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Neural Correlates of Intentional Actions

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Chapter 1

Introduction

An essential characteristic of human behavior is the ability to act out of intrinsic motivation to achieve desired goals. These kinds of actions have been denoted in the scientific literature as intentional, voluntary, willed, or internally guided. They contrast with actions that are performed in response to external stimuli.

Despite the importance of voluntary actions for human behavior, psychological research for a long time focused its efforts on actions that are guided by environmental cues (i.e., externally guided or stimulus-based actions).

Although this fact is mainly due to the influence of ‘behaviorism’, another reason for this imbalance in action research is the difficulty to study intentional actions experimentally. This latter point may be simply due to the fact that it is not easy to ‘measure’ an action that is independent of any external stimulation, such that the classical index ‘reaction time’ cannot be used.

In general, contemporary research on voluntary actions is interdisciplinarily motivated. For example, there has always been a philosophical interest in voluntary actions with emphasis on the question whether or not humans have free will. It has been suggested that the experience of free will is only a subjective by-product of acting and not more than an illusion (Wegner, 2003; Prinz, 2004). However, the focus of this thesis is not on the existence of free will although there is some overlap with the concept of intentional actions.

To get a deeper understanding of intentional actions, recent research has begun to explore the functional and neurophysiological underpinnings of internally guided actions and how they differ from externally guided actions. However, contrasting the two types of actions necessitates that the two experimental conditions differ only with respect to the action mode and not with respect to the kinematics of the action, its

timing, and/or its sensorimotor context. In many of the recent functional magnetic resonance imaging (fMRI) studies this was not the case, resulting in inconsistent and contradictory patterns of results.

Nevertheless, the general conclusion one can draw from these studies is that the two action modes differ with respect to their neural and behavioral correlates. Most importantly in the present context, functional neuroimaging as well as lesion studies point to a crucial role of the frontomedian cortex in intentional action control.

The aim of the present thesis is to further specify the role of the frontomedian cortex in intentional action control. Study 1 compares internally guided actions to externally guided actions using a paradigm that does not confound perceptual, motorical, or attentional factors. In particular, using fMRI, it focuses on the functional role of two substructures of the frontomedian wall, viz. the rostral cingulate zone (RCZ) and the presupplementary motor area (preSMA). Study 2 aims at answering the question of whether two different components of intentional action (*what* and *when*) can be dissociated at the functional neuroanatomical level.

In the following, I will briefly describe the theoretical background underlying the present thesis. The first chapter gives a definition of what is usually subsumed under the concept of intentional action (Chapter 1.1). Chapter 1.2 describes the neuroanatomical substrates involved in intentional actions. Chapter 1.3 is about the clinical consequences of an impaired willed action system. Thereafter, I will give an overview of behavioral, electroencephalographic (EEG) and fMRI research on intentional actions (Chapter 1.4 and 1.5). Chapter 1.6 describes the experimental approach and research questions of the present thesis. In Chapter 1.7 the main findings and conclusions from the two studies are summarized. Finally, Chapter 1.8 addresses some shortcomings and future prospects related to research on intentional actions.

1.1 Defining intentional actions

Even though everyone is familiar with the concept of intentional, willed actions, it is difficult to give a proper scientific definition of what exactly constitutes intentional actions. William James (1890/1950) addresses this problem in his principles of psychology in the chapter about the will, with the often-cited opening sentence:

Desire, wish, will, are states of mind which everyone knows, and which no definition can make plainer. [...] (James, 1890,1950, p. 486).

James thereafter tries to make clearer what is meant by intentional actions by contrasting them with automatic or reflex actions. He argues that the latter kinds of actions are unforeseen by the agent. Voluntary actions, in contrast, are performed purposefully and intended to reach a certain goal. Therefore, James argues that an action can be performed voluntarily only if the subject has first acquired knowledge of its consequences.

Nowadays, much more is known about intentional actions. However, there is still no generally accepted definition, and a common way to define intentional actions is simply to contrast them with reflexive, or automatic actions (Brass & Haggard, 2008; Haggard, 2008; Jahanshahi & Frith, 1998; Frith, 1992).

In addition to being purposive, intentional actions are considered to be endogenously or internally controlled and to be generally stimulus independent (Brass & Haggard, 2008; Haggard, 2008). Furthermore, they require attention and offer a choice between alternatives (Jahanshahi & Frith, 1998). Intentional actions can principally be inhibited and must not be directly executed once the intention to perform the action has been made, but can be conducted after a delay. Reflexive, automatic actions, in contrast, are caused by an external, environmental stimulus and are conducted in an immediate and stereotyped manner. Once the action program has started, they are unable to be stopped and inhibited.

Even though the notion of contrasting intentional actions with automatic actions is helpful for theoretical considerations, the distinction does not capture human behavior as it takes place in everyday life. Human actions are rarely totally externally determined, nor are they ever completely internally guided. Rather, they almost always comprise external and internal components. Therefore, it might be more realistic to assume that human actions exist along a continuum between the two extremes. Considering the predominant component, actions can then be categorized into those that are more internally guided, for example switching on the TV to watch the news, and

those that are more externally guided by environmental stimuli, for example stopping in front of a red traffic light.

Moreover, it is important that voluntary action should not be considered to be a unitary concept. Rather, it comprises at least three different components, which can be denominated in short as *what*, *when* and *whether* (Brass & Haggard, 2008; Haggard, 2008). The *what-component* comprises the decision *which* action to perform, the *when-component* the decision *when* to perform the action and the *whether-component* represents the decision *whether* or not to perform the action. In view of this, voluntary action can be seen as a form of decision-making (Haggard, 2008). In the following, I will refer to the *what-decision* as internal / external action selection and to the *when-decision* as internal / external action timing. The terms internally / externally guided actions will be used whenever no differentiation between the *what*- and *when*-component is made.

1.2 Neuroanatomical substrates of intentional actions

1.2.1 The two routes to action hypothesis

Based on the work of Sanides (1964), Goldberg (1985) proposed the existence of two distinct neuroanatomical routes to action more than twenty years ago. The core of his theory are a medial and a lateral motor system, subserving internally and externally guided behavior respectively. Both routes converge in the primary motor cortex (M1) (see Figure 1.1).

According to Goldberg's hypothesis (1985), each of the two motor systems has a 'premotor center' which is the supplementary motor area (SMA) for internally guided actions and the arcuate premotor area (APA) [equivalent to the ventrolateral premotor area (ventrolateral PMA)] for externally guided actions.

The SMA resides in the medial portion of Brodmann's area (BA) 6 (i.e., BA 6c) anterior to the leg representation of the primary motor cortex. The APA is located on the lateral convexity of the cortex in area 6a α (according to Vogt & Vogt, 1919), BA44 and BA45. According to Goldberg (1985), both motor areas differ with respect to their subcortical and cortical connections. The SMA receives subcortical input from the basal ganglia through the nucleus ventralis lateralis pars oralis (VLo) while the APA receives subcortical input from the cerebellum through area X of the thalamus. The medial system is related to the superior parietal lobe, sensory association areas, primary sensory motor area, lateral area 6, medial-dorsolateral prefrontal regions, and

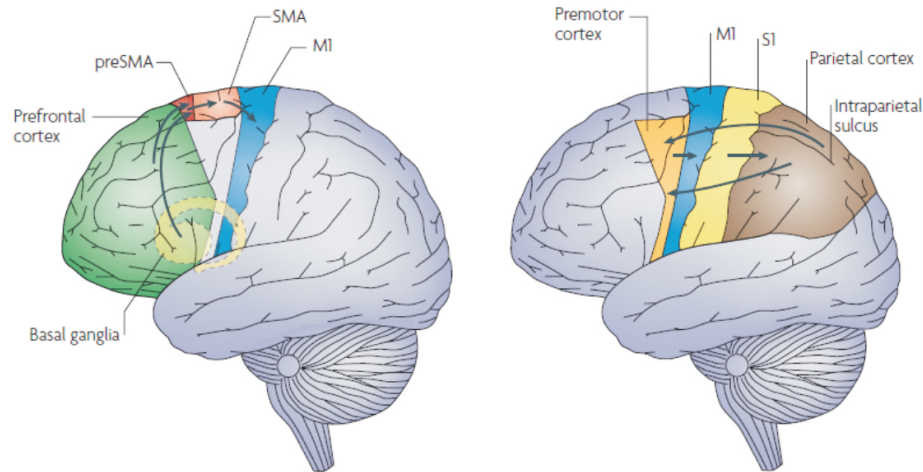


Figure 1.1: Schematic illustration of the two routes to action. Adapted from Haggard (2008). Left panel: Medial route to M1 via preSMA/SMA which receive input from the prefrontal cortex and basal ganglia. Right panel: Lateral route to M1 via sensory cortex, parietal cortex and lateral premotor cortex.

the anterior cingulate cortex (ACC). The APA is connected to the inferior parietal lobe, secondary somatosensory area, the frontoparietal operculum, the insula, orbito prefrontal cortex, auditory association cortex, and the prestriate area.

In its extremes, this theory suggests that the medial motor system is exclusively involved in internally guided behavior, whereas the lateral system is exclusively involved in externally guided behavior. However, neither recent animal nor human studies support this strict distinction. Rather, the distinction seems to be a matter of degree (Tanji, 1994; Jahanshahi & Frith, 1998). For example, the SMA receives input from both the cerebellum and the basal ganglia, but to a greater extent from the basal ganglia (Akkal, Dum, & Strick, 2007).

In addition, it is important to note that the view about the organization of the cortical motor system has changed dramatically during the last decades (Rizzolatti, Luppino, & Matelli, 1998). At the time when Goldberg (1985) proposed the two routes to action hypothesis, the SMA was regarded as one single motor area (Penfield & Welch, 1951). Today, on the basis of neurophysiological, cyto- and chemoarchitectonic differences, it is well-established that the SMA (in the monkey as well as in humans) represents two distinct motor areas (Dum & Strick, 1991; Strick, Dum, & Picard, 1998; Matelli, Luppino, & Rizzolatti, 1991): SMA proper and preSMA corre-

sponding to area 6a α and 6a β of Vogt and Vogt (1919), respectively. Furthermore, it is now established that the ACC, too, contains additional motor areas involved in the performance of internally guided actions (e.g., Cunnington, Windischberger, Deecke, & Moser, 2002; Deiber, Honda, Ibanez, Sadato, & Hallett, 1999). In the following, the frontomedian areas involved in intentional actions - preSMA/SMA and ACC - will be described in more detail.

1.2.2 The medial motor system

1.2.2.1 The SMA complex: SMA proper and preSMA

As mentioned above, the SMA proper and the preSMA are located in the medial portion of BA6. In imaging studies, the vertical commissure anterior (VCA) line is often used to differentiate between preSMA and SMA (see Figure 1.2).

The SMA proper resides caudal to the genu of the arcuate sulcus, which is caudal to the anterior commissure. It is somatotopically organized, and projects directly to the primary motor cortex (M1), and spinal cord (e.g., Dum & Strick, 1991, 2005; He, Dum, & Strick, 1995). The preSMA is located anterior to the SMA proper, is not clearly somatotopically organized, and has almost no projections to M1 and the spinal cord. Rather, the preSMA is strongly interconnected with regions of the prefrontal cortex and other nonprimary motor areas (Luppino, Matelli, Camarda, & Rizzolatti, 1993).

Both areas also differ with respect to their subcortical input: The SMA proper receives thalamic input from parts of the nucleus ventralis lateralis pars oralis (VLo) (Schell & Strick, 1984), whereas the preSMA receives input from the nucleus ventralis anterior pars parvocellularis and area X (Wiesendanger & Wiesendanger, 1985). They also receive input from spatially separate and neurochemically distinct regions of the cerebellum and basal ganglia. Neurons from the dentate nucleus that project to the SMA proper are located more dorsally than those projecting to the preSMA. Neurons projecting from the internal segment of the pallidum to the SMA proper are located in a more caudal region than those projecting to the preSMA (Akkal et al., 2007). Interestingly, both the cerebellar and basal ganglia segments projecting to the SMA proper are known to have motor-related functions, whereas cerebellar and basal ganglia segments projecting to the preSMA are located in regions usually considered to be non-motor (Middleton & Strick, 2001, 2002; Dum & Strick, 2003).

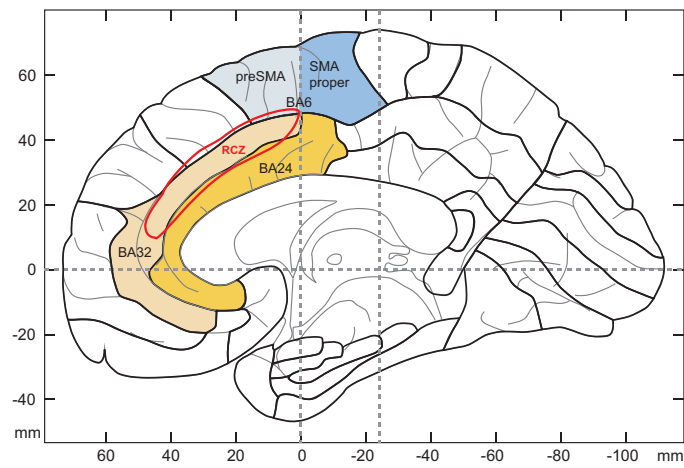


Figure 1.2: Frontomedian wall of the right hemisphere integrated into the coordinate system of Talairach and Tournoux (1988) which is aligned to the anterior commissure-posterior commissure (AC-PC). The Brodmann areas (BAs) of interest are colored. The location of the RCZ is schematically drawn in.

Altogether, neurochemical, neurophysiological as well as neuroimaging studies come to the conclusion that the preSMA is not a typical premotor area but rather a prefrontal area, related to cognitive functions. In contrast, the SMA proper seems to be a typical premotor area in the sense that it has strong connections to M1 and is directly related to motor output (Picard & Strick, 1996).

1.2.2.2 The Anterior Cingulate Cortex

The anterior cingulate cortex is part of the cingulate cortex which lies like a collar (lat. cingulum) around the corpus callosum and has traditionally been regarded as one of the largest parts of the limbic system (MacLean, 1990). Based on cytoarchitecture, patterns of connectivity, and function, it can be roughly subdivided into an anterior part (Anterior Cingulate Cortex; ACC) that plays a role in emotion and motor functions and a posterior part (Posterior Cingulate Cortex; PCC) involved in visuospatial and memory functions (Devinsky, Morrell, & Vogt, 1995). Due to its role in the internal action route, the ACC deserves to be described more thoroughly.

The ACC comprises a large region around the rostrum of the corpus callosum and is characterized by prominent layer V neurons (i.e., large pyramidal neurons). Differences in morphology of these neurons demarcate distinct areas of the ACC. BA24, 32, 33, 23, 25 are regarded as parts of the ACC and have further subparts (Devinsky et al., 1995).

A further parcellation in affect and cognition components of the ACC has been suggested based on functional neuroimaging, cytoarchitecture, and connectivity studies (Devinsky et al., 1995; Bush, Luu, & Posner, 2000). These authors suggested a rostral-ventral affect division (ACad) consisting of BA25, BA33 and rostral BA24a-c and BA32 and a dorsal cognitive division (ACcd) including area 24b'-c' and 32', the cingulate motor areas and nociceptive cortex (Devinsky et al., 1995; Bush et al., 2000) (see Figure 1.3). The ACad is connected with other limbic structures, such as the amygdala, the periaqueductal gray, nucleus accumbens, hypothalamus, anterior insula and hippocampus, as well as with the orbitofrontal cortex. The ACcd, in contrast, has connections with the lateral prefrontal cortex (BA46/9), parietal cortex (BA7), premotor cortex and SMA/preSMA (Bush et al., 2000).

Most important in the present context is the ACcd, more specifically, the cingulate motor areas (CMA) (Picard & Strick, 1996, 2001; Dum & Strick, 1991). According to Picard and Strick (1996, 2001) and Dum and Strick (1991), in monkeys, the cingulate motor areas consist of a rostral cingulate motor area (CMAr) and a dorsal and ventral

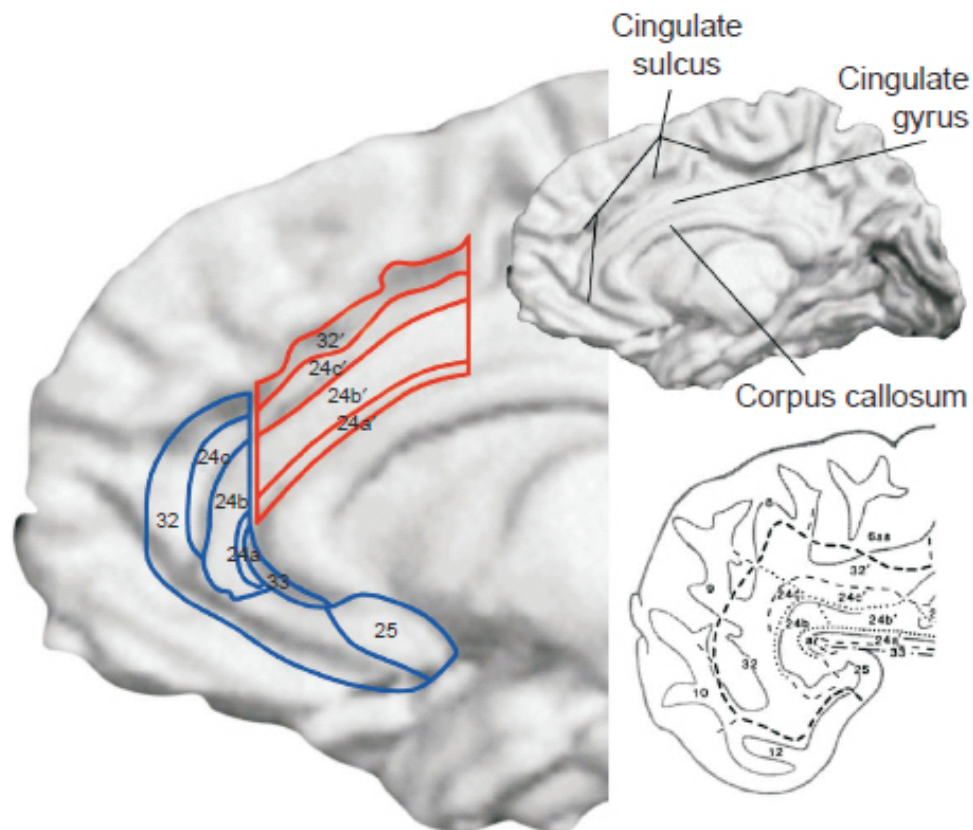


Figure 1.3: Anatomy of the Anterior cingulate cortex (ACC). The upper right part of the figure contains a reconstructed MRI of the medial surface of the right hemisphere of a single human brain. The left part of the figure shows an enlarged, schematic representation of cytoarchitectural areas of the ACC (numbered). Red: Anterior Cingulate, Cognitive division areas; Blue: Anterior Cingulate, Affective division areas. The bottom right panel shows a schematized flat map of actual anterior cingulate cortical areas. Thin unbroken black lines = borders of each sulcus; combination of broken and dotted lines = cingulate areas. Figure adapted from Bush et al., 2000.

CMA. The CMAr is located in area 24c at both sides of the cingulate sulcus anterior to the VCA line, while the dorsal and ventral CMA are located posterior to the VCA line. The dorsal CMA (CMA_d) is located in area 6c in the dorsal bank of the cingulate sulcus, whereas the ventral CMA (CMA_v) is located in area 23c in the ventral bank of the cingulate sulcus. It has been shown that the rostral and caudal parts of the CMA differ with respect to their influence on the spinal cord. Thus, there is some similarity with the distinction between preSMA and SMA.

Picard and Strick (1996) proposed the existence of corresponding areas in humans: a rostral cingulate zone with an anterior part (RCZ_a) and a posterior part (RCZ_p) (corresponding to the CMA_v), as well as a caudal cingulate zone (CCZ) (corresponding to the CMA_d).

It is important to note that this correspondence -like any other human analogies of the monkey cortex- is not so much a matter of exact location but rather of functional similarities. Additionally, the distinction in humans is not as clear as in other primates. The main reason for this is that, in contrast to the non-human primate where the cingulate sulcus is always single, constant and non-segmented, the cingulate sulcus in humans has extremely variable surface features. Therefore, it is uncertain whether the RCZ is buried in the sulcus or in the gyrus or both (Ono, Kubik, & Abernathey, 1990). By averaging in functional neuroimaging studies, this inconsistency even increases. Along the lines of Ullsperger and Cramon (2006, p. 484), I will refer to the RCZ as the brain area at the border between proisocortical parts of the anterior cingulate cortex (BA 24), neocortical areas (BA 32 and 8), as well as the SMA (BA 6) (see Figure 1.2 which schematically shows the RCZ as well as the SMA/preSMA).

1.2.3 Summary

The Goldberg (1985) model proposes two routes to action. Central to intentional actions is the medial motor system. The most important structures of this medial system, the preSMA/SMA, and ACC (including the RCZ), have been described in more detail. Nowadays, the strict distinction of two absolutely independently working routes has been abandoned. Instead, data from neuroanatomy as well as neuroimaging studies (which will be presented later on) suggest two *interdependent* rather than *independent* routes to action.

1.3 Two systems in balance

In addition to the evidence cited above, neuropsychological and neurological disorders such as the Alien (or Anarchic) Hand Syndrome, Utilization Behavior, akinesia and bradykinesia in Parkinsons Disease (PD) provide evidence that the lateral and medial action systems do not work in isolation from each other but rather, that they interact and need to be in balance. All of these disorders involve a dysfunction of the mesial frontal lobe and fronto-striatal pathways, such as the preSMA/SMA, the cingulate gyrus, the basal ganglia, and related thalamocortical circuits. The present chapter aims to describe these disorders in more detail.

In Alien (or Anarchic) Hand Syndrome and Utilization Behavior, patients are not able to refrain from performing stimulus-driven actions and therefore perform actions elicited by objects in the environment, even if these actions may be inappropriate in the given context (Archibald, Mateer, & Kerns, 2001).

Two different constellations of Alien (or Anarchic) Hand Syndrome (AHS) have been described (Spence, 2002). The mesial syndrome is important to the current topic. It involves damage to the anterior part of the corpus callosum, the SMA, ACC and medial prefrontal cortex (PFC). Patients having lesions in these areas issue involuntary movements of the hand contralateral to the lesion (Archibald et al., 2001; DellaSala, Marchetti, & Spinnler, 1991). For example, the right hand of a patient may aim to reach an apple to eat it, while the left hand hinders the right hand in doing so.

The term Utilization Behavior (UB) was first coined by Lhermitte (1983) referring to the automatic triggering of instrumentally correct but highly exaggerated and/or inappropriate motor responses to environmental cues and objects (Esslinger, 1991; Hashimoto, 1995). Imagine, for example, a patient being presented with a pair of shoes. The patient may immediately start to try to put them on, even though he is already wearing shoes. UB can arise from frontal cortical lesions (especially the preSMA) and certain subcortical lesions, particularly of the thalamus (Esslinger, Warner, Grattan, & Easton, 1991; Hashimoto, Yoshida, & Tanaka, 1995). It has been suggested that UB and AHS constitute an imbalance between the medial internal and the lateral external motor system (Lhermitte, Pillon, & Serdaru, 1986). In neurologically normal humans, the internal system functions upstream to the external system and usually inhibits its activity. Damage to the medial internal system therefore may result in the reduction of internally generated movement and the release of unintended, stimulus-triggered movements (Archibald et al., 2001) and therefore is related to behaviors typically ascribed to AHS and UB.

Despite these behavioral similarities between AHS and UB, there is a phenomenological difference between these two diseases since patients experience their actions differently. While AHS patients report their actions to be unintentional and complain about their hand being uncontrolled, UB patients, in contrast, are not aware that their behavior is inappropriate to the context (Pacherie, 2007).

The symptoms observed in Parkinsons Disease (PD) result from a loss of dopaminergic neurons in the substantia nigra. This, in turn, results in a reduction of the activating influence of the basal ganglia on the cerebral cortex. PD has been suggested to represent a failure to generate intended actions. That is, PD patients know what they want to do, but they are not able to implement their intentions (Frith, 1992). Akinesia (poverty of spontaneous movements) in PD is also referred to as ‘paralysis of the will’ (Wilson, 1925, cited in Jahanshahi & Frith, 1998, p. 502). This assumption is in line with the observation of paradoxical kinesis in some cases: PD patients can walk or run normally when there is an external cue such as fire. Generally, there is evidence that the provision of external guidance can improve movement-related symptoms in PD (Georgiou et al., 1993). In line with these observations, imaging studies which compared PD patients with healthy controls showed less activation in areas associated with internally guided actions such as preSMA/SMA, ACC and the putamen. In contrast, areas associated with externally guided actions did not differ between PD patients and healthy controls (Playford et al., 1992; Jahanshahi et al., 1995). These findings are further supported by EEG studies examining the readiness potential (RP). The RP is a slow cortical potential that usually precedes voluntary movements. These studies show a reduced RP-amplitude in PD patients preceding internally selected movements (Praagstra, Cools, Stegeman, & Horstink, 1996; Touge, Werhahn, Rothwell, & Marsden, 1995).

1.4 Behavioral studies on intentional action

Compared to the larger number of neuroscientific studies, the number of behavioral studies exploring the nature of intentional actions is rather small. However, three interesting lines of research will be described in the following.

1.4.1 Intention in ideomotor learning

One promising line of research is based upon the ideomotor theory (for a historical overview, see Stock & Stock, 2004). According to the ideomotor theory (Lotze, 1852;

Harless, 1861; James, 1890,1950), actions are selected with respect to their perceptual consequences. To be able to anticipate the consequences of an action, the causal relationship between actions and ensuing effects must have previously been learned. Therefore, as noted above, no action can be performed voluntarily for the first time. Mediated by the learning of which action is accompanied by which consequence/s, a bidirectional association between an action and its consequence/s is established. This in turn affords that the anticipation of a desired effect automatically activates the movement by which this effect is achieved.

Herwig, Prinz & Waszak (2007) and Herwig & Waszak (2009) used the ideomotor approach to explore whether internally and externally guided actions are associated with different types of learning. Herwig, Prinz, and Waszak (2007) compared action-effect learning in two conditions [see also Elsner and Hommel (2001)]. In an acquisition phase, subjects performed actions that were followed by certain effect tones. Two groups of subjects were examined: In the internally selected group, subjects were required to freely select between two possible actions. In the externally selected group, subjects' actions were determined by external stimulus events. The results of the test phase showed action-effect learning only for the internally selected acquisition group. Herwig and colleagues suggested that this is because, when reacting to an external event, subjects pass on control to the stimuli and actions are selected with respect to their perceptual antecedents. When internally selecting an action, by contrast, actions are guided by the ideomotor principle, (i.e., they are selected with respect to their perceptual consequences). It is only in this case that action and effect are associated. Herwig et al. (2007) suggest that externally selected actions and internally selected actions are accompanied by different types of learning: While externally selected actions are accompanied by stimulus-response (sensorimotor learning), internally selected actions are accompanied by action-effect (ideomotor learning).

1.4.2 Differences in temporal binding

In a study using a modified Libet-Paradigm (Libet, Gleason, Wright, & Pearl, 1983), subjects watched a rotating clock face and had to judge onset times of actions they performed either in response to a stimulus or at their own intention (Haggard, Aschersleben, Prinz, & Gehrke, 2002). The authors found that perceptual onset times of actions and their ensuing effects, on the one hand, and of stimuli and subsequent actions in response to them, on the other, attracted each other in time.

Similar findings were reported by Waszak et al. (2005). They developed a paradigm in which the differences between internally and externally guided actions were compared by means of EEG. For this study, subjects performed a temporal bisection task, making left or right key presses at the midpoint between isochronous pacing signals (a sequence of 'X's presented to the left or the right of the fixation cross). The button presses were either internally selected by the subjects and produced the next stimulus on the screen or they were externally selected, in that subjects had to react to the previous stimulus presented on the screen. The behavioral results showed that reaction times of externally guided actions are shifted towards the triggering stimuli, whereas reaction times of internally guided actions are shifted towards the produced effects. Waszak and colleagues considered these effects of the mode of movement on the actual timing of movements to be an analogue in the behavioral domain of the perceptual effects found by Haggard et al. (2002). Taken together, these findings are in line with the notion of two functional action modes suggested by Herwig et al. (2007), one that is based on stimulus-response representations and one that is based on action-effect representations.

1.4.3 Evidence for different physical control mechanisms

Astor-Jack and Haggard (2005) showed that when subjects had to interrupt an internally timed action in order to perform an externally timed action, response times are increased compared to when the action was externally timed from the start. This was the case even though the interrupted internal action and the externally timed action were physically identical. This result strongly suggests that internally and externally guided actions do not share the same representation.

In order to study the physical characteristics of internal and external movements, Obhi and Haggard (2004) measured the electromyogram (EMG) activity during three conditions. They found internally timed finger presses to elicit greater and longer EMG activity than did externally timed finger presses. Moreover, during a truncation condition, subjects had to prepare an internally timed action. However, similar to the study by Astor-Jack and Haggard (2005) the preparation was interrupted by an external cue triggering a certain action. Again, subjects showed significantly longer RTs in the truncation condition than in the externally timed condition. However, there was no effect of truncation on the EMG activity. Instead, the basic EMG characteristics of internally and externally timed movements were preserved, suggesting that subjects were indeed switching between the two types of action in the truncation condition,

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and were not producing some form of 'hybrid' action. This switch between movement modes is reflected in the longer RT times in the truncation condition as compared to the pure externally timed condition. The greater EMG activity in the internally timed condition was explained by internally timed movements being more forceful and eliciting stronger motor preparation than externally timed actions do. This finding was compatible with the possibility that internally and externally guided actions are planned and produced by the same central structures but that these structures were simply less active in the production of externally timed actions.

1.4.4 Summary

Altogether, the behavioral results are in line with Goldberg's hypothesis described previously. Although internally and externally guided actions seem to be physically identical, they differ in behavioral measurements. Specifically, there are differences with respect to the appearance of motor learning (Chapter 1.4.1) and the amount of temporal binding (Chapter 1.4.2). Furthermore, the costs that result from a switch from one action mode to the other indicate that the two modes are independently controlled (Chapter 1.4.3).

1.5 Neurophysiological antecedents of voluntary actions

1.5.1 Electroencephalographical studies on intentional actions

EEG studies examining intentional action usually focus on the readiness potential (RP). The RP is a slow cortical potential that precedes voluntary movements, beginning about 1.5 sec before movement onset (Kornhuber & Deecke, 1965).

In the seminal study by Libet et al. (1983) subjects were presented with a rotating clock and were instructed to press a button at some point in time of their own choice. Thereafter, they were either asked to estimate the time of their button press on the clock or the point in time when they first had the intention to act. The authors found the RP to precede the conscious intention to act by about 206 ms. Although various aspects of the study's design, including inaccuracy and unreliability of subjective estimates on the onset of an intention, have been criticized, the results have been interpreted as evidence for the non-existence of free will (e.g., Grind, 2002; Wegner, 2003).

More important to the present context, is a line of research that focused on the differences in the RP in internally and externally guided actions. Most of these studies re-

port that freely selected movements showed a higher RP amplitude than predetermined, fixed movements (Papa, Artieda, & Obeso, 1991; Dirnberger, Fickel, Lindinger, Lang, & Jahanshahi, 1998; Praamstra et al., 1996; Waszak et al., 2005; Keller et al., 2006). Since the effect of the action mode on the RP can be best explained by differences in activity in the mesial frontal cortex, the finding is usually considered to reflect increased SMA activity in internally selected movements (Praamstra et al., 1996). In accordance with this interpretation, some EEG studies seem to indicate increased activity in the SMA during internally guided tasks and increased activity in the PMA during externally guided tasks (Gerloff et al., 1998; Jahanshahi et al., 1995; Thut et al., 2000). However, one has to keep in mind that EEG measurements have only limited spatial resolution.

In a recent EEG study, Waszak and colleagues (2005) compared movement timing and EEG correlates of internally and externally selected actions, with the sensorimotor context, kinematics, and dynamics of the actions being identical in the two conditions. Waszak et al. (2005) analyzed stimulus-locked as well as response-locked event-related-potentials (ERPs). For the stimulus-locked ERPs, they observed a centro-parietal P3 and a fronto-central stimulus-locked LRP (lateralized readiness potential) only in the stimulus-based condition. Waszak et al. (2005) suggest that these two components reflect stimulus-driven processes that take effect whenever specific movements are to be carried out in response to specific stimuli. They speculate that these ERP reflect processes taking place in the lateral premotor cortex and the parietal cortex. In the response-locked ERPs, Waszak et al. (2005) observed a strong negative shift resembling the RP that began much earlier in the internally selected condition than in the externally selected condition, probably reflecting internal motor preparation in the mesial frontal cortex. No differences were observed between the two action conditions over hand motor areas, suggesting that the motor execution itself does not differ in the two modes of movement. Altogether Waszak et al.'s. (2005) results were compatible with the notion of a lateral system mediating externally guided actions and a medial system mediating internally guided actions, both converging on a common final pathway.

1.5.2 Intentional actions in functional neuroimaging research

This chapter aims to give a brief overview of the results obtained from functional magnetic resonance (fMRI) studies. On the basis of the two components of intentional

actions that are important to the present thesis, *when* and *what*, the chapter is subdivided respectively.

1.5.2.1 Selecting *when* to act

Studies dealing with internally timed actions usually compare a condition in which subjects have to press a button at a moment of their own choice with a condition in which subjects are prompted by a visual or acoustic cue to press the button (Cunnington et al., 2002; Wiese et al., 2004). As a main finding, these studies report activation differences in the frontomedian wall between internally and externally timed actions that are located in the SMA/preSMA complex and the ACC (Jenkins, Jahanshahi, Jueptner, Passingham, & Brooks, 2000; Deiber et al., 1999; Debaere, Wenderoth, Sunaert, Hecke, & Swinnen, 2003; Wiese et al., 2004). Further activations have been found in the dorsolateral prefrontal cortex (dlPFC) (Jenkins et al., 2000; Jahanshahi et al., 1995), basal ganglia (Jenkins et al., 2000; Debaere et al., 2003; Wiese et al., 2004), in the parietal lobe in BA 40 and BA 7 (Jenkins et al., 2000; Debaere et al., 2003; Wiese et al., 2004), and in the insula and cerebellum (Jenkins et al., 2000). Activations in the dlPFC and in the parietal lobe are thought to reflect attention and working memory related processes due to random generation of button presses in the internally timed but not externally timed condition. In contrast, activations in the frontomedian wall are assumed to reflect processes involved in internal action timing.

For the comparison of externally timed versus internally timed actions, most of the studies report activation which is due to the type of external trigger signal that is in the visual or auditory cortex respectively (Jenkins et al., 2000; Wiese et al., 2004; Cunnington et al., 2002). Evidence supporting the existence of a lateral motor route for externally guided actions as suggested by Goldberg (1985) could only be found by one study (Debaere et al., 2003).

1.5.2.2 Selecting *what* to do

Generally, there are a greater number of studies dealing with internal action timing than studies dealing with internal action selection. This might be due to the fact that it is even more difficult to develop a paradigm that does not confound factors such as attention, working memory or the sensorimotor context.

However, some fMRI studies do address the issue of intentional selection of actions. For example, Lau, Rogers, Ramnani & Passingham (2004b) compared a free selection condition in which subjects selected an image randomly out of several im-

ages with a specified condition in which subjects had to identify the image that matched the cursor image. For the main effect of free selection, they reported activation in the ACC, preSMA, and parietal cortex.

Other studies are in line with these results and report activations in different parts of the frontomedian wall (ACC and preSMA), as well as in the dlPFC, premotor cortex, parietal lobe, basal ganglia and cerebellum (Eimeren et al., 2006; H. C. Lau, Rogers, Ramnani, & Passingham, 2004; H. Lau, Rogers, & Passingham, 2006; Cunningham, Windischberger, Robinson, & Moser, 2006). As in studies on intentional action timing, the most consistent activation was found in the preSMA and/or the RCZ. Again, usually, these studies do not find stronger activations in the lateral motor system for externally as compared to internally selected actions.

1.5.3 Conclusions from EEG and fMRI studies

Taken together, most of the EEG studies generally support Goldberg's (1985) hypothesis of the medial and the lateral motor system being involved in internally and externally guided actions, respectively. In contrast, the majority of the fMRI studies do not find activations in the lateral motor system when comparing externally guided and internally guided actions. Instead, there is some evidence that the medial system is involved in both types of actions. Specifically, internally guided actions appear to be supported by the medial system to a greater degree than externally guided actions, suggesting that the difference between internally and externally guided actions is a matter of degree rather than absolute. This inconsistency between EEG and fMRI results might be due to the fact that EEG and fMRI pick up different dimensions of action preparation. While in EEG measurements, the temporal resolution is high and the spatial resolution is low, the reverse is true for fMRI. One might therefore assume that the differences between externally and internally guided actions in the lateral motor system take place only for a short amount of time and therefore can only be detected by means of EEG but not fMRI.

With respect to the brain structures involved in intentional action control, fMRI and EEG studies indicate that the preSMA and RCZ play an important role in internal action selection and internal action timing.

The activations reported in internal action selection and internal action timing were very similar, with the most consistent activation for both components found in the RCZ and/or preSMA. To date, it is an open question whether these two areas dissociate functionally.

1.6 Experimental approach and research questions

The review of the literature presented above illustrates two main points:

1. Internally and externally guided actions are at least partially controlled by different neuroanatomical networks (e.g., Goldberg, 1985). Findings from EEG studies, lesion studies and behavioral studies also support this theory. In contrast, findings from fMRI studies suggest a level difference rather than an absolute difference. Although these studies point to an important role of the frontal median wall in internally guided actions, to date, there is no consistency concerning the specific locus of activations: Some studies show activations in the RCZ/ACC, and others in the preSMA or in both structures.
2. Voluntary action is not adequately described by a unitary concept, rather it comprises different components such as deciding *what* to do, *when* to do it and *whether* to do it at all. To date, nothing is known about possible neurophysiological dissociations or functional interactions between these components.

The present thesis aims to address these two points. Study 1 asked which role the preSMA and RCZ play in intentional action under well controlled conditions. In Study 2, we addressed the question of whether there are different neural representations for intentional *what*- and *when*-decisions.

1.6.1 Study 1: Which role do the rostral cingulate zone and preSMA play in internally selected actions?

As indicated above, in studies dealing with intentional action timing and action selection, perceptual and/or motor factors were often confounded with the contrast in question (Cunnington et al., 2002; Debaere et al., 2003; Wiese et al., 2005; Lau et al., 2004; Cunningham 2006). At the same time, there is no consistency regarding the exact loci of activations. It remains unclear whether it is the preSMA and/or the anterior cingulate cortex with the rostral cingulate zone that is the most crucial structure in internally guided actions.

We hypothesized that this inconsistency might be due to the above-mentioned confounds and argued that the two action modes were not directly comparable in many of these former studies. A major challenge for the investigation of the neural correlates of internally guided actions was thus to develop a paradigm in which internally and externally guided actions differ in nothing more than the action mode. A paradigm that

tried to address this challenge was developed by Waszak et al. (2005). We adapted this paradigm to use in fMRI and addressed the question of which role the rostral cingulate zone and preSMA play in internally selected actions.

Subjects performed a temporal bisection task, making left and right key presses at the midpoint of isochronous pacing signals (a sequence of 'X's presented on the left or right side of a fixation cross). In the internally selected condition, subjects selected left or right key presses and so determined the side at which the next stimulus would appear. In the externally selected condition, they had to react to the previous stimulus with a button press corresponding to the side at which the preceding stimulus appeared. Thus the action itself and the sensorimotor context of the action were identical in both conditions. The only difference was the mode in which the actions were performed: internally selected or externally selected. We hypothesized we would find activation differences between internally and externally selected actions in the preSMA and/or the RCZ.

1.6.2 Study 2: Can we dissociate the *what* and *when* component of intentional actions using functional magnetic resonance imaging?

Study 1 revealed that the RCZ but not the preSMA is more strongly involved in internally selected as compared to externally selected actions. Instead, the preSMA was activated to the same degree in both action modes. Given the fact that in Study 1, subjects were required to self-initiate their button presses in both conditions, we hypothesized that these results might point to a neural dissociation of *what*- and *when*-components, with the RCZ being involved in deciding *which* action to perform and the preSMA being involved in the decision *when* to act.

This hypothesis was tested in Study 2. Subjects were presented with a cue and, as quickly as possible, had to decide, *which* action to perform and *when* to do it. The two decisions were either taken by the participants (internally) or based on the cue (externally), enabling us to differentiate between internal and external *what* and *when* decisions. We, furthermore, addressed the question of whether the same brain areas are involved in the decision processes (which occur in the cue phase) as in the implementation of the action. Therefore, we dissociated the moment when the subjects have to make the decision *what* to do, and *when*, from the moment when the subjects actually

execute the action. We hypothesized that activation differences in the frontomedian wall reflect mainly decisional aspects of voluntary action control.

1.7 Summary of the main results and conclusions

The neuroimaging results of Study 1 revealed a widespread neural network for the comparison of internally vs. externally selected actions that included frontolateral and inferior parietal brain areas and most importantly an activation in the RCZ. A signal-strength analysis conducted post-hoc showed preSMA and RCZ activation for both internally and externally selected actions. However, in contrast to the RCZ, the preSMA did not differentially contribute to internally selected actions.

We argue that the RCZ is primarily involved in the internal selection of actions (*what*-component), whereas the preSMA is more closely linked to the internal timing of an action (*when*-component), that is to determine the right moment for the execution of the action. The activity in the preSMA did not differ between the two conditions, because the timing was identical in both conditions (subjects had to issue a keypress at the midpoint between two consecutive stimuli). Moreover, we found activations in the lateral prefrontal cortex and inferior parietal lobe. These activations possibly reflect working memory and attention-related processes due to the random generation of button presses and due to higher attentional load in the internally selected condition.

As concerns Study 2, data from the whole brain analysis revealed a neurofunctional dissociation between two areas in the frontomedian wall. The RCZ was involved in the decision *which* action to perform, whereas an area of the superior frontal gyrus (SFG) in the left paramedian frontal cortex was involved in the decision *when* to perform an action. However, data from a post-hoc signal-strength analysis relativized this strong dissociation. This analysis revealed an interaction of action timing and action selection in the paramedian frontal cortex, suggesting that processes related to the decision of internal action timing and internal action selection are not completely dissociated but interdependent. We found the strongest differential activations in the RCZ and paramedian frontal cortex in the analysis of the cue-related signal and not in the analysis of the implementation-related signal. Therefore, the data suggest that the activations in the RCZ and paramedian SFG reflect processes concerned with preparing the upcoming action (viz. the internal specification of the *what* and *when* action parameters) and not processes related to the execution of the action. Thus, from the present thesis we can conclude the following:

1. The RCZ but not the preSMA is involved in internal action selection (Study 1 and Study 2).
2. The paramedian SFG is involved in deciding *when* to act (Study 2).
3. Internally and externally guided actions are not processed by two totally different systems. Rather, the two types of actions involve the same brain systems which are involved more strongly in internally than in externally guided (i.e., timed and selected) actions (Study 1 and Study 2).
4. Brain areas that are involved in processing intentional *what* and *when* decisions do not seem to operate totally independently of each other (Study 2).
5. Brain areas involved in the decision of *which* action to perform and *when* to do it are not involved in the initiation of the action itself (Study 2).

1.8 Shortcomings and future prospects

1.8.1 Shortcomings

The aim of the present thesis was to get a deeper understanding of the brain mechanisms involved in intentional action control. However, it should be noted that, in the laboratory, one has to instruct subjects to act voluntarily, a fact which is rather paradoxical but inevitable. In contrast to most situations in everyday life in which an intentional decision is associated with a certain (personal) value, there is no such value in an experimental setting. In order to have a well-controlled experimental setting, subjects can usually choose only between a very restricted number of alternatives, a situation which is oversimplified compared to the decisions people have to take outside the laboratory. However, it should also be noted that the brain areas found to be activated in functional neuroimaging studies are similar to those involved in impairments of the willed action system. This validates the experimental paradigms used, however simplified they might be (see Chapter 1.3 and Chapter 1.5). Nevertheless, one should pay attention to these issues when talking about psychological and neuroscientific research on voluntary action.

Furthermore, the finding of the RCZ as the neural correlate of intentional action selection has to be interpreted with care. One should at least be aware of the fact that the RCZ is also found to be related to conflict-monitoring and error detection (e.g.,

Botvinick, Braver, Barch, Carter, & Cohen, 2001; Botvinick, Cohen, & Carter, 2004; Ullsperger & Cramon, 2001). In view of the conflict-monitoring hypothesis (Botvinick et al., 2001), each underdetermined response form (i.e., when there is no preferred response, as is the case in intentional actions) represents a form of response conflict. Conversely, paradigms that are used to explore conflict monitoring such as the Stroop-Task (Stroop, 1935) or the Eriksen-Flanker-Task (Eriksen & Eriksen, 1974) compare an automatic, predominant response with an action that is less automatically prompted. Thus, Nachev, Rees, Parton, Kennard, and Husain (2005) argue that these paradigms are confounded by volition. We do not believe that paradigms on intentional actions are ‘confounded’ by response conflict and vice versa. Rather, as argued in the discussion of Study 2, we believe that response conflict and volition represent two sides of the same coin. That is, there is no will without ‘conflicting’ ideas, an idea that was already mentioned by (James, 1890,1950):

The express fiat, or act of mental consent to the movement, comes in when the neutralization of the antagonistic and inhibitory idea is required. [...] (James, 1890,1950, p. 526).

There are some studies that have tried to address this issue (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Nachev et al., 2005; H. Lau et al., 2006). However, the results were not consistent. Nachev and colleagues (2005) revealed a dissociation between response conflict and intentional action within the preSMA. Activity in the rostral preSMA was increased by trials that were high in conflict, regardless of whether action selection was intentional or not. The caudal preSMA, in contrast, was related to intentional actions irrespective of whether there was response conflict or not. They did not find any activation within the ACC/RCZ. In a study by Lau and colleagues (2006) who used a modified version of the Eriksen Flanker task, subjects were presented with compatible (low in conflict) and incompatible (high in conflict) flanker conditions. Additionally, there was a free selection condition during which subjects freely chose between left and right button presses. For the comparison free vs. compatible, the authors reported activation in the preSMA, whereas they reported activation in the ACC for the comparison incompatible vs. compatible. From this, they concluded that the ACC is involved in response conflict while the preSMA is involved in response selection. Most critical to this study is the fact that the authors do not report the contrast of most interest (i.e., the direct comparison of free vs. incompatible trials). Therefore,

they cannot really argue which brain area is more strongly involved in response conflict or response selection.

To conclude, data currently available neither allow us to draw conclusions in favor of the conflict-monitoring hypothesis of the RCZ nor in favor of an unbiased involvement of the RCZ in intentional actions. Thus, when interpreting studies on intentional action, one has to keep in mind that there might be an alternative interpretation for an activation within the RCZ.

1.8.2 Future prospects

The two fMRI studies described in the present thesis pointed to the important role of the frontomedian cortex in intentional action control. Moreover, they were able -at least partially- to dissociate different components of intentional action (*what* and *when*) within the frontomedian cortex. However, the experiments conducted do not only answer questions but also raise new ones. Thus, there is still much research to be done to get a finer grasp of the neural correlates of intentional actions. Some of the open questions can be addressed by a few modifications of Study 2.

Firstly, Study 2 could not show a complete dissociation of the *what*- and the *when*-component. This raises the questions of how independent the two components are, whether one decision could be made without the other and whether one component is superior to the other. A first step to explore this issue, is to temporarily disentangle the two decisions by presenting the *what* and *when* cue not at the same time but one after the other, such that they are jittered and therefore allow the dissociation of the underlying BOLD-responses. This manipulation would answer the question of whether one decision can be made without knowledge of the other component.

Another interesting issue is also related to Study 2. In everyday life, the timing of an intentional action rarely requires an explicit decision on which point in time to perform an action (as it was the case in Study 2). Rather, the timing of an intentional action depends on the coordination of the chosen action with other actions. The timing of an action often depends on environmental circumstances and internal motivations (Haggard, 2008).

In view of this, the term *when-decision*, as used in Study 2 is possibly better described in terms of the decision ‘under which environmental condition’ to perform an action. Imagine yourself deciding to make a bike trip at the first sunny weekend in spring. In this case, your decision is not related to a certain point in time but to the fulfillment of some environmental conditions. Although this sort of conditional action

planning corresponds to many of our daily actions, it is still unexplored. Using an experiment similar to Study 2, it could be tested whether the paramedian SFG that was identified to be involved in the decision *when* to act is part of a network involved in the decision ‘under which condition’ to implement a certain action. As for Study 2, subjects could be presented with a cue that either indicates an internal or an external *what*-decision as well as an internal or external setting of conditions. In contrast to deciding at which tone to press the button (*when*-decision), subjects could decide at which of six colors (presented in random order) of a color patch to press the button. For the contrast internal vs. external condition setting, one would assume increased activity in a network including the paramedian SFG. For the contrast internal vs. external action selection, one would expect to find a replication of Study 2 (i.e., an activation in the RCZ).

Additionally, it might be interesting to perform a version of the paradigm used in Study 2 with patients suffering from Parkinsons’ Disease (PD). Jahanshahi et al. (1995) asked normal subjects and PD patients to perform button presses at a point of their own choosing. They reported weaker activation in the preSMA and ACC for internally as compared to externally timed actions in PD patients than in healthy controls. However, this study confounded intentional action timing with the initiation of the action. It is therefore unclear whether the patients had a problem in the decision at which point in time to press the button or a problem in initiating the action. Another open issue is whether PD patients also have a problem related to the *what*-decision. From the results of the Jahanshahi et al. (1995) study which reported also weaker activation in the ACC, one could assume that there might also be less strong activation for PD patients related to the *what*-decision.

In sum, future research should focus on a further functional dissociation of the different concepts of voluntary action to make the concept itself and its associated components clearer. The two fMRI studies presented in this thesis represent a good starting point towards this, they have the potential to be rearranged to test new ideas and models.

Chapter 2

Empirical Section I



The role of the preSMA and the rostral cingulate zone in internally selected actions

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In everyday life, one can differentiate between actions that are primarily internally guided and actions that are primarily guided by external events. fMRI studies investigating the neural correlates of internally guided actions usually report activation maxima in the rostral cingulate zone (RCZ) as well as the preSMA. However, the pertinent contrasts were often confounded by perceptual and motor differences between the different conditions. In the current study, we reinvestigated the neural correlates of internally vs. externally selected actions using a paradigm that avoids any such perceptual or motor confound. By doing so, we wanted to address the yet unsolved question which differential role the preSMA and RCZ play in internally guided actions. Subjects were required to make left or right key presses at the midpoint between isochronous pacing signals (a sequence of 'X's presented to the left or the right of the fixation point). In the internally selected condition, the location of the 'X' was determined by the location of the preceding key press that the subjects selected freely. In the externally selected condition, by contrast, the location of the 'X' prescribed the location of the subsequent key press response. We found that the RCZ was differentially activated by internally as compared to externally selected actions. In contrast to previous studies, the preSMA showed equal activity in both conditions and thus did not differentiate between the two modes of action selection. This suggests a primary role for the RCZ in internally selected actions.

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Keywords: fMRI; Internally selected action; Externally selected action; RCZ; PreSMA

Introduction

In everyday life, actions are either more internally guided, for example switching on TV to watch the news, or they are more

externally guided by environmental stimuli, for example stopping in front of a red traffic light. Voluntary, internally guided actions are not prompted by external cues, but rather guided by intentions. An internally guided action commonly helps the agent to produce a desired effect in the environment (Prinz, 1997). According to the ideomotor theory, voluntary action control is based on learned associations between movements and their perceivable consequences (James, 1890, 1950). An intentional action, according to the ideomotor theory, can be triggered simply by anticipating these consequences (action–effect or A–E bindings) (Hommel et al., 2001; Prinz, 1997). Externally guided actions, on the other side, help the agent to adapt his behavior to environmental demands. This type of behavior is based on associations between cueing stimuli and subsequent actions (stimulus–response or S–R bindings).

For a long time, the focus of psychological research was on the exploration of the functional and neural underpinnings of externally guided actions. During the last years, however, research focused increasingly on the exploration of internally guided actions and how they differ from externally guided actions (Cunnington et al., 2002; Jahanshahi et al., 1995; Keller et al., 2006; Waszak et al., 2005; Wiese et al., 2004, 2005). Differences between the two modes of action are observed on the behavioral as well as on the neural level. On the behavioral level, it has been shown that reaction times of externally guided actions are shifted toward the triggering stimuli, whereas reaction times of internally guided actions are shifted towards the produced effects (Keller et al., 2006; Waszak et al., 2005). Similarly, Haggard et al. (2002) found that perceptual onset times of actions and their ensuing effects, on the one hand, and of stimuli and subsequent actions in response to them, on the other hand, attracted each other in time. These findings are in line with the notion that stimuli and responses as well as actions and effects share combined representations (S–R and A–E bindings) (Hommel et al., 2001; Prinz, 1997).

Regarding the underlying neuroanatomical differentiations between the two action modes, Goldberg (1985) emphasized the distinction between a medial and a lateral premotor system, which are involved in internally vs. externally guided actions, respectively.

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However, as Jahanshahi et al. (1995) outlined, even though the concept is very attractive, recent data question the anatomical and functional distinctiveness of major components of the two systems and suggest that their specialization is a matter of degree rather than absolute. This is supported by findings from electrophysiological as well as neuroimaging experiments which suggest that in both action conditions the same areas are activated, but to a stronger degree in the internally guided condition. On the neurophysiological level, there is evidence that the medial wall of the frontal lobe plays a major role in the execution of internally as compared to externally guided actions. According to Picard and Strick (1996), the fronto-medial wall consists of the supplementary motor area (SMA), subdivided into the preSMA and the SMA proper, as well as the cingulate motor areas (CMA), which are subdivided into the rostral cingulate zone (RCZ), and the caudal cingulate zone (CCZ).

It is important to note that the decision to perform an internally guided action has at least two components. First, the agent must decide which action out of a certain subset of actions to perform ('what-component'), and he must determine when to perform the action ('when-component'). Most studies that have been published in recent years explored the second component. Usually, in these studies, a condition during which subjects self-initially conducted a key press was compared with a condition in which subjects responded to a visual (Debaere et al., 2003; Deiber et al., 1999; Wiese et al., 2004) or acoustic cue (Cunnington et al., 2002; Jahanshahi et al., 1995; Jenkins et al., 2000). From now on, whenever we refer to the when-component of an action, we will call the action internally or externally *timed*.

However, more recently some studies also dealt with the 'what-component' of voluntary action (Cunnington et al., 2006; Lau et al., 2004a, 2006; van Eimeren et al., 2006). Most of these studies report activation loci in the medial wall of the frontal lobe as a neural correlate of internally guided actions, although the exact locations of activation differ from study to study. While some report peak activation in the preSMA (Deiber et al., 1999; Lau et al., 2006), others show activation in the cingulate motor areas (Debaere et al., 2003; Deiber et al., 1999; Jenkins et al., 2000; Wiese et al., 2004) or in both areas (Cunnington et al., 2006; Deiber et al., 1999; Lau et al., 2004a; van Eimeren et al., 2006). From now on, whenever we refer to the what-component of an action, we will call the action internally or externally *selected*. (We use the term internally or externally *guided* in a neutral manner, whenever *timed* and *selected* are inappropriate.) In the present study, we varied whether an action was internally or externally selected, whereas the timing of the actions was always internally controlled.

On the neuroanatomical level, it is still not clear which role the preSMA and the RCZ play in internally guided actions. One reason for the ambiguity of these findings might be the fact that in most previous studies perceptual and/or motor factors were confounded with the contrast in question (Cunnington et al., 2002; Debaere et al., 2003; Wiese et al., 2005). In some studies, the externally guided condition consisted of a signal that was missing in the internally guided condition (e.g., Cunnington et al., 2002). Thus the two action modes were not directly comparable. Other studies reported only one experimental (internally timed) condition which was compared with a rest condition (Cunnington et al., 2003; Wiese et al., 2005). Therefore activations could not be unequivocally attributed to the internally timed action itself but might have been part of action generation as a whole.

The problem of confounding factors was especially pertinent in this kind of research, because internally and externally guided

actions differed in the sensorimotor context in which they took place. A major challenge for the investigation of the neural correlates of internally guided actions is thus, to develop a paradigm in which externally and internally controlled actions differ only in the action mode.

Recently Waszak et al. (2005) conceived a paradigm in which the two modes of action were directly comparable. They studied the electrophysiological signatures of internally and externally selected key presses. In their paradigm, subjects performed a temporal bisection task, making left or right key presses at the midpoint between 35 isochronous pacing signals (a sequence of 'X's presented to the left or the right of the fixation cross). In the internally selected condition, the subjects' key press determined the location of the *subsequent* 'X' on the screen. In this condition, subjects were instructed to generate a random sequence of left and right 'X's. In the externally selected condition, by contrast, the subjects' key press was prompted by the location of the *preceding* stimulus. The movements in a given externally selected run were yoked (in a disguised fashion) to the movements produced in the preceding internally selected run. This paradigm enabled Waszak et al. (2005) to compare movement timing and EEG-correlates of internally and externally selected actions, although the sensorimotor context of the actions and the kinematics and dynamics of the actions were identical in the two conditions. In order to illuminate the neural correlates of internally selected actions, the present experiment used the Waszak paradigm in an fMRI study. Waszaks' (2005) EEG study told us a lot about the timing of the underlying electrophysiological processes of internally selected actions (for details, see Waszak et al., 2005). However, due to the poor spatial resolution of EEG, it could not tell us for sure where the differences in the neural correlates between the two action modes are manifested in the brain. Because we were mainly interested in the yet unsolved question as to which role the preSMA and the RCZ play in internally selected actions, we expected that combining the advantages of Waszak et al.'s paradigm described above with fMRI would help us to shed some light on answering exactly this question.

Material and methods

Subjects

Sixteen healthy subjects (eight males, eight females) with a mean age of 26.33 years ($SD \pm 2.92$) with normal or corrected to normal vision participated in the study. All subjects were right-handed as indicated by scores on the Edinburgh Handedness Inventory (Oldfield, 1971) with a mean laterality quotient higher than 80. Subjects gave written informed consent to the study. All subjects had extensive experience with participating in fMRI studies and had no history of psychiatric, major medical, or neurological disorder. Because of strong movement artifacts, one subject was not included in the analysis.

Stimuli

The stimulus consisted of an 'X' ($1.2^\circ \times 1.2^\circ$ degree of visual angle), which was presented about 2.2° to the left or to the right of a central fixation point. The 'X' was presented in yellow on a black background. Additionally, an auditory pacing-signal composed of sine tones (600 Hz; 100 ms in duration) was presented at the start of a data collection run through the headphones at a loudness level of

95 dBA. As 95 dBA was uncomfortably loud for one subject, the loudness level was reduced to 70 dBA for this person.

Stimulus presentation, synchronization of stimulus presentation, image pulse acquisition, and recordings of motor responses were carried out with the software package Presentation (www.nbs.neuro-bs.com).

Task

The study consisted of two experimental conditions: Internally and Externally selected action conditions that were presented in a blocked order (see Fig. 1). We conducted 20 blocks per condition in an alternating fashion (IEIEIE...). Each block consisted of 35 internally or 35 externally selected actions. A resting phase, lasting about 12,400 ms, followed each block. During this period we showed a blank screen.

In both conditions, the stimuli were presented at a constant inter-stimulus-interval (ISI) of 1200 ms. Each run began with 10 pacing signals, with which participants had to synchronize their key presses. Visual stimuli were presented 600 ms before and 600 ms after the pacing signal, respectively. Afterwards participants continued pressing the keys without the pacing tones, attempting to maintain the target interval as accurately as possible and so as to bisect the interval between two visual stimuli.

In the internally selected condition, subjects could freely choose whether to press the left or the right button and so determined the position of the next stimulus (a left button press was followed by an 'X' on the left side of the fixation cross and a right button press was followed by an 'X' on the right side of the fixation cross, respectively). In the externally selected condition, subjects reacted with compatible button presses to the preceding stimulus. The S–R mapping was compatible throughout the whole experiment (a left 'X' guided a left key press, a right 'X' guided a right key press). The sequence of stimuli presented in a given externally selected condition was yoked to the sequence the subject created in the preceding internally selected condition. To prevent subjects from recognizing the sequence, the sequence was presented backwards and the position of the stimuli was vertically mirrored. The whole experiment lasted about 55 min.

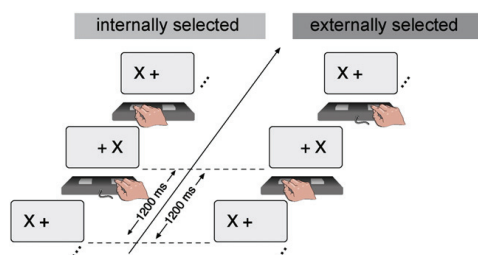


Fig. 1. Paradigm. Illustration of the two conditions. In the internally selected condition, subjects performed left (with the right index finger) or right button presses (with the right middle finger) in order to produce an 'X' on the left or right side of a fixation cross. In the externally selected condition, subjects reacted to the stimuli with compatible button presses. Both conditions were identical concerning motor performance, but differed in the action mode in which they were conducted.

fMRI data acquisition

The experiment was carried out on a 3T scanner (Siemens, Erlangen, Germany). Twenty axial slices were acquired (19.2 cm field of view, 64×64 matrix, 4 mm thickness, 1 mm gap) parallel to the AC–PC axis and covering the whole brain. Slice gaps were interpolated to generate output data with a spatial resolution of $3 \times 3 \times 3$ mm. A single shot, gradient recalled echo planar imaging (EPI) sequence was used (repetition time 2400 ms, echo time 30 ms, 90° flip-angle, acquisition bandwidth 100 kHz). Prior to functional runs, corresponding 20 anatomical MDEFT slices and 20 EPI-T₁ slices were acquired with the same geometrical parameters (slices, resolution) and the same bandwidth as used for the fMRI data. Stimuli were displayed using VisuaStim (Magnetic Resonance Technologies, Northridge, USA), consisting of two small TFT-monitors placed directly in front of the eyes, simulating a distance to a normal computer screen of about 100 cm with a resolution of 800×600 and a refresh rate of 60 Hz.

fMRI data analysis

Data processing was performed using the software package LIPSIA (Lohmann et al., 2001). This software package contains tools for pre-processing, co-registration, statistical evaluation, and visualization of fMRI data. First, functional data were corrected for motion using a matching metric based on linear correlation. Then, a sinc-interpolation algorithm was applied to correct for the temporal offset between the slices acquired in one scan. Data were filtered with a spatial Gaussian filter with 5.65 mm ($\sigma=0.8$) full width at half maximum (FWHM). A temporal high-pass filter with a cut-off frequency of 1/160 Hz was used for baseline correction of the signal. All functional data sets were individually registered into stereotaxic Talairach space using participant's individual high-resolution anatomical images. This 3D reference data set was acquired for each participant during a previous scanning session. The 2D anatomical MDEFT slices, geometrically aligned with the functional slices, were used to compute a transformation matrix containing rotational and translational parameter, which registers the anatomical slices with the 3D reference T1 data set. These transformation matrices were normalized to the standard Talairach stereotaxic space (Talairach and Tournoux, 1988) by linear scaling and finally applied to the individual functional data. The statistical evaluation was based on a least-squares estimation using the general linear model for serially autocorrelated observations (Friston et al., 1995; Worsley and Friston, 1995). The design matrix was generated with a boxcar function which was convolved with the hemodynamic response function. The two experimental conditions and the resting period were modeled as separate regressors. The model equation, including the observation data, the design matrix, and the error term, was convolved with a Gaussian kernel of dispersion of 4 s FWHM to deal with the temporal autocorrelation (Worsley and Friston, 1995). In the following, contrast images were generated for each subject. As noted before, each individual functional data set was aligned with the standard stereotaxic reference space, so that a group analysis based on the contrast images could be performed. The single-participant contrast images were then entered into a second-level random effects analysis for each of the contrasts. The group analysis consisted of a one-sample *t*-test across the contrast images of all subjects that indicated whether observed differences between conditions were significantly distinct from zero. Subsequently, *t*-values were transformed into *z*-scores. Results were

corrected for multiple comparisons using a combination of individual voxel probability thresholding and minimum cluster-size thresholding (Forman et al., 1995; Xiong et al., 1995). Given an original significance threshold of $z=3.09$ (uncorrected), 1000 iterations of Monte-Carlo simulations were used to confirm that the true false-positive probability of $p<0.001$ corresponds to a minimum cluster size of 1323.00 mm³.

Furthermore, we were interested in obtaining region*condition interactions in the signal-strength between a region in the rostral cingulate zone (RCZ) and a region in the preSMA. The RCZ coordinate was derived from the random effects analysis of the contrast between internally and externally selected condition and was centered at a local maximum of the z -map. The preSMA coordinate (2 4 54) was derived from Lau et al. (2004b). As the study of Lau et al. (2004b) used MNI coordinates, we transformed these MNI coordinates to Talairach space using Matthew Bretts' non-linear transformation (<http://imaging.mrc-cbu.ac.uk/imaging/MNITalairach>).

We defined a mask around each region with a radius of 6 mm. Within each subject and region (Voxel), a mean contrast was calculated separately for each condition. The mean values of the RCZ and preSMA subsequently entered a repeated measures ANOVA with factors condition and region. Effects were considered to be significant at an alpha of 0.05 with a Bonferroni correction for multiple comparisons. In a post hoc analysis, we then calculated differences between the two conditions for each region using two-sided Student's t -tests with effects to be considered significant at an alpha of 0.05.

Analysis of behavioral data

Only action times (time of key press [ms] after onset of the preceding stimulus) within the time window between 250 and 950 were retained for further analysis. Mean action times of the two conditions were compared with a two-tailed t -test. Moreover, for each condition, we ran a t -test against the bisection point (=600 ms).

Results

Behavioral data

T -tests against the bisection point revealed that action times differed in both conditions significantly from 600 ms (internally selected: $t(14)=-3.025$, $p<0.009$; externally selected: $t(14)=-5.440$, $p<0.000$). Furthermore, action times in the internally and externally selected condition differed significantly in the expected direction (MEAN: 569 ms vs. 501 ms; SE: 39.59 ms vs. 70.60 ms), $t(14)=4.238$, $p<0.001$. Mean asynchronies were smaller for the internally selected (-31 ms) than for the externally selected condition (-99 ms) (Fig. 2).

fMRI data

Whole-brain analysis

Internally vs. externally selected actions. As expected, the direct comparison of internally vs. externally selected actions revealed activation in the medial wall of the frontal lobe, namely in the rostral cingulate zone (RCZ). Moreover, we found activations in the lateral prefrontal cortex (IPFC) extending to anterior PFC, in the inferior parietal lobe (IPL), and bilaterally in the insula (Fig. 3) (Table 1). Most importantly, in contrast to previous studies, we

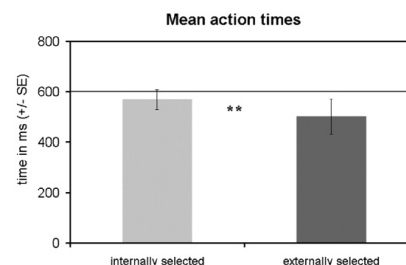


Fig. 2. Behavioral data. Action time (\pm SE) during internally and externally selected condition. The asterisk indicates significant differences between internally and externally selected actions. The bold line indicates the bisection point.

found no activity in the preSMA for this contrast. The reverse contrast of externally vs. internally selected actions showed no significant activations. Baseline contrasts are reported in the Supplementary data.

Signal-strength analysis

Because we were mainly interested in the role of the RCZ and the preSMA in internally selected actions, we ran an ANOVA with the factors region (RCZ and preSMA) and condition (internally vs. externally selected). The analysis revealed a significant region*condition interaction ($F(1,14)=13.706$; $p=0.002$; Fig. 3). As already obvious from the whole-brain analysis, the post hoc analysis revealed significant differences between the internally and externally selected condition only in the RCZ but not the preSMA (preSMA: $t(14)=1.369$, $p=0.193$; RCZ: $t(14)=5.053$; $p=0.000$). Thus it seems as if only the RCZ differentiated between internally and externally selected actions. The preSMA showed equal activity in both conditions and thus did not differentiate between internally and externally selected actions.

Discussion

The aim of the current fMRI study was to disentangle the role of the preSMA and the RCZ in internally selected actions without confounding motor and perceptual differences. We employed the paradigm developed by Waszak et al. (2005) in which internally and externally selected actions did not differ as concerns the timing, the sensorimotor context, and the kinematics of the movements. In the direct comparison of internally vs. externally selected actions, a widespread cortical network was found to be activated including frontolateral and inferior parietal brain areas. Most crucially, an activation in the RCZ was observed. A signal-strength analysis showed preSMA and RCZ activation for both internally and externally selected actions. However, in contrast to the RCZ, the preSMA did not differentially contribute to internally selected actions.

The behavioral data showed that movements generally preceded the true bisection point (for a discussion of these "negative asynchronies" see for example Aschersleben and Prinz, 1995). More importantly, the results replicated the finding from Waszak et al. (2005; in the behavioral domain) and Haggard et al. (2002) that triggering stimulus and response, on the one hand, and action and ensuing effect, on the other hand, attract each other temporally. This finding suggests that depending on the mode of movement the

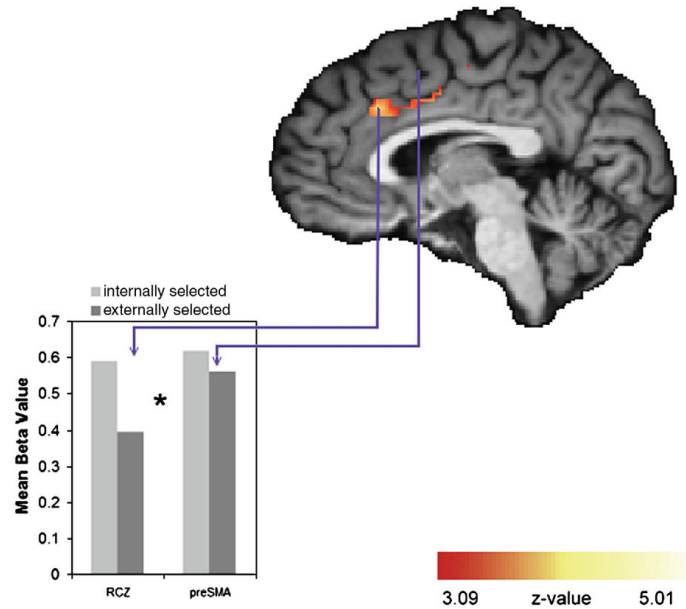


Fig. 3. Contrast between internally and externally selected action. The contrast was averaged over 15 subjects (z -threshold at $z=3.09$, corrected) and mapped to an individual brain from the in-house database. The diagram reports mean beta values for internally and externally selected actions in a region of the RCZ and a region of the preSMA (RCZ Talairach-coordinates: $x: 3, y: 23, z: 33$ and preSMA MNI-coordinates: $x: 2, y: 4, z: 54$, Talairach-coordinates: $x: 2, y: 6, z: 49$). RCZ coordinate is from the contrast internally vs. externally selected actions; preSMA coordinate is from Lau et al. (2004b). The asterisk indicates the significant interaction region* condition.

subjects operate in, sensory-motor integration involves stimuli and responses on one hand or actions and effects on the other hand (see Herwig et al., in press; Waszak et al., 2005).

The role of the RCZ in internally selected actions

As most of the previous studies dealing with internally selected actions, the results of the present study showed that both RCZ and

preSMA are involved in internally selected actions. However, when controlling for perceptual and motor confounds, only the RCZ is differentially involved in internally selected as compared to externally selected actions. The preSMA seems to contribute equally to both kinds of actions.

That the RCZ is involved in internally selected actions has been shown in several other fMRI studies (Cunnington et al., 2003, 2006; Debaere et al., 2003; Deiber et al., 1999; Lau et al., 2004a; van Eimeren et al., 2006; Wiese et al., 2004, 2005).

However, the functional role of the RCZ is still under discussion. The RCZ has been associated with a multitude of cognitive control processes, from “higher” cognitive functions to more motor-related functions like relating actions to their effects (Rushworth et al., 2004). In this latter vein, Walton et al. (2004) argue that it is not performance monitoring or reward guided action selection per se that causes RCZ activity but the process of assessing the consequences of a choice made by the subject. This notion nicely fits to the present results. In our study, the subjects’ actions resulted in the presentation of the corresponding stimulus only in the condition with internally selected actions. Along the lines of the ideomotor principle (James, 1890, 1950; Prinz, 1997), we assume that in this condition the action representation is activated by anticipation of the actions’ effect. In the externally selected condition, by contrast, there was no action–effect contingency. In this condition, so our reasoning goes, the action representation is activated by the triggering stimulus. Hence, RCZ activation might be higher in internally selected actions as compared to externally selected

Table 1
Anatomical location and Talairach coordinates with $z>3.09$ ($p=0.001$, corrected)

Anatomical area	Side	z_{\max}	Talairach coordinates		
			x	y	z
<i>Frontal</i>					
Rostral cingulate zone	R	4.18	3	23	33
Anterior prefrontal cortex	L	3.53	−18	68	18
Insula	L	4.03	−39	5	6
Insula	R	4.90	39	8	0
<i>Parietal</i>					
Inferior parietal lobe	R	5.00	54	−31	36
Inferior parietal lobe	R	4.35	48	−37	45

Activations with a minimum cluster size of 1323 mm^3 are shown. Comparison internally vs. externally selected actions. The table contains Talairach coordinates (x, y, z) of the most intense activated voxels of the cluster.

actions, simply because only the former necessitate action–effect anticipation.

Support for this notion comes also from the behavioral domain. Herwig et al. (in press) compared action–effect learning in two conditions similar to the two conditions investigated in the present study. The experiment consisted of an acquisition and a test phase. In the acquisition phase, subjects performed actions that were followed by certain effect tones. Importantly, one group of subjects – the internally selected group – was required to freely select between the two possible actions. In another group – the externally selected group – subjects' actions were determined by external stimulus events. Thus Herwig et al. tested two conditions that probably involve high and low activation of the RCZ, respectively. The results of the test phase showed action–effect learning only for the internally selected acquisition group (for details, see Herwig et al., in press). The results are thus consistent with the idea that RCZ activation is related to effect anticipation (and therefore also with action–effect learning), as supposed by the theoretical framework put forward by Rushworth et al. (2004).

However, there is another possible explanation for the RCZ activation found in the present study. Lau et al. (2004a,b) as well as Cunnington et al. (2005), for example, argue that randomly selecting one out of a set of possible responses constitutes an underdetermined response and therefore triggers response conflict. Monitoring response conflict has repeatedly been related to RCZ activation (Botvinick et al., 2001; Botvinick et al., 2004; Carter et al., 1998; Kerns et al., 2004). Thus the RCZ activation reported above may reflect a sort of conflict monitoring. However, notice that this notion can hardly explain why several studies found RCZ activation when subjects could choose *when* to press a certain *pre-determined* button (Cunnington et al., 2003; Deiber et al., 1999; Jenkins et al., 2000; Wiese et al., 2004, 2005). In these studies, there was only one response required and, therefore, no response conflict of the type outlined above.

At any rate, that the RCZ plays a major role in internally selected actions is also supported by neuroanatomical considerations. The RCZ sends efferents both to the primary motor cortex and to the spinal cord, thus having direct influence on motor behavior (Dum and Strick, 1991). Shima and Tanji (1998) suggest that, because of their anatomical connectivity with the preSMA and primary motor cortex, the cingulate motor areas are in a pivotal position to process the information which is necessary to select voluntary actions. Support for this assumption comes from the fact that, in voluntarily timed actions, the cingulate motor areas have been shown to be activated before the preSMA and the primary motor cortex (Ball et al., 1999; Cunnington et al., 2003).

Role of the preSMA

The second main result of this study is that preSMA activation did not differ between internally and externally selected actions. This is to be expected if the role of the preSMA is not linked to the selection of the action, but rather to its timing or initiation. Notice that in both conditions we investigated if subjects had to time the action such as to meet the bisection point. Accordingly, whether externally or internally *selected*, the trigger to initiate the action is necessary in both conditions to the same degree, such that preSMA activation was bound to be the same in both conditions.

This idea is in line with previous studies that associate the preSMA to the generation of self-initiated and self-paced (internally timed) actions (Cunnington et al., 2002, 2003; Debaere et al., 2003;

Deiber et al., 1999; Wiese et al., 2004). Likewise, bilateral lesions impaired the ability to generate simple internally timed actions (Thaler et al., 1995). More recently, Cunnington et al. (2006) suggested that the preSMA plays a major role in maintaining responses in readiness for action.

To sum up, our findings are thus compatible with the view that the RCZ activation is more closely linked to internally selected actions ('what-component'), whereas the preSMA might be more closely linked to the internal timing of an action ('when-component'), i.e., to find the right moment for the action. This latter point has already been suggested more than 20 years ago by Kornhuber and Deecke who hypothesized in the commentary to Goldberg's article (1985) (p. 591):

Because of this functional uniqueness a motivational role with emphasis on the will has been ascribed to the SMA (Kornhuber, 1980). However, motivation is a complex function with several independent subfunctions concerning *what* to do, *how* to do it and *when* to start. The latter function that of finding the right moment for action, is in our view the task of the SMA (Kornhuber, 1984).

Activations due to working memory and attentional load

Lateral and anterior PFC

Besides activation in the medial frontal wall, we observed significant activation differences between the two action conditions which were located in the right IPFC, extending to the anterior PFC. Even though these activations were not in the focus of our interpretations about the neural bases of internally selected actions, we have some clear ideas about their function. One possible explanation for the IPFC activation might be working memory processes due to the generation of random button presses (Jahanshahi et al., 1998). Another possible explanation for the IPFC activation in our study is that it reflects stronger attentional demands during internally selected actions (Lau et al., 2004a).

Another detail worthwhile to be reported is that, in contrast to previous imaging studies, the IPFC activation we found reaches up to the anterior PFC (BA 10). This activation might be due to branching processes. According to Koechlin et al. (1999), branching is the ability to keep in mind primary goals while exploring and processing secondary goals. Related to our study, this would mean that while our subjects had to bisect the task with left or right button press, they should randomize their button presses and thus hold in mind which buttons they pressed before.

IPL

As several previous fMRI studies, we found for internally selected actions a stronger bilateral activation in the inferior parietal lobe (BA 40) (Ball et al., 1999; Jahanshahi et al., 1995; Jenkins et al., 2000; Wiese et al., 2005). This area is reciprocally connected to the IPFC (Cavada and Goldman-Rakic, 1989), which, as outlined above, was also strongly activated during the internally selected action condition. Hence, we suggest that the parietal activation also reflects stronger attentional demand due to the random number generation.

To conclude, given the obvious requirement of generating random sequences in the internally but not the externally selected condition, we found a nice dissociation in the fMRI data between areas that are primarily involved in the generation of random sequences (IPFC activations) and activations associated primarily

with internally selected actions (activations in the medial frontal wall).

Conclusion

The present fMRI study aimed at investigating the neural correlates of internally selected actions. For this purpose, we compared internally and externally selected actions within a paradigm in which both conditions differed only in the action mode in which they were conducted. The behavioral as well as the functional imaging findings are in general agreement with previous studies that – compared to the current study – were less strictly controlled and therefore confounded by perceptual and motoric differences. We were able to show, first, that the preSMA contributes to both internally and externally selected actions in a similar way and, second, that the RCZ is differentially activated in internally as compared to externally selected actions. We suggest a primary role for the RCZ in the internal selection of actions ('what-component'), whereas the preSMA might be more closely linked to the internal timing of an action ('when-component'), i.e., to find the right moment for the action. Activations in the IPFC and IPL that were also found during internally selected actions possibly reflect working memory and attention-related processes due to the random generation of button presses as well as due to higher attentional load in the internally selected condition.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2007.06.018](https://doi.org/10.1016/j.neuroimage.2007.06.018).

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2.1 Supplementary Materials Empirical Section I

Baseline contrasts

Significant activations for the baseline contrast of internally selected actions vs. rest were found in the left precentral gyrus, extending to the preSMA, in the right central sulcus of the insulae, bilaterally in the superior temporal gyrus as well as in the right cerebellum (Table 2). A similar network of activations was found for the contrast of externally selected actions vs rest, namely in the left precentral gyrus, extending to the preSMA, in the right lateral prefrontal cortex and in the left putamen (Table 3).

Table 2:

Anatomical location and Talairach coordinates with $z=3.09$ ($p=0.001$, corrected).

Anatomical area	Side	Z _{max}	Talairach coordinates		
		x	y	z	
<i>Frontal</i>					
precentral gyrus	L	5.55	-36	-16	54
sulcus centralis insulae	R	4.87	33	14	18
<i>Temporal</i>					
superior temporal gyrus	L	4.56	-63	-31	9
	R	4.10	48	-43	18
<i>Others</i>					
Cerebellum	R	3.92	24	-55	-18

Activations with a minimum cluster size of 1323 mm^3 are shown. Comparison internally selected actions vs. rest. The table contains Talairach coordinates (x y z) of the most intense activated voxels of the cluster.

Table 3:

Anatomical location and Talairach coordinates with $z=3.09$ ($p=0.001$, corrected).

Anatomical area	Side	Z_{\max}	Talairach coordinates		
		x	y	z	
<i>Frontal</i>					
precentral gyrus	L	5.63	-39	-25	54
lateral prefrontal cortex	R	4.78	42	-1	33
<i>Others</i>					
Putamen	L	4.21	-21	5	12

Activations with a minimum cluster size of 1323 mm^3 are shown. Comparison externally selected actions vs. rest. The table contains Talairach coordinates (x y z) of the most intense activated voxels of the cluster.

Chapter 3

Empirical Section II



Dissociating what and when of intentional actions

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Recent brain imaging research revealed that internally guided actions involve the frontomedian wall, in particular the preSMA and the rostral cingulate zone (RCZ). However, a systematic decomposition of different components of intentional action is still lacking. We propose a new paradigm to dissociate two components of internally guided behavior: Which action to perform (selection component) and when to perform the action (timing component). Our results suggest a neuro-functional dissociation of intentional action timing and intentional action selection. While the RCZ is more strongly activated for the selection component, a part of the superior medial frontal gyrus is more strongly activated for the timing component. However, in a *post hoc* conducted signal strength analysis we did also observe an interaction between action timing and action selection, indicating that decisional processes concerning action timing and action selection are not completely dissociated but interdependent. Altogether this study challenges the idea of a unitary system supporting voluntary action and instead suggests the existence of different neuroanatomically dissociable subfunctions.

Keywords: fMRI, intentional action, action timing, action selection, frontal medial wall

INTRODUCTION

Human actions exist along a continuum with regard to whether they are externally or internally controlled. In every day life, actions rarely correspond to the extremes of the continuum. Nevertheless, they can be classified into actions guided foremost by internal factors, for example switching on TV to watch the news, and actions guided rather by environmental stimuli, for example stopping in front of a red traffic light.

The two types of actions differ in functional terms and in the neurophysiological substrate that controls the actions. Herwig et al. (2007) suggest that, in the stimulus-based mode, the agent passes on control to the environment in that the system merely acts upon presentation of a particular stimulus in a prespecified way (prepared reflex, see Hommel, 2000). These actions are selected with respect to their sensory antecedents. By contrast, in the intention-based mode actions are guided by the ideomotor principle, that is, they are selected with respect to the intended sensory consequences (e.g., Greenwald, 1970; Prinz, 1997). Regarding the underlying neuroanatomical differences between the two action modes (Goldberg, 1985) emphasized the distinction between a medial and a lateral motor system which are involved in internally and externally guided actions, respectively.

As concerns voluntary actions, fMRI studies show that several areas in the frontomesial cortex including the preSMA and the anterior cingulate cortex (ACC) play a major role in the internal selection and timing of action, as well as in related functions like the inhibition of competing action alternatives and the evaluation of likely outcomes and rewards of actions (e.g., Cunnington et al., 2002, 2005; Lau et al., 2004a,b, 2006; Rushworth et al., 2004). However, performing a voluntary action necessitates a large amount of information to be generated and processed. The areas involved in

voluntary action control are not only in charge of the prediction of the sensory consequences of the action (see Blakemore et al., 1998) and of the conscious experience of intending to act (see Haggard and Clarke, 2003), they also have to take care of a series of decisions regarding whether to act (see Brass and Haggard, 2007), what action to perform and when to perform it. It is at present unclear how precisely these different cognitive antecedents of voluntary actions are controlled in the brain.

The present study is meant to fill one of the gaps in our current knowledge of the neurophysiological substrate of voluntary action control. To be precise, we aimed at providing further insights into the role of frontomesial cortical regions in two different decision processes that are basic for carrying out a voluntary action: When people perform voluntary actions, they do not only have to choose which action to perform, they also have to determine an appropriate point in time to perform it. Imagine a soccer player approaching the goal. He has to decide whether to pass the ball or to shoot on the goal. He also has to choose the right moment to act. Thus, there are at least two components of internally guided actions: 'what' and 'when' (see Mueller et al., 2007). In the following we label actions referring to the 'when-component' internally or externally *timed*, whereas we label actions referring to the 'what-component' internally or externally *selected*.

Usually studies on voluntary action investigate one or the other component of voluntary action control. A direct comparison of both components within one paradigm has never been carried out. Typically, in studies exploring internal action *timing*, a condition in which subjects self-initiate a key press is compared with a condition in which subjects respond to a visual or acoustic cue (c.f. Deiber et al., 1999). As a correlate of internal action timing those studies reported activation in the preSMA and/or cingulate motor

areas (Cunnington et al., 2002; Debaere et al., 2003; Deiber et al., 1999; Jahanshahi et al., 1995; Jenkins et al., 2000; Wiese et al., 2004). Similar activations were found in studies exploring the internal selection of actions (Cunnington et al., 2006; Lau et al., 2006; van Eimeren et al., 2006). van Eimeren et al. (2006), for example compared a full-selection condition in which subjects could freely select which one out of four buttons to press with different restricted conditions (two or three response possibilities) as well as with a full restricted condition (forced choice). The most prominent activation they found as a correlate for internal action selection was located in the ACC, and the preSMA. Taken together there seems to be no evidence for a specific activation related to the selection or timing component of intentional action. This finding is in line with the conclusion (Jahanshahi and Frith, 1998) drew from a review of several neuroimaging studies: They found several cortical (dorsolateral prefrontal cortex, ACC and SMA) and subcortical structures (thalamus and basal ganglia) to be involved in the control of voluntary actions regardless of whether they are internally selected, timed or inhibited and proposed the existence of a uniform 'willed action system'.

However, contrary to this notion, Mueller et al. (2007) provided evidence for a dissociation of the 'what-' and the 'when-component' of intentional action, using a paradigm introduced by Waszak et al. (2005). In this paradigm, subjects performed a temporal bisection task, making left or right key presses at the midpoint between isochronous pacing signals (a sequence of 'X's presented to the left or the right of the fixation cross). In the internally selected condition the subjects' key press determined the location of the subsequent 'X' on the screen. In this condition, subjects were instructed to generate a random sequence of left and right 'X's. In the externally selected condition, by contrast, the subjects' key press was prompted by the location of the preceding stimulus. The movements in a given externally selected run were yoked (in a disguised fashion) to the movements produced in the preceding internally selected run. The results of the study by Mueller et al. (2007) revealed that the rostral cingulate zone (RCZ) but not the preSMA was related to internal action selection. Mueller and colleagues speculated that the preSMA might be more closely linked to the internal action timing. However, a direct comparison of both components – necessary to demonstrate a dissociation between the two aspects of action control within the frontomedian wall – has never been carried out.

In the present study we directly tested for a functional dissociation of 'when-' and 'what-component' within regions of the frontomedian wall. To do so, we independently manipulated these two components of voluntary action control within one task. Subjects were instructed to decide as fast as possible after presentation of a cue which action to perform, and when. The two decisions were either taken by the participants (internal) or based on the cue (external), enabling us to differentiate between internal and external 'when' and 'what' decisions. Based on the findings of Mueller et al. (2007), we expected to find increased activation in the RCZ for internally selected actions and increased activation in the preSMA for internally timed actions. In this previous study we could show a similar network of activations for internally and externally selected actions, but to a stronger degree for internally selected actions. From this result we concluded that externally guided actions are generally less complex than internally guided actions. Therefore we

did not expect to find activation differences for the main effects of the reversed contrasts (externally selected and externally timed actions respectively).

While the primary goal of our study was to investigate brain areas that are involved in the decision processes that occur in the cue phase, we tested whether frontomedian activation was also related to the implementation of the action. In our paradigm the moment when the subjects have to make the decision what to do, and when, and the moment when the subjects actually have to execute the action were experimentally dissociated. Subjects were instructed to decide as fast as possible after cue presentation which action to perform, and when. However, it is only after a variable cue-target-interval (CTI) that they were required to perform the action, enabling us to separate cue and target BOLD-response (reflecting decisional processes and processes related to the implementation of the action, respectively).

We assumed that activation differences in the frontomedian wall reflect mainly decisional aspects of voluntary action control. Since we were especially interested in these 'what' and 'when' decisions, the fMRI analysis focused on activations upon cue presentation. By contrast, we presumed that the implementation of the decision should not differentially involve frontomedian brain regions. Thus we hypothesized to find no activation differences contingent on the target in the frontomedian wall. The data of the target period are also presented below.

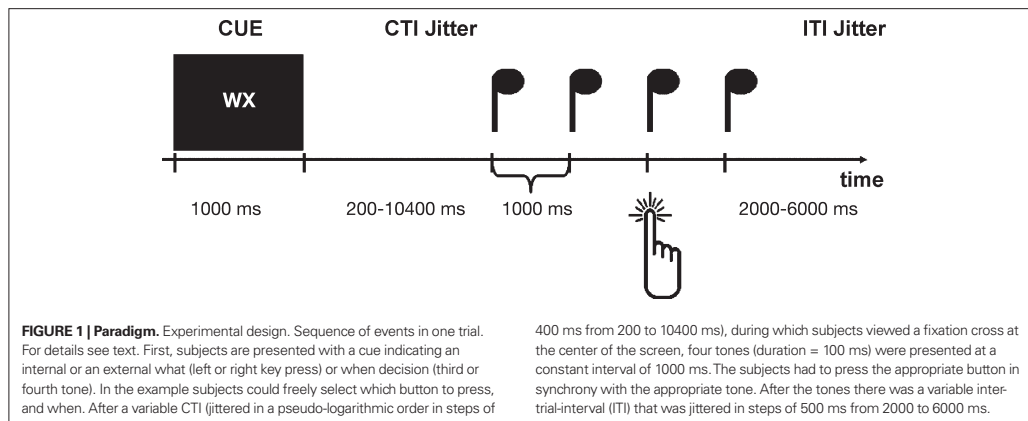
MATERIALS AND METHODS

SUBJECTS

Sixteen healthy subjects (eight females) with a mean age of 25.44 years ($SD \pm 2.87$) with normal or corrected to normal vision participated in the study. Two subjects were excluded from the analysis because they were not able to synchronize key presses with the pacing signals. Hence, 14 subjects remained (6 females). All subjects were right-handed as indicated by scores on the Edinburgh Handedness Inventory (Oldfield, 1971). Subjects gave written informed consent to the study. All subjects had extensive experience with participating in fMRI studies and had no history of psychiatric, major medical, or neurological disorder.

TASK

The sequence of events in one trial was as follows (see Figure 1). At the beginning of each trial subjects were presented with a cue consisting of two letters. After a variable CTI (jittered in a pseudo-logarithmic order in steps of 400 ms from 200 to 10400 ms), during which subjects viewed a fixation cross at the center of the screen, four tones (duration = 100 ms) were presented at a constant interval of 1000 ms. The rationale behind the intense jittering of the CTI was to separate cue-related activation from target-related activation. This separation was critical to the present study as we wanted to look at processes underlying action planning rather than action execution. Furthermore it is important to note that we introduced four target tones rather than two target tones to assure that subjects could prepare the two possible action times equally well. This manipulation also guarantees that subjects responded with the tone rather than reacted on the tone as they were able to anticipate the appearance of the target tone. The task of the subject was to perform a left or a right key press on the third or the fourth tone.



The first letter of the cue informed the subject about the ‘what-decision’: it indicated either that the subject was to freely choose between left and right (W), or it indicated which key to press [L or R (left/right in German)]. That is the first letter indicated either an internal ‘what-decision’ or an external ‘what-decision’. The second letter of the cue informed the subject about the ‘when-decision’: it indicated either that the subject was to freely choose between the third and the fourth key press (X), or it indicated the tone on which the subject had to press the key [D or V (third/fourth in German)]. That is the second letter indicated either an internal ‘when-decision’ or an externally cued ‘when-decision’. Subjects were instructed to decide as fast as possible after the cue presentation which action to perform, and when.

Both factors [‘what’ (externally vs. internally) and ‘when’ (externally vs. internally)] were independently crossed, resulting in four action conditions: both parameters internal (entirely internal condition), ‘what’ internal and ‘when’ external (internal selection condition), ‘what’ external and ‘when’ internal (internal timing condition), and ‘what’ and ‘when’ external (entirely external condition). After the tones there was a variable inter-trial-interval (ITI) that was jittered in steps of 500 ms from 2000 to 6000 ms. Due to the intense jittering the total trial length varied between 6600 ms (for the shortest trial) and 20800 ms (for the longest trial).

We conducted an event-related-design and stimuli were presented in randomized order. For each of the four conditions there were 36 trials; the whole experiment lasted about 30 min. Prior to the scanning session subjects underwent a training session outside the scanner to become familiar with the paradigm. The procedure was identical to the main session with the exception that we introduced feedback after the button press. Subjects then started the next trial themselves to give them time to ask questions if they had some. The training phase lasted about 5 min.

STIMULI

The stimuli used as the cue consisted of six letters (L, R, D, V, W, X; see above). The letters were presented in pairs of two in the center of the screen. They were presented in white on a black background.

The auditory pacing signals were sine tones (600 Hz; 100 ms in duration) presented at a constant interval of 1000 ms after the CTI at a loudness level of 80 dBA. Stimulus presentation, synchronization of stimulus presentation, image pulse acquisition and recordings of motor responses was carried out with the software package Presentation (<http://www.neurobs.com>).

MRI SCANNING PROCEDURE

The experiment was carried out on a 3T scanner (Siemens, Erlangen, Germany). Twenty-four axial slices were acquired (19.2 cm field of view, 64×64 matrix, 4 mm thickness, 25% gap) parallel to the AC-PC-axis and covering the whole-brain. Slice gaps were interpolated to generate output data with a spatial resolution of $3 \text{ mm} \times 3 \text{ mm} \times 3 \text{ mm}$. A single shot, gradient recalled echo planar imaging (EPI) sequence was used (repetition time 2000 ms, echo time 30 ms, 90° flip-angle, acquisition bandwidth 100 kHz). Prior to functional runs corresponding 24 anatomical MDEFT slices and 24 EPI- T_1 slices were acquired with the same geometrical parameters (slices, resolution) and the same bandwidth as used for the fMRI data. Stimuli were displayed by an LCD projector on a back-projection screen mounted in the bore of the magnet behind the participants’ head.

fMRI DATA ANALYSIS

Data processing was performed using the software package LIPSIA (Lohmann et al., 2001). This software package contains tools for pre-processing, co-registration, statistical evaluation, and visualization of fMRI data. First, functional data were motion-corrected offline with the Siemens motion correction protocol (Siemens, Erlangen, Germany). Then, a sinc-interpolation algorithm was applied to correct for the temporal offset between the slices acquired in one scan. Data were filtered with a spatial Gaussian filter with 5.65 mm ($\sigma = 0.8$) full width at half maximum (FWHM). A temporal high-pass filter of 90 s was used for baseline correction of the signal. All functional data sets were individually registered into 3-D space using participant’s individual high-resolution anatomical images. This 3-D reference data set was acquired for each

participant during a previous scanning session. The 2-D anatomical MDFET slices, geometrically aligned with the functional slices, were used to compute a transformation matrix containing rotational and translational parameter, which register the anatomical slices with the 3-D reference T1 data set. These transformation matrices were normalized to the standard Talairach stereotactic space (Talairach and Tournoux, 1988) by linear scaling and finally applied to the individual functional data. The statistical evaluation was based on a least-squares estimation using the general linear model for serially autocorrelated observations (Friston et al., 1995; Worsley and Friston, 1995). The design matrix for event-related analysis was created using a model of the hemodynamic response with a variable delay. Brain activations were analyzed in an event-related design. The four experimental conditions were modeled for cue and target as separate regressors with the trigger set on the appearance of the cue and the button press respectively (duration of analyzed events: 1000 ms). Furthermore CTI and ITI were also modeled as separate regressors with the trigger set on the start of the CTI and ITI. Here the duration of the events was identical with the respective CTI and ITI duration. Only correct trials, that is, trials with correct button press (L/R) and action times [time of key press (ms) before or after onset of the tone] within the time window between 250 ms before and 250 ms after the tone were retained for further analysis. The model equation, including the observation data, the design matrix and the error term, was convolved with a Gaussian kernel with a dispersion of 4-s FWHM to account for the temporal autocorrelation (Worsley and Friston, 1995). Contrast maps were generated for each participant. As the individual functional datasets were all aligned to the same stereotactic reference space, a group analysis was then performed. A one-sample *T*-test of contrast maps across participants (random effects model) was computed to indicate whether observed differences between conditions were significantly different from 0. Subsequently, *T*-values were transformed into *z*-scores. Results were corrected for multiple comparisons using a combination of individual voxel probability thresholding and minimum cluster size thresholding (Forman et al., 1995; Xiong et al., 1995). Given an original significance threshold of $z = 3.09$ (uncorrected), 1000 iterations of Monte Carlo simulations were used to confirm that the true false-positive probability of $p = 0.001$ corresponds to a minimum cluster size of 1134.00 mm³.

For the signal strength analysis we defined a mask around each region with a radius of 9 mm. Within each subject and region (Voxel) a mean contrast was calculated separately for each condition. The mean values of the regions subsequently entered SPSS for further analysis as described in the results part.

ANALYSIS OF BEHAVIORAL DATA

As for the fMRI analysis, only correct trials were retained for further analysis. To test for differences between conditions we ran a repeated measures ANOVA with factor condition. Moreover, for each condition we ran a one-sampled *T*-test against the point of perfect synchrony (=0 ms).

RESULTS

BEHAVIORAL DATA

Subjects performed the task with high accuracy. The timing (correct tone as well as valid action time) was correct in 96.92%

(SD = 3.35%) of all trials. Button presses were correct in 99.15% of all trials (SD = 1.104%). In the 'selection internal' conditions subjects pressed the left button more often than the right button (53.4% compared to 46.6%; paired-samples *T*-test: $t(13) = -3.066$; $p = 0.009$). In the 'timing internal' conditions subjects pressed the buttons more often with the third tone than with the fourth tone (56.77% compared to 43.23%; paired-samples *T*-test: $t(13) = 2.646$; $p = 0.020$). Our subjects were thus slightly biased. This is in correspondence with the common finding that people cannot generate sequences that are really random.

Subjects showed in all conditions a negative asynchrony, i.e., they performed the key press slightly in advance of the target tone ['both internal': -38.84 ms (SE 14.97); $t(13) = -2.594$; $p = 0.022$; 'timing internal': -39.66 ms (SE 15.76); $t(13) = -2.517$; $p = 0.026$; 'selection internal': -41.37 ms (SE 15.11); $t(13) = -2.737$; $p = 0.017$; 'both external': -45.66 ms (SE 14.61); $t(13) = -3.126$; $p = 0.008$], a common finding in synchronization experiments (Aschersleben and Prinz, 1995). This shows that subjects did not simply react to the tones. However, there were no significant differences in action times between the four conditions [$F(3, 11) = 1.077$; $p = 0.399$].

fMRI DATA

Whole-brain analysis

To analyze activity contingent on the cue and activity contingent on the target we computed two separate ANOVAs with the factors action selection (internal, external) and action timing (internal, external).

Cue-related activity. We found stronger activations for internal action selection than for external action selection in the right RCZ extending to medial BA 8 (Figure 2A) and in the right precuneus (BA 7) (Table 1). We did not find any activation that was significantly stronger for external action selection than for internal action selection.

Stronger activations for internal action timing than for external action timing were found in the left superior frontal gyrus (SFG) in BA 6 that extended from the medial wall to the lateral convexity of the SFG, hereinafter referred to as paramedian frontal cortex (Figure 3A; Table 1). Additionally we found activations that were stronger for external action timing than for internal action timing. These were located bilaterally at the border between inferior occipital lobe and fusiform gyrus (Table 1). Finally, the interaction of action timing and action selection did not yield any activation that survived the cluster threshold.

Target-related activity. Although our main focus was on activations appearing around the point in time when subjects made their decisions (i.e., on cue-related activation) we also analyzed the processes taking place around the implementation of the decision. Stronger activations for internal action selection than for external action selection were found bilaterally in the middle frontal gyrus (BA 10), in the inferior parietal lobe (BA 40), as well as at the border between inferior frontal gyrus (BA 47) and the insula (BA 13) (see Table 2). The reverse comparison revealed no activation that survived the threshold. When computing the main effect for the when component, we found only an activation that was stronger for external action timing than for internal action timing. This was located in the lingual gyrus (BA 18).

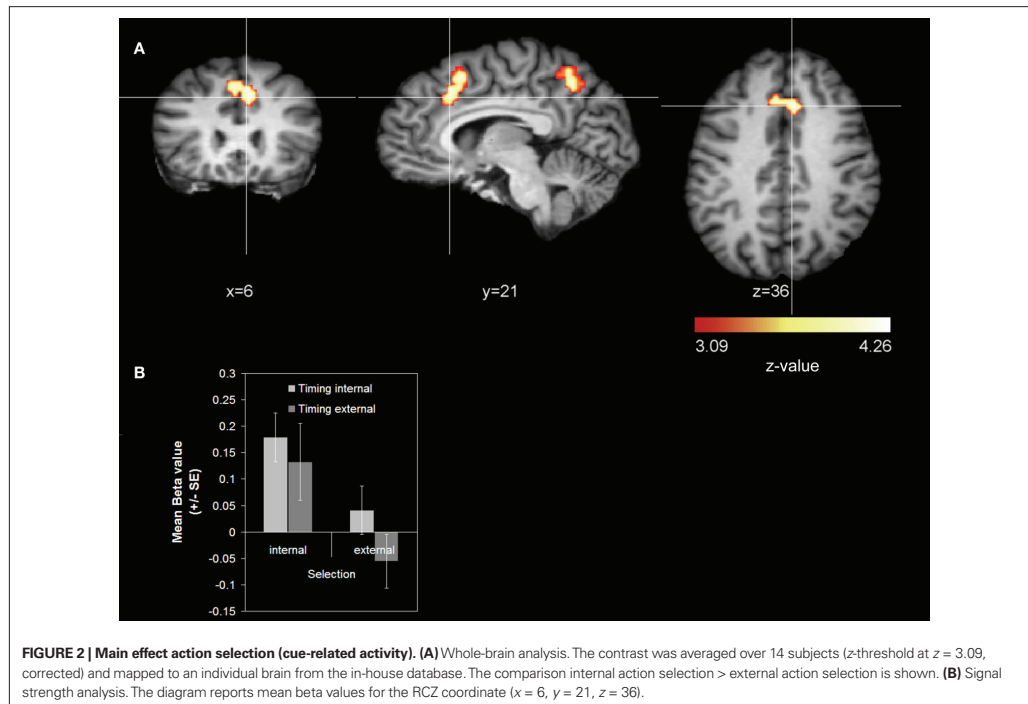


Table 1 | Anatomical location, hemisphere, maximum Z value ($p = 0.001$, corrected) and Talairach coordinates. Cue-related activations with a minimum cluster size of 1134 mm^3 are shown.

Anatomical area	Side	Z _{max}	Talairach coordinates		
			x	y	z
MAIN EFFECT ACTION SELECTION					
Internal > external					
Rostral cingulate zone	R	4.26	6	21	36
Precuneus	R	3.72	3	−60	45
MAIN EFFECT ACTIONTIMING					
Internal > external					
Superior frontal Gyrus (paramedian frontal cortex)	L	4.48	−18	12	51
External > internal					
Inferior occipital lobe/fusiform gyrus	L	4.95	−42	−66	−3

We observed no activations in the frontomedian wall, neither for the main effect action selection, nor for the main effect action timing. However, if we lowered the threshold to a more liberal one ($z > 3.09$; $p = 0.05$, corrected) we observed an activation in the RCZ for the main effect action selection. However, this activation was much smaller compared to the cue-related activation (567 mm^3 compared to 1944 mm^3). As for the cue-related activation we did not find any

activation that survived the cluster threshold when computing the interaction term of action selection and action timing.

Signal strength analysis. To gain more detailed information about the pattern of activation of the cue-related activations that were linked to the two voluntary action components in the whole-brain analysis we performed a signal strength analysis in the two main

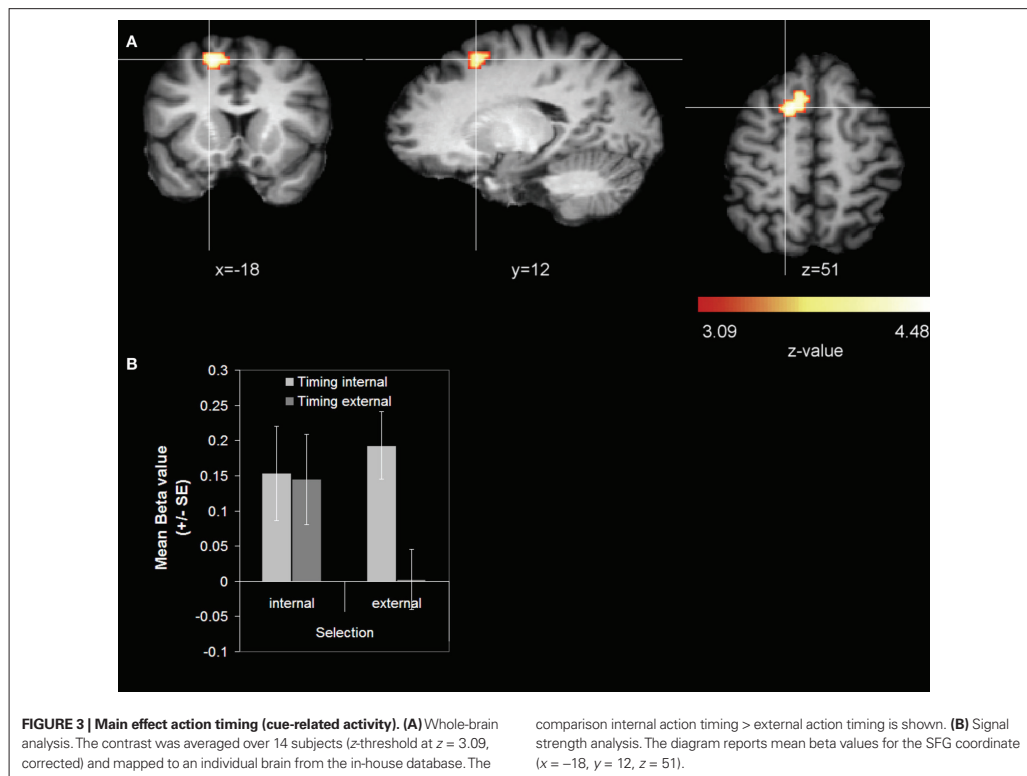


Table 2 | Anatomical location, hemisphere, maximum Z value ($p = 0.001$, corrected) and Talairach coordinates. Target-related activations with a minimum cluster size of 1134 mm³ are shown.

Anatomical area	Side	Z _{max}	Talairach coordinates		
			x	y	z
MAIN EFFECT ACTION SELECTION					
Internal > external					
Middle frontal gyrus (BA 10)	R	4.17	30	51	21
Middle frontal gyrus (BA 10)	L	3.93	−39	60	9
Inferior frontal Gyrus/Insula (BA 47/13)	L	4.52	−45	18	−3
Inferior parietal lobe (BA 40)	R	3.89	48	−36	51
Inferior parietal lobe (BA 40)	L	5.28	−51	−42	48
MAIN EFFECT ACTION TIMING					
External > internal					
Lingual gyrus (BA 18)	L	−4.90	−9	−72	−3

clusters for internal action selection (RCZ) and internal action timing (paramedian frontal cortex). A repeated measures ANOVA with factors action selection (internal vs. external) and action timing (internal vs. external) was computed for each region.

For the RCZ the results replicated the findings of the whole-brain analysis showing a significant main effect for action selection (internal > external) [$F(1, 13) = 15.456$; $p = 0.002$] (see Figure 2B). The main effect action timing (internal > external) was not

significant [$F(1, 13) = 3.77; p = 0.074$]. For the paramedian frontal cortex the results showed a significant main effect action timing (internal > external) [$F(1, 13) = 16.808; p = 0.001$], while the main effect action selection was not significant [$F(1, 13) = 3.016; p = 0.104$]. Additionally there was a significant interaction of action selection \times action timing [$F(1, 13) = 8.151; p = 0.014$]. Only when the action selection was externally, internal action timing resulted in a stronger activation than external action timing (see Figure 3B).

However, it is important to note that the results of the signal strength analysis were obtained *post hoc* and are based on a much more liberal threshold than the whole-brain analysis and therefore should be interpreted with care.

DISCUSSION

The aim of the present study was to dissociate the ‘when-’ and the ‘what-component’ of intentional action on the functional neuro-anatomical level. In order to do so, participants were instructed to perform one of two possible actions at one of two possible points in time. We varied whether participants freely chose between the two actions and the two points in time, or whether action and point in time were indicated by a stimulus. In other words, ‘what’ and/or ‘when’ of the to-be-produced action (selection and timing) were based either on some internal decision or were specified by an external stimulus.

We were primarily interested in activation differences underlying the decisional aspects of voluntary action that is reflected in the BOLD response contingent on the cue. The fact that we observed different activation maxima for internal action selection and internal action timing in decision relevant areas of the frontomedian wall stresses the fact that subjects really decided on the cue. The whole-brain analysis revealed two areas in the frontomedian wall that fulfill different functions. The RCZ is involved in the internal selection of an action, whereas an area of the SFG in the left paramedian frontal cortex is involved in the decision ‘when’ to perform an action. However, the signal strength analysis revealed an interaction of the action timing and action selection in the paramedian frontal cortex. When action selection was internally specified the activation level was equally high for internal and external action timing. Only when action selection was externally specified the activation level in the paramedian frontal cortex differed between internal and external action timing.

Notice that we found the strongest differential activations in the RCZ and paramedian frontal cortex in the analysis of the cue-related signal and not in the analysis of the target-related signal, indicating that these activations reflect processes preparing the upcoming action (viz. the internal specification of the when and what action parameters) and not processes related to the execution of the action.

THE ROLE OF THE RCZ IN INTERNALLY SELECTED ACTIONS

The finding that the RCZ is primarily involved in internal action selection, but not in internal action timing confirms the results from Mueller et al. (2007). These authors demonstrated increased RCZ activity for internally selected actions as compared to externally selected actions, while keeping the timing of the action constant. While involvement of the RCZ in internal action selection has also

been found in several other studies (Cunnington et al., 2003, 2006; Deiber et al., 1999; Lau et al., 2004b; van Eimeren et al., 2006; Wiese et al., 2004, 2005) the present study is to our knowledge the first that shows that this region is more sensitive for a selection manipulation than for a timing manipulation.

The functional role of the RCZ in voluntary action selection is still under discussion. Walton et al. (2004) argue that RCZ activity is related to the internal selection of an action and to assessing the consequences of the chosen action. This notion fits to the ideomotor principle of action control (Herwig et al., 2007; Hommel et al., 2001; James, 1890, 1950; Prinz, 1997; Waszak and Herwig, 2007) that assumes that action representations are activated by anticipation of the actions’ effect, including body-related afferent information, that is, proprioceptive feedback (Hommel et al., 2001). The view of representing actions in terms of their action goals is widely spread (Jeannerod, 1999; Rizzolatti et al., 1997).

On the other hand it has been argued that the RCZ might be involved in conflict monitoring (Botvinick et al., 2001, 2004; Carter et al., 1998; Lau et al., 2004b, 2006) rather than in voluntary selection of action. Lau et al. (2006, 2004b) argue that, if a response has to be selected randomly from a set of possible responses, the response is underdetermined and, therefore, triggers response conflict.

We believe that both interpretations are complimentary rather than contradictory. Selecting one response implies to reject all alternative responses. This idea is not new, but already expressed by James (1890, 1950) who said ‘The express fiat, or act of mental consent to the movement, comes in when the neutralization of the antagonistic and inhibitory idea is required’ (p. 526). The less the selection is predetermined, the more the alternative responses interfere with the selection and the more internal effort is required (Forstmann et al., 2006). This idea is in accordance with the suggestion from Brass and Haggard (2008) that response conflict is an inherent property of all action.

In addition to the hypothesized activation in the RCZ we found increased activation in the posterior precuneus that was related to internal action selection. The precuneus is extensively connected with the RCZ (Leichnetz, 2001; Petrides and Pandya, 1984). Furthermore there is evidence that the precuneus plays a role in voluntary action. In a recent neuroimaging study, Soon et al. (2008) found the anterior precuneus – in addition to the frontopolar cortex – to be a predictor of subjects’ free decisions ahead of time.

THE ROLE OF THE SUPERIOR FRONTAL GYRUS IN INTERNALLY TIMED ACTIONS

Activation in a part of the left SFG in the paramedian frontal cortex was found to be stronger for internally timed than for externally timed actions. This region is located slightly anterior and lateral to the preSMA. This is to our knowledge the first evidence for an involvement of the SFG in the ‘when-component’ of intentional action. At first sight this finding seems to be at odds with studies that indicated the preSMA to be involved in the decision when to act (Cunnington et al., 2002, 2003; Deiber et al., 1999; Jahanshahi et al., 1995; Jenkins et al., 2000; Wiese et al., 2004, 2005). However, in contrast to the present study, these studies did not disentangle processes related to the decision when to act from processes related to the instantaneous initiation of the action and therefore

presumably confounded these two factors. Moreover, the activation we found is located very close to the preSMA. The existence of a functional link between paramedian frontal cortex and preSMA is thus probable.

The results from the signal strength analysis extend the results from the whole-brain analysis by showing an additional interaction between selection and timing manipulation. Thus it seems that the paramedian frontal cortex is stronger activated for internal than for external action timing only if action selection is externally specified. If action selection is internally specified, paramedian frontal activation is almost the same for internal and external action timing.

Other structures that are considered to be involved in the timing of actions are the basal ganglia and the cerebellum (e.g., Elsinger et al., 2006; Jahanshahi et al., 2006; Taniwaki et al., 2003). We did not observe activation differences in these structures contingent on the cue, probably because they are not involved in the decision process (that takes place right after cue presentation), but only in the implementation of the action (that takes place during the target period). Furthermore we did not observe activation differences in the basal ganglia and cerebellum during the target period either, probably because at this processing stage both internally and externally timed actions draw equally on these structures.

DIFFERENTIATING WHAT- AND WHEN-COMPONENT OF INTENTIONAL ACTIONS

Our findings suggest the existence of at least partially dissociable neural networks underlying the 'what-' and 'when-component' of intentional action: the RCZ and paramedian frontal cortex are differentially activated for intentional action selection and action timing, respectively. Nonetheless, the interaction between action timing and action selection within the paramedian frontal cortex revealed by the signal strength analysis indicates that decisional processes concerning action timing and selection are not completely dissociated. This finding is not surprising in the light of the functional interdependency of these two components of voluntary action control: For an action and its consequences to be evaluated both components have to be taken into account. This interdependency can be illustrated by looking at the example of the soccer player who has to decide whether to pass the ball or to shoot on the goal. His choice strongly depends on the moment when he intends to act. The optimal timing, in turn, depends largely on the action he chooses.

The nature of the interdependency between internal action selection and timing remains subject for future research. Deecke (1996) suggested a hierarchical organization with 'what' and 'how' decision preceding the 'when-decision'. Although we have not investigated the sequential order in which the two decisions are taken, we consider our data to be in line with a superordinate role of the 'what'-decision that is subsequently timed and integrated into an action plan.

ACTIVATIONS RELATED TO THE TARGET

Although the present study focused mainly on decisional processes of voluntary action control taking place contingent on the presentation of the cue, activations related to the target tone should be considered briefly.

The activations found for the main effect action selection are similar to those found in prospective memory tasks such as the middle frontal gyrus (BA 10) and the inferior parietal lobe (BA 40) (c.f. Simons et al., 2006). In event-based prospective memory the intended action has to be remembered until the intention is retrieved upon presentation of the triggering stimulus condition (c.f. Einstein et al., 1992). Evidently, in our task subjects have to remember the selected action parameters until execution. Our results seem to indicate that the retrieval of internally generated action intentions draws especially heavily on the prospective memory network. This may be due to the quality of a representation specified by some distinct external stimulus being better than the quality of an internally generated representation. That this effect was observed for internally selected actions only and not for internally timed actions may be due the fact that, concerning the timing component of our task, the to-be-retrieved action parameter (which tone) and 'retrieval cue' (target tone) are basically identical.

Most important in the present context is the absence of target-related activation differences within the frontomedian wall. Only when the threshold was lowered we could observe activation in the RCZ for the main effect action selection. However, compared to the cue-related activation this activation has a much smaller extend. Given the above mentioned stronger involvement of prospective memory in the implementation of internal action selection the activation in the RCZ might reflect processes related to the updating of the decision. This finding confirms the notion that activation differences in the frontomedian wall reflect primarily decisional aspects of voluntary action control, rather than processes related to the implementation of the action.

CONCLUSIONS

The aim of the present study was to experimentally differentiate between different components of intentional action. Our experiment shows that the intentional decision when to execute an action is associated with activation in a part of the SFG, the paramedian frontal cortex, while the intentional decision which action to execute activates the RCZ.

Thus, we were able to dissociate the processes underlying 'what' and 'when' based voluntary decision processes. This challenges the idea of a unitary system supporting voluntary action. Instead, we propose that voluntary action control is an interplay of different neuroanatomically dissociable subfunctions. It is conceivable that in addition to the when- and what-component of intentional action other components might be dissociable as well (Brass and Haggard, 2007, 2008). Such a functional segregation of intentional action will certainly help to understand the confusing pattern of empirical findings. Furthermore, it is consistent with philosophical conceptions of intentions related to action which also distinguish different levels of action-related intentions.

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List of Abbreviations (Chapter 1)

AC-PC	Anterior Commissure–Posterior Commissure
ACad	Anterior Cingulate, affect division
ACC	Anterior Cingulate Cortex
ACcd	Anterior Cingulate, cognitive division
AHS	Alien (Anarchic) Hand Syndrome
APA	Arcuate Premotor Area
BA	Brodmann’s Area
CCZ	Caudal Cingulate Zone
CMA	Cingulate Motor Area
CMA _d	dorsal Cingulate Motor Area
CMA _r	rostral Cingulate Motor Area
CMA _v	ventral Cingulate Motor Area
dlPFC	dorsolateral Prefrontal Cortex
EEG	Electroencephalogram
e.g.	latin: Exempli gratia; for example
EMG	Electromyogram
ERP	Event-Related Potential
fMRI	functional Magnetic Resonance Imaging
i.e.	latin: id est; that is
LRP	Lateralized Readiness Potential
M1	Primary Motor Cortex
p.	page
PCC	Posterior Cingulate Cortex
PD	Parkinsons Disease
PFC	Prefrontal Cortex
PMA	Pre Motor Area
preSMA	pre Supplementary Motor Area

RCZ	Rostral Cingulate Zone
RCZa	Rostral Cingulate Zone, anterior part
RCZp	Rostral Cingulate Zone, posterior part
RP	Readiness Potential
RT	Reaction Time
SFG	Superior Frontal Gyrus
SMA	Supplementary Motor Area
UB	Utilization Behavior
VCA	Vertical Commisure Anterior
viz.	latin: vide licet; namely
Vlo	Nucleus Ventralis pars oralis

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NEURAL CORRELATES OF INTENTIONAL ACTIONS

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Paper

The aim of the present thesis was to investigate the neural mechanisms involved in intentional actions. In experimental settings intentional or internally guided actions are often contrasted with externally guided actions. Different components of an intentional action can be differentiated. One can choose which action to perform, when to perform the action and whether to perform it at all. Functional Magnetic Resonance Imaging (fMRI) studies investigating the neural correlates of intentional actions usually report activation maxima in the rostral cingulate zone (RCZ) as well as the pre Supplementary Motor Area (preSMA). However, the pertinent contrasts were often confounded by perceptual and sensorimotor differences between the different conditions. The first fMRI study of this thesis investigated the neural correlates of internally vs. externally selected actions using a paradigm that avoids any such perceptual or motor confounds. By doing so, we addressed the question which differential role the preSMA and RCZ play in internally guided actions. Subjects were required to make left or right key presses at the midpoint between isochronous pacing signals (a sequence of 'X's presented to the left or the right of the fixation point). In the internally selected condition, the location of the 'X' was determined by the location of the preceding key press that

the subjects selected freely. In the externally selected condition, by contrast, the location of the 'X' prescribed the location of the subsequent key press response. We found that the RCZ was differentially activated by internally as compared to externally selected actions. In contrast to previous studies, the preSMA showed equal activity in both conditions and thus did not differentiate between the two modes of action selection. This suggests a primary role for the RCZ in internally selected actions.

The second fMRI study was meant to further decompose what- and when-component of intentional actions. Subjects were presented with a cue and had to decide as fast as possible which action to perform and when. The two decisions were either taken by the participants (internally) or based on the cue (externally) enabling us to differentiate between internal and external when- and what-decisions. We furthermore addressed the question whether the same brain areas are involved in the decision processes (which occur in the cue phase) as in the implementation of the action. Therefore we dissociated the moment when the subjects have to make the decision what to do, and when, from the moment when the subjects actually executed the action. The results suggest a neuro-functional dissociation of intentional action timing and intentional action selection. While the RCZ is more strongly activated for the selection component, the paramedian frontal gyrus is more strongly activated for the timing component. However, in a signal strength analysis which was conducted post-hoc we did also observe an interaction between action timing and action selection, indicating that decisional processes concerning action timing and action selection are not completely dissociated but interdependent. Altogether this study challenges the idea of a unitary system supporting voluntary action and instead suggests the existence of different neuroanatomically dissociable subfunctions.

In sum, this thesis showed that the RCZ but not the preSMA is involved in internal action selection (Study 1 and Study 2). The paramedian frontal gyrus in contrast is involved in deciding when to act (Study 2). Furthermore the brain areas that are involved in processing intentional what- and when-decisions do not seem to operate totally independent from each other (Study 2). As could be shown from Study 2, brain areas involved in the decision which action to perform and when are not involved in the initiation of the action itself.

Summary

Introduction

An essential part of human behavior is the ability to act out of intrinsic motivation to achieve specific goals instead of simply reacting to external stimuli from the environment. These kinds of actions have been denoted in scientific literature as intentional, voluntary, willed, or internally guided. Even though everyone is familiar with the concept of intentional, willed actions, it is difficult to give a proper scientific definition of what exactly constitutes intentional actions. Instead, it is a common approach to contrast intentional actions with reflexive, or automatic actions (James, 1890/1950; Brass & Haggard, 2008; Haggard, 2008; Jahanshahi & Frith, 1998; Frith, 1992). In addition to being purposive, intentional actions are described as being endogenously or internally controlled by an agent and are generally stimulus independent (Brass & Haggard, 2008; Haggard, 2008). Furthermore, they require attention and offer a choice between alternatives (Jahanshahi & Frith; 1998).

However, human actions are rarely totally externally determined nor are they ever completely internally guided. Rather, they almost always comprise external and internal components. Therefore, it might be more realistic to assume that human actions exist along a continuum between the two extremes. Considering the predominant component, actions can then be categorized into those that are more internally guided, for example switching on the TV to watch the news, and those that are more externally guided by environmental stimuli, for example stopping in front of a red traffic light.

However, voluntary action should not be regarded as a unitary concept. At least three different components of voluntary action can be differentiated, which can shortly be denominated as *what*, *when* and *whether* (Brass & Haggard, 2008; Haggard, 2008). The *what*-component comprises the decision *which* action to perform (intentional action selection), the *when*-component the decision *when* to perform the action (inten-

tional action timing) and the *whether*-component represents the decision *whether* or not to perform the action (intentional action inhibition).

Despite the fact that voluntary action control represents such an important characteristic of human behavior, for a long time psychological research neglected voluntary actions. However, during the last years, research focused increasingly on internally guided actions and how they differ from externally guided actions. There is evidence that the two action modes differ with respect to their neural and behavioral correlates (e.g., Cunnington, Windischberger, Deecke, & Moser, 2002; Herwig, Prinz, & Waszak, 2007; Obhi & Haggard, 2004; Deiber, Honda, Ibanez, Sadato, & Hallett, 1999).

Goldberg (1985) suggested the existence of a lateral and a medial motor system representing externally and internally guided actions respectively, which converge only in the primary motor cortex. In line with this, functional neuroimaging as well as lesion studies point to a crucial role of the frontomedian cortex in intentional actions (e.g., Cunnington et al., 2002; Jahanshahi & Frith, 1998; Lau, Rogers, Ramnani, & Passingham, 2004).

Existing fMRI studies on intentional action timing and action selection often suffered from a badly controlled experimental design. Perceptual and/or motor factors were confounded with the contrast in question (e.g., Cunnington et al., 2002; Lau et al., 2004; Cunnington, Windischberger, Robinson, & Moser, 2006). At the same time, there is no consistency regarding the exact locus of activations. It remains unclear whether it is the presupplementary motor area (preSMA) and/or the anterior cingulate cortex with the rostral cingulate zone (RCZ) that is the most crucial structure in internally guided actions. We hypothesized that this inconsistency might be due to the above mentioned confounds and argued that the two action modes were not directly comparable in many of these former studies. Therefore we designed a study in which the two conditions differed only in the action mode.

Experimental approach and research questions

Study 1 was meant to answer the question which role exactly two frontomedian brain structures -the preSMA and RCZ- play in internally selected actions if subjects perform the very same action once in an internally selected action mode and the other time in an externally selected action mode with all other factors, such as perception and sensorimotor context being the same in both conditions. Therefore, the paradigm used by Waszak et al. (2005) was adapted for use in fMRI.

Subjects performed left and right button presses at the midpoint of an isochronous pacing interval (a sequence of 'X' es presented at the left or right side of a fixation cross). In the internally selected condition, subjects freely selected between left or right button presses, thereby determining the side on which the next 'X' would appear. In the externally selected condition, subjects had to react to the previous stimulus with a button press corresponding to the side at which the preceding stimulus appeared. Thus the action itself and the sensorimotor context of the action were identical in both conditions. The only difference was the mode in which the actions were performed: internally selected or externally selected. We hypothesized we would find activation differences between internally and externally selected actions in the preSMA and/or the RCZ.

The results revealed that the RCZ but not the preSMA is more strongly involved in internally selected as compared to externally selected actions. The preSMA instead was activated to the same degree in both action modes. Given the fact that subjects were required to self-initiate their button presses in both conditions, we hypothesized that the results might point to a neural dissociation of *what*- and *when*-component with the RCZ being involved in deciding *which* action to perform and the preSMA being involved in the decision *when* to act.

Thus Study 2 was conducted to investigate whether *what*- and *when*-component of intentional actions are represented in different brain areas.

Subjects were presented with a cue and, as quickly as possible had to decide *which* action to perform and *when*. The two decisions were either taken by the participants (internally) or based on the cue (externally), enabling us to differentiate between internal and external *what*- and *when*- decisions. We, furthermore, addressed the question whether the same brain areas are involved in the decision processes (which occur in the cue phase) as in the implementation of the action. Therefore, we dissociated the moment when the subjects had to make the decision *what* to do, and *when*, from the moment when the subjects actually executed the action. We hypothesized that activation differences in the frontomedian wall reflect mainly decisional aspects of voluntary action control.

Data from the whole brain analysis revealed a neurofunctional dissociation between two areas in the frontomedian wall. The RCZ was involved in the decision *which* action to perform, whereas an area of the superior frontal gyrus (SFG) in the left paramedian frontal cortex was involved in the decision *when* to perform an action. However, data from a signal-strength analysis that was conducted post-hoc, relativized this strong dis-

sociation. This analysis revealed an interaction of action timing and action selection in the paramedian frontal cortex. Only when action selection was externally specified the activation level in the paramedian frontal cortex differed between internal and external action timing. This suggests that processes related to the decision of internal action timing and internal action selection are not completely dissociated but interdependent.

With respect to the 2nd question whether the same brain areas were involved in the decision and implementation of the action, the strongest differential activations were found in the RCZ and paramedian frontal cortex in the analysis of the cue-related signal and not in the analysis of the implementation-related signal. Therefore, the data suggest that the activations in the RCZ and paramedian SFG reflect processes concerned with preparing the upcoming action (viz. the internal specification of the *what* and *when* action parameters) and not processes related to the execution of the action.

Conclusions

Altogether, the results showed that:

1. The RCZ but not the preSMA is involved in internal action selection (Study 1 and Study 2).
2. The paramedian SFG is involved in deciding *when* to act (Study 2).
3. Internally and externally guided actions are not processed by two totally different systems. Rather, the two types of actions involve the same brain systems which are involved more strongly in internally than in externally guided (i.e., timed and selected) actions (Study 1 and Study 2).
4. Brain areas that are involved in processing intentional *what* and *when* decisions do not seem to operate totally independently from each other (Study 2).
5. Brain areas involved in the decision of *which* action to perform and *when* to do it are not involved in the initiation of the action itself (at least not to the same degree) (Study 2).
6. Altogether the results challenge the idea of a formerly proposed 'unitary voluntary action system' (Jahanshahi & Frith, 1998). Rather they suggest the existence of different neuroanatomically dissociable subfunctions.

Zusammenfassung

Einleitung

Eine herausragende Eigenschaft menschlichen Verhaltens ist die Fähigkeit aus intrinsischer Motivation heraus zu handeln (d.h. zu *agieren*), anstatt nur auf Reize aus der Umwelt zu *reagieren*. Derartige Handlungen werden auch als intentionale, willentliche oder internal gesteuerte Handlungen bezeichnet. Obwohl jeder mit dem Begriff der ‘willentlichen Handlung’ vertraut zu sein scheint, ist es schwierig, eine exakte Definition dafür zu geben, was man exakt unter einer solchen Handlung versteht. Stattdessen ist es gängige Methode, intentionale Handlungen mit externalen, reflexhaften oder automatischen Handlungen zu kontrastieren (Brass & Haggard, 2008; Haggard, 2008; Jahanshahi & Frith, 1998; Frith, 1992). In diesem Zusammenhang werden intentionale Handlungen als absichtliche Handlungen beschrieben, die vom Agierenden selbst, d.h. internal kontrolliert werden und im Allgemeinen unabhängig von äußeren Reizen sind (Brass & Haggard, 2008; Haggard, 2008). Zudem erfordern sie Aufmerksamkeit und bieten die Wahl zwischen Alternativen (Jahanshahi & Frith, 1998) weshalb sie auch als spezielle Form des Entscheidens aufgefasst werden (Haggard, 2008).

Betracht man menschliche Handlungen jedoch im Alltag, sind diese im seltensten Fall komplett external gesteuert. Genausowenig ist eine Handlung in den meisten Fällen komplett internal gesteuert. Stattdessen beinhalten menschliche Handlungen meist interne und externe Komponenten. Aus diesem Grund scheint es angemessener anzunehmen, dass menschliche Handlungen entlang eines Kontinuums zwischen den zwei Extremen existieren. Bezüglich der vorherrschenden Komponente können Handlungen dann in solche unterteilt werden, die mehr internal gesteuert sind, wie z.B. das Einschalten des Fernsehers, um die Nachrichten anzusehen, und in solche, die mehr external gesteuert sind, wie z.B. das Anhalten vor einer roten Verkehrsampel.

Intentionale Handlungen sollten jedoch nicht als einheitliches Konzept betrachtet werden. Man kann mindestens drei verschiedene Komponenten intentionaler Hand-

lungen unterscheiden: Was, Wann und Ob (Brass & Haggard, 2008; Haggard, 2008). Die Was-Komponente bezieht sich auf die Entscheidung, welche Handlung ausgeführt wird (internale Handlungsselektion), die Wann-Komponente auf die Entscheidung, wann eine Handlung ausgeführt wird (internale Selektion des Zeitpunktes), die Ob-Komponente auf die Entscheidung, ob eine Handlung überhaupt ausgeführt werden soll oder nicht (internale Handlungsinhibition).

Es gibt Evidenz aus behavioralen und neurophysiologischen Untersuchungen, dass sich intentionale, d.h. internale Handlungen von externalen Handlungen unterscheiden auch wenn die ausgeführten Handlungen motorisch und perzeptuell identisch sind (z.B.: Cunnington, Windischberger, Deecke & Moser, 2002; Herwig, Prinz & Waszak, 2007; Obhi & Haggard, 2004; Deiber, Honda, Ibanez, Sadato, & Hallett, 1999).

Goldberg (1985) propagierte die Existenz einer lateralen und einer medialen Handlungsroute, die entsprechend externale bzw. internale Handlungen verarbeiten und sich nur im primären Motorkortex treffen. In Übereinstimmung damit deuten sowohl Funktionale-Magnetresonanztomographie (fMRT)-Studien als auch Läsionsstudien auf eine kritische Rolle des frontomedianen Kortex bei internal gesteuerten Handlungen hin (z.B.: Cunnington et al., 2002; Jahanshahi & Frith, 1998; Lau, Rogers, Ramnani, & Passingham, 2004).

Die meisten bisherigen fMRT-Studien zur intentionalen Handlungssteuerung waren schlecht kontrolliert und so waren perzeptuelle und/oder motorische Faktoren mit dem interessierenden Kontrast konfundiert (z.B.: Cunnington et al., 2002; Lau et al., 2004; Cunnington, Windischberger, Robinson, & Moser, 2006). Gleichzeitig gibt es bezüglich des genauen Ortes der Aktivierungen in der Frontomedianwand keine Konsistenz: Es ist unklar welche konkrete Rolle das präsupplementärmotorische Areal (präSMA) und die rostrale zinguläre Zone (RCZ) (ein Teil des anterioren cingulären Kortex) im Bezug auf intentionale Handlungen spielen. Es ist zu vermuten, dass diese Inkonsistenz unter Anderem auch durch die schlecht kontrollierten Paradigmen bedingt wird.

Experimenteller Ansatz und Fragestellungen

Die erste fMRT-Studie untersuchte, welche Rolle präSMA und RCZ bei der internalen Handlungsselektion spielen, wenn die Probanden ein und dieselbe Handlung einmal internal ausgewählt und einmal external ausgewählt durchführen, während alle anderen Faktoren, wie Wahrnehmung und Motorik, absolut identisch gehalten werden.

Zu diesem Zweck wurde ein von Waszak et al. (2005) entwickeltes Paradigma für den Gebrauch im Kernspintomographen adaptiert.

Die Probanden führten eine temporale Bisektionsaufgabe aus, indem sie in der Mitte eines isochronen Schrittgeberintervalls (eine Sequenz von 'X' en, die auf der linken oder rechten Seite eines Fixationskreuzes präsentiert wurden) rechte und linke Tastendrucke ausführten. In der internal ausgewählten Bedingung konnten die Probanden zwischen linken und rechten Tastendrucken wählen und bestimmten dadurch die Seite, auf der das 'X' anschließend erschien. In der external ausgewählten Bedingung mussten sie auf das vorhergehende 'X' mit einem kompatiblen Tastendruck reagieren. Somit waren motorische Handlung und Wahrnehmung der Probanden identisch, der einzige Unterschied zwischen beiden Handlungen war der Modus in dem die Handlung ausgeführt wurde: Internal ausgewählt oder external ausgewählt. Basierend auf oben genannten Studien wurden für den Vergleich internale versus externale Handlungssteuerung Aktivierungen in der präSMA und/ oder RCZ vermutet.

Die Ergebnisse zeigten beim Vergleich internal und external ausgewählter Handlungen stärkere Aktivierungen in der RCZ jedoch nicht in der präSMA. Letztere wurde in beiden Bedingungen gleich stark aktiviert. Unter Berücksichtigung der Tatsache, dass die Probanden in beiden Bedingungen den Zeitpunkt ihrer Tastendrucke selbst initiieren mussten (d.h. in der Mitte des Intervalls die Taste drücken mussten), deuten die Ergebnisse auf eine neuronale Dissoziation von Was- und Wann-Komponente intentionaler Handlungen hin: Möglicherweise ist die RCZ an internaler Handlungsselektion beteiligt, während die präSMA mehr an der internalen Selektion des Zeitpunktes beteiligt ist.

Die Beantwortung dieser Hypothese stand im Mittelpunkt der zweiten fMRT-Studie, die folglich untersuchte, ob Was- und Wann-Komponente intentionaler Handlungen in unterschiedlichen neuronalen Arealen repräsentiert sind. Zusätzlich wurde untersucht, ob die gleichen Hirnareale an den Entscheidungsprozessen während der Cue-Phase sowie an der Implementation der Handlung beteiligt sind.

Den Probanden wurde ein Cue präsentiert aufgrunddessen sie so schnell wie möglich entschieden, welche Handlung sie wann ausführten. Diese beiden Entscheidungen konnten jeweils von der Person selbst getroffen werden (internal) oder sie wurden durch den Cue vorgegeben (external). Dies ermöglichte eine Differenzierung zwischen internaler und externaler Wann- und Was-Entscheidung. Zur Beantwortung der zweiten Frage wurde der Entscheidungsprozess (welcher in der Cue-Phase stattfand)

vom Implementationsprozess durch einen starken Jitter getrennt. Dies ermöglichte die Hirnaktivitäten beider Prozesse zu trennen.

Die Daten der Gesamthirnanalyse zeigten zwei Areale im frontalen Kortex, die an der internalen Selektion der Handlung bzw. des Zeitpunktes beteiligt waren: Die RCZ war an der internalen Selektion der Handlung beteiligt, während ein Areal im Gyrus frontalis superior (SFG), der linke paramediane Frontalkortex, an der internalen Selektion des Zeitpunktes beteiligt war. Eine post-hoc durchgeführte Analyse der Signalstärke relativierte diese Dissoziation jedoch. Nur wenn die Handlungsauswahl external vorgegeben war, unterschieden sich die Aktivierungen im paramedianen Frontalkortex zwischen internaler und externaler Selektion des Zeitpunktes. Dieses Ergebnis legt nahe, dass die an beiden Selektionsprozessen beteiligten Strukturen nicht komplett dissoziierbar, sondern interdependent sind. Bezogen auf die zweite Grundfrage der Studie zeigte sich, dass die stärksten differentiellen Aktivierungen cue-bezogen auftraten. Daraus lässt sich folgern, dass die Aktivierungen in der RCZ und im paramedianen SFG auf Prozesse der Handlungsauswahl und -Vorbereitung bezogen sind, nicht auf Prozesse der Handlungsimplementation.

Schlussfolgerungen

1. Die RCZ jedoch nicht die präSMA wird durch interne Handlungsauswahl stärker aktiviert als durch externe (1. und 2. fMRT-Studie).
2. Der paramediane SFG spielt eine Rolle bei der internalen Auswahl des Zeitpunktes (fMRT-Studie 2).
3. Hirnareale, die an internaler Auswahl der Handlung und des Zeitpunktes beteiligt sind, sind nicht komplett dissoziierbar, sondern scheinen interdependent zu sein (fMRT-Studie 2).
4. Internal und external gesteuerte Handlungen werden nicht in komplett verschiedenen neuronalen Systemen verarbeitet, sondern beide Handlungstypen involvieren (zumindest teilweise) die gleichen Hirnareale, jedoch zu einem stärkeren Maß bei internal gesteuerten Handlungen (1. und 2. fMRT-Studie).
5. Hirnareale, die an der Selektion der Handlung und des Zeitpunktes beteiligt sind, sind nicht an der Initiierung der Handlung selbst beteiligt, zumindest nicht im selben Maß (fMRT-Studie 2).
6. Insgesamt stellen die Ergebnisse der beiden Studien die Idee eines von Jahanshahi and Frith (1998) vorgeschlagenen einheitlichen Systems der willentlichen Handlungssteuerung in Frage und deuten eher auf verschiedene, neuroanatomisch unterscheidbare Unterfunktionen hin.

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