res 156, 31-51.

Shibasaki, H. and Hallet, M. (2006). What is the Bereitschaftspotential?. Clin Neurophysiol 117, 2341-2356.

Takeuchi, S., Mochizuki, Y., Masaki, H., Takasawa, N. and Yamazaki, K. (2005). Stimulus preceding negativity represents arousal induced by affective picture. Int Congr Ser 1278, 385-388.

Ueda, K., Okamoto, Y., Okada, G., Yamashita, H., Hori, T. and Yamawaki, S. (2003). Brain activity during expectancy of emotional stimuli: an fMRI study. NeuroReport 14, 51–55.

Van Boxtel, G.J.M. and Böcker, K.B.E. (2004). Cortical measures of anticipation. J Psychophysiol 18, 61-76.

Van de Laar, M. C., Licht, R., Franken, I. H. and Hendriks, V. M. (2004). Event-related potentials indicate motivational relevance of cocaine cues in abstinent cocaine addicts. Psychopharmacology 177, 121-129.

Wessa, M. and Flor, H. (2007). Failure of extinction of fear responses in posttraumatic stress disorder: evidence from second-order conditioning. Am J Psychiatry 164, 1684-1692.

3. Individual differences in response speed and accuracy are associated to specific activities of two interacting brain systems

3.1. Introduction

In a typical go/no-go task subjects are required to quickly respond to go trials (e.g. pressing a button) and to refrain the response to no-go trials. This task has been widely investigated because it involves many cognitive processes, such as motor preparation (Rinkenauer et al., 2004; Berchicci et al., 2012), sensory evidence accumulation (Burle et al., 2004; Perea et al., 2010), decision-making (Schall, 2001; Heekeren et al., 2008), proactive and reactive inhibition (Aron et al., 2004; 2011) and motor response. The neural basis of these processing have been investigated at various levels, from animal (Mishkin, 1964) to humans (Konishi et al., 1998; Garavan et al., 1999; Konishi et al., 1999). However, neurocognitive processes underlying the perceptual decision-making are not entirely defined, and particularly the processes supporting the trade-off between speed and accuracy of the response in the go/no-go task has received little attention.

In the context of a perceptual discriminative task, decisions can be viewed as a result of continuous accumulation of sensory information from a baseline point until reaching a threshold (Ratcliff, 1978). Fast decisions are more error prone, while careful ones take longer (Wenzlaff et al., 2011); this phenomenon is known as the speed-accuracy tradeoff (hereafter, SAT) (for a review see Bogacz et al., 2010).

The cognitive models of decision making consider the SAT as the outcome of an evidence accumulation process. One of the most important accumulation models is the Ratcliff's diffusion model (Ratcliff and Rouder, 2000; Ratcliff, 2002; Ratcliff and Tuerlinckx, 2002;

Ratcliff et al., 2004); this model considers the response execution as a result of different processes, such as the quality of evidence accumulation, the decision criteria and the stimulus encoding. This model assumes that decisions are taken through a noisy process that accumulates information over time (Ratcliff and McKoon, 2008). Differently to the Ratcliff's model, the leaky competing accumulator model (Usher and McClelland, 2001) also considers the effects of leakage and amplification of differences (partly attributable to the noise), while the linear ballistic accumulation model (Brown and Heathcote, 2005, 2008) includes the between-trial variability in input strength and in the starting point of accumulation. Summarizing, all the accumulation models share the assumption that SAT can be explained by changes in the distance between a baseline and a threshold, so that a larger distance yield slower but more accurate responses (Reddi and Carpenter, 2000; Usher and McClelland, 2001; Bogacz et al., 2006; Simen et al., 2006). Computationally, a baseline increase would be equivalent to a threshold decrease. Despite the large amount of evidence supporting the modeling of behavioral results according to mathematical models of decision-making, the neural mechanisms for adjusting the baseline-to-threshold distance are only partially understood (Kim and Lee, 2011).

Several functional magnetic resonance imaging (fMRI) studies attempted to identify the brain regions involved in SAT by means of instructions emphasizing either response speed or accuracy; these studies used a Simon task with right/left hand response (van Veen et al., 2008; Forstman et al 2008a) or a cued motion direction discrimination task (Forstmann et al., 2008b; Ivanoff et al., 2008; Forstman et al, 2010). Forstmann et al (2008b) showed that the preparation for fast actions was associated with larger activity of the anterior striatum and the rostral part of the supplementary motor area (pre-SMA). Two other studies (Ivanoff et al., 2008; van Veen et al, 2008) confirmed that speed emphasis leads to greater activation in the striatum and pre-SMA, but showed also the involvement of other areas: the premotor area (PMA), the dorsolateral prefrontal cortex (DLPFC) and left parietal cortices. Forstmann et al (2008a) noted individual differences in the task, i.e. under speed constraint some participants adjusted their response thresholds more than others; the participants who had a relatively large decrease in response caution

also had a relatively large increase in activation for the right anterior striatum and right pre-SMA. On the other hand, none of these studies found SAT-related changes in sensory cortical areas.

This latter result was also reported by the electroencephalographic (EEG) studies on the SAT, which used tasks such as Simon, flankers and letter recognition and focused on the motor stages evaluating the lateralized readiness potential (LRP). Sangals, Sommer and Leuthold (2002) found that time pressure increased the LRP amplitude. Other studies (Osman et al., 2000; Van der Lubbe et al, 2001; Rinkenauer et al., 2004) considered the LRP latency and found that the faster the response time (RT), the earlier the LRP peak. Only Brunia et al. (2003) used a go/no-go task: they found that under speed instructions the preparatory activity was enhanced with respect to the instruction of being as fast and accurate as possible. Considering the locus of SAT, these studies concluded that SAT mechanism operated at the late motor stage, although some effects were also detected at the premotor stage (Rinkenauer et al., 2004). Finally, a recent MEG study using a face/house categorization task described the timing of the decision processing affected by SAT, and its dependence on sensory evidence (Wenzlaff et al., 2011). Emphasis on speed resulted in a higher activation of SMA and precuneus, whereas the left DLPFC showed larger activity under accuracy than speed instructions, possibly reflecting a higher level of accumulated evidence; however, they did not find SAT effects in sensory areas.

Overall, these studies provide convergent, but also divergent evidence. It is likely that the differences between results are caused by differences in tasks (such as perceptual categorization vs. Simon task), experimental designs (such as single trial cueing vs. cuing blocks), signal analyses (stimulus-locked vs. response-locked activity) and computational reference modeling. These contrasting results call for further investigations of SAT, particularly using other tasks and other analyses. To this aim, in the present study we investigated both pre- and post-stimulus SAT-related processes by means of high-density EEG and stimulus-locked analyses in a go/no-go task.

A key methodological difference with previous studies is that we did not force subjects to emphasize speed or accuracy, rather we sought to separately describe the neural processes subserving speed or accuracy on the basis of the subjects' spontaneous behavioral

tendency; thus, subjects were assigned a posteriori to each group (high or low accuracy; fast or slow speed) based on the observed performance. Spontaneous (idiosyncratic) employment of speed and accuracy strategies reflects, at least in part, a trait disposition (Ashcraft and Faust, 1994; Ashcraft and Kirk, 2001; Szymura and Wodniecka, 2003; Flehmig et al., 2010); thus, we thought that speed or accuracy behaviors could be better unfolded in their habitual trend. A limit of the approaches based on instructions manipulation is the individual differences in copying with the instructions themselves; for example, a spontaneously fast subject can easily behave more slowly, while a slow subject may have trouble to speed up. Consistently, these two subjects may engage different cognitive resources to fulfill with the instructions because of their basic dispositions, and this could influence the individuation of the SAT-neural correlates. Following this idea, we hypothesize that the idiosyncratic, behaviorally measured, individual speed-disposition or accuracy-disposition may reflect the dominance of a motor-related (in case of speed-oriented subjects) vs. decision making-related (in case of accuracy-oriented subjects) cortical mechanisms more clearly than it can be observed in studies manipulating either the speed or accuracy emphasis in the same subject. Moreover, we wonder whether, using this approach, speed- and accuracy-related neural processes were identifiable also at the perceptual level; this expectation was not supported by fMRI and MEG literature, because SAT-related effects were not found in sensory areas (Forstmann et al., 2008b; Ivanoff et al., 2008; van Veen et al., 2008; Wenzlaff et al., 2011). However, we hypothesize that the idiosyncratic behavioral performance can also express at perceptual processing level; this view was supported by previous event-related potentials (ERPs) evidence from our group (Di Russo et al., 2006) showing that the amplitude of the visual N1 evoked in a go/no-go task was increased in subjects with very fast RTs. Further, we expected to find a difference in the occurrence of a pre-movement brain component, which might partly explain the performance in the speed domain. Particularly, we hypothesized that this component could be represented by the prefrontal positivity (pP), previously associated to the stimulus-response (S-R) mapping process (see, e.g., Berchicci et al., 2014): indeed, if that component triggers the response execution in the go trials, a latency modulation at that level should predict the speed of

the response execution, while an amplitude modulation could reflect the quality of the subserved processing, as probably reflected by the accuracy comparison.

3.2. Methods

3.2.1. Subjects

From a database of 130 subjects who participated in the go/no-go task (described below), we firstly ordered them based on the values of two behavioral parameters: 1) speed: the individual median RTs of correct trials and 2) accuracy: the individual mean percentage of false alarms (FAs) (i.e. responses to no-go stimuli). We calculated the quartiles from each data set (i.e., mean value for the lower and upper quartiles for RTs was 524 and 372 ms respectively; mean value for the lower and upper quartiles for FAs was 18.00 and 2.18% respectively). Then, we selected the groups of subjects falling into the lower (33 and 32 subjects for speed and accuracy, respectively) and upper (32 and 34 subjects for speed and accuracy, respectively) quartiles. Afterwards, the groups were matched for age, gender and, most important, for the value of the other reference parameter, i.e. the two Speed-groups were FA-matched, and the two Accuracy-groups were RT-matched. Finally, we selected 63 participants for the final groups, each of one was composed by about 21 subjects (see Table 1); 23 of them belonged to two groups. Obviously, the main risk of this approach is that it does not allow a perfect groups match according to demographic and behavioral data, but it is important to note that in the final groups the statistical differences were significant between the reference parameter only (see Table 3.1). The demographic and behavioral data of the four groups and their relative comparisons (performed by t-test) are also shown in Table 3.1. The participants had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders; all of the subjects were right-handed (Edinburgh handedness inventory; Oldfield, 1971). After explanations of the procedures, all of the participants provided written informed consent, approved by the local ethical committee.

	Speed			Accuracy		
	Fast	**Slow**	**t (pvalue)**	**Accurate**	**Inaccurate**	**t (p value)**
N. (males)	23 (18)	22 (15)		20 (14)	21 (16)	
Age (SD)	34.4 (10.3)	39.9 (11.3)	-1.7 (>.05)	34.3 (12.2)	33.6 (13.4)	0.17 (>.05)
RT (SD)	388 (34)	489 (30)	**-10.7 (<.0001)**	435 (47)	413 (57)	1.4 (>.05)
FA (SD)	10.3 (7.7)	7.1 (5.3)	1.6 (>.05)	2.3 (1.2)	15.4 (5.9)	**-9.7 (<.0001)**

Tab. 3.1. Comparison of demographic and behavioral data in the Speed- and Accuracy-groups. Age is expressed years, RT in milliseconds and FA in percentage.

3.2.2. Procedure and Task

Subjects were tested in a sound attenuated, dimly lit room; they were comfortably seated in front of a computer screen at a distance of 114 cm, and a board was fixed on the armchair allowing them to push freely the button panel positioned on it. Four visual stimuli (i.e. four squared configurations made by vertical and horizontal bars) were randomly presented for 260 ms with equal probability (p=0.25). Two stimuli were defined as targets (go stimuli, p=0.5), the other two were defined as non-targets (no-go stimuli, p=0.5). The stimulus-onset asynchrony varied from 1 to 2 s to avoid time prediction effects on the RTs (for more details on the paradigms, see Berchicci et al., 2012). All of the participants were asked to be very accurate in discriminating the stimuli and to press the button as fast as possible with the right hand when a target appeared on the screen (go stimuli) and withhold the response when a non-target appeared (no-go stimuli). A minimum of 400 trials were recorded for both go and no-go stimuli.

3.2.3. Electrophysiological recording and data analysis

The EEG signal was recorded using BrainVisionTM system (BrainProducts GmbH, Munich, Germany) with 64 electrodes mounted according to the 10-10 international system. All electrodes were referenced to the left mastoid. Horizontal and vertical

electrooculogram (EOG) were also recorded using electrode at the right external canthi and below the left eye, respectively. Electrode impedances were kept below 5KΩ. The EEG was digitized at 250 Hz, amplified (band-pass of 0.01-80 Hz including a 50 Hz notch filter) and stored for offline averaging. Artifact rejection was performed prior to signal averaging to discard epochs contaminated by blinks, eye movements or other signals exceeding the amplitude threshold of ±100μV. In order to investigate both the pre- and the post-stimulus activities, the artifact-free signals were separately segmented into go and no-go trials, and then averaged in 2000 ms epochs (from 1100 ms before to 900 ms after the stimulus onset). The baseline was defined as the mean voltage during the initial 200 ms of the averaged epochs. To further reduce high frequency noise, the averaged signals were low pass filtered (i.e. Butterworth) at 25 Hz (slope 24 dB/octave). All of the statistical analyses were separately performed for Speed- and Accuracy-groups.

Pre-stimulus activities

Statistical differences in the pre-stimulus mean amplitude of Speed- and Accuracy-groups were initially assessed with sample-by-sample t-test in all electrodes in order to select the locations and the time windows where the differences were consistently significant.

For the Speed-groups, the mean amplitude on Cz derivation in the -500/0 time window, reflecting the Bereitschaftspotential (BP), was submitted to a repeated measures ANOVA with Group (Fast vs. Slow) and Condition (go vs. no-go) as factors.

Based on preliminary analysis on the Accuracy-groups, we selected the following electrodes on the left (AF3-F3-F7-FC5) and right (AF4-F4-F8-FC6) prefrontal cortex (PFC); the ERPs recorded at these electrodes were averaged in order to obtain a representative pool of activities in each hemisphere of the PFC. The mean amplitude between 250 ms before and 50 ms after stimulus onset at the two selected pools was submitted to a 2x2x2 ANOVA(Group x Pool x Condition). Post-hoc comparisons were conducted using Fisher's least significant difference (LSD) test. Furthermore, the correlation coefficients (Pearson's r coefficients) were performed between behavioral and pre-stimulus electrophysiological data for the Speed- and Accuracy-groups. The overall alpha level was fixed at 0.05.

Post-stimulus activities

Based on the peak electrodes, the typical post-stimulus ERPs components were measured as follows: the P1 on PO8, the N1 on PO7, the N2 on Cz, and the P3 on Pz and Cz in the go and no-go condition, respectively. The peak amplitude and latency of these components were submitted to separate 2x2 ANOVAs with Group (Fast vs. Slow or Accurate vs. Inaccurate) as between factor and Condition (go vs. no-go) as within factor. Post-hoc comparisons were conducted using Fisher's least significant difference (LSD) test. The correlation coefficients (Pearson's r coefficients) were performed between behavioral and post-stimulus electrophysiological data; further, in order to look for the relationship between pre- and post-stimulus neural activities in the decision-making process, we also performed the correlation analyses between the electrophysiological data in both Speed- and Accuracy-groups. The results of analyses will be reported only when they are significant ($p<0.05$).

Differential waves

In a study combining EEG and fMRI measures (Di Russo et al., 2013b), it was showed that stimulus perception in the go/no-go task triggers early activity in anterior insula, corresponding to the pP component of the EEG. The positivity enhancement over the frontopolar derivations was closely associated to the go condition as triggering the response execution (Berchicci et al., 2014): it started bilaterally 80 ms after the stimulus and peaked at 300-350 ms, as also reported in a study with neurological patients (Di Russo et al., 2013a).

In the present study, to better isolate the pP component, we adopted the differential method subtracting the individual no-go ERP from the go ERP of the same subject; the individual subtraction waves were then separately averaged for Speed- and Accuracy-groups. Obviously, the risk in adopting this method is to indistinctly subtract different activities taking place in the same period. In order to avoid this, we limited our analyses on the Fp1 and Fp2 sites in the time window following the stimulus appearance. This method was motivated by the fact that we wanted to emphasize the prefrontal positive activity, expecting to find latency modulations as a consequence of difference in response speed. We also looked at that component in the accuracy-groups, in which the speed-match should

not produce a modulation in the peak latency. The data were band pass filtered (1-20 Hz; slope 24 dB/octave) to reduce the low-frequency noise and to facilitate the peak detection. The visual inspection of the averaged differential waves showed a positive peak at approximately 330 ms bilaterally over the frontopolar electrodes (i.e.Fp1 and Fp2); since both topography and latency of this difference wave were similar to that of the pP elsewhere reported (Di Russo et al., 2013a,b; Berchicci et al., 2014), this component will be called differential prefrontal positivity (dpP) wave.

The onset latency (calculated as the first deflection larger than twice the absolute value of the baseline mean) and the peak amplitude and latency of the dpP were submitted to 2x2 ANOVAs with Group and Site (Fp1, Fp2) as factors, repeated for both Speed- and Accuracy-groups. The correlation coefficients (Pearson's r coefficients) were computed between behavioral and dpP data. The overall alpha level was fixed at 0.05.

3.3. Results

Figure 3.1 illustrates the ERP waveforms of both Speed- (Figure 3.1 a) and Accuracy-groups (Figure 3.1 b) at three relevant sites (AF4, Cz, PO8) for both go and no-go conditions. Time zero represents the stimulus onset; inspection of the figure indicates that these stimulus-locked ERPs using long pre-stimulus analysis allow to appreciate the motor preparation activity, which is usually obtained by the motor response-locked ERPs, called movement-related cortical potentials (MRCPs).

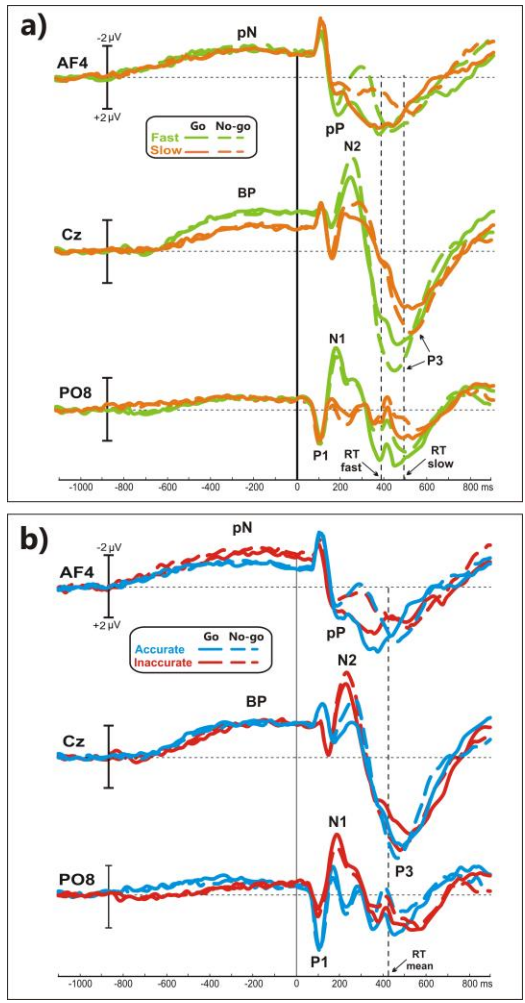

Fig. 3.1: Grand averaged waveforms of Speed- (a) and Accuracy-groups (b) in the three relevant sites (AF4, Cz, PO8); time 0 corresponds to the stimulus onset. The different groups and task conditions are superimposed with different colors. pN: prefrontal negativity; BP: Bereitschaftspotential.

Pre-stimulus activities

No differences were found between go and no-go conditions before stimulus onset. In all groups, the prefrontal negativity (pN) started about 800 ms before the stimulus appearance (see AF4); 200 ms later, over Cz, emerged the BP that progressively raised reaching its maximum at about 300 ms before the stimulus onset. The BP

component was larger in the fast than the slow group, while the two Accuracy-groups had identical BP component. By contrast, the pN was modulated by the accuracy only, i.e. the inaccurate group showed a larger negativity than accurate group.

Figure 3.2 a) shows the topographical distribution of the aforementioned pre-stimulus activities. The activity over the medial frontal-central areas (likely the SMA) in the fast group was larger than the slow group; on the other hand, the inaccurate group showed a greater negativity than the accurate over the PFC, especially in the right-hemisphere. In order to visually enhance the presence of hemispheric differences in the inaccurate group, Figure 3.2 b) shows the differential waves obtained over lateral PFC by subtraction of the grand averaged ERP of accurate group from that of the inaccurate.

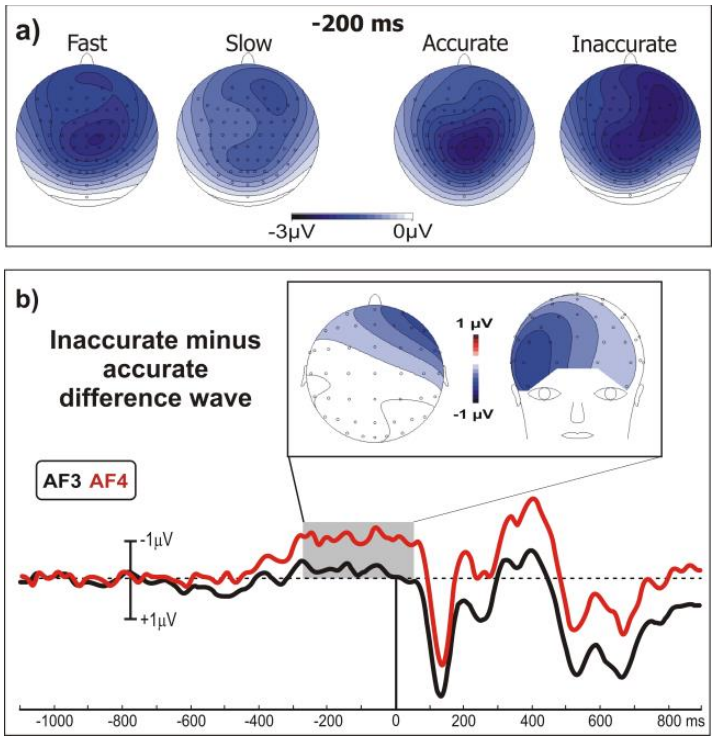

Fig. 3.2. (a) Scalp topographies (top-flat view) of the grand averaged pre-stimulus activities in the Speed- and Accuracy-groups. (b) Topographical distribution in the -250/+50 ms time window and waveforms at relevant sites of the left and right PFC pools of the differential activity in the Accuracy-groups (inaccurate minus accurate group). Time 0 corresponds to the stimulus onset

As for the statistical analysis of the Speed-groups, ANOVA revealed a significant effect of Group on the BP time window ($F_{1,43}=5.35$, $p<0.05$), which was larger in fast (-2.2μV) than in slow (-1.3 μV) group; at the opposite, no differences emerged by analysis on the pN component ($F_{1,43}=0.33$). For the Accuracy-groups, ANOVA on the BP revealed no significant effect of Group ($F_{1,39}=0.24$), while the pN showed a main effect of Pool ($F_{1,39}=16.97$, $p=0.0001$) and a significant interaction Group x Pool ($F_{1,39}=5.26$, $p<0.05$). Post hoc revealed that the pN was larger ($p<0.05$) in the inaccurate (-2.4 μV) than accurate (-1.4 μV) group. Moreover, the pN amplitude at the right side of the inaccurate group was larger than the left pN of both inaccurate ($p<0.0001$) and accurate ($p<0.01$) groups.

Pearson's analysis showed that the BP amplitude of the Speed-groups correlated positively with the RTs ($r=0.33$, $p<0.05$); on the other hand, the analysis on the Accuracy-groups showed a significant correlation between the percentage of FAs and the pN activity of the left ($r=-0.34$, $p<0.05$) and especially right ($r=-0.48$, $p=0.001$) pools (Figure 3.3 a). At the opposite, the correlations were neither significant between RTs and BP in the Accuracy-groups ($r=0.01$, $p>0.05$), nor between FAs and right pN in the Speed-groups ($r=-0.08$, $p>0.05$). These results suggest that a) the larger the BP component, the faster the behavioral response, and b) the larger the pN activity (especially on the right side), the worst the accuracy performance. Moreover, significant correlations emerged between the BP and the pN in both Speed- ($r=0.61$, $p<0.0001$) and Accuracy-groups ($r=0.4$, $p<0.01$), pointing to an interaction between SMA and right PFC activities.

Post-stimulus ERPs

The P1 and N1 components peaked at about 110 and 170 ms, respectively, on bilateral parietal-occipital sites (PO7/PO8). At about 240 ms emerged the N2 peaking on medial frontal sites (Cz). Finally, the P3 component peaked between 470 and 545 ms over medial parietal and frontal sites. Statistical comparisons of the aforementioned components are shown in Figure 3.3 b).

P1 component

For the Accuracy-groups, ANOVA showed a larger amplitude of the P1 in the accurate than inaccurate ($F_{1,39}=5.9$, $p=0.01$) group, and

the Pearson's test revealed a negative correlation between P1 amplitudes and FAs percentages (r=-0.35, p<0.05).

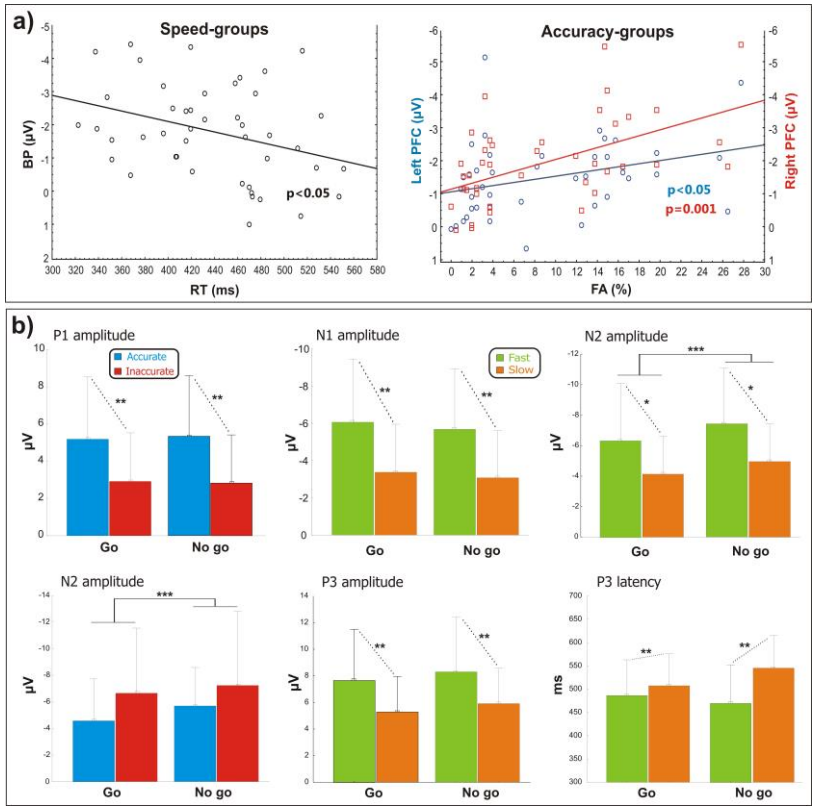

Fig. 3.3: (a) Pre-stimulus activity. Left side: correlation scatterplot of the RT with the BP amplitude in the Speed-groups. Right side: correlation scatterplot of the FA with both the left and right PFC activity (indexed by the pN) in the Accuracy-groups. (b) Post-stimulus activity: means and standard deviations of the main ERPs components. From the upper left: P1 amplitude in Accuracy-groups; N1 amplitude in Speed-groups; N2 amplitude in Speed-groups; N2 amplitude in Accuracy-groups; P3 amplitude in Speed-groups; P3 latency in Speed-groups. *p<.05 **p<.01 ***p<.001.

N1 component.

For the Speed-groups, the N1 component was larger in the fast than the slow group (F1,43=9.78, p<0.01); further, its amplitude positively correlated with RTs in both Speed- (r=0.48, p<0.001) and Accuracy-groups (r=0.36, p=0.001), indicating that an enhancement of this component was associated with faster RTs in both cases.

N2 component.

For the Speed-groups, ANOVA on the N2 component showed a main effect of Condition ($F_{1,43}=47.75$, $p<0.0001$), indicating that it was larger in no-go than go, and a main effect of Group ($F_{1,43}=5.03$, $p<0.05$), reflecting a larger N2 in the fast than slow group. For the Accuracy-groups, only the main effect of Condition ($F_{1,39}=19.98$, $p<0.0001$) was present, which was comparable to that observed for Speed-groups. Further, the N2 amplitude was positively correlated with the RTs in both Speed- ($r=0.38$, $p<0.001$) and Accuracy-groups ($r=0.47$ $p<0.001$), and negatively correlated with the FAs in both Speed- ($r=-0.26$, $p<0.001$) and Accuracy-groups ($r=-0.28$, $p<0.001$). In other words, larger N2 components were associated with faster RTs and more errors in both groups.

P3 component.

ANOVA on the Speed-groups showed a main effect of Group for both P3 amplitude ($F_{1,43}=6.97$, $p=0.01$) and P3 latency ($F_{1,43}=7.46$, $p<0.01$), indicating an earlier and larger P3 component in the fast than the slow group. In the Accuracy-groups the effects on the P3 were not significant. Pearson's analyses showed a negative sign correlation between RTs and P3 amplitude of both Speed- ($r=-0.39$, $p<0.001$) and Accuracy-groups ($r=-0.28$, $p<0.01$); further, the RTs was also positively correlated with the P3 latency of the Speed-groups ($r=0.27$, $p<0.01$) only. These data indicate that faster responses were associated with earlier and larger P3 peaks.

The results of the correlation analyses between electrophysiological data in the Speed- and Accuracy-groups are reported in Table 2. Overall, accuracy modulated the P1 and the N2 components in two opposite ways. The more accurate performance correlated with larger P1 amplitude and smaller N2 amplitudes. Speed modulated the N1, N2 and P3 components; the larger their amplitudes, the faster the RTs. For the P3 component, also the latency was related to RTs speed (the shorter P3 latency, the faster RTs).

Differential waves

To enhance the go-related pP, the differential waves (go minus no-go) were calculated on the frontopolar derivations (Fp1, Fp2), limiting the analyses to the time window following the stimulus. By this

method, the no-go condition acted as baseline for the go ERP in each subject: this procedure was motivated by the fact that the pP activity was closely associated to the response trials (i.e. Go); furthermore, the adopted spatial and temporal restrictions allowed us to isolate the known component without extending the observation to unknowable and interpretable waves.

Figure 3.4 shows the difference waveforms (restricted to the post-stimulus period) over the left prefrontal site (Fp1), in which the dpP was largely pronounced. In the Speed-groups, the dpP of the fast group started approximately 60 ms earlier than the slow group, and this difference partially remains until the peak, which was reached at 309 ms and 351 ms by the fast and slow group, respectively. Furthermore, the peak was larger in the fast than slow group. On the other hand, the accurate group had larger dpP than the inaccurate group, but latency differences were not present. These trends were confirmed by the ANOVAs, which in the Speed-groups revealed significant effects on the onset latency ($F_{1,43}=20$, $p<0.0001$), peak latency ($F_{1,43}=8.3$, $p<0.01$) and peak amplitude ($F_{1,43}=7.8$, $p<0.01$). For the Accuracy-groups, only the peak amplitude was different between groups ($F_{1,39}=5.5$, $p<0.05$).

Pearson's analyses showed that the RTs were positively correlated with the onset latency of the Speed-groups ($r=0.46$, $p=0.001$), and with the peak latency of both Speed- ($r=0.39$, $p<0.01$) and Accuracy-groups ($r=0.37$, $p<0.05$). Moreover, significant negative correlation emerged between the dpP amplitude and the RTs of the Speed-groups ($r=-0.4$, $p<0.01$), confirming that the larger the dpP, the faster the response. Overall, this differential wave enhancing go-related processing at prefrontal level was a sensitive marker of the efficiency of the decision processing in both Speed- and Accuracy-groups.

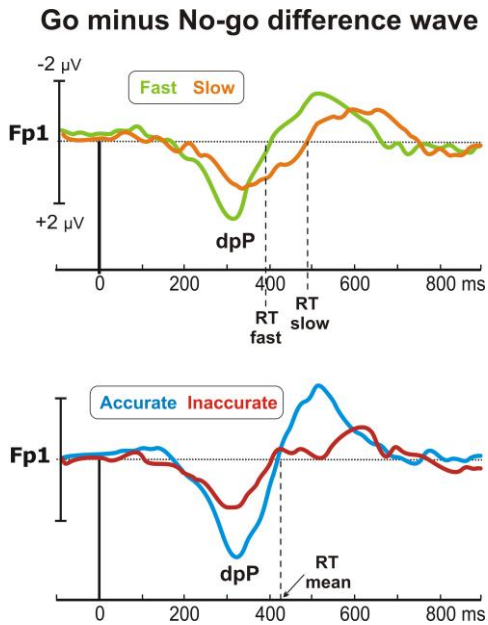

Fig. 3.4: Go minus no-go difference wave: the differential prefrontal positivity (dpP). Differential activity is reported for the left frontopolar electrode (Fp1) for both Speed- (top) and Accuracy-groups (bottom). Time zero represents stimulus onset

3.4. Discussion

This study aimed at identifying the neural processing stages associated with the SAT using a novel approach, i.e. selecting subjects based on their spontaneous speed or accuracy tendency rather than manipulating speed or accuracy requirements. Moreover, we recorded the frontal activity with a much more dense electrode array than previous electrophysiological studies (Osman et al., 2000; Van der Lubbe et al, 2001; Sangals et al., 2002; Band et al 2003 Rinkenauer et al., 2004) allowing discrimination of two different frontal activities in the temporal window before stimulus onset. Finally, we considered the characteristics of ERP components after stimulus, highlighting different levels of perceptual processing associated with response speed or response accuracy.

Pre-stimulus activities

The anticipatory brain activities (the BP and pN components)

showed group differences depending on the speed or the accuracy of the subsequent motor response. Fast and slow groups (matched in accuracy) had different BP amplitudes and similar pN amplitudes; at the opposite, accurate and inaccurate groups (matched in speed) had different pN amplitudes and similar BP amplitudes. The sources of these components were located in different areas of the frontal cortex: the SMA for the BP component (Di Russo et al., 2005; Berchicci et al., 2012), and the PFC for the pN (Di Russo et al., 2013a,b; Berchicci et al., 2013). An enhanced SMA activity in the last half second before the stimulus onset characterized subjects with fast responses with respect to slow subjects. By contrast, an enhanced rPFC activity starting 250 ms before the stimulus onset characterized inaccurate subjects with respect to very accurate subjects. Correlations between SMA amplitude and RTs on one side, and between rPFC amplitude and accuracy on the other further support the different roles played by these two frontal areas into speed and accuracy processing. However, it is noteworthy that the pre-stimulus activities were correlated (the larger the BP, the larger the pN) within both Speed and Accuracy groups, pointing to a stable relationship between SMA and rPFC activity.

The enhanced SMA activity was associated with speed instructions in fMRI (Forstmann et al., 2008b; Ivanoff et al., 2008; van Veen et al., 2008), MEG (Wenzlaff et al., 2011) and EEG (Brunia and Vingerhoets, 1980; Band et al., 2003; Rinkenauer et al., 2004) studies. Neurophysiologically, larger SMA activity under speed constrain might contribute to overcome the tonic inhibition provided by the output nuclei of basal ganglia (Lo and Wang, 2006). Present findings showed that the subjects with a spontaneous tendency to be fast had an enhanced SMA activity starting 500 ms before the stimulus onset, suggesting that baseline activity increased in fast performers. Indeed, a reduced baseline-to-threshold distance could account for the shorter time needed to reach a motor response (Bogacz et al., 2010).

On the other hand, it is still a matter of debate the role played by prefrontal areas in the SAT processing, although the engagement of the rPFC in the response accuracy is supported by studies on the response inhibition (Garavan et al., 1999, 2002; Stuss et al., 2002), and the ability to differentiate correct stimuli (Stuss et al., 2003), especially in tasks requiring sustained attention (Wilkins et al., 1987; Glosser and

Goodglass, 1990) such as the present one. Present findings indicate that the rPFC activity starting 250 ms before the stimulus onset was accuracy-related (larger in the inaccurate than accurate group).

Based on present results, we propose that: 1) speed and accuracy tendencies are settled by the activity of two distinct frontal areas (the SMA and rPFC, respectively) long before the stimulus onset (for this reason called "baseline"); 2) although there is a trade-off between SMA and rPFC activities (i.e. the BP and pN were correlated), it is not total: indeed, each group was marked by amplitude differences in only one component, without affecting the other. Thus, two interacting but separate neurocognitive systems may represent the basis of the individual tendencies underlying the baseline modulation of different baseline-to-threshold systems. In the "speed system" (modulated by the SMA), the increased baseline could lead to fast responses, while in the "accuracy system" (modulated by the rPFC) the increased baseline could lead to inaccurate performance, because of the reduced possibility of accumulating sufficient evidences until threshold reaching. Thus, we propose that SAT is the result of the co-activation of the two interacting systems. Indeed, considering the anatomo-functional connections between the SMA and rPFC (for a review see Aron, 2011), it could be proposed that an increased baseline activity in the SMA-rPFC network leads to fast and inaccurate performance, while the decreased baseline accounts for the trade-off in the sense of slow and accurate responses.

Post-stimulus activities

Data on post-stimulus activities are consistent with the view that accuracy- or speed-related individual tendency might affect also the activity of visual cortical areas. We observed a dissociation of the two visual components P1 and N1, which had larger amplitudes in the accurate and fast groups than slow and inaccurate groups, respectively. The dissociation was further confirmed by the correlation analyses, showing that larger P1 amplitude was associated with high accuracy, and larger N1 amplitude was associated with high speed.

A vast literature showed that spatial attention produces an amplification of stimulus-evoked activity in extrastriate areas and posterior parietal cortex (PPC) during the 80-250 ms following the stimulus onset (Luck et al., 1990; Clark and Hillyard, 1996; Wijers et

al., 1997; Hillyard et al., 1998; Martinèz et al., 1999; Di Russo et al., 2003). These studies support the "early selection" theories of visual-spatial attention (Bashinski and Bacharach, 1980; Johnston and Dark, 1986; Downing, 1998); however a different role of the P1 and N1 components should be considered (Luck et al., 1990). The P1 component enhancement represents facilitation at the early sensory processing level for items presented at attended location (Di Russo et al., 2003), while the N1 component is associated with the discrimination processes within the focus of attention (Luck et al., 1990; Vogel and Luck, 2000). In addition to the modulation of the extrastriate areas, visual attention control relies on a network of cortical and subcortical regions, including the DLPFC and PPC, the anterior cingulate gyrus, and the pulvinar nucleus of the thalamus (Mesulam, 1990; Nobre et al., 1997). Thus, it is likely that the modulations of the visual areas observed in the present study are part of a perceptual decision-making process, starting with pre-stimulus baseline adjustments and ending up with the response threshold reaching. We propose that individual speed- and accuracy-oriented neural strategies provide "bias signals" that exert a selective amplification of sensory information flow in different visual pathways. Support to this hypothesis comes from a single cell recording (Heitz and Schall, 2012) showing that the SAT-related cues induced a shift of baseline firing rates in the visually responsive neurons of the frontal eye field (FEF). At the same time, under the framework of the drift-diffusion models, recent studies (Rae et al., 2014; Zhang et Rowe, 2014) suggest that not only the boundary threshold but also other parameters are affected by the speed or accuracy; for example, it was proposed that emphasis on accuracy increased the allocation of attention on the task (i.e. the drift rate) and the non-decision time, i.e. the time reserved to the stimulus encoding. These latter hypotheses are consistent with the present findings, pointing to a greater allocation of visual-spatial attention in the accurate group, as revealed by the P1 amplitude. Further studies are needed to shed light into the brain networks underlying the speed- and accuracy-oriented perceptual processes, as indexed by the P1-N1 modulation.

Difference between groups was also observed for the N2 component: it was larger in the fast than slow group, showing also the

'typical' no-go enhancement (e.g. Donkers and van Boxtel, 2004). The N2 modulation is generally described as an index of inhibitory control (e.g. Van Boxtel et al., 2001) or as conflict monitoring between go and no-go stimuli (Nieuwenhuis et al., 2003; Donkers and van Boxtel, 2004). However, we will not discuss the N2 data in these terms, because in a recent study (Di Russo et al., 2013b) combining ERP and fMRI measures using the same paradigm of the present one, we found that the no-go condition did not produce larger activity than the go condition in any brain areas, indicating that the no-go N2 cannot be the expression of extra (inhibitory or conflict-related) activity, but more likely the summation of negative and positive waveforms originating in premotor, prefrontal and parietal areas in the same time period (200-400 ms after the stimulus). Further studies are required to clarify this issue, which is outside the scope of present work.

The P3 component, usually described as an index of the stimulus categorization process (Mecklinger and Ullsperger, 1993), started earlier and was larger in the fast than slow group, whereas no differences emerged between accurate and inaccurate groups. The correlation analyses further confirmed the relationship between the RT and the P3 component, suggesting that the P3 could also provide an estimation of the stimulus evaluation time that is closely related to the response processing time.

Finally, are crucial the effects found on the prefrontal positivity (pP). We confirmed that this newly discovered components, compared to no-go, is larger in the go condition as previously described by our group (Di Russo et al., 2013a,b; Berchicci et al., 2014). The neural generator of the pP was localized in the anterior Insula in a study combining fMRI and ERP data collected with the same task used in the present study (Di Russo et al., 2013b), and its function would be to trigger the response when enough information are accumulated. Other studies showed that insular activation indicates the stimulus-response (S-R) association to guide response selection (Boettiger and D'Esposito, 2005), and reflects both self and motor awareness (Berti et al., 2005). In the present study, we additionally adopted the subtraction method to better focus on the pP modulation on prefrontal sites: the main risk of this procedure is to compare different activities acting in the same period. For this reason, our analyses and interpretation were limited to the differential activity resulting from

the frontopolar derivations in the time window following the stimulus. In line with our predictions, we observed a positive component, called dpP, peaking at about 330 ms after the stimulus: thus, differential analyses further confirmed the presence of a positive activity closely related to the response execution, as previously observed in other studies (Di Russo et al., 2013a,b; Berchicci et al., 2014). Taking into account these views and the present data, we suggest that the dpP might reflect the S-R mapping finalized to the response execution in a perceptual discrimination task, representing the final stage of the decision process before the movement onset. Analyses on the dpP showed that the latency of this differential wave reflects the speed of the decision-making processing. Indeed, the dpP started earlier in the fast than slow group (see Fig. 4), explaining about the 60% of the RT difference between the two groups. Moreover, the dpP wave was larger in both fast and accurate groups than their respective counterparts, suggesting that its amplitude reflects the efficiency of the decision process in both cases.

Speed and accuracy decision systems: an integrative view

In summary, present results showed different brain activities both before and after stimulus onset in Speed- and Accuracy-groups. Pre-stimulus activity in the SMA and rPFC seems to reflect the baseline modulation of the speed and accuracy decision systems: they are interacting, as revealed by present analyses and anatomo-functional connections between SMA and rPFC (for a review see Aron, 2011). Thus, we suggest that the typical trade-off between response speed and accuracy is accounted by the baseline activity in the SMA-rPFC network. A baseline increase in this network could prepare subjects to fast and inaccurate performance, while a reduced baseline may predict slow and accurate performance because of the greater baseline-to-threshold distance in both the speed and accuracy systems. In addition, we showed that the speed and accuracy baselines can also be separately modulated, leading to either high or low group performance in one system without affecting (or affecting very little) the other, as indicated by comparable mean performance in the other system. Thus, as previously suggested, the two systems should be considered interacting but not totally dependent. Finally, after stimulus onset, ERP components reflecting perceptual processing, S-R

mapping and stimulus categorization were also differentially affected by speed and accuracy idiosyncratic tendencies.

Overall, the present study suggests that the motor response in a perceptual discrimination task should be considered as the final output of a series of neurocognitive processes starting long before the stimulus onset. For this reason, and based on our results, we sketched in Figure 3.5 the time course of the main processes supporting the go/no-go task. Obviously, all brain areas were active in both speed and accuracy processing; however, some areas were more involved in the speed with respect to accuracy system, and we tried to distinguish them by using different colors.

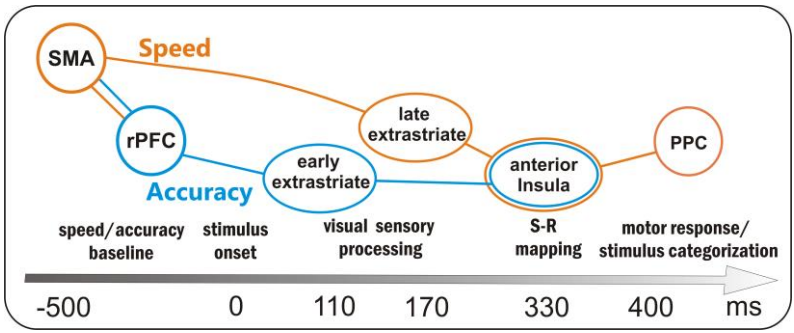

Fig. 3.5: Sketch of the processing in the preparation-perception-action cycle and associated brain areas as a function of time (not scaled). Obviously the same brain areas were involved in both speed- (orange) and accuracy (blue)- processing; however, the activity of some areas was more affected by either one or the other condition: the orange and blue lines depict the two main flows within speed and accuracy systems. SMA=supplementary motor area, rPFC=right prefrontal cortex, PPC=posterior parietal cortex.

Before stimulus onset the baseline activity of the speed and accuracy systems was modulated by the SMA (reflected by the BP) and the rPFC (reflected by the pN), respectively. Even if the activity of these prefrontal areas was correlated (accounting for the interaction between the two systems), the larger SMA activity marked only the fast group, while the larger rPFC activity marked only the inaccurate group. About 110 ms after the stimulus onset, the early sensory processing of the extrastriate areas (P1 component) was modulated by the accuracy level, with the accurate group focusing greater attention to the attended location. Immediately after, extrastriate visual and

parietal areas (N1 component) showed a more intense processing, likely corresponding to the discrimination stage, in the fast than the slow group. Because of this enhanced sensory processing, the response-oriented S-R mapping in the anterior Insula (as reflected by the dpP) was reached earlier and Insula activity was larger in fast with respect to slow group; moreover, also accuracy affected the anterior Insula activity (larger dpP in the accurate than inaccurate group), although its activity was not directly correlated with the rPFC modulation. In a time window around 400 ms, the activity corresponding to the stimulus categorization in the PPC (P3 component) and response execution in the case of go stimuli, was especially affected by response speed.

Summarizing, present data suggest that the behavioral speed-accuracy trade-off is explained by the neurocognitive processing of two "decision systems", starting to work before the stimulus appearance and reflecting the neural substrate of idiosyncratic tendencies. A limitation of the present study is that we did not observe if speed is traded for accuracy (or vice versa) at a single-subject level, and we matched the groups by a posteriori criteria based on behavioral performance; however, considering that task instructions equally emphasized speed and accuracy, we thought it might represent a sort of spontaneous sorting, enhancing idiosyncratic individual tendency.

References

Aron, A. R. (2011). From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. Biological psychiatry, 69(12), e55-e68.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in cognitive sciences, 8(4), 170-177.

Ashcraft, M. H., & Faust, M. W. (1994). Mathematics anxiety and mental arithmetic performance: An exploratory investigation. Cognition & Emotion, 8(2), 97-125.

Ashcraft, M. H., & Kirk, E. P. (2001). The relationships among working memory, math anxiety, and performance. Journal of experimental psychology: General, 130(2), 224.

Band, G. P., Ridderinkhof, K. R., & van der Molen, M. W. (2003). Speed-accuracy modulation in case of conflict: the roles of activation and inhibition. Psychological Research, 67(4), 266-279.

Bashinski, H. S., & Bacharach, V. R. (1980). Enhancement of perceptual sensitivity as the result of selectively attending to spatial locations. Perception & Psychophysics, 28(3), 241-248.

Berchicci, M., Lucci, G., & Di Russo, F. (2013). Benefits of Physical Exercise on the Aging Brain: The Role of the Prefrontal Cortex. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 68(11), 1337-1341.

Berchicci, M., Lucci, G., Pesce, C., Spinelli, D., & Di Russo, F. (2012). Prefrontal hyperactivity in older people during motor planning. Neuroimage, 62(3), 1750-1760.

Berchicci, M., Lucci, G., Perri, R.L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. Frontiers in Aging Neuroscience, 6:48.

Berti, A., Bottini, G., Gandola, M., Pia, L., Smania, N., Stracciari, A., Castiglioni, I., Vallar, G., & Paulesu, E. (2005). Shared cortical anatomy for motor awareness and motor control. Science, 309(5733):488-491.

Boettiger, C. A., & D'Esposito, M. (2005). Frontal networks for learning and executing arbitrary stimulus-response associations. The Journal of neuroscience, 25(10), 2723-2732.

Bogacz, R., Brown, E., Moehlis, J., Holmes, P., & Cohen, J. D. (2006). The physics of optimal decision making: a formal analysis of models of performance in two-alternative forced-choice tasks. Psychological review, 113(4), 700.

Bogacz, R., Wagenmakers, E. J., Forstmann, B. U., & Nieuwenhuis, S. (2010). The neural basis of the speed–accuracy tradeoff. Trends in neurosciences, 33(1), 10-16.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. Psychological review, 108(3), 624.

Brown, S., & Heathcote, A. (2005). A ballistic model of choice response time. Psychological review, 112(1), 117.

Brown, S. D., & Heathcote, A. (2008). The simplest complete model of choice response time: Linear ballistic accumulation. Cognitive psychology, 57(3), 153-178.

Brunia, C. H. M., & Vingerhoets, A. J. J. M. (1980). CNV and EMG preceding a plantar flexion of the foot. Biological Psychology, 11(3), 181-191.

Burle, B., Vidal, F., Tandonnet, C., & Hasbroucq, T. (2004). Physiological evidence for response inhibition in choice reaction time tasks. Brain and Cognition, 56(2), 153-164.

Clark, V. P., & Hillyard, S. A. (1996). Spatial selective attention affects early extrastriate but not striate components of the visual evoked potential. Journal of Cognitive Neuroscience, 8(5), 387-402.

Di Russo, F., Martínez, A., & Hillyard, S. A. (2003). Source analysis of event-related cortical activity during visuo-spatial attention. Cerebral Cortex, 13(5), 486-499.

Di Russo, F., Pitzalis, S., Aprile, T., & Spinelli, D. (2005). Effect of practice on brain activity: an investigation in top-level rifle shooters. Medicine and science in sports and exercise, 37(9), 1586.

Di Russo, F., Taddei, F., Aprile, T., & Spinelli, D. (2006). Neural correlates of fast stimulus discrimination and response selection in top-level fencers. Neuroscience Letters, 408(2), 113-118.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013a). A passive exoskeleton can push your life up: Application on multiple sclerosis patients. PloS One, 8(10), e77348.

Di Russo, F., Lucci, G., Sulpizio, V., Berchicci, M., Spinelli, D., Pitzalis, S., Galati, G. (2013b). Spatiotemporal mapping of response inhibition in the prefrontal cortex. Neuropsychological Trends, Abstr. 79.

Donkers, F. C., & van Boxtel, G. J. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. Brain and cognition, 56(2), 165-176.

Downing, C. J. (1988). Expectancy and visual-spatial attention: effects on perceptual quality. Journal of Experimental Psychology: Human Perception and Performance, 14(2), 188.

Flehmig, H. C., Steinborn, M. B., Westhoff, K., & Langner, R. (2010). Neuroticism and speed-accuracy tradeoff in self-paced speeded mental addition and comparison. Journal of Individual Differences, 31(3), 130.

Forstmann, B.U., van den Wildenberg, W.P., Ridderinkhof, K.R. (2008a) Neural mechanisms, temporal dynamics, and individual differences in interference control. Journal of Cognitive Neuroscience, 20(10):1854-65.

Forstmann, B. U., Anwander, A., Schäfer, A., Neumann, J., Brown, S., Wagenmakers, E. J., & Turner, R. (2010). Cortico-striatal connections predict control over speed and accuracy in perceptual decision making. Proceedings of the National Academy of Sciences, 107(36), 15916-15920.

Forstmann, B. U., Dutilh, G., Brown, S., Neumann, J., von Cramon, D. Y., Ridderinkhof, K. R., & Wagenmakers, E. J. (2008b). Striatum and pre-SMA facilitate decision-making under time pressure. Proceedings of the National Academy of Sciences, 105(45), 17538-17542.

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: an event-related functional MRI study. Proceedings of the National Academy of Sciences, 96(14), 8301-8306.

Garavan, H., Ross, T. J., Murphy, K., Roche, R. A. P., & Stein, E. A. (2002). Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction. Neuroimage, 17(4), 1820-1829.

Glosser, G., & Goodglass, H. (1990). Disorders in executive control functions among aphasic and other brain-damaged patients. Journal of Clinical and experimental Neuropsychology, 12(4), 485-501.

Heekeren, H. R., Marrett, S., &Ungerleider, L. G. (2008). The neural systems that mediate human perceptual decision making. Nature Reviews Neuroscience, 9(6), 467-479.

Heitz, R. P., & Schall, J. D. (2012). Neural mechanisms of speed-accuracy tradeoff. Neuron, 76(3), 616-628.

Hillyard, S. A., & Anllo-Vento, L. (1998). Event-related brain potentials in the study of visual selective attention. Proceedings of the National Academy of Sciences, 95(3), 781-787.

Hillyard, S. A., Vogel, E. K., & Luck, S. J. (1998). Sensory gain control (amplification) as a mechanism of selective attention: electrophysiological and neuroimaging evidence. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 353(1373), 1257-1270.

Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. PLoS One, 3(7), e2635.

Johnston, W. A., & Dark, V. J. (1986). Selective attention. Annual review of psychology, 37(1), 43-75.

Kim, S., & Lee, D. (2011). Prefrontal cortex and impulsive decision making. Biological psychiatry, 69(12), 1140-1146.

Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. Brain, 122(5), 981-991.

Konishi, S., Nakajima, K., Uchida, I., Sekihara, K., & Miyashita, Y. (1998). No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging. European Journal of Neuroscience, 10(3), 1209-1213.

Lo, C. C., & Wang, X. J. (2006). Cortico–basal ganglia circuit mechanism for a decision threshold in reaction time tasks. Nature neuroscience, 9(7), 956-963.

Luck, S. J., Heinze, H. J., Mangun, G. R., & Hillyard, S. A. (1990). Visual event-related potentials index focused attention within bilateral stimulus arrays. II. Functional dissociation of P1 and N1 components. Electroencephalography and clinical Neurophysiology, 75(6), 528-542.

Martinez, A., Anllo-Vento, L., Sereno, M. I., Frank, L. R., Buxton, R. B., Dubowitz, D. J., ... & Hillyard, S. A. (1999). Involvement of striate and extrastriate visual cortical areas in spatial attention. Nature neuroscience, 2(4), 364-369.

Mecklinger, A., & Ullsperger, P. (1993). P3 varies with stimulus categorization rather than probability. Electroencephalography and clinical neurophysiology, 86(6), 395-407.

Mesulam, M. (1990). Large-scale neurocognitive networks and distributed processing for attention, language, and memory. Annals of neurology, 28(5), 597-613.

Mishkin, M. (1964). Preservation of central sets after frontal lesions in monkeys. In J. M. Warren & K. Akert (Eds.), The frontal granular cortex and behavior (pp. 219-241). New York: McGraw-Hill.

Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. Cognitive, Affective, & Behavioral Neuroscience, 3(1), 17-26.

Nobre, A. C., Sebestyen, G. N., Gitelman, D. R., Mesulam, M. M., Frackowiak, R. S., & Frith, C. D. (1997). Functional localization of the system for visuospatial attention using positron emission tomography. Brain, 120(3), 515-533.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 104, 199-206.

Osman, A., Lou, L., Muller-Gethmann, H., Rinkenauer, G., Mattes, S., & Ulrich, R. (2000). Mechanisms of speed–accuracy tradeoff: evidence from covert motor processes. Biological psychology, 51(2), 173-199.

Perea, M., Gómez, P., & Fraga, I. (2010). Masked nonword repetition effects in yes/no and go/no-go lexical decision: A test of the evidence accumulation and deadline accounts. Psychonomic bulletin & review, 17(3), 369-374.

Rae, B., Heathcote, A., Donkin, C., Averell, L., & Brown, S. (2014). The hare and the tortoise: emphasizing speed can change the evidence used to make decisions. Journal of Experimental Psychology: Learning, Memory, and Cognition.

Ratcliff, R. (1978). A theory of memory retrieval. Psychological review, 85(2), 59.

Ratcliff, R., & Rouder, J. N. (2000). A diffusion model account of masking in two-choice letter identification. Journal of Experimental Psychology: Human perception and performance, 26(1), 127.

Ratcliff, R. (2002). A diffusion model account of response time and accuracy in a brightness discrimination task: Fitting real data and failing to fit fake but plausible data. Psychonomic Bulletin & Review, 9(2), 278-291.

Ratcliff, R., & Tuerlinckx, F. (2002). Estimating parameters of the diffusion model: Approaches to dealing with contaminant reaction times and parameter variability. Psychonomic bulletin & review, 9(3), 438-481.

Ratcliff, R., Gomez, P., & McKoon, G. (2004). A diffusion model account of the lexical decision task. Psychological review, 111(1), 159.

Ratcliff, R., & McKoon, G. (2008). The diffusion decision model: Theory and data for two-choice decision tasks. Neural computation, 20(4), 873-922.

Reddi, B. A. J., & Carpenter, R. H. S. (2000). The influence of urgency on decision time. Nature neuroscience, 3(8), 827-830.

Rinkenauer, G., Osman, A., Ulrich, R., Müller-Gethmann, H., & Mattes, S. (2004). On the locus of speed-accuracy trade-off in reaction time: inferences from the lateralized readiness potential. Journal of Experimental Psychology: General, 133(2), 261.

Sangals, J., Sommer, W., & Leuthold, H. (2002). Influences of presentation mode and time pressure on the utilisation of advance information in response preparation. Actapsychologica, 109(1), 1-24.

Sasaki, K., Gemba, H., Nambu, A., & Matsuzaki, R. (1993). No-go activity in the frontal association cortex of human subjects. Neuroscience Research, 18(3), 249-252.

Schall, J. D. (2001). Neural basis of deciding, choosing and acting. Nature Reviews Neuroscience, 2(1), 33-42.

Simen, P., Cohen, J. D., & Holmes, P. (2006). Rapid decision threshold modulation by reward rate in a neural network. Neural networks, 19(8), 1013-1026.

Stuss, D. T., Binns, M. A., Murphy, K. J., & Alexander, M. P. (2002). Dissociation within the anterior attentional system: Effects of task complexity and irrelevant information on reaction time speed and accuracy. Neuropsychology, 16(4), 500.

Stuss, D. T., Murphy, K. J., Binns, M. A., & Alexander, M. P. (2003). Staying on the job: the frontal lobes control individual performance variability. Brain, 126(11), 2363-2380.

Szymura, B., & Wodniecka, Z. (2003). What really bothers neurotics? In search for factors impairing attentional performance. Personality and individual differences, 34(1), 109-126.

Usher, M., & McClelland, J. L. (2001). The time course of perceptual choice: the leaky, competing accumulator model. Psychological review, 108(3), 550.

van Boxtel, G. J., van der Molen, M. W., Jennings, J. R., & Brunia, C. H. (2001). A psychophysiological analysis of inhibitory motor control in the stop-signal paradigm. Biological Psychology, 58, 229–262.

Van Veen, V., Krug, M. K., & Carter, C. S. (2008). The neural and computational basis of controlled speed-accuracy tradeoff during task performance. Journal of Cognitive Neuroscience, 20(11), 1952-1965.

Vogel, E. K., & Luck, S. J. (2000). The visual N1 component as an index of a discrimination process. Psychophysiology, 37(02), 190-203.

Wenzlaff, H., Bauer, M., Maess, B., & Heekeren, H. R. (2011). Neural characterization of the speed–accuracy tradeoff in a perceptual decision-making task. The Journal of Neuroscience, 31(4), 1254-1266.

Wijers, A. A., Lange, J. J., Mulder, G., & Mulder, L. J. (1997). An ERP study of visual spatial attention and letter target detection for isoluminant and nonisoluminant stimuli. Psychophysiology, 34(5), 553-565.

Wilkins, A. J., Shallice, T., & McCarthy, R. (1987). Frontal lesions and sustained attention. Neuropsychologia, 25(2), 359-365.

Zhang, J., & Rowe, J. B. (2014). Dissociable mechanisms of speed-accuracy tradeoff during visual perceptual learning are revealed by a hierarchical drift-diffusion model. Frontiers in neuroscience, 8.

4. Why do we make mistakes? Neurocognitive processes during the preparation-perception-action cycle and error processing

Abstract

The event-related potential (ERP) literature described two error-related brain activities: the error-related negativity (Ne/ERN) and the error positivity (Pe), peaking immediately after the erroneous response. ERP studies on error processing adopted a response-locked approach, thus, the question about the activities preceding the error is still open. In the present study, we tested the hypothesis that the activities preceding the false alarms (FA) are different from those occurring in the correct (responded or inhibited) trials. To this aim, we studied a sample of 36 Go/No-go performers, adopting a stimulus-locked segmentation also including the pre-motor brain activities. Present results showed that neither pre-stimulus nor perceptual activities explain why we commit FA. In contrast, we observed condition-related differences in two pre-response components: the fronto-central N2 and the prefrontal positivity (pP), respectively peaking at 250 ms and 310 ms after the stimulus onset. The N2 amplitude of FA was identical to that recorded in No-go trials, and larger than Hits. Because the new findings challenge the previous interpretations on the N2, a new perspective is discussed. On the other hand, the pP in the FA trials was larger than No-go and smaller than Go, suggesting an erroneous processing at the stimulus-response mapping level: because this stage triggers the response execution, we concluded that the neural processes underlying the pP were mainly

responsible for the subsequent error commission. Finally, sLORETA source analyses of the post-error potentials extended previous findings indicating, for the first time in the ERP literature, the right anterior insula as Pe generator.

4.1. Introduction

The ancient philosopher Seneca wrote "errare humanum est, perseverare autem diabolicum" (i.e., to err is human, but to persist in error is diabolical). Indeed, being aware of own errors is a crucial skill of the human brain. In the last decades neuroscientists investigated the neural substrates of error detection through electrophysiological techniques using cognitive tasks requiring decision making and motor responses, such as Odd-ball, Go/No-go, Flanker and Stop-Signal tasks (Braver et al., 2001; Debener et al., 2005; Matthews et al., 2005; Dhar et al., 2011). The error negativity (Ne; Falkenstein et al., 1991) or error-related negativity (ERN; Gehring et al., 1993), a frontal wave peaking at 50-100 ms after the erroneous response, is the most investigated error-related brain activity. After the Ne, at 200-400 ms after the erroneous response, a second activity, called error positivity (Pe; Falkenstein et al., 1994, 1996), is commonly observed in posterior areas. These two components are associated to different aspects of the error processing. The Ne is thought to reflect both the response conflict processing (Yeung et al., 2004) and the mechanism of early mismatch between the intended and actual response (Falkenstein et al., 1991; Coles et al., 2001). The main generator of the Ne was localized within the fronto-medial wall (FMW), specifically in the anterior cingulate cortex (ACC) and pre-supplementary motor area (pre-SMA) (Dehaene et al., 1994; Holroyd et al., 1998; Miltner et al., 1998; Luu et al., 2000; van Veen and Carter, 2002). However, recent evidences suggest also the contribution of a more distributed network in its generation, including the dorsolateral and ventrolateral prefrontal cortex (dlPFC and vlPFC), the cingulate motor area (CMA), and the lateral parietal cortex (typically Brodmann area 40) (Menon et al., 2001; Ullsperger and von Cramon, 2001; Bràzdil et al., 2002; Garavan et al., 2003; Ramautar et al., 2006; Taylor et al., 2007). The Pe component is usually linked to the awareness of the error commission because its amplitude was larger in case of consciously perceived error than in the

undetected error condition (Davies et al., 2001; Nieuwenhius et al., 2001; Mathalon et al., 2003; Dhar et al., 2011). The main neural sources of the Pe component were localized in the ACC and parietal cortices (van Veen and Carter, 2002), while an intracerebral recording study suggested also the participation of the orbitofrontal cortex and the mesio-temporal regions (Bràzdil et al., 2002). Further, recent evidences revealed an insular source of the Pe component, suggesting the involvement of this brain area in a more general process of error detection that includes both the conscious perception of response errors (Klein et al., 2007; Ullsperger et al., 2010; Dhar et al., 2011) and the detection of a failure in inhibition (Ramautar et al., 2006).

The main literature in this field typically investigated the processes related to the error detection stage, that is, the brain activities immediately following the fallacious response; consequently, the brain activity prior to the execution of the erroneous action has never been described. Thus, the fundamental question about what went wrong before we commit error is lacking. The main goal of the present study is to answer this question. To this aim, we used a Go/No-Go task, testing the hypothesis that the false alarms (FA; i.e. responses to No-go stimuli) could be associated to processing deficits taking place at one or multiple stages before response emission. We considered both the cognitive and premotor anticipatory processing in the pre-stimulus activities, and the post-stimulus stages such as perceptual processing, inhibitory- or conflict-related activities and stimulus-response mapping. Differently from previous studies, which used response-locked ERPs, we used a stimulus-locked ERPs with a large time window including both pre- and post- stimulus response activities. In previous works (Berchicci et al., 2014; Di Russo et al., 2013b; Perri et al., 2014, 2015) we demonstrated that this method allows to investigate the typical post-stimulus ERPs (related to sensory, motor and cognitive processing) without masking the motor preparation and cognitive anticipation processes.

At pre-stimulus level, we might expect error-related modulations at one or multiple anticipatory activities. Specifically, three pre-stimulus processing should be considered. First, an increased negative activity on the right frontal electrodes could reflect an increased baseline of the accuracy decision system (Perri et al., 2014); this should restrict the possibility to accumulate enough sensorial evidences to

reach the decision (Reddi and Carpenter, 2000; Usher and McClelland, 2001; Simen et al., 2006; Bogacz et al., 2010). Second, the FA could be caused by lapses of attention: this would be associated to a reduced PFC top-down control (e.g. Weissman et al., 2006), reflected by a reduction of the prefrontal negativity (pN) component over the frontopolar derivations (Perri et al., 2015). Third, the FA could be the outcome of a defective processing in the motor unit during the motor preparation phase; this latter is mainly processed by the SMA activity, as electrophysiologically reflected by the Bereitschaftspotential (BP; Deecke and Kornhuber 1978; Shibasaki and Hallett, 2006). An amplitude increase of this component could reflect a greater baseline level in the speed system (Perri et al., 2014), accounting for fast but inaccurate performance (Bogacz et al., 2010).

As regard the earliest stage of the post-stimulus phase, i.e. the sensory processing, we considered the visual P1 and N1 components. The P1 reflects task accuracy, since it makes possible to discriminate accurate performers (Perri et al., 2014), while the N1 component mainly reflects the orienting of attention to task-relevant stimuli (Luck et al., 1990; Vogel and Luck, 2000); thus, we may expect error-related modulations at these levels.

Finally, we evaluated two other post-stimulus components preceding the response emission: the well-know N2 component, usually peaking at 250-300 ms after the stimulus, and the recently described prefrontal positivity (pP) peaking about 300 ms after stimulus onset (Berchicci et al., 2014; Di Russo et al, 2013 a,b; Lucci et al., 2013; Perri et al., 2014). In the context of a Go/No-go task, the fronto-central N2 was mainly related to the inhibitory processing because it is usually enhanced when motor responses are correctly inhibited, such as in the case of No-go trials (e.g., Van Boxtel et al., 2001). However, the functional role of this component is still an open question. According to the inhibitory control theory (Bokura et al., 2001; Van Boxtel et al., 2001; Schmajuk et al., 2006), the N2 reflects the inhibitory control to No-go trials; thus, since FA represent instances of failed inhibition, the amplitude of N2 in case of FA is expected to be smaller than that recorded in correctly inhibited No-go trials, and comparable to the Go condition. On the other hand, according to the conflict monitoring theory (Nieuwenhuis et al., 2003; Donkers and van Boxtel, 2004), the enhancement of the N2 component should be linked

to the high conflict level: this latter would mainly increase as effect of the low frequency stimuli, independently of their category (Botvinick et al., 2001). According to this view, the present task should induce a low conflict level, because Go and No-go stimuli had equal probability of occurrence. As consequence, we should not expect differences between the N2 amplitude of Go and No-go trials. In case of FA, literature on the N2 is currently lacking, because the typically adopted motor-locked segmentations mask the pre-response activities such as the N2.

The pP component is a positive wave peaking on the frontopolar derivations, and previously localized in the anterior Insula (aIns; Di Russo et al., 2013b). We showed that the pP amplitude is larger in the Go than No-go trials, suggesting that it reflects the stimulus-response (S-R) mapping process finalized to response execution (Di Russo et al., 2013b; Berchicci et al., 2014; Perri et al., 2014). As also suggested by Boettiger and D'Esposito (2005), the function of aIns would be to trigger the motor response when enough action-related information are accumulated. Based on these latter suggestions we hypothesized that error-related activity could be detected also at this stage of processing, as probably reflected by a different pP amplitude of FA when compared to the other conditions. It is noteworthy that a frontal positive wave in the pP interval was also described by Makeig et al. (1999) that labeled it as P3f. Shortly after, Bruin et al. (2001) challenged the traditional view of the N2 suspecting that response activation (instead of response inhibition) processes might take place immediately before the response emission. Finally, in the same year when our group firstly described the pP (Di Russo et al., 2013a,b; Lucci et al., 2013), Gajewski and Falkenstein (2013) reached similar conclusions reporting the so-called Go-P2 that can be assimilated to the present pP.

An additional goal of this study was to contribute to the knowledge about the neural sources of the post-error potentials, i.e., the Ne and Pe components. To this aim we used the Standardized Low Resolution Electromagnetic Tomography (sLORETA) method, which does not assume a priori generators.

Furthermore, a common issue in studying the error-related brain activity is represented by the low number of erroneous trials available, leading to a small signal to noise ratio. In the present study we tried to

overcome this limit by selecting subjects from a large database and focusing only on participants who made a relevant number of errors.

4.2. Material and methods

4.2.1. Subjects

From a large database of 136 subjects who participated in the Go/No-go task (described below), we firstly excluded subjects who did not report FA, i.e. responses to No-go stimuli. Then, we processed the electroencephalographic (EEG) data of the remaining subjects (n=127), selecting only the subjects with at least 20 artifact-free trials of FA. Following this procedure, 36 subjects were selected for further analyses (6 females; age mean=38.9, SD=11.3).

The participants had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders; all of the subjects were right-handed (Edinburgh handedness inventory; Oldfield, 1971). After procedures were explained, all of the participants provided written informed consent, approved by the local Ethical Committee.

4.2.2. Procedure and Task

Subjects were tested in a sound attenuated, dimly lit room; they were comfortably seated in front of a computer screen at a distance of 114 cm. A board was fixed on the armchair in order to allow participants to push with the right index finger the button panel positioned on it. Four visual stimuli (i.e. four squared configurations made by vertical and horizontal bars) were randomly presented for 260 ms with equal probability (p=0.25). Two stimuli were defined as targets (Go stimuli, p=0.5), the other two were defined as non-targets (No-go stimuli, p=0.5). The stimulus-onset asynchrony varied from 1 to 2 s to avoid overlapping ERPs activities and to limit time prediction effects on the RTs. The entire experiment consisted of 8 blocks, each of one contained 100 trials and lasted 2.5 min with a rest period in between: the total duration was about 30 min, depending on the subjective pauses time. A total of 800 trials were delivered in the experiment: 400 for both Go and No-go condition. All of the participants were asked to be very accurate in the stimuli discrimination and to press a button as fast as possible with the right

hand when a target appeared (Go stimuli) and withhold the response when a non-target appeared (No-Go stimuli) on the monitor. In other words, speed and accuracy performances were equally emphasized in the task instructions.

4.2.3. Electrophysiological recording and data analysis

The EEG signal was recorded using BrainVisionTM system and analyzed by means of the Brain Vision Analyzer 2.0 software (BrainProducts GmbH, Munich, Germany). We employed 64 electrodes were referenced to the left mastoid. Horizontal electrooculogram (HEOG) was recorded using bipolar montage electrodes at the right external canthi; vertical EOG (VEOG) was also recorded using bipolar montage electrodes below the left eye and Fp1. Electrode impedances were kept below 5KΩ. The EEG was digitized at 250 Hz, amplified (band-pass of 0.01-80 Hz including a 50 Hz notch filter) and stored for offline averaging. Artifact rejection was performed prior to signal averaging to discard epochs contaminated by blinks, eye movements or other signals exceeding the amplitude threshold of ±120 μV. In order to investigate both the pre- and the post-stimulus activities, the artifact-free signals were separately segmented into three conditions, i.e. Go, No-go and FA, and then averaged in 2000 ms epochs: from 1100 ms before to 900 ms after the stimulus onset (corresponding to zero). The baseline was defined as the mean voltage during the initial 200 ms of the averaged epochs (from -1100 to -900 ms). To further reduce high frequency noise, the averaged signals were low pass filtered (i.e. Butterworth) at 25 Hz (slope 24 dB/octave).

Statistical differences in the pre-stimulus mean amplitudes were initially assessed with the Brain Vision Analyzer 2.0 sample-by-sample t-test in all electrodes in order to select the locations and the time windows where the differences were consistently significant. The comparisons were repeated for the three conditions; since this preliminary test did not reveal significant differences, no further analyses were performed on the pre-stimulus EEG activity. The remaining analyses were conducted using Statsoft Statistica version 10 (Statistica for Windows, StatSoft, Inc., Tulsa, OH, USA). Specifically, the post-stimulus ERPs detectable in all conditions were measured as follows: the P1 on PO8, the N1 on PO7 and the N2 on Cz. The relevant sites were identified on the basis of both the grand-average visual

detection of the maximal peak electrodes and the indications emerged by previous studies using the same task of the present one (e.g. Perri et al., 2014). The peak amplitude and latency of these components were submitted to ANOVAs with the three Conditions (Go, FA and No-go) as repeated measures. On the other hand, the activity of the pP, P3, Ne and Pe components was calculated as the mean amplitude of the 40 ms surrounding the grand-average peak latency (from 20 ms before to 20 ms after the peak). These ERP activities were calculated in the following time-windows and electrodes: the pP in the 290-330 ms interval on Fp1 and Fp2; the P3 and the Ne 460-500 ms interval on Cz; the Pe in the 680-720 ms interval on Pz. ANOVA with Condition as repeated measure was performed on the mean amplitude of the P3, Ne and Pe components, while the pP activity was submitted to a 2x3 ANOVA with Site (Fp1 vs. Fp2) and Condition as repeated measures. Post-hoc comparisons were conducted using Fisher's least significant difference (LSD) test. The overall alpha level was fixed at 0.05.

4.2.4. sLORETA analysis

We used the Standardized Low Resolution Electromagnetic Tomography (sLORETA) to determine the brain sources of the Ne and Pe components. sLORETA is a functional imaging method based on certain electrophysiological and neuroanatomical constraints (Pascual-Marqui et al., 2002). The cortex has been modeled as a collection of volume elements (voxels) in the digitized Montreal Neurological Institute (MNI) coordinates corrected to the Talairach coordinates. The sLORETA algorithm solves the inverse problem by assuming related orientations and strengths of neighboring neuronal sources (represented by adjacent voxels) and, accordingly, it computes the ''smoothest'' of all possible activity distributions (i.e. no a priori assumption is made on the number and locations of the sources). sLORETA estimates the 3-dimensional intracerebral current density distribution in 6239 voxels (5 mm resolution). The previous version of sLORETA (LORETA, Pascual-Marqui et al., 1994) has received considerable validation from studies combining LORETA with other localization methods as fMRI (Vitacco et al., 2002; Mulert et al., 2004), structural MRI (Worrell et al., 2000) and Positron Emission Tomography (PET, Pizzagalli et al., 2004). These results serve also as validation for sLORETA, since it is an improved version of the original

LORETA method; it is useful to note that deep structures such as the ACC (Pizzagalli et al., 2004) and mesial temporal lobes (Zumsteg et al., 2006) can be correctly localized with this method. In order to identify the brain areas activated by error commission, the EEG activity of the erroneous trials was compared with that of the correct inhibition, making possible to compare brain activities associated to different performance after the same set of stimuli (i.e. No-go). Nonparametric statistical analyses of sLORETA (Statistical non-Parametric Mapping, SnPM) were performed for the Ne and Pe in the respective time windows employing a log-F-ratio statistic for paired groups, with 5000 random permutations (i.e., bootstrapping) and levels of significance ($p<0.05$) corrected for multiple comparisons and false positives. By this method, the SnPM bypasses the assumption of Gaussianity and reaches the highest possible statistical power (Nichols and Holmes, 2002).

4.3. Results

4.3.1. Behavioural data

The mean percentage of FA in the selected group was 11.1% (SD=6.2). For each subject, the median response times (RT) were calculated for both FA and correct-Hits (i.e., Go trials). Statistical analyses on RT data showed that FA-RT (mean=396, SD=65.4) were significantly faster than correct Go-RT (mean=435, SD=67.1) ($t=-2.52$, $df=70$, $p=0.01$).

4.3.2. ERP data

4.3.2.1. Pre-stimulus components

Figure 4.1 illustrates the ERP waveforms at the Fp2 and Cz sites as electrodes of maximum amplitude for the prefrontal and premotor activities, respectively. The earliest anticipatory activity, i.e., the pN component, started to raise 800 ms before the stimulus onset, reaching its maximum approximately at -500 ms on Fp2. The motor preparation, represented by the BP component, initiated at 700 ms before the stimulus onset, reaching its maximum at about -400 ms on Cz. No statistical differences were detected between the three conditions in the pre-stimulus period (all $ps>0.05$).

4.3.2.2. Post-stimulus components

In Figure 4.1 the post-stimulus components could be also detected. The visual P1 and N1 emerged on the parieto-occipital regions (see PO7), without showing differences between conditions, neither in amplitude nor in latency (all ps>0.05).

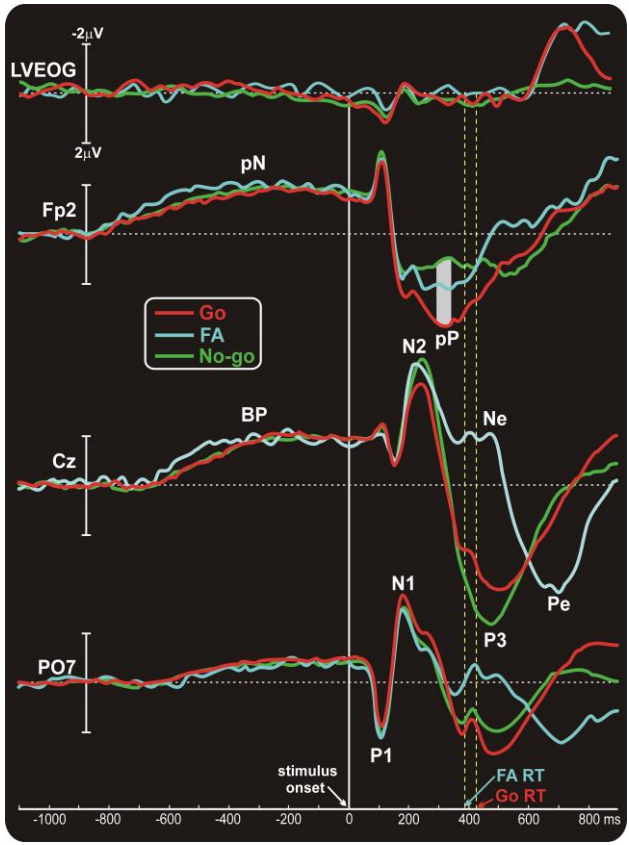

Fig. 4.1. Grand average waveforms in the prefrontal (Fp2), central (Cz) and parieto-occipital (PO7) scalp sites; time 0 corresponds to the stimulus onset. The three task conditions are represented by different colors (labeled in legend). Left vertical EOG (VEOG) is also displayed.

The waveforms on the top of Figure 4.1 show the pP components, starting at about 150 ms on the frontopolar derivations and peaked at 310 ms, corresponding to 100-150 ms before the motor response. The pP showed the largest amplitude for Go condition (3.50 μV), the

smallest for No-go (0.95 μV), whereas it reached an intermediate value in the case of FA trials (1.99 μV).

Figure 4.2 shows the surface electrical distribution of the pP, revealing a bilateral pronounced activity on the prefrontal derivations. ANOVA did not show a significant effect of Site, while the Condition effect was significant ($F_{2,70}=17.5$, $p<0.0001$) revealing that the pP in FA condition was larger than No-go condition ($p<0.001$) and smaller than Go condition ($p=0.01$); the Go pP was also significantly larger than No-go pP ($p<0.0001$).

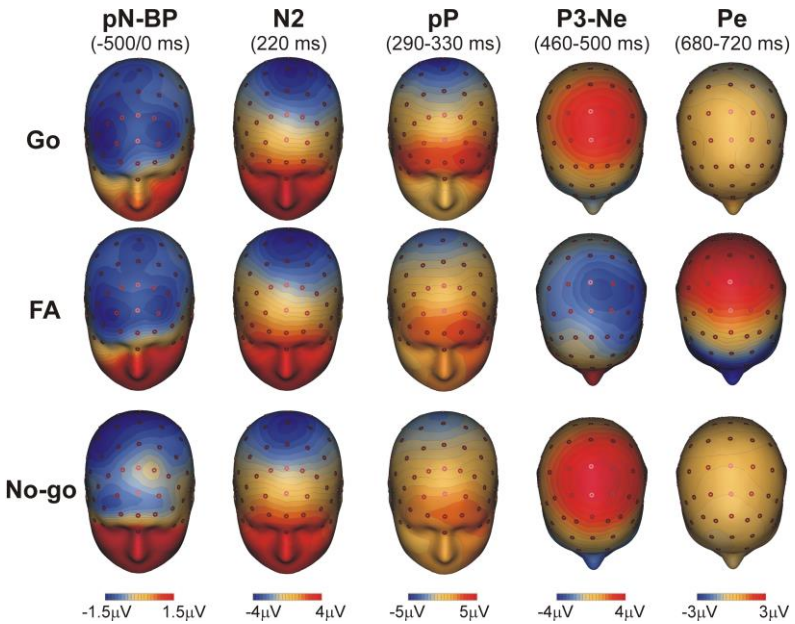

Fig. 4.2. Scalp topographies of the main ERP components in the three task conditions. pN: prefrontal negativity; BP: Bereitschaftspotential; Ne: error-negativity; Pe: error positivity.

In Figure 4.1, the N2 component is showed on Cz site; this component peaked at 240 ms in the three experimental conditions and no differences emerged with respect to their latency ($p>0.05$). Statistical analysis on the N2 amplitude showed a significant effect of Condition ($F_{2,70}=4.99$, $p<0.01$); post-hoc analysis revealed that the amplitude in FA condition (-7.80 μV) was larger than Go condition (-6.20 μV) ($p<0.01$); in contrast, there was no difference between FA and

No-go (-7.00 μV), as well as between Go and No-go conditions. Figure 4.1 (at Cz site) and Figure 4.3 a) show the P3 component peaking in the Go (4.10 μV) and No-go (5.50 μV) condition at about 480 ms; in Figure 4.3 c) the same component is also showed on Pz. Statistical analysis on the P3 and Ne time window (i.e. 460-500 ms) showed a significant effect of Condition ($F_{2,70}=37.1$, $p<0.0001$), indicating a reduced activity in the FA condition with respect to the Go and No-go conditions (both $ps<0.0001$). Figure inspection strongly suggests that this reduction was due to the negative Ne potential (-2.00 μV) emerging at the same latency. No difference emerged between Go (4.10 μV) and No-go (5.50 μV) conditions ($p>0.05$). Finally, at 700 ms after the stimulus onset (i.e., at about 300 ms after the motor response), the late error-related Pe was evident on Pz site in case of FA (see Fig. 3c). Inspection of the figure shows that the typical P3 component was not present in FA trials, even if the Pe was similar in topography, as evident in the maps of Figure 4.2. ANOVA on the Pe revealed a significant effect of Condition ($F_{2,70}=27.3$, $p<0.0001$), indicating a larger amplitude in the FA (3.90 μV) than in the Go (0.30 μV) and No-go (0.00 μV) (all $ps<0.0001$).

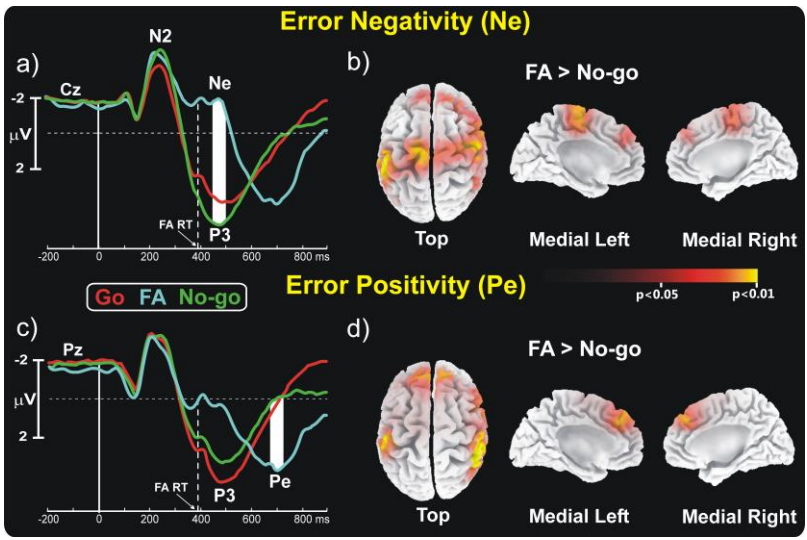

Fig. 4.3. a) Grand-average waveforms in the Cz site showing the time-course of the Ne. b) Cortical representation of the Ne neural sources. c) Grand-average waveforms in the Pz site showing the time-course of the Pe. d) Cortical representation of the Pe neural sources. The waveforms of the three task conditions are superimposed with different colors and restricted to the post-stimulus period.

Since ERPs from frontopolar electrodes were analyzed, EOG tracks were also considered to ensure that prefrontal activity was not driven by any kind of ocular artifacts. The EOG analysis showed that there was no residual ocular activity after artifact correction up to 200 ms after the response emission. Vertical EOG (LVEOG) in Figure 4.1 shows small activity peaking 700 ms after the stimulus in the Go and FA trials, but nothing for the No-go condition. This late ocular activity seems not to affect the electrical signal in prefrontal sites.

4.3.3. sLORETA analyses

Table 4.1 and 4.2 list the brain regions and the relative Talairach coordinates and Brodmann areas (BA) where the log-F-ratio achieved statistical significance in the Ne- and Pe-time range, respectively. Figure 4.3 b,d show the cortical localization of the regions more active in the FA than No-go condition, separately for the two error-related components.

Anatomical region	Brodmann areas	Hemisphere	Talairach coordinates			Log-F-ratio
			x	y	z	
Inferior Frontal Gyrus	6, 9, 45	R	45	6	32	2.01*
Medial Frontal Gyrus	6	L	-10	-11	65	2.07**
Middle Frontal Gyrus	6	L	-15	-7	60	2.08**
	6, 9	R	35	-7	46	2.13**
Superior Frontal Gyrus	6	L	-15	-6	65	2.08**
	8, 6	R	25	41	39	1.93*
Precentral Gyrus	6, 4	L	-10	-16	65	2.04**
	6, 4, 9	R	40	-7	46	2.14**
Postcentral Gyrus	1, 2, 3, 40	L	-50	-22	52	2.18**
	3, 1	R	50	-12	51	2.07**
Sub-Gyral	6	L	-20	-7	56	1.96*
	6	R	35	-3	42	2.11**
Cingulate Gyrus	24	L	-15	-7	46	1.87*
Middle Temporal Gyrus	21	L	-64	-29	1	2.13**
Superior Temporal Gyrus	22, 42	L	-64	-24	1	2.13**
Inferior Parietal Lobule	40	L	-54	-36	48	2.15**
Paracentral Lobule	31	L	-10	-12	47	1.87*

Tab. 4.1. Brain regions more strongly activated in FA vs. No-go condition in the Ne-time range. Talairach coordinates and Log-F-ratio values are referred to the peak activity in each brain region. L= left, R= right; *p<0.05 **p<0.01.

The analyses revealed that the Ne and the Pe components presented both similar and different neural generators. The two resulting waves originated by a network of frontal, temporal and parietal regions including the Middle Frontal Gyrus (BA 6/9), Superior

Frontal Gyrus that includes also the pre-SMA (BA 8), Precentral Gyrus, corresponding to the SMA and Primary Motor Cortex (M1) (BA 4/6), Post Central Gyrus (BA 1/2), Inferior Parietal Lobule (BA 40) and Superior Temporal Gyrus (BA 22/43): in BA 22/43 a laterality effect emerged, showing greater activation in the left and right hemisphere for the Ne and Pe, respectively.

Anatomical region	Brodmann areas	Hemisphere	Talairach coordinates			Log-F-ratio
			x	y	z	
Inferior Frontal Gyrus	9, 45, 44	R	50	6	27	3.14**
Medial Frontal Gyrus	8, 6, 9, 32	L	-5	41	39	3.20**
	6, 8	R	5	41	35	3.18**
Middle Frontal Gyrus	8, 9	L	-20	36	40	2.94*
	9, 46	R	50	16	27	3.11**
Superior Frontal Gyrus	8, 9, 6	L	-5	46	44	3.15**
	8	R	15	46	39	3.21**
Precentral Gyrus	4	L	-45	-12	47	2.86*
	6, 4, 44, 46	R	50	1	28	3.11**
Postcentral Gyrus	1, 2, 3, 40	L	-50	-22	52	3.26**
	1, 2, 3, 40	R	50	-31	52	3.50**
Superior Temporal Gyrus	42, 22	R	64	-33	20	2.99*
Cingulate Gyrus	32	L	-10	26	31	2.88*
Anterior Insula	13	R	40	15	13	2.96*
Inferior Parietal Lobule	40	L	-50	-32	43	3.36**
	40, 39, 7	R	50	-41	53	3.88**
Superior Parietal Lobule	7	R	40	-56	49	2.99*
Angular Gyrus	39	R	40	-61	35	2.83*
Supramarginal Gyrus	40	R	64	-47	25	2.82*

Tab. 4.2. Brain regions more strongly activated in FA vs. No-go condition in the Pe-time range. Talairach coordinates and Log-F-ratio values are referred to the peak activity in each brain region. L= left, R= right; *p<0.05 **p<0.01.

The Cingulate Gyrus was also activated by both components, but it should be noted that the Ne was generated by the BA 24, corresponding to the CMA of the dACC (Ullsperger and von Cramon, 2001), while the neural source of the Pe was localized in the rostral region of the ACC (BA 32). The Ne showed also specific generators, such as more extended areas of the BA 6 (i.e. the Sub-Gyral) and the left Middle Temporal Gyrus (BA 21). At the opposite, the Pe was specifically accounted by activation of the right Insula (BA 13) and more diffused areas in the right Posterior Parietal Cortex (PPC), such as the Superior and Inferior Parietal Lobule and the Supramarginal Gyrus (BA 7/39/40).

4.4. Discussion

In the present study we investigated the error commission exploring the brain activities both preceding and following the stimuli onset in a group of Go/No-go performers. At behavioral level we found faster RT in case of erroneous than hit responses, suggesting the view of the FA as a "too fast" action that does not allow the accumulation of enough action-related evidences. However, because the similarity of BP and right frontal activity between conditions, the hypotheses of the FA as a consequence of a pre-stimulus increased baseline in the speed or accuracy systems were not confirmed. At the same time, the error commission cannot be attributed to lapses in attention in the anticipatory phase (i.e., the bilateral pN did not differ between conditions), nor to attentional effects at perceptual level, where the P1 and N1 visuo-attentional components (Luck et al., 1990; Vogel and Luck, 2000) were not modulated as effect of the erroneous response.

4.4.1. The N2: a new perspective

In the present study no N2 differences were found between the failed (FA) and correct inhibition (No-go). At the same time, we did not observe significant differences between inhibited (No-go) and executed (Go) responses (similar to Di Russo et al, 2013b; for similar observation in the auditory domain, see Falkenstein et al., 1995, 1999, 2002). Present findings clearly challenge the inhibitory control theory of N2 (Bokura et al., 2001; Van Boxtel et al., 2001; Schmajuk et al., 2006); moreover, considering the equal probability of Go and No-go stimuli, present results are also not consistent with the conflict monitoring theory of this component (Botvinick et al., 2001; Nieuwenhuis et al., 2003; Donkers and van Boxtel, 2004).

Furthermore, we showed that the N2 for false alarms was larger than hits, and this result does not have an explanation that can be based on the aforementioned N2 literature. However, in a recent study using the same Go/No-go paradigm (Di Russo et al., 2013b), which combined ERP and fMRI measures, we suggested that the modulation of the N2 component results from the summation of negative and positive waveforms originating in prefrontal, premotor and parietal areas overlapping each other in the same time period (200-400 ms after

the stimulus). The N2 was related to the proactive inhibitory control, reflecting thus the activity of the late motor-preparation phase (late BP or NS' component) in premotor areas, and the No-go effect was explained by the concomitant modulation of positive prefrontal activity (pP) in the anterior Insula (Di Russo et al., 2013b). Within this frame, the larger N2 in false alarms than hits could be interpreted as (1) the result of the summation of different surface potentials emerging at the same time (i.e., the P3 and especially the pP component, or the Go-P2 according to Gajewski and Falkenstein (2013) that proposed a similar interpretation) or (2) in terms of an enhanced (negative) activity in the later premotor stage in case of FA. This latter enhancement might reflect a greater baseline level in the speed system that occur at a later stage (i.e., post-stimulus) than that hypothesized on the basis of Perri et al. (2014) study (i.e., at pre-stimulus phase), and would account for fast but inaccurate performance (Bogacz et al., 2010). However, this latter explanation needs more experimental support to be confirmed.

4.4.2. Decision to act: the role of the pP component

Considering the functional role of the processes acting in the preparation-perception-action cycle (Di Russo et al., 2013b; Perri et al., 2014), we conclude that the main neurocognitive mechanism determining the commission of false alarms is represented by the pP component, peaking 310 ms after the stimulus (corresponding to 80 ms before the erroneous response). Compared to Go and No-go conditions, the amplitude of the FA pP was respectively smaller and larger. Since in a previous study (Di Russo et al., 2013b) we identified the anterior Insula (especially the left aIns, contralateral to the responding hand) as the main generator of the electrophysiological pP component, we conclude that the difference between the false alarms and the other conditions reflects different processing at insular level. The key-role of the aIns before error commission was also described by other studies reporting the engagement of this area in tasks involving pre-response conflict and decision uncertainty (Klein et al., 2007; Ullsperger et al., 2010). In the context of discrimination tasks, the activation of the aIns could reflect the S-R mapping processing finalized to the response execution (Boettiger and D'Esposito, 2005; Di Russo et al., 2013b; Berchicci et al., 2014). In other words, the pP

component represents the final stage of the decision-making process before the response emission (Perri et al., 2014). Further, we also proposed that the pP component amplitude reflects the efficiency of the accuracy decision system, because its amplitude was larger in the more accurate performers (Perri et al., 2014).

Overall, it is possible to describe the erroneous response (FA) as the outcome of a mistake at the S-R mapping level; according to this view, the false alarms are risky responses which are emitted before sufficient evidences are accumulated. This is also supported by the RT, consistently faster (of about 40 ms) in the false alarms than hits. An alternative explanation could be that the low quality of the S-R mapping is not the cause of the FA, rather the consequence of a reduced response threshold that might account for the faster RT as predicted by computational models in this field (for a review see Bogacz et al., 2010). However, while we were able to describe the neural activities associated to the baseline level of the individual speed dispositions (Perri et al. 2014), it seems more difficult to derive a hypothetical response threshold modulation with the surface electrophysiology.

4.4.3. Neural sources of the Ne and Pe components

In the FA condition the Ne and Pe components peaked respectively at 480 ms and 700 ms after the stimulus onset (corresponding to 90 ms and 310 ms after the motor response). sLORETA analyses on the Ne and Pe largely replicated previous findings of neuroimaging literature (Braver et al., 2001; Menon et al., 2001; van Veen and Carter, 2002; Garavan et al., 2003; Mathalon et al., 2003; Debener et al., 2005). Specifically, we observed regions in the SMA, dlPFC, ACC, temporal and lateral parietal cortex to be significantly activated in the time-range of both components, suggesting the engagement of a common error-processing network in their generation.

The pre-SMA activation (more diffused in the Ne) was typically associated with greater levels of response conflict rather than error detection per se (Braver et al., 2001; Ullsperger and von Cramon, 2001; Garavan et al., 2003). The ACC and PFC were described as key regions of an error-processing system (see, e.g., Taylor et al., 2007): consistently, we reported error-related activation in those regions, specifically in the middle and superior frontal gyrus, such as in the

ACC. The co-activation of the lateral PFC and ACC could reflect the processing of a conflict detection system (Carter et al., 1998; Gehring and Knight, 2000), in which the PFC maintains online information for the appropriate response and the ACC facilitates the implementation of the selected action (Paus et al., 1993). However, it should be noted that the Ne was accounted by greater activation of the dACC, specifically the CMA (BA 24), while the generator of the Pe was localized in the rACC (BA 32). According to previous evidences (Vogt and Pandya, 1987; Paus et al., 1993; Devinsky et al., 1995; Bush et al., 2000; van Veen and Carter, 2002; Margulies et al., 2007), we suggest that the dorsal division of the ACC is mainly involved in the earlier stage of error processing because of its association with the high-order motor control, while the rostral ACC could reflect the affective reaction to the subsequent error awareness, as revealed by the Pe component (Davies et al., 2001; Nieuwenhius et al., 2001; Mathalon et al., 2003; Dhar et al., 2011). On the other hand, the functional role of the temporal generators in error processing remains unclear, since, to the best of our knowledge, they were reported only by one fMRI (Critchley et al., 2005a) and two intracerebral ERP (Bràdzil et al., 2002, 2005) studies. A possible explanation comes from Bràdzil and colleagues (2002), suggesting that the engagement of these areas in affective processing could reflect the presence of emotional aspects in the error processing. With respect to the Ne, the Pe was further generated by the activation of the right aIns and more diffused areas of the PPC, as well as reported in previous studies (van Veen and Carter, 2002; Ullsperger et al., 2010). Considering the involvement of the PPC in the internal error detection (for a review see Desmurget and Grafton, 2000), we propose that posterior regions process the motor error by detecting the discrepancy between the executed and the expected action, as evoked by the stimulus features. In fact, the sensory signals of different modalities (e.g. visual, auditory, proprioceptive and vestibular), as well as efferent copy signals from motor structures, are integrated in the PPC (Andersen et al., 1997).

As for the enhanced activity of the insular cortex in the Pe component, we may note that it was reported by several fMRI studies (Menon et al., 2001; Ullsperger and von Cramon, 2001; Mathalon et al., 2003; Critchley et al., 2005a,b; Debener et al., 2005; Matthews et al., 2005; Polli et al., 2005; Ramautar et al., 2006; Klein et al., 2007), while

only a recent ERP study (Dhar et al., 2011) was able to localized this area as the Pe generator. However, probably due to a sample smaller than the present one, or to the difficulty to measure the activity of a deep region with the surface EEG, the authors localized the main generator of the Pe in the posterior insula. At the opposite, consistently with neuroimaging literature, present analysis revealed significant activation in the anterior Insula, specifically on the right hemisphere. The key-role of the insular cortex in experimental conditions implying pre-response conflict and response errors was accurately described in the Turkeltaub et al. (2002) meta-analysis. Interestingly, the authors consistently reported a laterality effect of the aIns, showing an association between the left aIns and the pre-response conflict, and between the right aIns and the post-response processing, in line with our previous (Di Russo et al., 2013b) and present findings showing the left and the right aIns to be mainly involved in the pP and Pe generation, respectively. The aIns activation after the FA might reflect the engagement of a "salience network", suggesting the conscious detection of inhibition failure (Ramautar et al., 2006; Klein et al., 2007), such as the recruiting of additional cognitive and physical resources in response to the error (Ullsperger et al., 2010).

4.5. Conclusion

The present study investigated the neural correlates of the error commission by means of high density EEG and a large signal segmentation, also including the pre-motor activities. We also investigated the neural sources of the error-related potentials by means of sLORETA method. Present results largely confirmed the previous findings on the neural generators of Ne and Pe components and, for the first time in the ERP literature, we found that the right aIns was activated in the generation of the electrophysiological Pe.

With respect to the original question "Why do we commit errors?", we found no differences between false alarms and correct (responded or inhibited) trials at pre-stimulus and perceptual level. In contrast, we observed that the false alarms showed a larger N2 when compared to the correct Go trials; because the equiprobability of the stimuli and the lack of differences between No-go N2 and Go N2, the present study challenges the main previous theories on the functional role of this

component (i.e., the inhibitory and the conflict-monitoring account). Otherwise, based on recent evidences, we describe the N2 component in terms of late premotor activity, whose modulation could result from the algebraic summation of the prefrontal and parietal ERPs emerging in the same time range.

Most important, we observed a significant effect on the pP amplitude as a function of error commission; this component emerged about 80 ms before the erroneous response, originating in the anterior Insula. Since the pP activity reflects the S-R mapping finalized to the response execution, we described this mechanism as the main process predicting error commission. Therefore, we can conclude that the processing acting at this stage of the motor preparation might induce subjects to erroneous and hasty responses, constituting the main reason for which we make errors in a perceptual decision-making task.

References

Andersen, R. A., Snyder, L. H., Bradley, D. C., & Xing, J. (1997). Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annual review of neuroscience*, *20*(1), 303-330.

Berchicci, M., Lucci, G., Pesce, C., Spinelli, D., & Di Russo, F. (2012). Prefrontal hyperactivity in older people during motor planning. *Neuroimage*, *62*(3), 1750-1760.

Berchicci, M., Lucci, G., Perri, R. L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. *Frontier in Aging Neuroscience*, 6, 48.

Boettiger, C. A., & D'Esposito, M. (2005). Frontal networks for learning and executing arbitrary stimulus-response associations. *The Journal of neuroscience*, 25(10), 2723-2732.

Bogacz, R., Wagenmakers, E. J., Forstmann, B. U., & Nieuwenhuis, S. (2010). The neural basis of the speed–accuracy tradeoff. *Trends in neurosciences*, 33(1), 10-16.

Bokura, H., Yamaguchi, S., & Kobayashi, S. (2001). Electrophysiological correlates for response inhibition in a Go/NoGo task. *Clinical Neurophysiology*, *112*(12), 2224-2232.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. *Psychological review*, 108(3), 624.

Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L., & Snyder, A. (2001). Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. *Cerebral Cortex*, *11*(9), 825-836.

Brázdil, M., Roman, R., Daniel, P., & Rektor, I. (2005). Intracerebral error-related negativity in a simple go/nogo task. *Journal of Psychophysiology*, *19*(4), 244.

Brázdil, M., Roman, R., Falkenstein, M., Daniel, P., Jurák, P., & Rektor, I. (2002). Error processing–evidence from intracerebral ERP recordings. *Experimental Brain Research*, *146*(4), 460-466.

Bruin, K. J., Wijers, A. A., & Van Staveren, A. S. J. (2001). Response priming in a go/nogo task: do we have to explain the go/nogo N2 effect in terms of response activation instead of inhibition?. *Clinical Neurophysiology*, 112(9), 1660-1671.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in cognitive sciences*, *4*(6), 215-222.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*, *280*(5364), 747-749.

Coles, M. G., Scheffers, M. K., & Holroyd, C. B. (2001). Why is there an ERN/Ne on correct trials? Response representations, stimulus-related components, and the theory of error-processing. *Biological psychology*, *56*(3), 173-189.

Critchley, H. D., Rotshtein, P., Nagai, Y., O'Doherty, J., Mathias, C. J., & Dolan, R. J. (2005b). Activity in the human brain predicting differential heart rate responses to emotional facial expressions. *Neuroimage*, *24*(3), 751-762.

Critchley, H. D., Tang, J., Glaser, D., Butterworth, B., & Dolan, R. J. (2005a). Anterior cingulate activity during error and autonomic response. *Neuroimage*, *27*(4), 885-895.

Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature neuroscience*, *7*(2), 189-195.

Davies, P. L., Segalowitz, S. J., Dywan, J., & Pailing, P. E. (2001). Error-negativity and positivity as they relate to other ERP indices of attentional control and stimulus processing. *Biological Psychology*, *56*(3), 191-206.

Debener, S., Ullsperger, M., Siegel, M., Fiehler, K., Von Cramon, D. Y., & Engel, A. K. (2005). Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring. *The Journal of Neuroscience*, *25*(50), 11730-11737.

Deecke, L., & Kornhuber, H. H. (1978). An electrical sign of participation of the mesial 'supplementary'motor cortex in human voluntary finger movement. *Brain research*, 159(2), 473-476.

Dehaene, S., Posner, M. I., & Tucker, D. M. (1994). Localization of a neural system for error detection and compensation. *Psychological Science*, 5, 303–305.

Desmurget, M., & Grafton, S. (2000). Forward modeling allows feedback control for fast reaching movements. *Trends in cognitive sciences*, *4*(11), 423-431.

Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain*, *118*(1), 279-306.

Dhar, M., Wiersema, J. R., & Pourtois, G. (2011). Cascade of neural events leading from error commission to subsequent awareness revealed using EEG source imaging. *PLoS One*, *6*(5), e19578.

Di Russo, F., Martínez, A., &Hillyard, S. A. (2003). Source analysis of event-related cortical activity during visuo-spatial attention. *Cerebral Cortex*, 13(5), 486-499.

Di Russo, F., Pitzalis, S., Aprile, T., & Spinelli, D. (2005). Effect of practice on brain activity: an investigation in top-level rifle shooters. *Medicine and science in sports and exercise*, 37(9), 1586.

Di Russo, F., Taddei, F., Aprile, T., & Spinelli, D. (2006). Neural correlates of fast stimulus discrimination and response selection in top-level fencers. *Neuroscience Letters*, 408(2), 113-118.

Di Russo, F., & Spinelli, D. (2010). Sport is not always healthy: Executive brain dysfunction in professional boxers. *Psychophysiology*, 47(3), 425-434.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013a). A passive exoskeleton can push your life up: Application on multiple sclerosis patients. *PloS one*, 8(10), e77348.

Di Russo, F., Lucci, G., Sulpizio, V., Berchicci, M., Spinelli, D., Pitzalis, S., Galati, G. (2013b). Spatiotemporal mapping of response inhibition in the prefrontal cortex. *Neuropsychological Trends*, 79. ISSN 1970-321X

Donkers, F. C., & van Boxtel, G. J. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. *Brain and cognition*, 56(2), 165-176.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. *Electroencephalography and clinical neurophysiology*, *78*(6), 447-455.

Falkenstein, M., Hohnsbein, J., & Hoormann, J. (1994). Event-related potential correlates of errors in reaction tasks. *Electroencephalography and clinical neurophysiology*. Supplement, 44, 287-296.

Falkenstein, M., Hohnsbein, J., & Hoormann, J. (1996). Differential processing of motor errors. *Recent advances in event-related brain potential research*, 579-585.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (1999). ERP components in Go/Nogo tasks and their relation to inhibition. *Acta psychologica*, *101*(2), 267-291.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (2002). Inhibition-related ERP components: Variation with modality, age, and time-on-task. *Journal of Psychophysiology*, *16*(3), 167.

Falkenstein, M., Koshlykova, N. A., Kiroj, V. N., Hoormann, J., & Hohnsbein, J. (1995). Late ERP components in visual and auditory Go/Nogo tasks.

Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, *96*(1), 36-43.

Gajewski, P. D., & Falkenstein, M. (2013). Effects of task complexity on ERP components in Go/Nogo tasks. *International Journal of Psychophysiology*, *87*(3), 273-278.

Garavan, H., Ross, T. J., Kaufman, J., & Stein, E. A. (2003). A midline dissociation between error-processing and response-conflict monitoring. *Neuroimage*, *20*(2), 1132-1139.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal–cingulate interactions in action monitoring. *Nature neuroscience*, *3*(5), 516-520.

Gehring, W. J., Goss, B., Coles, M. G., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological science*, *4*(6), 385-390.

Hester, R., Fassbender, C., & Garavan, H. (2004). Individual differences in error processing: a review and reanalysis of three event-related fMRI studies using the GO/NOGO task. *Cerebral Cortex*, *14*(9), 986-994.

Holroyd, C. B., Dien, J., & Coles, M. G. (1998). Error-related scalp potentials elicited by hand and foot movements: evidence for an output-independent error-processing system in humans. *Neuroscience letters*, *242*(2), 65-68.

Klein, T. A., Endrass, T., Kathmann, N., Neumann, J., Von Cramon, D. Y., & Ullsperger, M. (2007). Neural correlates of error awareness. *Neuroimage*, *34*(4), 1774-1781.

Leuthold, H., & Sommer, W. (1999). ERP correlates of error processing in spatial SR compatibility tasks. *Clinical Neurophysiology*, *110*(2), 342-357.

Lucci, G., Berchicci, M., Spinelli, D., Taddei, F., & Di Russo, F. (2013). The effects of aging on conflict detection. *PloS one*, 8(2), e56566.

Luck, S. J., Heinze, H. J., Mangun, G. R., &Hillyard, S. A. (1990). Visual event-related potentials index focused attention within bilateral stimulus arrays. II. Functional dissociation of P1 and N1 components. *Electroencephalography and clinical Neurophysiology*, *75*(6), 528-542.

Luu, P., Flaisch, T., & Tucker, D.M. (2000). Medial frontal cortex in action monitoring. *The Journal of Neuroscience*, 20, 464–469.

Maier, M., Steinhauser, M., & Hübner, R. (2008). Is the error-related negativity amplitude related to error detectability? Evidence from effects of different error types. *Journal of Cognitive Neuroscience*, *20*(12), 2263-2273.

Makeig, S., Westerfield, M., Jung, T. P., Covington, J., Townsend, J., Sejnowski, T. J., & Courchesne, E. (1999). Functionally independent components of the late positive event-related potential during visual spatial attention. *The journal of neuroscience*, 19(7), 2665-2680.

Margulies, D. S., Kelly, A. M., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *Neuroimage*, *37*(2), 579-588.

Mathalon, D. H., Whitfield, S. L., & Ford, J. M. (2003). Anatomy of an error: ERP and fMRI. *Biological psychology*, *64*(1), 119-141.

Matthews, S. C., Simmons, A. N., Arce, E., & Paulus, M. P. (2005). Dissociation of inhibition from error processing using a parametric inhibitory task during functional magnetic resonance imaging. *Neuroreport*, *16*(7), 755-760.

Menon, V., Adleman, N. E., White, C. D., Glover, G. H., & Reiss, A. L. (2001). Error-related brain activation during a Go/NoGo response inhibition task. *Human brain mapping*, *12*(3), 131-143.

Miltner, W.H.R., Lemke, U., Holroyd, C., Scheffers, M.K., & Coles, M.G.H. (1998). Where does the brain process errors? On the neural generators of the ERN. *Psychophysiology*, 35, 7.

Mulert, C., Jäger, L., Schmitt, R., Bussfeld, P., Pogarell, O., Möller, H. J., ... & Hegerl, U. (2004). Integration of fMRI and simultaneous EEG: towards a comprehensive understanding of localization and time-course of brain activity in target detection. *Neuroimage*, *22*(1), 83-94.

Nichols, T. E., & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Human brain mapping*, 15(1), 1-25.

Nieuwenhuis, S., Ridderinkhof, K. R., Blom, J., Band, G. P., & Kok, A. (2001). Error-related brain potentials are differentially related to awareness of response errors: Evidence from an antisaccade task. *Psychophysiology*, *38*(5), 752-760.

Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., &Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. *Cognitive, Affective, & Behavioral Neuroscience*, 3(1), 17-26.

Niki, H., & Watanabe, M. (1979). Prefrontal and cingulate unit activity during timing behavior in the monkey. *Brain research*, *171*(2), 213-224.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 104, 199-206.

Pascual-Marqui, R. D., Michel, C. M., & Lehmann, D. (1994). Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *International Journal of psychophysiology*, *18*(1), 49-65.

Paus, T., Petrides, M., Evans, A. C., & Meyer, E. (1993). Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. *Journal of neurophysiology*,*70*(2), 453-469 in Brázdil, M., Roman, R., Daniel, P., & Rektor, I. (2005). Intracerebral error-related negativity in a simple go/nogo task. *Journal of Psychophysiology*, *19*(4), 244.

Perri, R.L., Berchicci, M, Spinelli, D. & Di Russo, F. (2014). Individual Differences in Response Speed and Accuracy are Associated to Specific Brain Activities of two Interacting Systems. *Frontiers in behavioral Neuroscience*, 8, 251.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015). The Premotor Role of the Prefrontal Cortex in Response Consistency. *Neuropsychology*. In press

Pizzagalli, D. A., Oakes, T. R., Fox, A. S., Chung, M. K., Larson, C. L., Abercrombie, H. C., ... & Davidson, R. J. (2004). Functional but not structural subgenual prefrontal cortex abnormalities in melancholia. *Molecular psychiatry*, *9*(4), 393-405.

Polli, F. E., Barton, J. J., Cain, M. S., Thakkar, K. N., Rauch, S. L., & Manoach, D. S. (2005). Rostral and dorsal anterior cingulate cortex make dissociable contributions during antisaccade error commission. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(43), 15700-15705.

Ramautar, J. R., Slagter, H. A., Kok, A., & Ridderinkhof, K. R. (2006). Probability effects in the stop-signal paradigm: the insula and the significance of failed inhibition. *Brain research*, *1105*(1), 143-154.

Reddi, B. A. J., & Carpenter, R. H. S. (2000). The influence of urgency on decision time. *Nature neuroscience*, 3(8), 827-830.

Schmajuk, M., Liotti, M., Busse, L., & Woldorff, M. G. (2006). Electrophysiological activity underlying inhibitory control processes in normal adults. *Neuropsychologia*, *44*(3), 384-395.

Shibasaki, H., & Hallett, M. (2006). What is the Bereitschaftspotential?. Clinical *Neurophysiology*, 117(11), 2341-2356.

Simen, P., Cohen, J. D., & Holmes, P. (2006). Rapid decision threshold modulation by reward rate in a neural network. *Neural networks*, 19(8), 1013-1026.

Taylor, S. F., Stern, E. R., & Gehring, W. J. (2007). Neural Systems for Error Monitoring Recent Findings and Theoretical Perspectives. *The Neuroscientist*, *13*(2), 160-172.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., & Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage*, *16*(3), 765-780.

Ullsperger, M., & von Cramon, D. Y. (2001). Subprocesses of performance monitoring: a dissociation of error processing and response competition revealed by event-related fMRI and ERPs. *Neuroimage*, *14*(6), 1387-1401.

Ullsperger, M., Harsay, H. A., Wessel, J. R., & Ridderinkhof, K. R. (2010). Conscious perception of errors and its relation to the anterior insula. *Brain Structure and Function*, *214*(5-6), 629-643.

Usher, M., & McClelland, J. L. (2001). The time course of perceptual choice: the leaky, competing accumulator model. *Psychological review*, 108(3), 550.

van Boxtel, G. J., van der Molen, M. W., Jennings, J. R., &Brunia, C. H. (2001). A psychophysiological analysis of inhibitory motor control in the stop-signal paradigm. *Biological Psychology*, 58, 229–262.

Van Veen, V., & Carter, C. S. (2002). The timing of action-monitoring processes in the anterior cingulate cortex. *Journal of cognitive neuroscience*, *14*(4), 593-602.

Vitacco, D., Brandeis, D., Pascual-Marqui, R., & Martin, E. (2002). Correspondence of event-related potential tomography and functional

magnetic resonance imaging during language processing. *Human brain mapping*, *17*(1), 4-12.

Vogel, E. K., & Luck, S. J. (2000). The visual N1 component as an index of a discrimination process. *Psychophysiology*, *37*(02), 190-203.

Vogt, B. A., & Pandya, D. N. (1987). Cingulate cortex of the rhesus monkey: II. Cortical afferents. *Journal of Comparative Neurology*, *262*(2), 271-289.

Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. *Nature neuroscience*, 9(7), 971-978.

Worrell, G. A., Lagerlund, T. D., Sharbrough, F. W., Brinkmann, B. H., Busacker, N. E., Cicora, K. M., & O'Brien, T. J. (2000). Localization of the epileptic focus by low-resolution electromagnetic tomography in patients with a lesion demonstrated by MRI. *Brain topography*, *12*(4), 273-282.

Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: conflict monitoring and the error-related negativity. *Psychological review*, *111*(4), 931.

Zumsteg, D., Friedman, A., Wieser, H. G., & Wennberg, R. A. (2006). Propagation of interictal discharges in temporal lobe epilepsy: correlation of spatiotemporal mapping with intracranial foramen ovale electrode recordings. *Clinical Neurophysiology*, *117*(12), 2615-2626.

5. Fixing errors: how the brain prevents a second error in a decision-making task

Abstract

In cognitive tasks, error commission is usually followed by behavioral performance characterized by post-error slowing (PES) and post-error improvement of accuracy (PIA). Three not mutually exclusive cognitive accounts were hypothesized to support the post-error adjustments: the cognitive, the inhibitory, and the orienting account. The aim of the present ERP study was to investigate the neural processes associated to the second error prevention. To this aim, we focused on the pre-stimulus and pre- movement brain activities in a large sample of subjects performing a visual equiprobable Go/No-go task. The main results were the enhancement of the prefrontal negativity (pN) component -especially on the right hemisphere- and the reduction of the Bereitschaftspotential (BP) -especially on the left hemisphere- in the trials following errors. These results are consistent with the three cognitive accounts of the post-error adjustments. In fact, we observed the increased top-down inhibitory control and the reduced excitability of the premotor areas in the preparatory phase of the trials following the infrequent (i.e., orienting) errors. Further, additional control analyses supported the view that the adjustments-related components (the post-error pN and BP) are separated by the error-related potentials (Ne and Pe), even if all these activities are part of a cascade of cognitive processes triggered by error-commission.

Keywords: ERPs; Bereitschaftspotential (BP); post-error slowing (PES); post-improvement in accuracy (PIA).

5.1. Introduction

The ancient Romans said that "tempus omnia medetur" (i.e., the time remedies everything); however, time is not always unlimited and sometimes it is important to immediately fix an error. Understanding how the brain fixes its own errors is a current challenge for neuroscientists. In healthy people, the error commission in tasks such as Go/No-go or stop signal is usually followed by conscious experience of incorrect response, allowed by a neural system specialized in error detection (see, e.g., Dehaene et al., 2004). This system has been largely investigated by means of event-related potentials (ERPs; Gehring and Knight, 2000; Herrmann et al., 2004; Chang et al., 2014) studies, showing the error-related negativity (ERN) or error negativity (Ne, peaking at 50-100 ms after the error), and the error positivity (Pe, peaking at 100-200 ms after the error) (Falkenstein et al., 1991; Gehring et al., 1993; Dhar et al., 2011). Also the functional magnetic resonance imaging (fMRI; for a review see Taylor et al., 2007) studies showed the frontal and parietal brain regions activation immediately after error commission. At behavioral level, several post-error adjustments were reported: the most frequently observed are the post-error improvement of accuracy (PIA; e.g., Marco- Pallarés et al., 2008) and the post-error slowing (PES; e.g., Rabbitt, 1966), reflecting increased accuracy and slower response times (RTs) in the post-error trials, respectively. According to the review of Danielmeier and Ullsperger (2011), three accounts may explain the PES. (1) The cognitive control account describes the PES as the result of increased top-down control, as revealed by the relationship between the activity of the medial frontal cortex (MFC) and the behavioral slowing (e.g., Kerns et al., 2004). Some studies also underlined the association between the MFC and the adjustments at level of the response priming unit (Botvinick et al., 2001): in other words, the reduced activity in motor areas would predict the post-error slowing (King et al. 2010; Danielmeier et al., 2011). (2) The inhibitory account states that PES is supported by increased inhibition in trials following the error commission (Ridderinkhof et al., 2002). The inhibition is sustained by the activation of the right PFC (Marco-Pallarés et al., 2008) and plays a central role in motor slowing, because the PFC is part of the proactive inhibitory network of the right hemisphere (e.g., Aron et al., 2007). (3) According

to the orienting account, PES emerges after any kind of infrequent event. In other words, response slowing may occur also after correct responses (i.e., post-correct slowing; Notebaert et al., 2009) if these latter are infrequent. fMRI studies shed light on the neural substrates of the post-error adjustments, especially on the engagement of the PFC and premotor regions in behavioral slowdown (Kerns et al., 2004; Li et al., 2008; King et al., 2010); however, due to the low temporal resolution, this technique does not always allow to distinguish between the error-detection processing and the following adjustment mechanisms (Li et al., 2008). On the other hand, several electroencephalographic (EEG) studies attempted to investigate the PES using approaches based on both frequency and ERP analysis. For example, Cavanagh et al. (2009) reported increased theta oscillation at mid- frontal and lateral frontal sites immediately after the error. Further, they showed a relationship between theta band and behavioral adjustments. However, since theta oscillations reflect the error-detection process (Luu et al., 2004), we can hypothesize that the relationship between theta power and post-error adjustments is not direct, but could be mediated by an additional processing occurring later than that described by Cavanagh (2009). This hypothesis is supported from the inconsistency among ERP results: some studies reported an association between PES and error negativity (Ne, emerging 50-100 ms after error; Gehring et al., 1993; Debener et al., 2005; West and Travers, 2008; Wessel and Ullsperger, 2011), while others found a correlation between PES and error positivity (Pe, emerging 200-300 ms after error; Nieuwenhuis et al., 2001; Hajcak et al., 2003; Chang et al., 2014). These contradictory findings could be partly explained by the results of Marco-Pallarés et al. (2008), who reported an association between the increased frontal-central beta activity at 600-800 ms after the error (i.e., 400 ms after the Pe) and the behavioral slowdown, suggesting that motor inhibition processes (as reflected by beta increase; Alegre et al., 2004) occur after the error and may account for the PES. It is noteworthy that the neurocognitive dissociation between error-detection and adjustment-oriented processes was also supported by a study on cocaine users that showed reduced awareness of errors, but intact performance adjustments (Hester et al., 2007). Summarizing, the ERP studies that investigated the post-error adjustments reported just an association between one of

the two error-related potentials (the Ne and Pe) and the post-error behavior (especially the post-error slowing). However, any decision-making behavior is "prearranged" by preparatory activities that have a direct relationship with the motor response (e.g., Band et al., 2003). Accordingly, our hypothesis is that the error commission yields to neural adjustment mechanisms that regulate the post-error performance much more than the error-detection processes. To the best of our knowledge, this is the first ERP study investigating the post-error neural adjustments, that is the stage of processing that follows the error awareness stage (the Pe component) and precedes the post-error behavior. To this aim, we focused on the preparation processing taking place long before action, considering both cognitive preparation (as indexed by the prefrontal negativity or pN; Perri et al., 2014) and motor preparation activities (as indexed by the Bereitschaftspotential or BP; Shibasaki and Hallett, 2006). Specifically, we compared the preparatory brain activity of trials following errors (hereafter post-error trials) with those following correct responses (hereafter post-correct trials) in a equiprobable Go/No-go task. Even if the 50/50 stimuli ratio produces a quite low number of errors, this choice has the advantage to exclude the participation of confounding factors like the prepotent response tendency and the oddball effect, typical of the error-prone tasks with high frequency of Go trials (Nieuwenhuis et al., 2003; Lavric et al., 2004; Li et al., 2008).

It is noteworthy that the ERP investigation of the post-error adjustment mechanisms would be possible just in case the error-related potentials (Ne and Pe) are not overlapped in time with the preparatory activities of the post-error trials. To verify this prerequisite, we made control analyses (see methods and results sections) confirming that the present paradigm does allow to isolate two sets of consecutive processing (related to the preparation in the current trial, and to the detection of the previous error).

According to the cognitive account of the PES (Kerns et al., 2004), we would expect an increased top-down control in the preparation of the post-error trials, which is associated to increased activity of the frontal-medial regions. At ERP level, the increased top-down control should emerge through bilateral enhancement of the pN component (Berchicci et al., 2014; Perri et al., 2015b). Further, since it was also proposed that the activation of the MPFC predicts the reduced

premotor activity (Danielmeier et al., 2011), we may expect an amplitude reduction of the BP component in the post-error trials. In fact, the BP mainly reflects the activity of the supplementary motor area (SMA; Shibasaki and Hallett, 2006) and its amplitude was associated to the motor baseline modulating the response speed (Band et al., 2003; Perri et al., 2014). According to the inhibitory account (as reviewed by Danielmeier and Ullsperger, 2011), we may expect a selective right-side enhancement of the pN: in fact, this component was localized in the inferior frontal gyrus (iFg; Di Russo et al., 2013b), which plays a key-role in the proactive inhibitory control (Aron et al., 2003, 2004, 2007). Because of the lack of conditions modulating the frequency of errors (or correct responses), the present study is not suited to directly test the orienting account. However, since in our paradigm the errors represent infrequent events, the present results can also be interpreted in terms of orienting adjustments.

Finally, since previous studies found a positive relationship between the amplitude of the N1 and P1 potentials, and the speed and accuracy performance, respectively (Di Russo et al., 2006; Perri et al., 2014), we also investigated whether the post-error behavior might be partly mediated at visual processing level.

5.2. Material and methods

5.2.1. Subjects

From a database of subjects who participated in the Go/No-go task (described below), we firstly excluded those who did not report false alarms (FAs), i.e. responses to No-go stimuli. After, we processed the electroencephalographic (EEG) data of the remaining subjects, and only those with a suitable number of artifact-free trials of FAs were considered for the grand-averages. By this procedure, 36 subjects were selected for the final sample (6 females; mean age =38.9, SD=11.3): the mean percentage of FAs was 11.1%, SD=6.2. The participants had normal or corrected-to- normal vision and no history of neurological or psychiatric disorders; all of the subjects were right-handed (Edinburgh handedness inventory; Oldfield, 1971). After explanations of the procedures, all of the participants provided written informed consent, approved by the Local Ethical Committee.

5.2.2. Procedure and Task

Subjects were tested in a sound attenuated, dimly lit room; they were comfortably seated in front of a computer monitor at a distance of 114 cm, and a board was fixed on the armchair allowing them to freely push the button panel positioned on it. A yellow circle (subtending 0.15°x0.15° visual angle) at the center of the screen was served as fixation point and was always displayed on the screen. The four visual stimuli consisted of squared configurations (subtending 4x4°) made of vertical or horizontal segments, or both of them with different orientation (vertical and horizontal) presented centrally on a dark gray background. Two configurations were defined as targets (Go stimuli), and two were defined as non-targets (No-go stimuli). The four stimuli were randomly presented for 260 ms with equal probability (p=0.25). The stimulus-onset asynchrony varied from 1to 2 sto avoid time prediction effects on the RTs. The entire experiment consisted of 10 blocks, each of which contained 80 trials and lasted 2.5 min with a rest period in between. The total duration was about 30 min, depending on the subjective rest time. A total of 800 trials were delivered in the experiment: 400 for Go and 400 for No-go category.

Participants were asked to be very accurate and to press a button as fast as possible with the right index finger when Go stimuli appeared on the monitor and withhold the response when No-Go stimuli appeared.

5.2.3. Behavioral recording and analysis

We calculated the error percentage in the post-correct and post-error conditions, and the median RT for FAs and hit responses in the pre-error and post- error conditions for each subject. Both speed and accuracy values served for the calculation of PIA and PES. According to what suggested by Dutilh et al. (2012), the PES was calculated as the RT difference between pre-error hits and post-error hits. Statistical analyses on behavioral data were performed by means of t-test.

5.2.4. Electrophysiological recording and analysis

The EEG signal was recorded using BrainVisionTM system with 64 electrodes mounted according to the 10-10 International system. All electrodes were referenced to the left mastoid. Horizontal and vertical

electrooculogram (EOG) were also recorded using electrode at the right external canthi and below the left eye, respectively. Electrode impedances were kept below 5KΩ. The EEG was digitized at 250 Hz, amplified (band-pass of 0.01-80 Hz including a 50 Hz notch filter) and stored for offline averaging. Artifact rejection was performed prior to signal averaging to discard epochs contaminated by blinks, eye movements or other signals exceeding the amplitude threshold of ±120 μV. We considered the stimulus onset as time 0, and each condition was averaged in a 2000 ms epoch (from 1100 ms before to 900 ms after the stimulus). The baseline was defined as the mean voltage during the initial 200 ms of the averaged epochs. To further reduce high frequency noise, the averaged signals were low pass filtered (i.e. Butterworth) at 25 Hz (slope 24 dB/octave). Since we were mainly interested in the preparatory brain activities and we have already demonstrated the lack of ERPs differences between Go and No-go stimuli, specifically in the cognitive and motor preparation phase (i.e., the pN and the BP components) and in the early sensory response (the P1 and the N1 components), the artifact-free signals were separately segmented into two trial conditions as sketched in Figure 5.1: post-correct (i.e., average of Go and No-go following correctly inhibited or responded trials) and post-error (i.e., average of Go and No-go trials following FAs). Because the averaging of Go/No-go trials, only the pN, the BP, the P1 and N1 components were considered for further analysis. At the opposite, the Pp, N2 and P3 components were excluded from analyses because of their sensitivity to Go/No-go categories (e.g. Salisbury et al., 2004; Schmajuk et al., 2006; Perri et al., 2014).

The pre-stimulus mean amplitudes of each condition were initially compared with a sample-by-sample t-test in the prefrontal (Fp1, Fp2) and central (C1, Cz, C2) electrodes previously associated to the pN and BP components: by this method we identified the time windows where the differences were consistently significant. Based on this preliminary analysis, we selected the Fp1 and Fp2 sites in the -600/0 ms time window, and the C1, Cz and C2 sites in the -500/0 ms: the mean amplitude on the selected electrodes was submitted to a repeated measures ANOVA with Site (Fp1, Fp2; C1, Cz, C2) and Condition (post-correct vs. post-error) as factors. The P1 and N1 components were respectively measured on the PO8 and PO7 sites as electrodes of maximum activity; for both components, the peak amplitude and

latency were submitted to repeated measures ANOVA with Conditions (post-correct vs. post-error) as repeated measure. Post-hoc comparisons were conducted using Bonferroni test. The correlation coefficients (Pearson's r coefficients) were performed in the post-error condition between electrophysiological data and RTs of hit responses (no analyses were possible on the RTs and percentage of FAs because of the floor effect of the errors in the post-error condition). The overall alpha level was fixed at 0.05. Note that the relevant comparison in the present study is between post-correct and post-error conditions; thus, statistical analyses considered these two conditions. The waveforms of error trials are presented in the figures only as a control for the possible confounding influence of the error-related activities (see section 3.2.1).

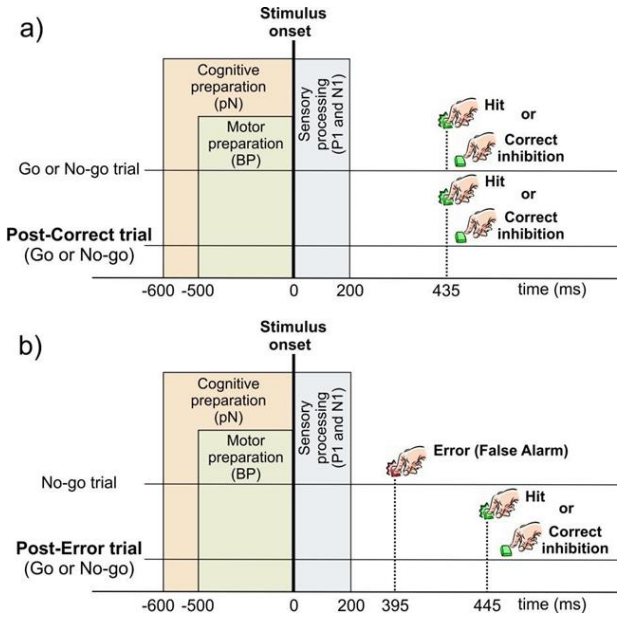

Fig. 5.1. Schematic representations of (a) post-correct and (b) post-error trials. In both a and b, the horizontal lines represent different single trials; the temporal sequence of these trials is from the upper line to the lower line. The rectangular areas represent the main brain processes (insensitive to stimulus category) taking place as a function of time (not scaled). In the preparation phase we investigated both the cognitive and motor preparation (as reflected by the BP and pN components, respectively); in the post-stimulus phase we investigated the visual sensory processing (the P1 and N1 components). The figure also shows the mean RTs for post-correct and post-error trials (hits in a and b), and for false alarms (in b).

5.3. Results

5.3.1. Behavioral performance

Statistical analyses on accuracy performance (Figure 5.2 a) showed that the percentage of FAs decreased significantly from the post-correct (mean=11.1%, SD=6.2) to the post-error (mean= 4.04%, SD=5.36) ($t=5.15$, $p<0.0001$) condition. After making an error, 50% of the subjects did not commit second FAs, while 33% committed a second FA, and 17% more than two at least once. Considering the overall low rate of FAs in the post-error condition (4%), two consecutive errors were present in less than 0.5% of trials following FAs.

Analyses on speed performance (Figure 2b) showed that the post-error RTs (mean=445 ms, SD=82.8) were slower than the pre-error RTs (mean=408 ms, SD=66.2) ($t=-2.1$, $p<0.05$). The FA RTs (mean=395, SD=65) were similar to the pre- error RTs ($t=-0.83$, $p>0.05$), and faster than the post-error RTs ($t=-2.84$, $p<0.01$).

Overall, analyses on behavioral data confirmed that error commission led to a more "conservative" performance characterized by post-error improvement in accuracy (PIA) and post-error slowing (PES).

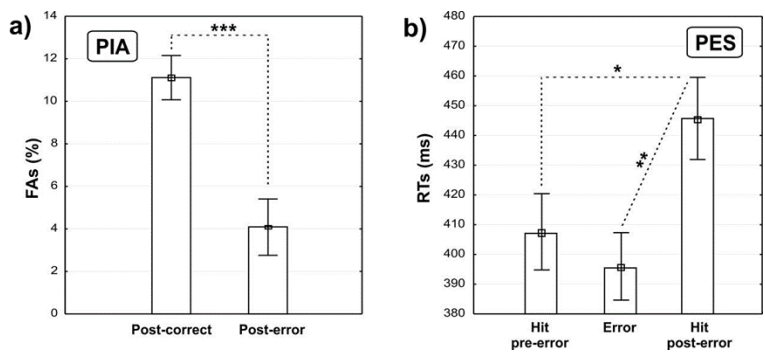

Fig. 5.2. Behavioral data. a) Percentage of false alarms b) Mean response times. PIA: Post-Improvement in Accuracy. PES: Post-Error Slowing; *p<0.05 **p<0.01 ***p<0.001.

5.3.2. Electrophysiological activities

Figure 5.3 shows the stimulus-locked activity for post-error (red lines) and post-correct (green lines) conditions over left and right sites on the prefrontal (Fp1, Fp2), central (C1, C2) and parietal-occipital

(PO7, PO8) areas. The errors waveforms are presented in the figure too (blue lines). To facilitate the visual inspection, the entire signal segmentation is reported in the figure even if, as previously indicated, no analyses were performed on the late ERP components (i.e., the pP, N2 and P3). Before the stimulus onset two main components are well detectable: the slow-rising pN and the BP components reflecting the cognitive and motor preparation at level of the prefrontal and premotor brain areas, respectively. The pN and BP of post-correct trials are comparable to those of the error trials. In contrast, the post-error trials showed specific modulations in the preparatory phase: the pN amplitude was enhanced, especially on the right hemisphere, while the BP was reduced in both hemispheres with a stronger effect on the left side. After the stimulus onset, the last activity (i.e., the Pe) peaks in the error condition at around 700 ms, reaching the baseline value within 900 ms (see C1 and C2). The visual inspection does not suggest significant effects on the P1 and N1 visual components that have similar amplitudes and latencies across conditions.

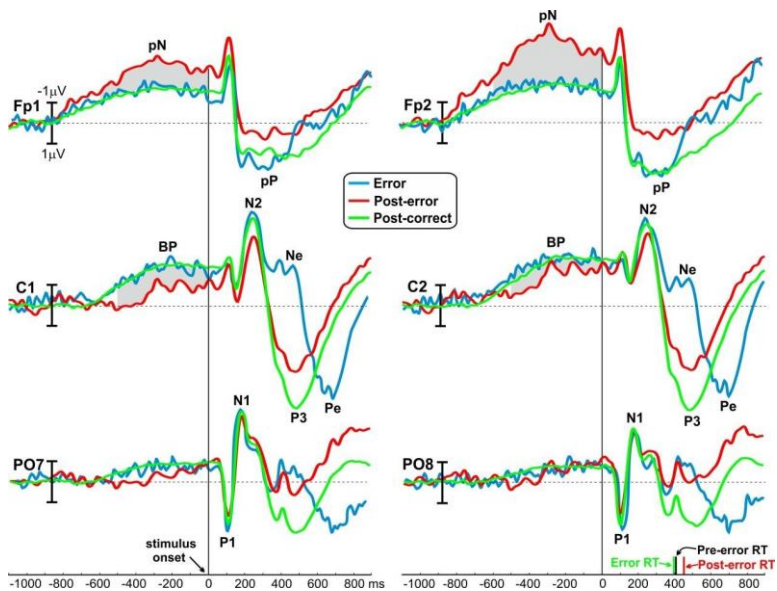

Fig. 5.3. Grand-averaged waveforms of the error, post-error and post-correct trials in bilateral prefrontal (Fp1, Fp2), central (C1, C2) and parieto-occipital (PO7, PO8) sites; time 0 corresponds to the stimulus onset. The gray areas indicate the time windows considered for statistical analyses. The bars on the abscissa line represent the RTs of different trials.

ANOVAs on the pre-stimulus ERP confirmed what suggested by visual inspection of Figure 5.3. The analyses of the pN component showed a significant effect of Condition ($F_{1,35}=9.1$, $p<0.01$), revealing more than 100% amplitude enhancement in the post-error (mean=-3μV, SD=3.4) with respect to the post-correct (mean=- 1.4μV, SD=1) condition; further, the effect of Site was significant ($F_{1,35}=12.4$, $p<0.01$) indicating a larger activity on Fp2 (mean=-2.5 μV, SD=2.9) than Fp1 (mean=-1.9 μV, SD=2.3) site. The interaction between Condition and Site was also significant ($F_{1,35}=5.3$, $p<0.05$). Post-hoc tests revealed that the laterality effect was mainly accounted by the post-error condition; in fact, the Fp2 activity was larger than Fp1 in the post-error ($p<0.001$), and not in the post-correct condition ($p>0.05$), as shown in Figure 5.4 a). Statistical analyses on the BP component also revealed significant effects of Condition ($F_{1,35}=4.3$, $p<0.05$) indicating a 56% amplitude reduction of the post-error condition amplitude (mean=-0.8 μV, SD=3.2) with respect to the post-correct condition amplitude (mean=-1.8μV, SD=1.2), and Site ($F_{2,70}=24$, $p<0.0001$) indicating smaller amplitudes on the left than right side. The interaction between Condition and Site was significant ($F_{2,70}=11.4$, $p<0.0001$). Post-hoc tests indicated that the BP laterality effect was present in the post-error condition only, where the amplitudes of C1 (mean=-0.6μV, SD=3.2) and Cz (mean=-0.51 μV, SD=3.6) were smaller than that of the C2 (mean=-1.4μV, SD=2.9) site ($p<0.0001$ for both comparisons); no laterality effects emerged in the post-correct condition (all ps were ns) as shown in Figure 5.4 b). The topographic distribution of the pre-stimulus brain activities is reported in Figure 5.5, showing the surface voltage distribution of the pN and BP components in the two conditions.

No significant effects emerged from the analyses on the amplitude and latency of the visual P1 and N1 components (all ps were ns).

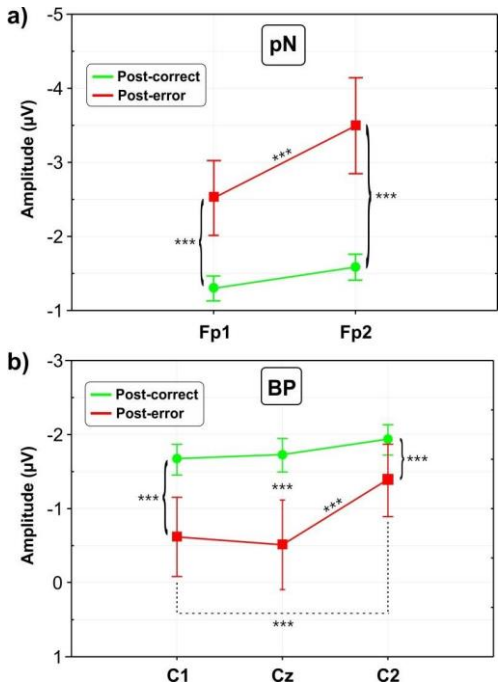

Fig. 5.4. Statistical comparisons of the two conditions (post-correct and post-error) for the (a) prefrontal negativity (pN) and (b) Bereitschaftspotential (BP) components. Vertical bars indicate standard deviations (SD). ***p<0.001.

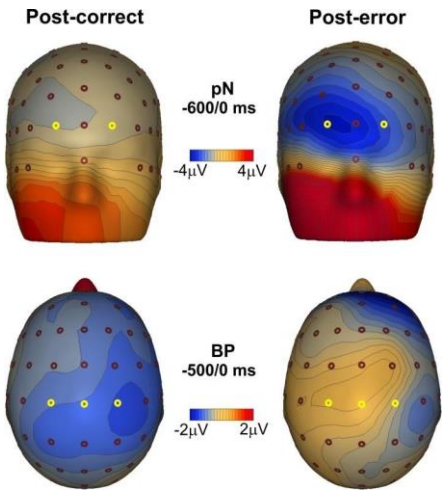

Fig. 5.5. Scalp topographies of the grand-averaged activities for post-correct and post-error conditions associated with the pN (top) and the BP (bottom) components. The yellow circles indicate the EEG sites selected for statistical analyses.

A significant correlation was found between the Go RTs and the BP amplitude in the post-error condition: the slower the RTs (i.e. greater the post-error slowing), the smaller the BP on C1 ($r=0.47$, $p<0.01$), Cz ($r=0.43$,$p<0.01$) and C2 ($r=0.47$, $p<0.01$) sites. In contrast, no significant correlations emerged between RTs and pN amplitudes, neither for Fp1 ($r=0.02$, $p>0.05$) nor for Fp2 ($r=0.07$, $p>0.05$) sites.

Overall, the comparison between post-error and post-correct trials indicates that error commission affects the preparation stage of the subsequent trials (i.e., pN and BP components). Further, these adjustment-oriented processes reflect a genuine adaptive preparatory mechanism and do not result from a confounding influence of the preceding Ne/Pe complex. Additional control analyses on this point are presented below.

5.3.2.1. Additional control analyses

To support the view that the post-error neural adjustments are not confounded with the Ne/Pe complex evoked by the error commission, additional controls are reported in Figure 5.6, where the pN and BP components are shown on Fp2 and Cz sites, respectively.

Figures 5.6 a) and b) show respectively the response- and stimulus-locked grand averages: however, these waveforms are locked to the trials preceding those considered so far (i.e., the error and correct trials instead of the post-error and post- correct trials); further, a larger time window is considered. Note that, since the signal is locked to the error trials, the “next-trial BP” and “next-trial pN” gray areas correspond to the BP and pN activities on the left side of Fig. 3 (and Fig. 6c: see later in this section).

In Fig. 6a the ERPs are response-locked: accordingly, the -1500/-1300 ms interval was taken as baseline. The error-related potentials emerge on Cz for error trials (blue line), and the pN and BP of the next trials are well detectable on the right side of the figure. Despite the different segmentation, the difference between the two conditions shows the same trend as previously reported in the results section, that is larger pN and smaller BP in the post-error trials than in the post-correct trials. The gray areas indicate the mean time-windows selected for the pN and BP analyses as reported in the methods section; the delay between areas depends on the difference between error- and correct-RTs.

Fig. 6b shows the same data of Fig. 6a, but the signal is stimulus-locked and a "traditional" baseline is adopted (100 ms pre-stimulus). Again, the pN and BP components of the next trials show the same difference between conditions as reported in the results section.

The additional evidence of Fig. 6a, b strengthen the findings of the present study; however, one could argue that, given the large ISI variability (from 1000 to 2000 ms; mean 1500 ms, SD 289), the BP and pN components of the next trials were smeared by the 1000 ms time-jitter of the next stimulus. For this reason, possibly the more convincing control is that of Fig. 6c. In this latter stimulus-locked analysis we adopted a larger time window than that of the original approach (see Fig. 3), that is the epoch was expanded until 2000 ms before the onset of the post-error (and post- correct) stimulus. In this way, the onset of the previous stimuli and the corresponding evoked activities were included in the time window. The main result of Figure 5.6 c) is that the waveforms are nearly aligned up to -800 ms: hence, the original baseline of Fig. 5.3 (marked in Figure 5.6 c) by dashed vertical lines) did not alter the difference between post-correct and post-error trials in the pN and BP components, which are the focus of the present study. Moreover, this analysis confirms that the large time-jitter of this paradigm did not allow the Ne and Pe components to emerge in the preparatory phase when ERPs are locked to the post-error stimulus.

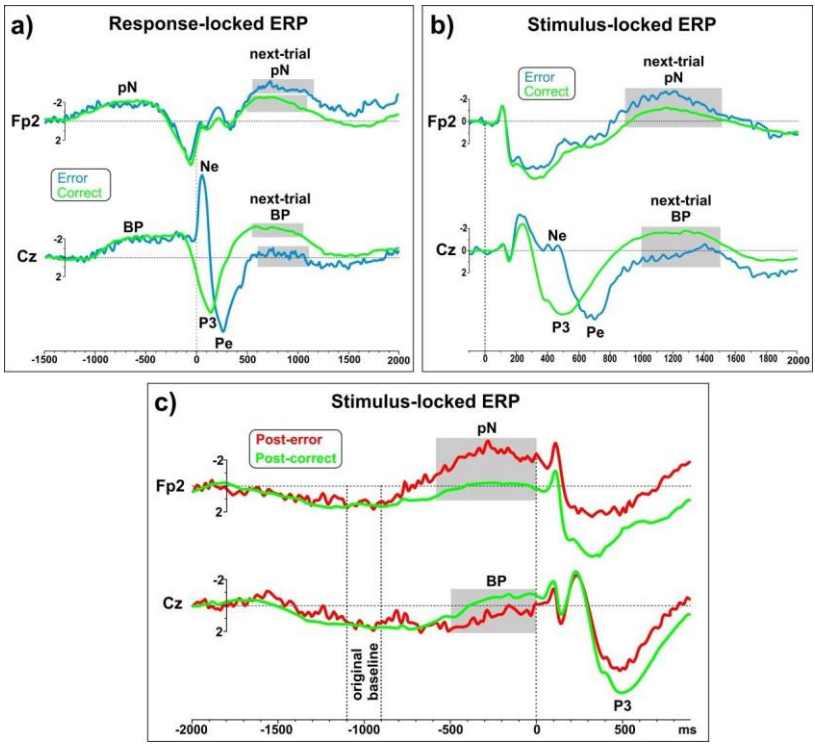

Figure 5.6. a) Response-locked ERPs of error and correct trials. In the error trials, the Ne and Pe potentials peak on Cz largely before the time-window considered for analysis of the next-trial BP. The waveforms on Fp2 are aligned until 300 ms after the motor response. b) Stimulus-locked ERPs of error and correct trials. As in the R- locked segmentation, the error-related activities emerge on Cz site without compromising the modulation of the next-trial BP. The waveforms on Fp2 site are aligned until 800 ms after the stimulus onset. c) Stimulus-locked ERPs of post- correct and post-error trials. The segment starts 2 s before the stimulus onset. The waveforms of the two trials do not differ until -800 ms, as in the original segmentation. The vertical dashed lines indicate the original baseline of Fig. 3.

5.4. Discussion

The present study confirmed previous behavioral findings showing post-error slowing (PES) and post-error improvement in accuracy (PIA) after error commission. In fact, the trials following errors were characterized by more accurate (i.e., most of the subjects did not commit two consecutive errors) and slower (about 50 ms) responses. However, the main novelty of this study concerns the ERP findings, revealing a reduction of the BP component (especially on the

left side) and a bilateral (but more pronounced on the right side) enhancement of the pN component in the post-error trials. These results are consistent with both the cognitive (Kerns et al., 2004) and inhibitory (Ridderinkhof et al., 2002) accounts of the PES. In previous studies that used the same task of the present one (Berchicci et al., 2014; Perri et al., 2015b) the pN enhancement has been associated with increased top-down control; consistently, we interpret the pN increase in the post-error trials as evidence of increased top-down control in the post-error trials. The cognitive account of the PES is also supported by the reduced BP amplitude in the post-error trials, reflecting neural adjustments at premotor level. Based on fMRI (Forstmann et al., 2008; King et al., 2010) and EEG (Band et al., 2003; Rinkenauer et al., 2004) studies, the BP reduction can be discussed in terms of reduced motor baseline, which in turn is responsible for the slower RTs. At neurophysiological level, the SMA activation (corresponding to the BP enhancement) overcomes the tonic inhibition provided by the output nuclei of the thalamus (Lo and Wang, 2006); at the opposite, the SMA hypo-activation (marked by the BP reduction) may be functionally interpreted as a mechanism slowing-down the motor response (Perri et al., 2014). This view is also supported by the significant correlation between the BP amplitude and the RTs: the smaller the BP, the slower the RTs (corresponding to greater PES). Taking into account also the absence of significant correlations between pN amplitude and RTs, we can conclude that the speed performance is mostly determined at SMA level, while the pN component reflects a more indirect, attentional-mediated, task control (Perri et al., 2015b).

It is also interesting to note that the BP reduction was larger over the left hemisphere, further suggesting task-related adjustments for the right responding hand. Conversely, the pN increase was more pronounced on the right hemisphere. This latter laterality effect, together with the observation of the iFg as the source of the pN (Di Russo et al., 2013b), and the role of the right-iFg as inhibitory control area (Aron et al., 2003, 2007; Hampshire et al., 2010), underlines the contribution of the inhibitory processes in the post-error adjustments, as postulated by the inhibitory account (Marco-Pallarés et al., 2008).

Since errors represented infrequent events in our task, current results might also be interpreted in terms of orienting account (Notebaert et al., 2009); in other words, the errors might be considered

as orienting cues (Hampshire et al., 2010) increasing the inhibitory and attentional control and reducing the preparatory activity of the motor areas.

Overall, because of the simultaneous presence of different neurocognitive processes (i.e., top-down, inhibitory and orienting mechanisms), we agree with other authors (Ridderinkhof et al., 2004; Danielmeier and Ullsperger 2011; Danielmeier et al., 2011) in suggesting that different preparatory processes account simultaneously for the post-error adjustments. Consistently, the post-error neural activity was modulated through prefrontal and premotor areas. It is noteworthy that, differently from studies that used error-prone paradigms by modulating the frequency of target stimuli (Li et al., 2008; Dhar et al., 2011), we adopted an equiprobable Go/No-go task. This choice has several advantages, like to maximize the stimuli uncertainty, to minimize the differences in response conflict between categories (Lavric et al., 2004), and to exclude that frequency-related processes (rareness or oddball effect) account for the ERP differences. Also, the 50/50 ratio has the peculiarity to bring out the individual behavioral disposition in performing the task (Perri et al., 2014), while the high target frequency yield to error commission by inducing a task-dependent pattern characterized by the prepotent response tendency (Nieuwenhuis et al., 2003). Moreover, based on a previous study that adopted the same paradigm of the present one (Perri et al., 2015a), we also have the chance to state that the Ne/Pe complex is temporally separated by the adjustments-related activities, further confirming that they reflect consecutive but different processes. In fact, the last error-related potential (the Pe) peaked 700 ms after the stimulus onset, that is on average 200 ms and 300 ms before the beginning of the present pN and BP modulation, respectively. This point is reinforced by the additional control analyses (see Fig. 6) revealing that the large inter-trial jitter of the present paradigm did not allow the Pe component to rise up and compromise the post-error ERPs.

As also suggested by Li et al. (2008), the distinction between activities following error is not trivial, because they subtend different neurocognitive processes. Specifically, there are processes related to the error-detection and- awareness (Ne and Pe, respectively; Hajcak et al., 2003; Dhar et al., 2011), and others related to the error prevention, as reflected by the reduced premotor activity and the increased top-

down control (BP and pN components in the present study). These different processes might well represent a connected cascade of events triggered by error commission. In fact, the action monitoring system of the medial PFC (as reflected by the ERN/Ne; Luu et al., 2000) may act as an alarm facilitating the conscious error perception (i.e., Pe; Dhar et al., 2011) and recruiting the attentional and inhibitory control networks of the PFC (Aron 2003; Stuss et al., 2003), as respectively indexed by the bilateral and right-side enhancement of the pN component. Finally, the activation of the MFC might predict the reduced activity of the motor system (Danielmeier et al., 2011), which in turn is associated with the response slowdown.

At post-stimulus level, the post-error trials did not present modulations of the visual sensory components. This result is in line with the findings of our previous studies, showing that the modulation of the P1 and N1 potentials does not reflect inter-trials, state-dependent performance fluctuations, but rather components marking the individual behavioral tendency in performing the whole task (Perri et al., 2014, 2015a). Also, the lack of significant effects at sensory level further confirms the view of the post-error adjustments as brain mechanisms mediated by high-level information processing.

Concluding, it is also noteworthy that the distinction between error-detection activities and post-error adjustment mechanisms might be relevant in the clinical research as well. Present findings foster the possibility to investigate the neurophysiological correlates of disorders impairing only specific stages of the error- triggered processing ranging from error detection to error prevention, as in the case, for example, of drug addiction (Hester et al., 2007), frontal lesion (Woods and Knight, 1986; Vendrell et al., 1995; Fellows and Farah, 2005) and obsessive- compulsive disorders (Schmidtkeet al., 1998).

References

Alegre, M., Gurtubay, I. G., Labarga, A., Iriarte, J., Valencia, M., &Artieda, J. (2004). Frontal and central oscillatory changes related to different aspects of the motor process: a study in go/no-go paradigms. Experimental Brain Research, 159(1), 14-22.

Aron, A. R., & Poldrack, R. A. (2006). Cortical and subcortical contributions to stop signal response inhibition: role of the subthalamic nucleus. The Journal of Neuroscience, 26(9), 2424-2433.

Aron, A. R., Fletcher, P. C., Bullmore, T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nature neuroscience, 6(2), 115-116.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in cognitive sciences, 8(4), 170-177.

Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J., & Poldrack, R. A. (2007). Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. The Journal of Neuroscience, 27(14), 3743-3752.

Band, G. P., Ridderinkhof, K. R., & van der Molen, M. W. (2003). Speed-accuracy modulation in case of conflict: the roles of activation and inhibition. Psychological research, 67(4), 266-279.

Berchicci, M., Lucci, G., Perri, R. L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. Frontier in Aging Neuroscience, 6, 48.

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). Conflict monitoring and cognitive control. Psychological review, 108(3), 624. Cavanagh, J. F., Cohen, M. X., & Allen, J. J. (2009). Prelude to and resolution of an error: EEG phase synchrony reveals cognitive control dynamics during action monitoring. The Journal of Neuroscience, 29(1), 98-105.

Chang, A., Chen, C.C., Li, H.H., Li, C.S. (2014). Event-related potentials for post- error and post-conflict slowing. PlosOne, 16;9(6).

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature reviews neuroscience, 3(3), 201-215.

Debener, S., Ullsperger, M., Siegel, M., Fiehler, K., Von Cramon, D. Y., & Engel, A.

K. (2005). Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifie the dynamics of performance monitoring. The Journal of Neuroscience, 25(50), 11730-11737.

Dehaene, S., Posner, M. I., & Tucker, D. M. (1994). Localization of a neural system for error detection and compensation. Psychological Science, 5, 303–305.

Danielmeier, C., & Ullsperger, M. (2011). Post-error adjustments. Frontiers in Psychology, 2, 233.

Danielmeier, C., Eichele, T., Forstmann, B. U., Tittgemeyer, M., & Ullsperger, M. (2011). Posterior medial frontal cortex activity predicts post-error adaptations in task-related visual and motor areas. The Journal of Neuroscience, 31(5), 1780-1789.

Dhar, M., Wiersema, J. R., & Pourtois, G. (2011). Cascade of neural events leading from error commission to subsequent awareness revealed using EEG source imaging. PLoS One, 6(5), e19578.

Di Russo, F., Taddei, F., Apnile, T., & Spinelli, D. (2006). Neural correlates of fast stimulus discrimination and response selection in top-level fencers. Neuroscience letters, 408(2), 113-118.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013a). A passive exoskeleton can push your life up: application on multiple sclerosis patients. PloS one, 8(10), e77348

Di Russo, F., Lucci, G., Sulpizio, V., Berchicci, M., Spinelli, D., Pitzalis, S., Galati,

G. (2013b). Spatiotemporal mapping of response inhibition in the prefrontal cortex. Neuropsychological Trends, 79. ISSN 1970-321X.

Dutilh, G., van Ravenzwaaij, D., Nieuwenhuis, S., van der Maas, H. L., Forstmann,

B. U., & Wagenmakers, E. J. (2012). How to measure post-error slowing: a confound and a simple solution. Journal of Mathematical Psychology, 56(3), 208-216.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. Electroencephalography and clinical neurophysiology,78(6), 447-455.

Fellows, L. K., & Farah, M. J. (2005). Different underlying impairments in decision- making following ventromedial and dorsolateral frontal lobe damage in humans. Cerebral cortex, 15(1), 58-63.

Forstmann, B. U., Dutilh, G., Brown, S., Neumann, J., Von Cramon, D. Y., Ridderinkhof, K. R., & Wagenmakers, E. J. (2008). Striatum and pre-SMA facilitate decision-making under time pressure. Proceedings of the National Academy of Sciences, 105(45), 17538-17542.

Gehring, W. J., Goss, B., Coles, M. G., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. Psychological science, 4(6), 385-390.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal–cingulate interactions in action monitoring. Nature neuroscience, 3(5), 516-520.

Hajcak, G., McDonald, N., & Simons, R. F. (2003). To err is autonomic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. Psychophysiology, 40(6), 895-903.

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage, 50(3), 1313-1319.

Herrmann, M. J., Römmler, J., Ehlis, A. C., Heidrich, A., & Fallgatter, A. J. (2004). Source localization (LORETA) of the error-related-negativity (ERN/Ne) and positivity (Pe). Cognitive Brain Research, 20(2), 294-299.

Hester, R., Simoes-Franklin, C., & Garavan, H. (2007). Post-error behavior in active cocaine users: poor awareness of errors in the presence of intact performance adjustments. Neuropsychopharmacology, 32(9), 1974-1984.

Hajcak, G., McDonald, N., & Simons, R. F. (2003). To err is autonomic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. Psychophysiology, 40(6), 895-903.

Kerns, J. G., Cohen, J. D., MacDonald, A. W., Cho, R. Y., Stenger, V. A., & Carter,

C. S. (2004). Anterior cingulate conflict monitoring and adjustments in control. Science, 303(5660), 1023-1026.

King, J. A., Korb, F. M., Von Cramon, D. Y., &Ullsperger, M. (2010). Post-error behavioral adjustments are facilitated by activation and suppression of task- relevant and task-irrelevant information processing. The Journal of Neuroscience, 30(38), 12759-12769.

Lavric, A., Pizzagalli, D. A., & Forstmeier, S. (2004). When 'go'and 'nogo' are equally frequent: ERP components and cortical tomography. European Journal of Neuroscience, 20(9), 2483-2488.

Li, C. S. R., Huang, C., Yan, P., Paliwal, P., Constable, R. T., & Sinha, R. (2008). Neural correlates of post-error slowing during a stop signal task: a functional magnetic resonance imaging study. Journal of Cognitive Neuroscience, 20(6), 1021-1029.

Lo, C. C., & Wang, X. J. (2006). Cortico–basal ganglia circuit mechanism for a decision threshold in reaction time tasks. Nature neuroscience, 9(7), 956-963.

Luu, P., Flaisch, T., & Tucker, D.M. (2000). Medial frontal cortex in action monitoring. The Journal of Neuroscience, 20, 464–469.

Luu, P., Tucker, D. M., & Makeig, S. (2004). Frontal midline theta and the error-related negativity: neurophysiological mechanisms of action regulation. Clinical Neurophysiology, 115(8), 1821-1835.

Marco-Pallarés, J., Camara, E., Münte, T. F., & Rodríguez-Fornells, A. (2008). Neural mechanisms underlying adaptive actions after slips. Journal of Cognitive Neuroscience, 20(9), 1595-1610.

Nieuwenhuis, S., Ridderinkhof, K. R., Blom, J., Band, G. P., & Kok, A. (2001). Error-related brain potentials are differentially related to awareness of response errors: Evidence from an antisaccade task. Psychophysiology, 38(5), 752-760.

Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. Cognitive, Affective, & Behavioral Neuroscience, 3(1), 17-26.

Notebaert, W., Houtman, F., Van Opstal, F., Gevers, W., Fias, W., & Verguts, T. (2009). Post-error slowing: an orienting account. Cognition, 111(2), 275-279.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia104, 199-206.

Perri, R. L., Berchicci, M., Spinelli, D., & Di Russo, F. (2014). Individual Differences in Response Speed and Accuracy are Associated to Specific

Brain Activities of two Interacting Systems. Frontiers in Behavioral Neuroscience, 8, 251.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015a). Why do we make mistakes? Neurocognitive processes during the preparation-perception- action cycle and error-detection. Neuroimage, 113, 320-328.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015b). The Premotor Role of the Prefrontal Cortex in Response Consistency. Neuropsychology, 29 (5), 767-775.

Rabbitt, P. M. (1966). Errors and error correction in choice-response tasks. Journal of experimental psychology, 71(2), 264.

Ridderinkhof, R. K. (2002). Micro-and macro-adjustments of task set: Activation and suppression in conflict tasks. Psychological research, 66(4), 312-323.

Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The role of the medial frontal cortex in cognitive control. Science, 306(5695), 443-447.

Rinkenauer, G., Osman, A., Ulrich, R., Müller-Gethmann, H., & Mattes, S. (2004). On the locus of speed-accuracy trade-off in reaction time: inferences from the lateralized readiness potential. Journal of Experimental Psychology: General, 133(2), 261.

Rubia, K., Smith, A. B., Brammer, M. J., & Taylor, E. (2003). Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. Neuroimage, 20(1), 351-358.

Salisbury, D. F., Griggs, C. B., Shenton, M. E., & McCarley, R. W. (2004). The NoGo P300 'anteriorization' effect and response inhibition. Clinical Neurophysiology, 115(7), 1550-1558.

Sangals, J., Sommer, W., & Leuthold, H. (2002). Influences of presentation mode and time pressure on the utilisation of advance information in response preparation. Acta psychologica, 109(1), 1-24.

Schmajuk, M., Liotti, M., Busse, L., &Woldorff, M. G. (2006). Electrophysiological activity underlying inhibitory control processes in normal adults. Neuropsychologia, 44(3), 384-395.

Schmidtke, K., Schorb, A., Winkelmann, G., &Hohagen, F. (1998). Cognitive frontal lobe dysfunction in obsessive-compulsive disorder. Biological Psychiatry, 43(9), 666-673.

Shibasaki, H., & Hallett, M. (2006). What is the Bereitschaftspotential?. Clinical Neurophysiology, 117(11), 2341-2356.

Stuss, D. T., Murphy, K. J., Binns, M. A., & Alexander, M. P. (2003). Staying on the job: the frontal lobes control individual performance variability. Brain, 126(11), 2363-2380.

Taylor, S. F., Stern, E. R., & Gehring, W. J. (2007). Neural Systems for Error Monitoring Recent Findings and Theoretical Perspectives. The Neuroscientist, 13(2), 160-172.

Vendrell, P., Junqué, C., Pujol, J., Jurado, M., Molet, J., & Grafman, J. (1995). The role of prefrontal regions in the Stroop task. Neuropsychologia, 33(3), 341- 352.

Vogel, E. K., & Luck, S. J. (2000). The visual N1 component as an index of a discrimination process. Psychophysiology, 37(02), 190-203.

Wessel, J. R., & Ullsperger, M. (2011). Selection of independent components representing event-related brain potentials: a data-driven approach for greater objectivity. Neuroimage, 54(3), 2105-2115.

West, R., & Travers, S. (2008). Tracking the temporal dynamics of updating cognitive control: An examination of error processing. Cerebral Cortex, 18(5), 1112-1124.

Woods, D. L., & Knight, R. T. (1986). Electrophysiologic evidence of increased distractibility after dorsolateral prefrontal lesions. Neurology, 36(2), 212-212.

6. Missing the target: the neural processing underlying response omission

Abstract

The omissions represent missing responses to the target stimuli; since omissions are infrequent errors, literature about them is lacking. This is the first ERP study aimed at investigating the brain activities associated to omissions in a equiprobable go/no- go task. By analyzing the preparatory brain activities preceding the stimulus onset in the correct and omitted trials, we found that omissions are predicted by the onset delay (in the range of half a second) of two pre-stimulus ERP components, that is the prefrontal negativity and the Bereitschaftspotential, associated to the top-down control and the motor preparation, respectively. Further, at post-stimulus stage the omission trials were characterized by the suppression of the prefrontal positivity component (emerging at around 300 ms), reflecting the stimulus-response mapping oriented to the stimulus categorization. No differences between omission and correct trials were detected at the level of the P1 and N1 visual components, as well as the P3. These findings suggest the view of omissions as attentional lapse-based errors, as reflected by the delayed pre-stimulus brain activation. The reduced cortical excitability during the preparation phase did not affect the visual processing, but compromised the cognitive-demanding process of the stimulus categorization, resulting in the inability to reach a decision.

Keywords: ERPs; prefrontal negativity (pN); Bereitschaftspotential (BP); prefrontal positivity (pP); decision-making; omission error.

6.1. Introduction

The decision-making literature literature has described the neurocognitive processes of error commission using tasks like the go/no-go; however, both neuroimaging (for a review see Taylor et al., 2007) and event-related potential (ERP; for a review see Olvet and Hajcak, 2008) studies focused on false alarm errors (FAs; i.e., the responses to non-target stimuli) and much less is known about omission errors. The omission is the failure to respond to the target stimulus and represents a quite rare error type: this might explain why literature is lacking.

According to the Latin proverb "in dubiis abstine" (i.e., in doubtful situations, abstain), the uncertainty is a possible cause of omissions; however, we do not know if omissions are the outcome of attentional lapses, or if they represent withheld responses to stimuli erroneously categorized as non-target. Subjects' feedback after each trial could partly help to clarify this point, but methodological issues like the task duration and the generation of feedback-related activities make unusual the auto-evaluation procedure.

In a complex visual discrimination task (Rousselet et al., 2004), the ERP data associated to missing targets are presented. However, the omission errors were not the focus of the investigation, and the authors just reported that the post-stimulus activity of no-go trials did not differ from omission trials. To the best of our knowledge there are no studies directly aimed at investigating the omissions. Accordingly, the hypotheses of the present study are based on previous findings about the motor and cognitive preparatory activities observed in the same task of the present one (Di Russo et al., 2013a,b; Berchicci et al., 2014; Perri et al., 2014, 2015a, b). Also, we aim to examine to what extent the brain processes preceding omissions are different from those preceding the FAs. In case of FAs (Perri et al., 2015a), we found that neither the top-down control of the prefrontal cortex (PFC), as reflected by the prefrontal negativity (pN; Berchicci et al., 2014; Perri et al., 2015b) component, nor the preparatory activity of the supplementary motor area (SMA), as reflected by the Bereitschaftspotential (BP; Shibasaki and Hallett, 2006), accounted for the erroneous responses. In contrast, the FAs were caused by the inaccurate stimulus-response (S-R) mapping, as reflected by the

prefrontal positivity (pP; Di Russo et al., 2013a; Berchicci et al., 2014; Perri et al., 2014, 2015a). The pP is a prefrontal distributed component emerging at about 300 ms after the stimulus onset, corresponding to 100-150 ms before the response time in the present go/no-go task. The pP reflects the categorization process as revealed by the larger amplitude after the larger than non-target stimuli (Di Russo et al., 2013a,b; Berchicci et al., 2014; Perri et al., 2015a). Further, the latency of the pP reflects the speed of the decision process, being correlated with the individual response times (RTs; Perri et al., 2014). It is noteworthy that the pP can be assimilated to other components independently described by different groups that in the context of different tasks (e.g., go/no-go and oddball) reached similar conclusions about the nature of the PFC positivity; this activity was labeled as Go-P2 (Gajewski and Falkenstein, 2013), anterior P2 (P2a; Potts et al., 2004), frontal selection positivity (FSP; Kenemans et al., 1993) and frontal P3 (P3f; Makeig et al., 1999). Combining fMRI and ERP data to investigate this frontal activity, we found that the anterior insula (aIns) was the main generator of the pP component (Di Russo et al., 2013a). Consistent with the view that the pP component reflects the S-R mapping process, the insular activation was referred to the S-R association to guide response selection (Boettiger and D'Esposito, 2005), and reflects both self and motor awareness (Berti et al., 2005). The main goal of the present study is to understand the neurocognitive processing predisposing to omission errors. To this aim, at least four not alternative mechanisms can be hypothesized:

1) Lapse of attention. A momentary lapse of attention during omission trials might emerge at different levels of processing such as a reduced top-down control in the preparation phase (as reflected by the reduced pN component; Berchicci et al., 2014; Perri et al., 2015b), a reduced attention allocated to the visual stimulus (as reflected by reduced P1 and N1 components; Di Russo et al., 2003; Luck et al., 1990), or a reduced P3, considered as an index of the attentional state (i.e., the P3 amplitude is smaller in conditions of low arousal, for a review see Nieuwenhuis et al., 2005). According to this view, the task preparation or the stimulus processing were neglected in the omission trials.

2) Reduced motor preparation. According to this hypothesis, the activity of the BP component reflecting the motor preparation (Shibasaki and Hallett, 2006) is reduced in the omission trials.

Accordingly, omissions would be missed responses due to the low excitability of the premotor areas in the preparation phase; in other words, since the reduced activity of the premotor areas predisposes to slow reaction times (Smith et al., 2006; Perri et al., 2014), the subjects would not be able to emit a response in the expected time (i.e., before the next stimulus onset).

3) Erroneous S-R mapping. The locus of error is at post-stimulus stage, and is marked by specific modulations of the pP component. Omissions would be associated to changes of this component with respect to the correct trials (as for the FA error; Perri et al., 2015a). A defective processing at this level would lead subjects to do not reach a decision, or to erroneously decide for the response inhibition.

4) Categorization error. The subjects perceive the target stimulus as a non- target. To confirm this hypothesis, the brain activity of omission trials should be identical to those recorded in the correctly inhibited trials. In other words, the preparatory BP and pN components, the visual P1 and N1, the pP component sensible to the stimulus category, and the attentional P3 should be comparable between omission and no-go trials. Particularly informative would be also the N2 component that, according to the inhibitory control theory (Bokura et al., 2001; Van Boxtel et al., 2001; Schmajuk et al., 2006), should be larger in case of inhibited than executed motor response. Thus, according to this theory, the N2 is expected to be enhanced in both omission and no-go trials.

6.2. Materials and methods

6.2.1. Subjects

From a large database of subjects who participated in the go/no-go task (described below), we first selected those who reported a relatively high number of omissions (i.e., 19 subjects). Then we analyzed the electroencephalographic (EEG) data of these subjects, and selected those with a suitable number of artifact-free trials of omissions for the grand-averages. By this procedure, we selected 12 subjects for the final sample (1 female; mean age=31.6, SD=12.9); their mean percentage of omissions was 7.6%, SD=7.8. For each subject, the median RT of the go trials was calculated; the group mean RT was 422

ms, SD=62.2. The participants had normal or corrected-to-normal vision and no history of neurological or psychiatric disorders; all of the subjects were right-handed (Edinburgh Handedness Inventory; Oldfield, 1971). After explanations of the procedures, all of the participants provided written informed consent, approved by the Local Ethical Committee.

6.2.2. Procedure and Task

Subjects were tested in a sound attenuated, dimly lit room; they were comfortably seated in front of a computer monitor at a distance of 114 cm, and a board was fixed on the armchair allowing them to freely push the button panel positioned on it. A yellow circle (subtending 0.15°x0.15° visual angle) at the center of the screen was served as fixation point and was always displayed on the screen. The four visual stimuli consisted of squared configurations (subtending 4x4°) made of vertical or horizontal segments, or both of them with different orientation (vertical and horizontal) presented centrally on a dark gray background. Two stimuli were defined as targets (go stimuli, p=0.5), and the other two were defined as non-targets (no-go stimuli, p=0.5). The four visual stimuli were randomly presented for 260 ms with equal probability (p=0.25). The stimulus-onset asynchrony varied from 1 to 2 s to avoid time prediction effects on the RTs. After receiving the task instructions, the participants were trained in a 40 trials block. The entire experiment consisted of 10 blocks, each of which contained 80 trials and lasted 2.5 min with a rest period in between. The total duration was about 30 min, depending on the subjective rest time. A total of 800 trials were delivered in the experiment: 400 for go and 400 for no-go category. Participants were asked to be very accurate and to press a button as fast as possible with the right index finger when go stimuli appeared on the monitor, and withhold the response when no-go stimuli appeared.

6.2.3. Behavioral analyses

In order to exclude that omissions were caused by very slow responses in the preceding trial, the pre-omission RTs (i.e., the correct go responses preceding the omission trials) of each subject were compared (t-test analyses) to his/her RT on the whole task.

6.2.4. Electrophysiological recording and data analysis

The EEG signal was recorded using BrainVisionTM system (BrainProducts GmbH, Munich, Germany) with 64 electrodes mounted according to the 10-10 International system. All electrodes were referenced to the left mastoid. Horizontal and vertical electrooculogram (EOG) were also recorded using electrode at the right external canthi and below the left eye, respectively. Electrode impedances were kept below 5KΩ. The EEG was digitized at 250 Hz, amplified (band-pass of 0.01-80 Hz including a 50 Hz notch filter) and stored for offline averaging.

The raw signal was segmented into go, no-go and omission trials. Task- related ERPs components, such as the pN, BP, N2, pP and P3, were analyzed adopting 2000 ms epochs with stimulus onset as time 0 (from 1100 ms before to 900 ms after the stimulus). The P1 and N1 components were analyzed adopting a standard -200/0 ms baseline. To further reduce high frequency noise, the signal was low pass filtered (i.e., Butterworth) at 25 Hz (slope 24 dB/octave). The removal of the eye-movement artifacts was performed using the ocular correction with the independent component analysis tool (ICA ocular correction) available in the Brain Vision Analyzer software: this method was introduced by Jung et al. (2000) and revealed better results when compared to other ocular correction methods (e.g., Hoffmann and Falkenstein, 2008). Then, the artifact rejection was performed to discard epochs contaminated by artifacts or other signals exceeding the amplitude threshold of ±120 μV. The artifact-free trials were finally averaged and the baseline was defined as the mean voltage during the initial 200 ms of the considered epochs. In order to look at the differences in the pN and BP components, we firstly compared the pre-stimulus activities of the three trials with a sample-by-sample t-test (Brain Vision Analyzer tool) at the frontal and central electrodes where the two components showed the maximal activity. This preliminary analysis indicated significant differences at AFz site in the -600/-200 ms time window (pN activity), and at Cz site in the -500/-300 ms time window (BP activity). The statistical analyses were conducted using Statsoft Statistica version 10 (Statistica for Windows, StatSoft, Inc., Tulsa, OH, USA). Specifically, the pre- stimulus mean amplitude on the selected electrodes was submitted to an ANOVA with Trials (go, no-go, omission) as dependent variables. The visual evoked P1 and N1

components, such as the fronto-central N2, were measured on the electrodes of maximum activity as follows: the P1 on the PO8, the N1 on the Iz and the N2 on the Cz site. The peak amplitude and latency of these components were submitted to ANOVAs with Trial as repeated measure. The P3 component was calculated as the mean amplitude of the range of maximum activity surrounding the grand-average peak latency: this method indicated the Cz and Pz electrodes, and the 450-500 ms as the sites and time interval to analyze. As regard the pP, we firstly defined the length of this component on the basis of the grand-average waveform of the go trial, as condition showing the largest pP amplitude (e.g., Perri et al., 2015a). By this method, the 300-460 ms interval was selected on the Fp1 and Fp2 sites. Because of the different trials modulation over time, we decided to split the selected interval of the pP in 4 temporal windows (hereafter T) of similar length: 300-340 ms (T1), 340-380 ms (T2), 380-420 ms (T3) and 420-460 ms (T4). The pP activity was submitted to a 4 x 3 x 2 ANOVA with Temporal window (T1, T2, T3, T4), Trial and Site (Fp1 vs. Fp2) as repeated measures. The amplitude and latency of the N2 were submitted to ANOVAs with Trial as repeated measure, while the P3 was calculated by means of a Site (Cz vs. Pz) x Trial ANOVA. Post-hoc comparisons were conducted using Fisher's least significant difference (LSD) test. The overall alpha level was fixed at 0.05.

6.3. Results

6.3.1. Behavioral data

Statistical analyses showed that the pre-omission RTs (mean=464, SD=140) were comparable to the overall RTs (mean=422, SD=62; t= -0.8, p>0.05). Accordingly, we can exclude the view of the omissions as the consequence of slow motor responses in the preceding trials.

6.3.2. ERP data

Pre-stimulus components

Figure 6.1 reports the grand-average waveforms over the most representative electrodes. The pN and BP components emerged over the medial prefrontal (AFz) and central (Cz) sites, respectively. The pre-stimulus activities were comparable between go and no-go trials;

in contrast, the preparatory activity in the omission trials was drastically reduced, as revealed by the delayed onset of both the pN and BP components. Specifically, in case of omissions the pN started about 200 ms before the stimulus onset, that is with a 500 ms delay with respect to correct trials; the BP started to rise at about 300 ms before the stimulus, corresponding to a delay of 400 ms with respect to correct trials. It is important to note that the modulation of the pre-stimulus activities was not driven by ocular artifacts, as indicated by the inspection of the EOG waveforms reported on the top row of Fig. 1. The above reported modulations of the pN and BP components are also confirmed by the topographical maps (Fig. 2, top row) where the surface activity of the omission trials is close to 0 μV. In contrast, negative activities can be clearly detected over the central and prefrontal areas in the correct trials.

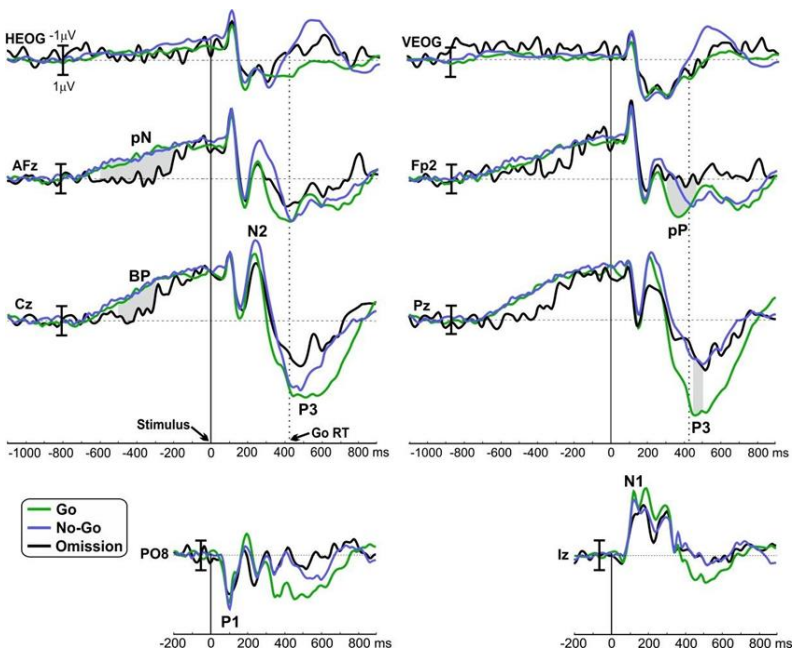

Fig. 6.1 Grand average waveforms in the ocular (HEOG, VEOG) prefrontal (AFz, Fp2), centro-parietal (Cz, Pz) and occipital (PO8, Iz) sites; time 0 corresponds to the stimulus onset. The grey labels indicate the temporal windows in which significant differences emerged between trials. The three trials are represented by different colors (labeled in legend). pN: prefrontal negativity; BP: Bereitschaftspotential; pP: prefrontal positivity.

ANOVA on the pN component showed a significant effect of Trial ($F_{2,22}=6.3$, $p<0.01$), revealing a smaller (i.e., close to 0 μV) activity in case of omission (mean= -0.6 μV, SD=3) compared to both go (mean= -1.5 μV, SD=1) and no-go (mean= -1.7 μV, SD=1.1) trials (all ps<0.01). ANOVA on the BP component showed a significant effect of Trial ($F_{2,22}=3.6$, $p<0.05$), indicating again smaller activity of omission trials (mean= -0.7 μV, SD=2.4) compared to go (mean= -1.9 μV, SD=1.2) and no-go (mean= -2 μV, SD=1.4) trials (all ps<0.05).

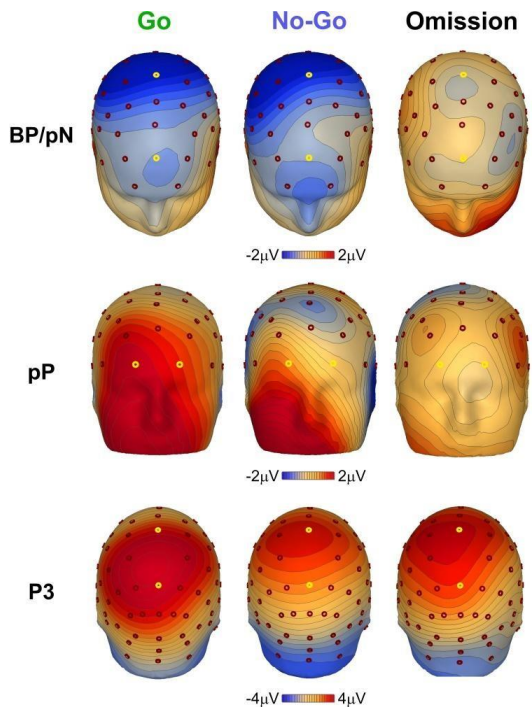

Figure 6.2 Scalp topographies of the main ERP components in the three trials (go, no-go, and omission). pN: prefrontal negativity; BP: Bereitschaftspotential; pP: prefrontal positivity.

Post-stimulus components

Figure 1 shows the P1 and N1 components peaking at 100 ms and 160 ms over PO8 and Iz, respectively. At 250 ms, the frontal-central N2 emerged in the three conditions (see Cz) and, immediately later, the pP component was detectable over the prefrontal derivations as shown in Figure 6.1 (see Fp2) and, more clearly, in Figure 6.3 a). As

expected (Perri et al., 2014, 2015a), the go trials showed the largest pP component, starting 300 ms after the stimulus and decreasing at about 460 ms. The no-go pP started at 340 ms and raised progressively, reaching its maximum only at 430 ms, that is concomitant to the response in the go trials. On the other hand, the pP component is undetectable in the omission trials, being the prefrontal activity in that interval close to the baseline level. The surface cortical distribution of the pP component is reported in the middle row of Figure 6.2, showing clear differences between trials in the selected time interval.

Finally, 500 ms after the stimulus the P3 component was detectable over the central-parietal derivations (see Cz and Pz in Fig 1) showing the largest activity in the go trials over Pz. The topographical maps (Fig 2, bottom row) show the well- known "no-go anteriorization" of the P3 (Pfefferbaum et al., 1985; Kopp et al., 1996; Fallgatter et al., 1997), while the topography of omissions was more similar to that of no-go trials.

The statistical analyses of the visual potentials did not reveal significant differences, neither for the amplitude nor for the peak latencies of the P1 and N1 components (all ps>0.05). Similarly, the amplitude and latency of the frontal-central N2 did not show differences between trials (all ps>0.05).

ANOVA on the pP component showed a significant main effect of Trial ($F_{2,22}=3.9$, $p<0.05$) and a significant interaction of Temporal window x Trial ($F_{6,66}=8.6$, $p<0.001$). As showed in Figure 6.3 b), the go activity was larger than no-go and omission at both T1 and T2 (all ps<0.0001); at T3, the pP was larger for no-go than omission ($p<0.01$), and for go than no-go trials ($p<0.05$). Finally, at T4 the pP was comparable between go and no-go trials (ps>0.05), and both the correct trials were larger than omission (ps<0.0001).

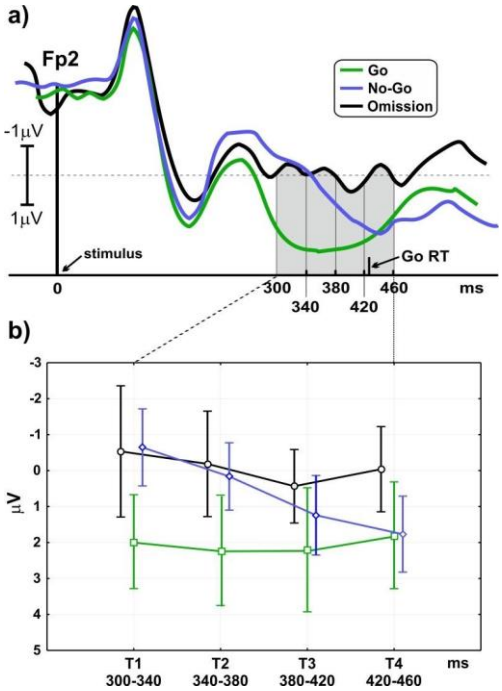

Fig. 6.3 a) Grand average waveforms of the prefrontal positivity (pP) in the Fp2 site. The waveforms of the three trials are superimposed and restricted to the post- stimulus period. The grey rectangles represent the 40 ms temporal windows (T) considered for statistical analyses. **b)** ANOVA interaction effect of Temporal window X Trial. Vertical bars denote the standard error.

Analyses on the P3 component showed a significant Site x Trial interaction ($F_{2,22}=12.8$, $p<0.001$): the P3 activity was comparable among trials over Cz, while the parietal P3 was larger for go if compared to both omission and no-go ($ps<0.0001$). No significant differences emerged between omission-P3 and no-go-P3.

6.3.3. Additional control analyses

Given the rarity of the omission errors and, consequently, the quite low number of averaged trials, one can argue that the present findings were partly compromised by the comparison between conditions of different signal-to-noise ratio. In order to control for this possible confounding factor, we made additional control analyses consisting in lowering the number of averaged trials in the go and no-go conditions. Specifically, we adopted an individual-based approach consisting in

re-averaging, for each subject, the same number of omission trials for the go and no-go conditions as well. By means of a random artifact-free trials selection, we obtained the same signal-to-noise ratio between conditions in each subject. As a result, the mean number of averaged trials was 25.9, SD=24 for each of the three conditions. The grand-average waveforms of this additional analysis are presented in Figure 6.4, where the main significant effects are labeled by the same time windows of the original analyses (see Figure 6.1). As can be seen, even if more noisy than in Figure 6.1, the go and no-go trials show the same waveforms as in the original approach. Figure 6.4 confirms the results of the previous section, showing that the omission trials were characterized by the onset delay of the pre-stimulus activities and the suppression of the pP component. Summarizing, we can conclude that the lower number of omission trials did not affect the findings of the present study, as revealed by the control analyses showing that the BP, the pN and the pP components of the correct trials were still preserved after the drastic trials reduction.

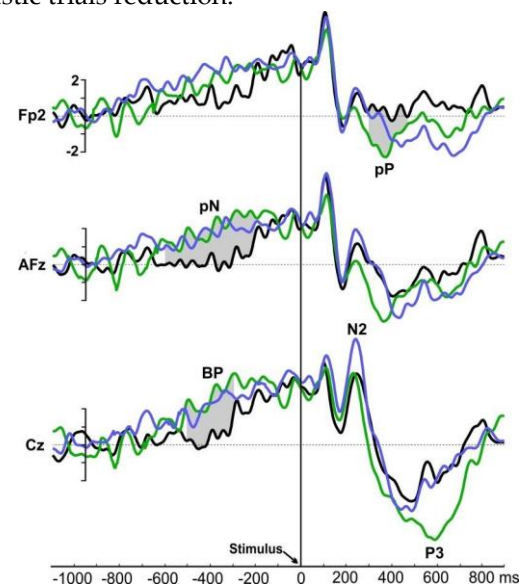

Fig. 6.4. Grand average waveforms of the additional control analyses. The average number of go and no-go trials has been drastically reduced in each subject in order to have similar signal-to-noise ratio between conditions. The gray labels correspond to the time windows where the statistical differences were found to be significant. The differences between conditions are the same of those reported in the original approach of Figure 6.1.

6.4. Discussion

In the introduction, we proposed four possible -not mutually exclusive- neural mechanisms predisposing to omission errors. We firstly hypothesized an attentional explanation: this view was supported by the results. In fact, the onset of the pN component, related to the top-down control (e.g., Perri et al., 2015b) showed a prominent delay (500 ms) in case of omissions; this is consistent with a lapse of attention in the early preparation phase. However, the P1-N1 components (modulated by visual-spatial attention; e.g., Luck et al., 1990) and the P3 component (also sensitive to attention) did not show difference between omission and correct trials.

Because of the relationship between the BP amplitude and the response speed (i.e., the smaller the BP, the slower the RT; Smith et al., 2006; Perri et al., 2014), we hypothesized that the omissions might be associated to reduced premotor activity, therefore to the inability to emit a response before the next stimulus onset. This second hypothesis was also supported by the results because the BP component presented a delayed onset (400 ms) in case of omissions, although its amplitude in the 300 ms before the stimulus was similar to that of correct trials.

The third hypothesis about the erroneous S-R mapping process was supported by the pP component data, as revealed by the significant difference between omission and correct trials. Specifically, the pP was larger in the go than no-go trials (as expected), and it was suppressed (i.e., the activity was close to the baseline level) in case of omissions.

The data did not support the fourth hypothesis that described the omission as an erroneous categorization of the go stimulus as a no-go one. In fact, no-go and omission trials were different in many respects. The pP amplitude of omissions was different from no-go trials, and both the BP and the pN components clearly distinguished the omissions from correct trials. As for the N2, data were not informative with respect to the categorization hypothesis because we did not found evidence in favor of the inhibitory control theory (Bokura et al., 2001; Van Boxtel et al., 2001; Schmajuk et al., 2006), and this latter was preliminary to the comparison between no-go N2 and omission N2. The inhibitory theory states that the N2 component is enhanced in case of inhibited than executed motor response; however, we found no

difference between go and no-go trials, as already reported by other studies (Falkenstein et al., 1995, 1999, 2002; Donkers and van Boxtel, 2004; Perri et al., 2015a).

Summarizing, the results confirmed that three (lapse of attention, reduced motor preparation, and erroneous S-R mapping) of the four proposed mechanisms might have a relevant role in the omission error. In fact, the neural pattern of omission trials was characterized by a strong delay (i.e., in the range of half a second) of the preparatory components, and by the suppression of the pP component after the stimulus onset.

Given the interaction between the BP and pN components (Perri et al., 2014), it is possible that the low excitability of the premotor areas (BP) and the reduced top- down control (pN) are associated with each other, and that both processes are compromised by a momentary lapse of attention in the omission trials. Attentional effects were not found on the P1, N1 and P3 components of omission trials. However, the lack of effect on the P1 and N1 is not surprising because several studies showed preserved visual cortex processing in case of attentional blink (Marois et al., 2004), inattention (Beck et al., 2001) and unconscious perception (Supèr et al., 2001). Also, Sergent et al. (2005) reported intact P1 and N1 after "unseen" stimuli, suggesting that these potentials can be dissociated from conscious perception. As for the P3, which is typically modulated by attention and suppressed when the stimuli are not consciously perceived (Fukuda et al., 1996; Luck et al., 1996; Vogel et al., 1998; Rolke et al., 2001), the similarity between no-go and omission trials (see also Rousselet et al., 2004) does not support the view of the "unseen" stimulus in the omission trials. A possible explanation for the lack of effects on the P1, N1 and P3 is that the lapse of attention involves a reduction of the top-down control before visual stimulus is presented (Weissman et al., 2006; Perri et al., 2015b), but the abrupt appearance of the stimulus served as a bottom-up trigger reorienting the attention back to the stimulus location. As also suggested by Weissman et al. (2006), the stimulus-guided reorienting occurs too late to aid the current trial, but it could improve the performance in the next trial.

Overall, an attentional failure in the preparatory phase is associated to scarce motor preparation (delayed BP onset) and reduced top-down control (delayed pN onset) which causes a specific loss of information

at the S-R mapping stage (absence of the frontal pP) without affecting the stimulus-driven components such as the P1, N1 and P3. In this way, even if the omitted stimulus is consciously perceived, the subjects are not ready enough to accomplish the cognitive-demanding request of stimulus categorization, resulting in the inability to reach a decision. Within this proposal, the pP suppression is considered a consequence of the delayed pre-stimulus preparation.

An important implication of these findings is the relationship between the onset and duration of the pre-stimulus ERPs and the efficacy of the S-R mapping process (i.e., the pP component). In other studies we found that the amplitude of the pN and BP components was not related to the pP activity (Berchicci et al., 2014; Perri et al., 2014, 2015b); in contrast, in the present study the onset delay of the pN and BP components compromised the pP. These results suggest that the prerequisite for the efficient S-R mapping is that the pre-stimulus cortical activities start and rise up for a critical amount of time. Consistently, the negative slow potentials in the preparatory phase generally reflect the increased excitability of the areas involved in the task execution (for a review see Birbaumer et al., 1990). In the omission trials, the consistent delay of the pre-stimulus components does not allow an adequate preparation of the prefrontal and premotor areas for executing the task. In this way, even if the visual processing is preserved, the cognitive-demanding process of the S- R mapping fails to start because of the poor readiness to fulfill the categorization request.

The analyses of behavioral data did not show any difference between the pre- omission trials and the individual performance on the whole task; accordingly, we can exclude the contribution of a preceding defective performance (i.e., long RTs) on the omission error. Finally, the neural pattern associated to omissions was very different from that of false alarms (see Perri et al., 2015a), indicating that the two errors reflect the behavioral outcome of different and specific neurocognitive "faults". Specifically, the omissions are associated to defective preparation, and suppression of the S-R mapping process. In contrast, the false alarms are associated to intact preparatory components and defective S-R mapping.

References

Beck, D. M., Rees, G., Frith, C. D., & Lavie, N. (2001). Neural correlates of change detection and change blindness. Nature neuroscience, 4(6), 645-650.

Berchicci, M., Lucci, G., Perri, R. L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. Frontier in Aging Neuroscience, 6, 48.

Berti, A., Bottini, G., Gandola, M., Pia, L., Smania, N., Stracciari, A., ... & Paulesu,

E. (2005). Shared cortical anatomy for motor awareness and motor control. Science, 309(5733), 488-491.

Birbaumer, N, Elbert, T., Canavan, A., & Rockstroh, B. (1990). Slow potentials of the cerebral cortex and behavior. Physiological reviews, (70), 1-41.

Boettiger, C. A., & D'Esposito, M. (2005). Frontal networks for learning and executing arbitrary stimulus-response associations. The Journal of neuroscience, 25(10), 2723-2732.

Bokura, H., Yamaguchi, S., & Kobayashi, S. (2001). Electrophysiological correlates for response inhibition in a Go/NoGo task. Clinical Neurophysiology, 112(12), 2224-2232.

Di Russo, F., Martínez, A., & Hillyard, S. A. (2003). Source analysis of event-related cortical activity during visuo-spatial attention. Cerebral cortex, 13(5), 486- 499.

Di Russo, F., Lucci, G., Sulpizio, V., Berchicci, M., Spinelli, D., Pitzalis, S., Galati,

G. (2013a). Spatiotemporal mapping of response inhibition in the prefrontal cortex. Neuropsychological Trends, 79. ISSN 1970-321X.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013b). A passive exoskeleton can push your life up: application on multiple sclerosis patients. PloS one, 8(10), e77348

Donkers, F. C., & van Boxtel, G. J. (2004). The N2 in go/no-go tasks reflects conflict monitoring not response inhibition. Brain and cognition, 56(2), 165-176.

Falkenstein, M., Koshlykova, N. A., Kiroj, V. N., Hoormann, J., & Hohnsbein, J. (1995). Late ERP components in visual and auditory Go/Nogo tasks. Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 96(1), 36-43.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (1999). ERP components in Go/Nogo tasks and their relation to inhibition. Acta psychologica, 101(2), 267-291.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (2002). Inhibition-related ERP components: Variation with modality, age, and time-on-task. Journal of Psychophysiology, 16(3), 167.

Fallgatter, A. J., Brandeis, D., & Strik, P. W. (1997). A robust assessment of the NoGo-anteriorisation of P300 microstates in a cued Continuous Performance Test. Brain topography, 9(4), 295-302.

Fukuda, M., Hata, A., Niwa, S. I., Hirmatsu, K. I., Yokokoji, M., Hayashida, S., ... & Iwanami, A. (1996). Event-related potential correlates of functional hearing loss: Reduced P3 amplitude with preserved Nl and N2 components in a unilateral case. Psychiatry and clinical neurosciences, 50(2), 85-88.

Gajewski, P. D., & Falkenstein, M. (2013). Effects of task complexity on ERP components in Go/No-go tasks. International Journal of Psychophysiology,87(3), 273-278.

Hoffmann, S., & Falkenstein, M. (2008). The correction of eye blink artefacts in the EEG: a comparison of two prominent methods. PLoS One, 3(8), e3004.

Jung, T. P., Makeig, S., Humphries, C., Lee, T. W., Mckeown, M. J., Iragui, V., & Sejnowski, T. J. (2000). Removing electroencephalographic artifacts by blind source separation. Psychophysiology, 37(02), 163-178.

Kenemans, J. L., Kok, A., & Smulders, F. T. Y. (1993). Event-related potentials to conjunctions of spatial frequency and orientation as a function of stimulus parameters and response requirements. Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 88(1), 51-63.

Kopp, B., Mattler, U., Goertz, R., & Rist, F. (1996). N2, P3 and the lateralized readiness potential in a nogo task involving selective response priming. Electroencephalography and clinical neurophysiology, 99(1), 19-27.

Luck, S. J., Heinze, H. J., Mangun, G. R., & Hillyard, S. A. (1990). Visual event-related potentials index focused attention within bilateral stimulus arrays. II. Functional dissociation of P1 and N1 components. Electroencephalography and clinical Neurophysiology, 75(6), 528-542.

Luck, S. J., Vogel, E. K., & Shapiro, K. L. (1996). Word meanings can be accessed but not reported during the attentional blink. Nature, 383(6601), 616-618.

Makeig, S., Westerfield, M., Jung, T. P., Covington, J., Townsend, J., Sejnowski, T. J., & Courchesne, E. (1999). Functionally independent components of the late positive event-related potential during visual spatial attention. The journal of neuroscience, 19(7), 2665-2680.

Marois, R., Yi, D. J., & Chun, M. M. (2004). The neural fate of consciously perceived and missed events in the attentional blink. Neuron, 41(3), 465-472.

Nieuwenhuis, S., Aston-Jones, G., & Cohen, J. D. (2005). Decision making, the P3, and the locus coeruleus-norepinephrine system. Psychological bulletin, 131(4), 510.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia104, 199-206.

Olvet, D. M., & Hajcak, G. (2008). The error-related negativity (ERN) and psychopathology: toward an endophenotype. Clinical psychology review, 28(8), 1343-1354.

Perri, R. L., Berchicci, M., Spinelli, D., & Di Russo, F. (2014). Individual Differences in Response Speed and Accuracy are Associated to Specific Brain Activities of two Interacting Systems. Frontiers in Behavioral Neuroscience, 8, 251.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015a). Why do we make mistakes? Neurocognitive processes during the preparation-perception- action cycle and error-detection. Neuroimage, 113, 320-328.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015b). The Premotor Role of the Prefrontal Cortex in Response Consistency. Neuropsychology, 29 (5), 767-775.

Pfefferbaum, A., Ford, J. M., Weller, B. J., & Kopell, B. S. (1985). ERPs to response production and inhibition. Electroencephalography and clinical neurophysiology, 60(5), 423-434.

Potts, G. F. (2004). An ERP index of task relevance evaluation of visual stimuli. Brain and Cognition, 56(1), 5-13.

Rolke, B., Heil, M., Streb, J., & Hennighausen, E. (2001). Missed prime words within the attentional blink evoke an N400 semantic priming effect. Psychophysiology, 38(02), 165-174.

Rousselet, G. A., Thorpe, S. J., & Fabre-Thorpe, M. (2004). Processing of one, two or four natural scenes in humans: the limits of parallelism. Vision research, 44(9), 877-894.

Schmajuk, M., Liotti, M., Busse, L., & Woldorff, M. G. (2006). Electrophysiological activity underlying inhibitory control processes in normal adults. Neuropsychologia, 44(3), 384-395.

Sergent, C., Baillet, S., & Dehaene, S. (2005). Timing of the brain events underlying access to consciousness during the attentional blink. Nature neuroscience, 8(10), 1391-1400.

Shibasaki, H., & Hallett, M. (2006). What is the Bereitschaftspotential? Clinical Neurophysiology, 117(11), 2341-2356.

Smith, J. L., Johnstone, S. J., & Barry, R. J. (2006). Effects of pre-stimulus processing on subsequent events in a warned Go/NoGo paradigm: response preparation, execution and inhibition. International Journal of Psychophysiology,61(2), 121-133.

Supèr, H., Spekreijse, H., & Lamme, V. A. (2001). Two distinct modes of sensory processing observed in monkey primary visual cortex (V1). Nature neuroscience, 4(3), 304-310.

Taylor, S. F., Stern, E. R., & Gehring, W. J. (2007). Neural Systems for Error Monitoring: Recent Findings and Theoretical Perspectives. The Neuroscientist,13(2), 160-172.

van Boxtel, G. J., van der Molen, M. W., Jennings, J. R., & Brunia, C. H. (2001). A psychophysiological analysis of inhibitory motor control in the stop-signal paradigm. Biological psychology, 58(3), 229-262.

Vogel, E. K., Luck, S. J., & Shapiro, K. L. (1998). Electrophysiological evidence for a postperceptual locus of suppression during the attentional blink.

Journal of Experimental Psychology: Human Perception and Performance, 24(6), 1656. Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. Nature neuroscience, 9(7), 971-978.

7. General conclusion

The studies of the present thesis provide two main kinds of implications: methodological and theoretical.

7.1. Methodological implications

The MRCPs have been usually analyzed by locking the ERP signal to the movement onset (identified by the EMG signal) or to the response execution (marked, for example, by the key-press). This "traditional" approach has the advantage to enhance (in both amplitude and duration) the brain activities oriented, or concomitant, to the movement execution, like the Bereitschaftspotential (BP), the Lateralized readiness potential (LRP) and the motor potential (MP). In addition, the response (R) -locked approach has been adopted by studies aimed at investigating some post-movement, but still movement-related, activities like the re-afferent potential (RAP), the error- negativity (Ne) and the error-positivity (Pe) potentials. However, one of the limitations of this segmentation is that the ERP signal is time-locked to an individual-based (i.e., variable) event instead of a task-based (i.e., stable) one. The main consequence is that, when interested in the neural correlates of the performance, the ERP researcher can just look at the premotor cortical activities, neglecting the perceptual and cognitive processes that determine and "drive" the motor behavior. In fact, given the stimulus-to-response jitter, the stimulus-related (but still pre-movement) components reflecting the sensory processing (e.g., the visual P1 and N1), the cognitive task control (e.g., the N2) and the categorization process (the pP) are mostly

suppressed when signal is locked to the motor response. Accordingly, this latter will be investigated through features that are closely related to the premotor areas excitability, resulting in a biased view of the human action, approached like an "independent brain function". Moreover, it should be noted that just the responded trials make possible the R-locked approach: this means that no R-locked segmentations are possible in case of inhibited trials, making impossible the comparison between conditions in tasks like the present Go/No-go.

Differently from the R-locked approach, the stimulus (S) –locked segmentation has the advantages to enhance the stimulus-related activities, to set as time 0 a task-based event, and to be suitable for both responded and inhibited trials. However, it is noteworthy that in a typical decision-making task the premotor activities are mostly pre-stimulus. Nevertheless, the S-locked approaches usually take as baseline the 100 ms or 200 ms before the stimulus, aligning on the 0 μV all the preceding activities like the BP and pN. Accordingly, the pre-stimulus preparatory differences between trials or groups (like the BP modulation between fast vs. slow responders; e.g., Band et al., 2003) are hidden by this method.

In order to overcome the above reported limitations, some studies used to adopt both the R- and S-locked approaches: in this way, they get different results and reach more conclusions about the same data (see, e.g., Rinkenauer et al., 2004). From one side, this solution can solve some issues: in fact, it allows to enhance the movement-related activities by through the R-locked segmentation, and to identify the stimulus-related activities by through the S-locked segmentation. On the other hand, however, this "double-side" approach does not take into account the specific contribution of the pre-movement activities on the post-stimulus potentials.

In the studies of the present thesis, we proposed a new solution, that is to S-lock the ERP signal, and to extend the "left edge" of the epoch much more than usual: starting, for example, 1 sec before the stimulus onset. When allowed by the paradigm (i.e., if the inter-stimulus interval is large enough to avoid the trials overlap, and the baseline is not contaminated by previous-trial ERPs), this method give the chance to investigate both the pre- and post-stimulus activities, such as the contribution they play on each other, and on the motor

performance as well. This view is supported by all the studies described in this thesis, and especially by those of Chapters 3 and 6, revealing a strong relationship between the preparatory brain activities and the post-stimulus processing, such as between these activities and the behavioral performance. To better understand how the difference between pre-stimulus activities can modulate the post-stimulus potentials, the comparison between the "typical" and the here adopted (i.e., the larger) S-locked segmentation can be seen on the real data of Figure 7.1 (adapted from Perri et al., 2014).

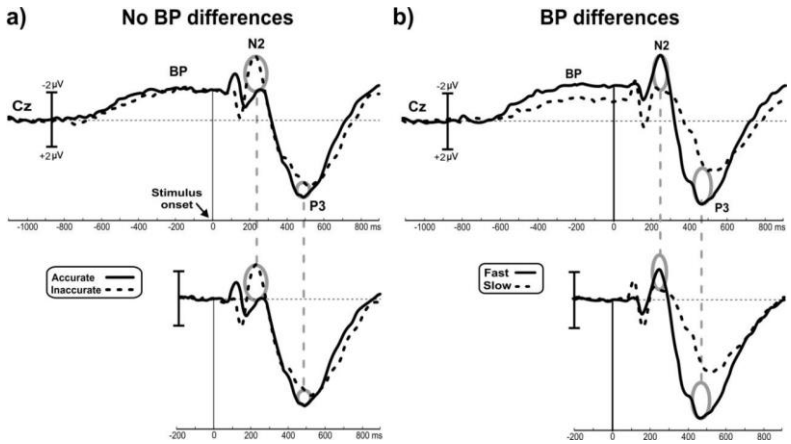

Fig. 7.1. Stimulus-locked ERP comparisons between groups of Go/No-go performers. The top figures show the large segmentation adopted in these studies, while in the bottom figures the "traditional" -200/0 ms baseline is adopted. The grey circles in the top figures mark the N2 and P3 peak-to-peak distance between groups. The same circles are superimposed on the bottom figures, revealing that a) if there are no BP differences, just the absolute ERP values are affected by the different baseline. At the opposite, b) if the BP differs between groups, both the absolute ERP values and the ERP modulation between groups are affected by the different baseline. Adapted from Perri et al. (2014)

Figure 7.1 suggests that in case of experimental paradigms requiring motor and/or cognitive preparation, the choice of where settle the S-locked baseline yield to two main consequences. 1) it modifies the absolute ERP values when the pre-stimulus activities are comparable between groups or conditions (Fig. 8a), and 2) it modifies both the absolute ERP values and the ERP modulations between groups when the differences emerge at pre-stimulus stage (Fig. 8b). Summarizing, since most of the post-stimulus activities still precede

the response execution, it would be useful to extend the signal analysis to the earlier stages of processing, so as to avoid to disentangle the stimulus-related activities from the concomitant cognitive and motor preparation.

7.2. Theoretical implications: the preparation-perception-action cycle.

The present studies confirm the view that the motor performance represent the outcome of different neuro-cognitive processes acting at different stages of processing. What is novel is that most of these processes can be well identified by the ERP technique too. In fact, one of the main limitations of the previous ERP studies is that most of them limited the investigation just to specific stages of processing, like the motor preparation or the error detection. Otherwise, studying the behavioral performance would require to investigate all the pre-response activities, in the different stages of processing (like the cognitive preparation, the sensory activity, the error detection and prevention, and so on). For this reason, in the present studies we tried to adopt an as eclectic as possible approach that looks at the modulation of the decision-making processes, such as at the relationship between each other in determining the final performance. This methodological approach, and the consequent "new way" to look at the data, has led us to conceptualize the so called "preparation-perception-action cycle". Before our group described this cycle the first time (Perri et al., 2014), it was already mentioned twice by Digiacomo et al. (2008) and Gómez et al. (2009). In its two papers, that group suggested that "the perception of a target stimulus is often preceded by a cue that creates expectations about the features and relevance of the target, and this leads to a more complex view of the perception–action cycle: there is a continuous expectancy bias for certain stimuli and actions, converting the former perception-action cycle into a preparation-perception-action cycle". The perception-action cycle they mentioned is referred to the continuous and reciprocal influences between sensation and movement within any given behavioral structure. In other words, this sensory-movement cycle underlines the link between the organism and its environment. Along the years the perception-action cycle has been given various names, as reviewed by

Fuster (1990): Weizsäcker (1950) called it the "Gestaltkreis" (gestalt cycle) and Neisser (1976) the "perception cycle", while Arbib (1981) called it the "action-perception cycle".

In our view, the "preparation-perception-action cycle" name comes from the need to summarize in the same concept the causality and the connection of the three macro processes (preparation, perception and action), such as the cyclical nature of their relationship. In fact, the action (here intended also as a cerebral activity, and not only as a peripheral event), does not represent just the end of a cycle, but also the beginning of a new one. Further, the action does not just trigger the next cycle, but it also affects its processing by through effects that act from the cycle preparation until the next action (see, for example, the post-error adjustments described in Chapter 5).

It should be noted that each of the three macro-processes consists of different micro processes, like the top-down control and the premotor activity in the preparation stage. Accordingly, the relationship between the micro processes of the macro processes needs to be considered too. In order to show all the macro and micro processes above mentioned, and to describe how they work together in making a decision, we summarized the findings of the present studies in a preliminary version of the ERP-based model of the preparation-perception-action cycle, as reported in Figure 7.2.

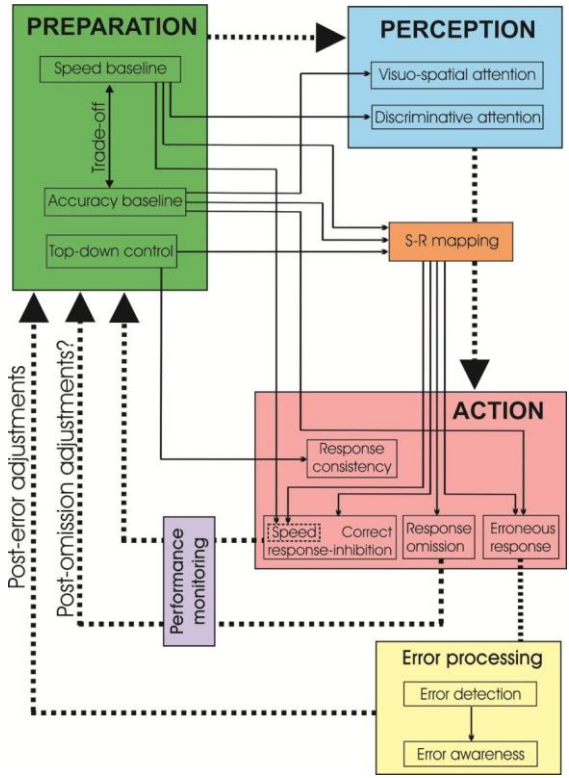

Fig. 7.2. ERP-based model of the preparation-perception-action cycle.

The neurocognitive model of Figure 7.2 is referred to the ERP-detectable processes of externally triggered visual tasks, and it consists of three main blocks reflecting the three macro processes of the preparation-perception-action cycle. The dashed arrows indicate the main order of communication between macro processes. However, they do not reflect a stringent temporal rule, but rather a basic sequence of processing. For example, it should be noted that the preparatory activities start before the perception stage, but they still work after stimulus is visually processed. On the other side, the solid arrows represent the main relationships between micro processes, as emerged in different studies (most of them are reported in the present thesis). Expect for the action block, each micro process reflects the main cognitive function of a single ERP component. The micro process-ERP couplings are reported below:

- Speed-baseline: the BP component over the central areas of the scalp.
- Accuracy-baseline: the right dorsolateral prefrontal negativity (rDLpN).
- Top-down control: the pN component.
- Visuo-spatial attention: the occipital P1 component.
- Discriminative attention: the occipital N1 component.
- Stimulus-response (S-R) mapping: the prefrontal positivity (pP) component.
- Performance monitoring: the P3 component.
- Error detection: the error-negativity (Ne) or error-related negativity (ERN) component.
- Error awareness: the error-positivity (Pe) component.

As regard the action block, each rectangle reflects the response performance as measured by specific behavioral indices. Specifically:

- Response consistency: measured by the intraindividual coefficient of variation (ICV) index.
- Correct response/inhibition: it reflects the correct responses to target stimuli, and the correct inhibition to non-target stimuli. In the former case, the speed (i.e., the response time) is measured too.
- Response omission: the percentage of erroneous inhibition to target stimuli.
- Erroneous response (or false alarm): the percentage of erroneous responses to non-target stimuli.

In the externally triggered tasks, the upcoming stimulus is attended and "prepared" before it appears. What is interesting is that most of the behavioral performance is already established at this early level of processing. In fact, the speed baseline, that is the premotor areas excitability marked by the BP component, is directly associated to the response speed: higher the BP, faster the response (Band et al., 2003). This relationship emerges at both group (i.e., trait-dependent; Perri et al., 2014) and trial-by-trial level (i.e., state-dependent; see Chapter 5), and is neurophysiologically explained by the fact that the larger SMA activity contributes to overcome the tonic inhibition provided by the output nuclei of basal ganglia (Lo and Wang, 2006). Before stimulus appears, the accuracy-baseline is settled too: in Perri et al. (2014) study,

we found that the excitability level of the right frontal cortex marks the accuracy performance between groups of accurate vs. inaccurate participants, showing strong correlations with the percentage of erroneous responses. However, since this relationship does not survive at trial-by-trial level (Perri et al., 2015a), it has to be considered as a "trait disposition index" in performing the task, rather than a trial-based predictor of performance. It should also be noted that the speed and accuracy baselines reflect the activity of different but interacting systems (Perri et al., 2014), as revealed by the typical speed-accuracy tradeoff (SAT; for a review see Bogacz et al., 2010), and by the relative independence between the two systems at both behavioral and electrocortical level.

Obviously, the behavioral performance is not just determined by the speed and accuracy level of activity in the respective neural systems, but it is also influenced by the attentional engagement in performing the task. In fact, it has been shown that the lapses of attention might affect the response in terms of increased variability or, in other words, less consistent performance (e.g, Weissman et al., 2006). At ERP level, we described the pN component as the electrocortical marker of the preparatory top-down control (Di Russo et al., 2013; Berchicci et al., 2014), which in turn is associated to the response consistency (i.e., larger the pN, more consistent the performance; Perri et al., 2015b). The above mentioned relationships between pre-stimulus processing and behavioral performance are represented in the model by the solid arrows linking the speed-baseline, the accuracy-baseline, and the top-down control to the speed, the erroneous response, and the response consistency, respectively. It should be noted that the links between preparation processes and action performance are based on findings that showed a direct (i.e., no perception-mediated) relationship between them. However, the preparation-action link is not always (or not necessarily) direct, but it might also be mediated by the perception stage, such as by the S-R mapping process. In fact, as can be seen in Figure 7.2, the speed-baseline and the accuracy-baseline are also linked to the discriminative attention (N1 component) and the visuo-spatial attention (P1 component), respectively: in other words, more fast and accurate was the performance, larger the P1 and the N1 components, respectively (Perri et al., 2014). These last relationships reflect a key role of the pre-

stimulus activities in modulating the sensory processing, which in turn might be associated to the behavioral performance (e.g., Weissman et al., 2006).

All the micro processes of the preparation stage are linked to the S-R mapping process, electrophysiologically marked by the pP component, also labeled as Go-P2 (Gajewski and Falkenstein, 2013), anterior P2 (P2a; Potts et al., 2004), frontal selection positivity (FSP; Kenemans et al., 1993) and frontal P3 (P3f; Makeig et al., 1999). Since the pP reflects the anterior insula-mediated process of categorization oriented to making a decision (Di Russo et al., 2016; Perri et al., 2014, 2015a), it has to be considered as the "linking process" between perception and action. This is the reason why the S-R mapping is graphically represented outside the three main blocks, but in the middle between the perception and the action stages.

The pP represents a categorization-oriented process: in fact, no pP is detectable in self-paced or simple response tasks where no stimulus categorization is required. At the opposite, the categorization demand evokes larger pP after the target than non-target stimuli, and this component reaches the maximum amplitude at 300-350 ms after the stimulus, corresponding to about 100 ms before the response in our Go/No-go paradigm. There are two main parameters to consider when analyzing the pP component: the latency and the amplitude. The former is associated to the speed of the decision process, while the last reflects its efficiency. In the present studies we found that the comparison between fast and slow subjects was the only one able to reveal a pP latency difference (Perri et al., 2014). In fact, in that study the pP started earlier in the fast than slow group, explaining about the 60% of the RT difference between the two groups. Also, the pP was larger in both fast and accurate groups than their respective counterparts (i.e., slow and inaccurate), suggesting that its amplitude reflects the efficiency of the decision process in both speed and accuracy systems.

In the study of Chapter 6 we found that the omission error is associated to the suppression of the pP component, which in turn is associated to the delayed onset of the pN component reflecting the top-down control. This observation led us to conclude that a severe lapse of attention in the preparatory stage might compromise the S-R mapping process, making impossible to accomplish the cognitive

demanding request of stimulus categorization. An important implication is the relationship between the efficiency of the S-R mapping process and the duration of the preparatory processing. In fact, while the pN amplitude modulations did not affect the pP component (Berchicci et al., 2014; Perri et al., 2014, 2015b), the onset delay of the pN did not allow the pP to start and raise up.

Summarizing, most of the behavioral indices of performance (expect for the response consistency) are modulated by the pP component. Indeed, also the erroneous response to non-target stimuli (i.e., the false alarm) represents the outcome of the erroneous S-R mapping processing (Perri et al., 2015a). In other words, while the trait disposition in being more or less accurate might be predicted by the pre-stimulus accuracy baseline, the cause of error commission is entirely explained by the S-R mapping efficacy at trial level.

After the motor response is correctly emitted or inhibited, or the response is omitted, the P3 component (corresponding to the performance monitoring process in the model of Fig. 9) can be detected over the centro-parietal areas of the scalp. Since the P3 represents a very heterogeneous component, and it is out of the main focus of the present thesis, no condition-related details will be discussed here. However, more information can be read in the previous chapters. What is important to state here is that the P3 is a basically attention-mediated component emerging after anytime a stimulus is processed: the P3 might be affected by several cognitive and biological factors like, for example, stimulus frequency and relevance, arousal state, motivation, age, drugs and exercise (for a review see Polich and Kok, 1995).

Basically, after the response is emitted or inhibited, a new cycle begins starting from the "first" macro process: the preparation. Therefore, as previously stated, in a decision making task consisting in the continuous trials presentation, the action represents both the end of a cycle and the trigger of a new one. In fact, depending on its performance, the action might also influence the nature of the next preparation (and action) as revealed for example by the post-error adjustments (see Chapter 5).

Error commission is followed by ERP activities reflecting the error detection and error awareness processes (the Ne and Pe components respectively; see Chapter 4) while, at behavioral level, the post-error

slowing (PES) and the post-error improvement in accuracy (PIA) are usually observed in the next trial (for a review see Danielmeier and Ullsperger, 2011). What is interesting is that we were able to identify the preparatory ERP activities subtending the post-error behavioral adjustments. These neural mechanisms are an excellent example of how the action might influence the subsequent trial preparation. In fact, we found that the PES and the PIA are respectively explained by the reduced activity of the premotor baseline (i.e., reduced BP, especially on the left hemisphere) and by the increased top-down and proactive inhibitory control (i.e., enhanced pN, especially on the right hemisphere) in the post-error trials. The post-error neural adjustments are reported in the model of Figure 7.2 showing that after error is processed, the preparation of the new cycle is influenced by the adjustments mechanisms oriented to the second error prevention. On the other hand, because of the lack of literature, we still do not know if the omission error is followed by some kind of adjustment too. For this reason, we just reported the possibility of the post-omission adjustments in the model (i.e., it is followed by the "?"), postponing the answer in a future study.

Concluding, present findings underline the importance of considering the human action as the result of neurocognitive processes acting long before the movement execution. From a theoretical perspective, this point might be considered as trivial or obvious. However, the main risk for the experimental neuroscience is to focus just on limited aspects of motor execution, neglecting the rich complex of processes around it. The EEG researchers are probably the most exposed to that risk; in fact, while the neuroimaging techniques "force" the need to look at different brain areas, the EEG users sometimes establish the number and position of the scalp-electrodes on the basis of a priori, goal-based, decision. Further, although the EEG high-temporal resolution, the ERP investigators might adopt signal analysis strategies that overshadow some important information coming from other stages of processing (for more details, see previous section).

The above presented ERP-based model of the preparation-perception-action cycle should stress the need to consider, at theoretical but especially at empirical experimental level, the human action as the final point of a cascade of processes that prearrange and

"build" the response before it is consciously driven. By this approach, it is possible to considerably increase the ERP contribution to the neurocognitive research, especially in the field of the human-environment interaction.

References

Arbib, M. A. (1981). Perceptual structures and distributed motor control. Comprehensive Physiology.

Aron, A. R. (2011). From reactive to proactive and selective control: developing a richer model for stopping inappropriate responses. Biological psychiatry, 69(12), e55-e68.

Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J., & Poldrack, R. A. (2007). Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. The Journal of Neuroscience, 27(14), 3743-3752.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in cognitive sciences, 8(4), 170-177.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. Trends in cognitive sciences, 18(4), 177-185.

Baddeley, A., & Wilson, B. (1988). Frontal amnesia and the dysexecutive syndrome. Brain and cognition, 7(2), 212-230.

Band, G. P., Ridderinkhof, K. R., & van der Molen, M. W. (2003). Speed-accuracy modulation in case of conflict: the roles of activation and inhibition. Psychological research, 67(4), 266-279.

Barkley, R. A., Grodzinsky, G., & DuPaul, G. J. (1992). Frontal lobe functions in attention deficit disorder with and without hyperactivity: A review and research report. Journal of abnormal child psychology, 20(2), 163-188.

Baumgartner, T., Willi, M., & Jäncke, L. (2007). Modulation of corticospinal activity by strong emotions evoked by pictures and classical music: a transcranial magnetic stimulation study. Neuroreport, 18(3), 261-265.

Bellgrove, M. A., Hester, R., & Garavan, H. (2004). The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. Neuropsychologia, 42(14), 1910-1916.

Berchicci, M., Lucci, G., Perri, R. L., Spinelli, D., & Di Russo, F. (2014). Benefits of physical exercise on basic visuo-motor functions across age. Frontiers in aging neuroscience, 6.

Bogacz, R., Wagenmakers, E. J., Forstmann, B. U., & Nieuwenhuis, S. (2010). The neural basis of the speed–accuracy tradeoff. Trends in neurosciences, 33(1), 10-16.

Braver, T. S., & Barch, D. M. (2006). Extracting core components of cognitive control. Trends in cognitive sciences, 10(12), 529-532.

Bunce, D., Anstey, K. J., Christensen, H., Dear, K., Wen, W., & Sachdev, P. (2007). White matter hyperintensities and within-person variability in community-dwelling adults aged 60–64 years. Neuropsychologia, 45(9), 2009-2015.

Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. Science, 280(5364), 747-749.

Chatrian, G. E., Petersen, M. C., & Lazarte, J. A. (1959). The blocking of the rolandic wicket rhythm and some central changes related to movement. Electroencephalography and clinical neurophysiology, 11(3), 497-510.

Chen, M., & Bargh, J. A. (1999). Consequences of automatic evaluation: Immediate behavioral predispositions to approach or avoid the stimulus. Personality and Social Psychology Bulletin, 25(2), 215-224.

Cheney, P. D. (1985). Role of Cerebral Cortex in Voluntary Movements A Review. Physical therapy, 65(5), 624-635.

Coombes, S. A., Cauraugh, J. H., & Janelle, C. M. (2007). Emotional state and initiating cue alter central and peripheral motor processes. Emotion, 7(2), 275.

Coombes, S. A., Gamble, K. M., Cauraugh, J. H., & Janelle, C. M. (2008). Emotional states alter force control during a feedback occluded motor task. Emotion, 8(1), 104.

Coombes, S. A., Tandonnet, C., Fujiyama, H., Janelle, C. M., Cauraugh, J. H., & Summers, J. J. (2009). Emotion and motor preparation: a transcranial magnetic stimulation study of corticospinal motor tract excitability. Cognitive, Affective, & Behavioral Neuroscience, 9(4), 380-388.

Cummings, J. L. (1993). Frontal-subcortical circuits and human behavior. Archives of neurology, 50(8), 873-880.

Cunnington, R., Bradshaw, J. L., & Iansek, R. (1996). The role of the supplementary motor area in the control of voluntary movement. Human Movement Science, 15(5), 627-647.

Damasio, H., Grabowski, T., Frank, R., Galaburda, A. M., & Damasio, A. R. (1994). The return of Phineas Gage: clues about the brain from the skull of a famous patient. Science, 264(5162), 1102-1105.

Danielmeier, C., & Ullsperger, M. (2011). Post-error adjustments. Frontiers in Psychology, 2, 233.

Deecke, L., Lang, W., Heller, H. J., Hufnagl, M., & Kornhuber, H. H. (1987). Bereitschaftspotential in patients with unilateral lesions of the supplementary motor area. Journal of Neurology, Neurosurgery & Psychiatry, 50(11), 1430-1434.

Desmurget, M., & Grafton, S. (2000). Forward modeling allows feedback control for fast reaching movements. Trends in cognitive sciences, 4(11), 423-431.

Desmurget, M., & Sirigu, A. (2012). Conscious motor intention emerges in the inferior parietal lobule. Current opinion in neurobiology, 22(6), 1004-1011.

Digiacomo, M. R., Marco-Pallarés, J., Flores, A. B., & Gómez, C. M. (2008). Wavelet analysis of the EEG during the neurocognitive evaluation of invalidly cued targets. Brain research, 1234, 94-103.

Di Russo, F., Martínez, A., & Hillyard, S. A. (2003). Source analysis of event-related cortical activity during visuo-spatial attention. Cerebral cortex, 13(5), 486-499.

Di Russo, F., Pitzalis, S., Aprile, T., & Spinelli, D. (2005). Effect of practice on brain activity: an investigation in top-level rifle shooters. Medicine and science in sports and exercise, 37(9), 1586.

Di Russo, F., Berchicci, M., Perri, R. L., Ripani, F. R., & Ripani, M. (2013). A passive exoskeleton can push your life up: application on multiple sclerosis patients. PLoS ONE, 8, e77348.

Dosenbach, N. U., Visscher, K. M., Palmer, E. D., Miezin, F. M., Wenger, K. K., Kang, H. C., ... & Petersen, S. E. (2006). A core system for the implementation of task sets. Neuron, 50(5), 799-812.

Evarts, E. V. (1968). Relation of pyramidal tract activity to force exerted during voluntary movement. J Neurophysiol, 31(1), 14-27.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components. II. Error processing in choice reaction tasks. Electroencephalography and clinical neurophysiology,78(6), 447-455.

Falkenstein, M., Hoormann, J., & Hohnsbein, J. (2002). Inhibition-related ERP components: Variation with modality, age, and time-on-task. Journal of Psychophysiology, 16(3), 167.

Ferreira, C. T., Verin, M., Pillon, B., Levy, R., Dubois, B., & Agid, Y. (1998). Spatio-temporal working memory and frontal lesions in man. Cortex, 34(1), 83-98.

Ferrier, D (1874). Experiments on the brain of monkeys - No. 1. Proc. R. Soc. Lond23 (156–163): 409–430

Ferrier, D. (1886). The functions of the brain. Smith, Elder.

Flehmig, H. C., Steinborn, M. B., Westhoff, K., & Langner, R. (2010). Neuroticism and speed-accuracy tradeoff in self-paced speeded mental addition and comparison. Journal of Individual Differences, 31(3), 130.

Folstein, J. R., & Van Petten, C. (2008). Influence of cognitive control and mismatch on the N2 component of the ERP: a review. Psychophysiology,45(1), 152-170.

Forstmann, B. U., Dutilh, G., Brown, S., Neumann, J., Von Cramon, D. Y., Ridderinkhof, K. R., & Wagenmakers, E. J. (2008). Striatum and pre-SMA facilitate decision-making under time pressure. Proceedings of the National Academy of Sciences, 105(45), 17538-17542.

Frijda, N. H., Kuipers, P., & Ter Schure, E. (1989). Relations among emotion, appraisal, and emotional action readiness. Journal of personality and social psychology, 57(2), 212.

Fritsch, G and Hitzig, E (1870). Über die elektrische Erregbarkeit des Grosshirns. Arch. f. Anatomische, Physiologische, und Wissenschaftliche Medizin: 300–332. Translated in:von Bonin, G., ed. (1960). Some Papers on the Cerebral Cortex. Springfield IL: Charles Thomas. pp. 73–96.

Fuster, J. M. (1990). Prefrontal cortex and the bridging of temporal gaps in the perception action cycle. Annals of the New York Academy of Sciences, 608 (1), 318-336.

Fuster, J. M. (2001). The prefrontal cortex—an update: time is of the essence. Neuron, 30(2), 319-333.

Gajewski, P. D., & Falkenstein, M. (2013). Effects of task complexity on ERP components in Go/Nogo tasks. International Journal of Psychophysiology, 87(3), 273-278.

Gehring, W. J., & Knight, R. T. (2000). Prefrontal–cingulate interactions in action monitoring. Nature neuroscience, 3(5), 516-520.

Gehring, W. J., Goss, B., Coles, M. G., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. Psychological science, 4(6), 385-390.

Ghez, C. (1991). Voluntary movement. Principles of neural science, 3, 622-624.

Gómez, C. M., Flores, A., Digiacomo, M. R., & Vázquez-Marrufo, M. (2009). Sequential P3 effects in a Posner's spatial cueing paradigm: Trial-by-trial learning of the predictive value of the cue. Acta neurobiologiae experimentalis, 69(2), 155-167.

Hallett, M. (2007). Volitional control of movement: the physiology of free will. Clinical Neurophysiology, 118(6), 1179-1192.

Harmon-Jones, E., Lueck, L., Fearn, M., & Harmon-Jones, C. (2006). The effect of personal relevance and approach-related action expectation on relative left frontal cortical activity. Psychological Science, 17(5), 434-440.

Hart, S. J., Lucena, N., Cleary, K. M., Belger, A., & Donkers, F. C. (2012). Modulation of early and late event-related potentials by emotion. Frontiers in integrative neuroscience, 6.

Hopf, J. M., Vogel, E., Woodman, G., Heinze, H. J., & Luck, S. J. (2002). Localizing visual discrimination processes in time and space. Journal of Neurophysiology, 88(4), 2088-2095.

Hultsch, D. F., MacDonald, S. W., & Dixon, R. A. (2002). Variability in reaction time performance of younger and older adults. The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 57(2), P101-P115.

Iacoboni, M., Woods, R. P., & Mazziotta, J. C. (1996). Brain-behavior relationships: evidence from practice effects in spatial stimulus-response compatibility. Journal of Neurophysiology, 76(1), 321-331.

Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. PLoS one, 3(7), e2635.

Jaffard, M., Longcamp, M., Velay, J. L., Anton, J. L., Roth, M., Nazarian, B., & Boulinguez, P. (2008). Proactive inhibitory control of movement assessed by event-related fMRI. Neuroimage, 42(3), 1196-1206.

Jahanshahi, M., Dirnberger, G., Liasis, A., Towell, A., & Boyd, S. (2001). Does the pre-frontal cortex contribute to movement-related potentials? Recordings from subdural electrodes. Neurocase, 7(6), 495-501.

Jones, E. G., Coulter, J. D., & Hendry, S. H. C. (1978). Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. Journal of Comparative Neurology, 181(2), 291-347.

Kenemans, J. L., Kok, A., & Smulders, F. T. Y. (1993). Event-related potentials to conjunctions of spatial frequency and orientation as a function of stimulus parameters and response requirements. Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 88(1), 51-63.

Karni A, Meyer G, Jezzard P, Adams MM, Turner R, Ungerlieder LG. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Nature, 377, 155-158.

Kim, S., & Lee, D. (2011). Prefrontal cortex and impulsive decision making. Biological psychiatry, 69(12), 1140-1146.

Kornhuber, H. H., & Deecke, L. (1965). Hirnpotentialänderungen bei Willkürbewegungen und passiven Bewegungen des Menschen: Bereitschaftspotential und reafferente Potentiale. Pflüger's Archiv für die gesamte Physiologie des Menschen und der Tiere, 284(1), 1-17.

Krakauer, J., & Ghez, C. (2000). Voluntary movement. Principles of neural science, 4, 756-781.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1998). Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. Biological psychiatry, 44(12), 1248-1263.

Laplane, D., Talairach, J., Meininger, V., Bancaud, J., & Orgogozo, J. M. (1977). Clinical consequences of corticectomies involving the supplementary motor area in man. Journal of the neurological sciences, 34(3), 301-314.

Libet, B., Gleason, C. A., Wright, E. W., & Pearl, D. K. (1983). Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). Brain, 106(3), 623-642.

Lo, C. C., & Wang, X. J. (2006). Cortico–basal ganglia circuit mechanism for a decision threshold in reaction time tasks. Nature neuroscience, 9(7), 956-963.

Luck, S. J., Heinze, H. J., Mangun, G. R., & Hillyard, S. A. (1990). Visual event-related potentials index focused attention within bilateral stimulus arrays. II. Functional dissociation of P1 and N1 components. Electroencephalography and clinical neurophysiology, 75(6), 528-542.

Luria, A. R. (1966). Higher cortical functions in man.

Lynch, J. C., Mountcastle, V. B., Talbot, W. H., & Yin, T. C. (1977). Parietal lobe mechanisms for directed visual attention. Journal of Neurophysiology,40(2), 362-389.

Makeig, S., Westerfield, M., Jung, T. P., Covington, J., Townsend, J., Sejnowski, T. J., & Courchesne, E. (1999). Functionally independent components of the late positive event-related potential during visual spatial attention. The journal of neuroscience, 19(7), 2665-2680.

Marsh, A. A., Ambady, N., & Kleck, R. E. (2005). The effects of fear and anger facial expressions on approach-and avoidance-related behaviors. Emotion, 5(1), 119.

Martinez, A., Anllo-Vento, L., Sereno, M. I., Frank, L. R., Buxton, R. B., Dubowitz, D. J., ... & Hillyard, S. A. (1999). Involvement of striate and extrastriate visual cortical areas in spatial attention. Nature neuroscience, 2(4), 364-369.

McAdam, D. W., & Seales, D. M. (1969). Bereitschaftspotential enhancement with increased level of motivation. Electroencephalography and Clinical Neurophysiology, 27(1), 73-75.

Mercado, F., Hinojosa, J.A., Peñacoba, C., and Carretiè , L. (2007).“The emotional S1-S2 paradigm for exploring brain mechanisms underlying affective modulation of expectancy,” in Brain Mapping Research Developments, ed L.N. Bakker (Hauppauge, NY:Nova Science Publishers),197–209.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. Annual review of neuroscience, 24(1), 167-202.

Naugle, K. M., Hass, C. J., Joyner, J., Coombes, S. A., & Janelle, C. M. (2011). Emotional state affects the initiation of forward gait. Emotion, 11(2), 267.

Neisser, U. (1976). Cognition and reality: Principles and implications of cognitive psychology. WH Freeman/Times Books/Henry Holt & Co.

Nesselroade, J. R. (2002). Elaborating the differential in differential psychology. Multivariate Behavioral Research, 37(4), 543-561.

Neubert, F. X., Mars, R. B., & Rushworth, M. F. (2013). Is there an inferior frontal cortical network for cognitive control and inhibition?. Principles of frontal lobe function, 332-352.

Neuper, C., & Pfurtscheller, G. (2001). Evidence for distinct beta resonance frequencies in human EEG related to specific sensorimotor cortical areas. Clinical Neurophysiology, 112(11), 2084-2097.

Nieuwenhuis, S., Yeung, N., Van Den Wildenberg, W., & Ridderinkhof, K. R. (2003). Electrophysiological correlates of anterior cingulate function in a go/no-go task: effects of response conflict and trial type frequency. Cognitive, Affective, & Behavioral Neuroscience, 3(1), 17-26.

Oathes, D. J., Bruce, J. M., & Nitschke, J. B. (2008). Worry facilitates corticospinal motor response to transcranial magnetic stimulation. Depression and anxiety, 25(11), 969-976.

Oliveri, M., Babiloni, C., Filippi, M. M., Caltagirone, C., Babiloni, F., Cicinelli, P., ... & Rossini, P. M. (2003). Influence of the supplementary motor area on primary motor cortex excitability during movements triggered by neutral or emotionally unpleasant visual cues. Experimental brain research, 149(2), 214-221.

Paus, T., Petrides, M., Evans, A. C., & Meyer, E. (1993). Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. Journal of neurophysiology,70(2), 453-469.

Penfield, W., & Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain: A journal of neurology.

Perri, R. L., Berchicci, M., Spinelli, D., & Di Russo, F. (2014). Individual Differences in Response Speed and Accuracy are Associated to Specific Brain Activities of two Interacting Systems. Frontiers in Behavioral Neuroscience, 8, 251.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015a). Why do we make mistakes? Neurocognitive processes during the preparation-perception-action cycle and error-detection. Neuroimage, 113, 320-328.

Perri, R.L., Berchicci, M., Lucci, G., Spinelli, D., Di Russo, F. (2015b). The Premotor Role of the Prefrontal Cortex in Response Consistency. Neuropsychology, 29 (5), 767-775.

Petersen, S. E., Van Mier, H., Fiez, J. A., & Raichle, M. E. (1998). The effects of practice on the functional anatomy of task performance. Proceedings of the National Academy of Sciences, 95(3), 853-860.

Petrides, M., & Pandya, D. N. (1984). Projections to the frontal cortex from the posterior parietal region in the rhesus monkey. Journal of Comparative Neurology, 228(1), 105-116.

Polich, J., & Kok, A. (1995). Cognitive and biological determinants of P300: an integrative review. Biological psychology, 41(2), 103-146.

Pfurtscheller, G. (1981). Central beta rhythm during sensorimotor activities in man. Electroencephalography and clinical neurophysiology, 51(3), 253-264.

Pfurtscheller, G. (1981). Central beta rhythm during sensorimotor activities in man. Electroencephalography and clinical neurophysiology, 51(3), 253-264.

Pfurtscheller, G. (1992). Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. Electroencephalography and clinical neurophysiology, 83(1), 62-69.

Pfurtscheller, G. (1992). Event-related synchronization (ERS): an electrophysiological correlate of cortical areas at rest. Electroencephalography and clinical neurophysiology, 83(1), 62-69.

Pfurtscheller, G., & Aranibar, A. (1979). Evaluation of event-related desynchronization (ERD) preceding and following voluntary self-paced

movement. Electroencephalography and clinical neurophysiology, 46(2), 138-146.

Pfurtscheller, G., & Aranibar, A. (1979). Evaluation of event-related desynchronization (ERD) preceding and following voluntary self-paced movement. Electroencephalography and clinical neurophysiology, 46(2), 138-146.

Pochon, J. B., Levy, R., Poline, J. B., Crozier, S., Lehéricy, S., Pillon, B., ... & Dubois, B. (2001). The role of dorsolateral prefrontal cortex in the preparation of forthcoming actions: an fMRI study. Cerebral Cortex, 11(3), 260-266.

Polich, J., & Kok, A. (1995). Cognitive and biological determinants of P300: an integrative review. Biological psychology, 41(2), 103-146.

Posner, M. I., & Petersen, S. E. (1989). The attention system of the human brain (No. TR-89-1). WASHINGTON UNIV ST LOUIS MO DEPT OF NEUROLOGY.

Potts, G. F. (2004). An ERP index of task relevance evaluation of visual stimuli. Brain and Cognition, 56(1), 5-13.

Praamstra, P., Stegeman, D. F., Cools, A. R., & Horstink, M. W. (1998). Reliance on external cues for movement initiation in Parkinson's disease. Evidence from movement-related potentials. Brain, 121(1), 167-177.

Ratcliff, R. (1978). A theory of memory retrieval. Psychological review, 85(2), 59.

Rinkenauer, G., Osman, A., Ulrich, R., Müller-Gethmann, H., & Mattes, S. (2004). On the locus of speed-accuracy trade-off in reaction time: inferences from the lateralized readiness potential. Journal of Experimental Psychology: General, 133(2), 261.

Roland, P. E., Larsen, B., Lassen, N. A., & Skinhoj, E. (1980). Supplementary motor area and other cortical areas in organization of voluntary movements in man. Journal of neurophysiology, 43(1), 118-136.

Rotteveel, M., & Phaf, R. H. (2004). Automatic affective evaluation does not automatically predispose for arm flexion and extension. Emotion, 4(2), 156.

Saito, N., Mushiake, H., Sakamoto, K., Itoyama, Y., & Tanji, J. (2005). Representation of immediate and final behavioral goals in the monkey prefrontal cortex during an instructed delay period. Cerebral Cortex, 15(10), 1535-1546.

Sanes, J. N., Suner, S., & Donoghue, J. P. (1990). Dynamic organization of primary motor cortex output to target muscles in adult rats I. Long-term patterns of reorganization following motor or mixed peripheral nerve lesions. Experimental Brain Research, 79(3), 479-491.

Sangals, J., Sommer, W., & Leuthold, H. (2002). Influences of presentation mode and time pressure on the utilisation of advance information in response preparation. Acta Psychologica, 109(1), 1-24.

Saville, C. W., Dean, R. O., Daley, D., Intriligator, J., Boehm, S., Feige, B., & Klein, C. (2011). Electrocortical correlates of intra-subject variability in

reaction times: Average and single-trial analyses. Biological psychology, 87(1), 74-83.

Shibasaki, H., & Hallett, M. (2006). What is the Bereitschaftspotential?. Clinical Neurophysiology, 117(11), 2341-2356

Stancák Jr, A., & Pfurtscheller, G. (1996). Mu-rhythm changes in brisk and slow self-paced finger movements. Neuroreport, 7(6), 1161-1164.

Stephan, K. M., Fink, G. R., Passingham, R. E., Silbersweig, D., Ceballos-Baumann, A. O., Frith, C. D., & Frackowiak, R. S. (1995). Functional anatomy of the mental representation of upper extremity movements in healthy subjects. Journal of neurophysiology, 73(1), 373-386.

Takakusaki, K., Habaguchi, T., Ohtinata-Sugimoto, J., Saitoh, K., & Sakamoto, T. (2003). Basal ganglia efferents to the brainstem centers controlling postural muscle tone and locomotion: a new concept for understanding motor disorders in basal ganglia dysfunction. Neuroscience, 119(1), 293-308.

Takeuchi, S., Mochizuki, Y., Masaki, H., Takasawa, N., & Yamazaki, K. (2005, March). Stimulus preceding negativity represents arousal induced by affective picture. In International Congress Series (Vol. 1278, pp. 385-388). Elsevier.

Tanji, J. (1994). The supplementary motor area in the cerebral cortex. Neuroscience research, 19(3), 251-268.

Tanji, J. (1996). New concepts of the supplementary motor area. Current opinion in neurobiology, 6(6), 782-787.

Tanji, J., & Kurata, K. I. Y. O. S. H. I. (1985). Contrasting neuronal activity in supplementary and precentral motor cortex of monkeys. I. Responses to instructions determining motor responses to forthcoming signals of different modalities. J Neurophysiol, 53(1), 129-141.

Taylor, M. J. (2002). Non-spatial attentional effects on P1. Clinical neurophysiology, 113(12), 1903-1908.

Tokuno, H., Kimura, M., & Tanji, J. (1992). Pallidal inputs to thalamocortical neurons projecting to the supplementary motor area: an anterograde and retrograde double labeling study in the macaque monkey. Experimental brain research, 90(3), 635-638.

van Boxtel, G. J., van der Molen, M. W., Jennings, J. R., &Brunia, C. H. (2001). A psychophysiological analysis of inhibitory motor control in the stop-signal paradigm. Biological Psychology, 58, 229–262.

van Veen, V., Krug, M. K., & Carter, C. S. (2008). The neural and computational basis of controlled speed-accuracy tradeoff during task performance. Journal of Cognitive Neuroscience, 20(11), 1952-1965.

Verfaellie, M., & Heilman, K. M. (1987). Response preparation and response inhibition after lesions of the medial frontal lobe. Archives of Neurology, 44(12), 1265-1271.

Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. Nature neuroscience, 9(7), 971-978.

Weizsäcker, V. (1950). Funktionswandel und Gestaltkreis. Journal of Neurology, 164(1), 43-53.

Wenzlaff, H., Bauer, M., Maess, B., & Heekeren, H. R. (2011). Neural characterization of the speed–accuracy tradeoff in a perceptual decision-making task. The Journal of Neuroscience, 31(4), 1254-1266.

Wiese, H., Stude, P., Nebel, K., Osenberg, D., Völzke, V., Ischebeck, W., ... & Keidel, M. (2004). Impaired movement-related potentials in acute frontal traumatic brain injury. Clinical Neurophysiology, 115(2), 289-298.

Wiesendanger, M. (1981). Organization of secondary motor areas of cerebral cortex. Comprehensive Physiology.

Williams, B. R., Hultsch, D. F., Strauss, E. H., Hunter, M. A., & Tannock, R. (2005). Inconsistency in reaction time across the life span. Neuropsychology, 19(1), 88.

Wright, D. J., Holmes, P., Di Russo, F., Loporto, M., & Smith, D. (2012). Reduced motor cortex activity during movement preparation following a period of motor skill practice. PloS one, 7(12), e51886.

Yeung, N., Botvinick, M. M., & Cohen, J. D. (2004). The neural basis of error detection: conflict monitoring and the error-related negativity. Psychological review, 111(4), 931.

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ISBN 978-88-9377-138-2

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