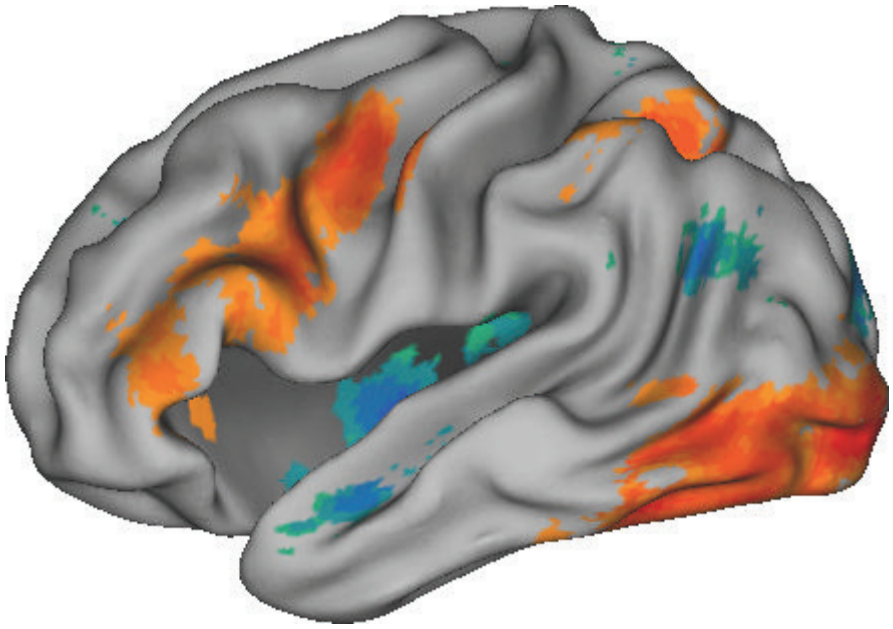
Aus der
Abteilung für Neuropsychologie und Verhaltensneurobiologie
Zentrum für Kognitionswissenschaften (ZKW)

Cognitive Control of coherent motion perception: functional MRI studies of response selection



vorgelegt dem Fachbereich 2 (Biologie/ Chemie)
Universität Bremen
als
Dissertation
zur Erlangung des akademischen Grades
eines Doktors der Naturwissenschaften (Dr. rer. nat.)

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April 2008

Abstract

Executive control is a human ability that allows to overcome automatic stimulus-response mappings and to act appropriate in the context of a task where the selection of relevant stimuli and the suppression of interfering information are crucial. The first study (Chapter 2) aimed at characterizing the neural correlates of conflict resolution in two variations of the Simon effect. Two different Simon tasks were introduced where subjects had to identify shapes on the basis of form-from-motion perception (FFM) within a randomly moving dot field, while (1) motion direction (motion-based Simon task) or (2) stimulus location (location-based Simon task) had to be ignored. Behavioral data revealed that both types of Simon tasks induced highly significant interference effects. Using event-related fMRI we could demonstrate that both tasks share a common cluster of activated brain regions during conflict resolution (pre-supplementary motor area (pre-SMA), superior parietal lobule (SPL), and cuneus) but also show task-specific activation patterns (left superior temporal cortex in the motion-based, and the left fusiform gyrus in the location-based Simon task). Although motion-based and location-based Simon tasks are conceptually very similar (Type-3 stimulus-response ensembles according to the taxonomy of Kornblum & Stevens (2002)) conflict resolution in both tasks results in the activation of different task-specific regions probably related to the different sources of task-irrelevant information. The second experiment (Chapter 3) aimed at investigating the influence of the degree of interfering information on error processing. The ability to detect errors is a crucial prerequisite for the appropriate adjustment of behavior to future situations. By means of fMRI, we provide evidence for the existence of different error-related networks within the human brain. While errors related to incompatible trials were mainly associated with activation of the rostral anterior cingulate cortex (rACC) and the precuneus / posterior cingulate, errors related to trials without pre-response conflict showed specific activation in right inferior parietal cortex. Despite this functional dissociation of brain networks, conjunction analysis revealed common clusters of activation in the medial wall (dorsal anterior cingulate cortex (dACC) and medial superior frontal cortex (msFC)), and bilateral inferior frontal gyrus / insula, consistent with earlier reports of error-related BOLD-signal increases. The results support the view that despite of an overlapping core system of error processing, additional brain areas come into play depending on the existence or absence of cognitive conflict. In order to address the question which brain areas are involved in the detection and processing of two simultaneously operating sources of

interference derived from a spatial incompatibility task, we used fMRI to directly contrast neural activity related to a double conflict situation to single incompatibility conditions (Chapter 6). Results show signal increase of left dorsolateral prefrontal cortex when monitoring simultaneously presented conflict. There was no additional activity in the medial prefrontal cortex or anterior cingulate cortex although these regions are expected to play an important role in all types of conflict monitoring. Further analyses also suggest a major role for the basal ganglia during error detection and resolution.

Zusammenfassung

Exekutive Kontrolle ist eine Fähigkeit des Menschen, die es ermöglicht automatisierte Reiz-Reaktionsverbindungen zu überwinden und sich dem Aufgabenkontext entsprechend angemessen zu handeln. Von besonderer Wichtigkeit sind hierbei die Auswahl relevanter Reize und die Unterdrückung interferierender Informationen. Das Ziel der ersten Studie (Kapitel 2) bestand in der Charakterisierung neuronaler Korrelate der kognitiven Konfliktlösung in Rahmen zweier Simon-Aufgaben. Dabei wurden zwei verschieden Arten benutzt, bei denen die Versuchsteilnehmer Formen innerhalb eines Zufallspunktefeldes zu erkennen hatten. Entweder sollte die (1) Bewegungsrichtung (bewegungsbasierte Simon-Aufgabe) oder der (2) Reizort (ortsbasierte Simon-Aufgabe) nicht beachtet werden. Verhaltensdatenergebnisse ließen darauf schließen, dass beide Variationen hochsignifikante Interferenzeffekte induzierten. Mittels funktioneller Magnetresonanztomografie (fMRT) konnte gezeigt werden, dass beide Aufgaben gemeinsame Aktivität bezüglich der Konfliktlösung aufwiesen (prä-supplementär-motorisches Areal [prä-SMA], superiorer parietaler Kortex und Cuneus), jedoch ebenfalls aufgabenspezifische Aktivierungsmuster zeigten (bewegungsbasierte Simon-Aufgabe: linker superiorer temporaler Kortex; ortsbasierte Simon-Aufgabe: linker fusiformer Gyrus). Trotz einer konzeptuellen Ähnlichkeit der bewegungsbasierten als auch der ortsbasierten Simon-Aufgabe (Typ-3 Reiz-Reaktions-Ensemble nach der Taxonomie von Kornblum & Stevens (2002)) resultierte Konfliktlösung während beider Aufgaben in unterschiedlicher Aktivierung aufgabenspezifischer Regionen, die vermutlich mit den unterschiedlichen Ursprüngen der jeweils aufgaben-irrelevanten Information in Beziehung stehen. Das Ziel des zweiten Experimentes (Kapitel 3) war die Untersuchung des Einflusses des Ausmaßes interferierender Information auf die Fehlerverarbeitung. Die Fähigkeit, Fehler zu erkennen, ist eine entscheidende Voraussetzung für die adäquate, zukünftige Verhaltensanpassung. Mittels fMRT konnten Belege für die Existenz verschiedener Fehlerverarbeitungsnetzwerke im menschlichen Gehirn gefunden werden. Während bei Fehlern in Reaktion auf inkompatible Ereignisse Aktivierungen im rostralen ACC (rACC) und im Precuneus/ posterioren Zingulum gefunden wurden, zeigte sich bei Fehlern auf Ereignissen ohne Antwortkonflikt spezifische Aktievierungen im rechten inferioren parietalen Kortex. Trotz dieser funktionellen Dissoziation der Hirnnetzwerke wurden auch gemeinsame Aktivierungsmuster in der medialen Wand (dorsales anteriores Zingulum (dACC), medialer superiorer frontaler Kortex (msFC)) und beidseitig in dem

inferioren frontalen Gyrus/ Inselrinde, was frühere Berichte von fehlerbezogenen BOLD-Signalerhöhungen konsistent widerspiegelt. Die Ergebnisse unterstützen die Ansicht, dass – trotz eines überlappenden Kernsystems der Fehlerverarbeitung – zusätzliche Hirnareale ins Spiel kommen; und dies in Abhängigkeit des Vorhandenseins kognitiver Konflikte. Um der Frage nachzugehen, welche Hirnareale bei der Detektion und Verarbeitung zweier gleichzeitig dargebotener Interferenzen bei räumlicher Inkompatibilität involviert sind, wurde mit Hilfe funktioneller MRT neurale Aktivität bezogen auf die doppelte Interferenz direkt mit neuraler Aktivität der jeweils einzelnen inkompatiblen Bedingungen kontrastiert (Kapitel 4). Die Ergebnisse zeigten einen Signalanstieg im linken dorsolateralen präfrontalen Kortex bei der Überwachung eines Doppelkonfliktes. Es zeigte sich keine zusätzliche Aktivierung im medialen präfrontalen Kortex oder im anterioren Zingulum, obwohl diese Regionen üblicherweise eine entscheidende Bedeutung bei allen Arten der Konfliktüberwachung spielen. Weitergehende Analysen deuten darauf hin, dass den Basalganglien bei der Fehlererkennung und –auflösung eine Hauptrolle zukommt.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1.0 General introduction

Attention is the cognitive process of selectively concentrating on one aspect of the environment while ignoring other aspects. The MIT encyclopedia of cognitive sciences (Wilson & Keil, 1999) explains that attention "refers to our ability to concentrate our perceptual experience on a selected portion of the available sensory information, and, in doing so, to achieve a clear and vivid impression of the environment" (p 41). And even as early as in the late nineteenth century William James emphasized that attention "implies withdrawal from some things in order to deal effectively with others" (James, 1890: pp. 403-404).

This psychological construct serves as one of a few basic and highly relevant cognitive principles, and it is self-explanatory that attention research is considered as one of the fastest growing within cognitive psychology and cognitive neuroscience (Posner & Rothbart, 2007). Its implications extend into various research fields. With regard to this, one can find an increasing number of neuro-scientific investigations of cognitive control. This term refers to the human ability to monitor and regulate attentional resources of concentrating on a task and ignoring irrelevant information.

All following experiments were conducted within the Center of Advanced Imaging (CAI) project under the title “Changes in brain activation patterns associated with top-down regulation of coherent motion perception”. The specific aims of this project were to examine the basic and (meta-) cognitive brain mechanisms underlying figure-ground segmentation and target selection in humans as well as in primates. Thereby, it was planned to not only investigate the brain activation reflected in functional magnetic resonance imaging (MRI) Blood Oxygen Level-Dependent (BOLD) changes of interference resolution, but also to test the hypothesis of comparable activation patterns in humans and macaques.

Attentional control, motor planning abilities, and executive cognitive functions are crucial for successfully managing our daily life. As children have been reported to be more susceptible to interference than adults, the development of these functions supposedly lasts throughout childhood (Bunge et al., 2002; Konrad et al., 2005).

The high relevance of this research field lies in the fact that these functions rapidly decline with age (Rosano et al., 2005). Moreover, many neurologic and neuropsychiatric disorders like Parkinson’s disease or schizophrenia show impairments in action control (Pagonabarraga et al., 2007; MacDonald et al., 2006; Opgen-Rhein et al., 2008). Understanding how to preserve or regain attentional and motor planning capacities may help reducing the burden of age- and disease-related functional decline. Brain research is still at the beginning of revealing mechanisms of executive functions. Promising approaches have been developed to elucidate the neural correlates of cognitive control. By combining neuroimaging with genetics, recent findings indicated that genes could have a role in shaping the biological substrates of attention (Fan et al., 2001; Parasuraman et al., 2005; Klein et al., 2007b). As an example, the dopamine

receptor gene D4 (DRD4) has been associated with novelty-seeking, as knockout mice that lack this gene show less explorative behavior (Grandy & Kruzich, 2004).

The present work intends to add new insights to the existing literature by introducing a novel experimental setup based not on static visual events, but on events which are formed by coherent motion. This was conducted on the basis of random dot kinematograms (RDKs): small light dots move along random trajectories on a dark background. With the manipulation of two aspects of human motion perception – coherence detection and form-from-motion (FFM) perception – a task was created in which subjects were able to detect target forms. These forms – a triangular and a rectangular shape – 'popped out' of the RDK because all dots in these forms were moving with 100 % coherence.

The underlying strategic way to manipulate higher brain functions was by inducing an irrelevant stimulus feature, thus inducing cognitive conflict. In order to achieve this, we made use of the Simon task. Besides the classic color Stroop task and the Eriksen flanker task, the Simon task is one of the most commonly used experimental strategies to generate conflict in the human brain. It was used in several neuroscientific studies aiming at investigating mechanisms of interference resolution (e.g., Peterson et al., 2002; Fan et al., 2003; Liu et al., 2004).

The Simon task is central to this thesis as it was used in variations throughout all experiments; thus, some further discussion about this task is warranted. In the following, further terms will be explained which are relevant in respect to the experiments in the present work.

1.1 The Simon task

The conflicting effect of the Simon task is generally achieved by presenting the target stimulus in the hemifield opposite to the response side. Conflict arises because the subjects' first intention is to quickly respond with the body side in which the stimulus occurs although this reaction would be incorrect with respect to the task at hand. On average, subjects usually react later and make more errors if this conflict between stimulus and response site is presented compared to events with no interfering information.

The Simon effect is usually defined as the difference between reaction times in the incompatible minus compatible condition. Based on a large amount of data, there is evidence that the Simon effect is caused by the parallel activation of two routes, namely a conditional (controlled) and an unconditional (direct) route. In the conditional route, an intentional process activates the appropriate response, whereas in the unconditional route, the response corresponding to the stimulus location is activated fast and automatically (Ridderinckhof, 2002). The processing of the direct and automatic route occurs because of dimensional overlap (Kornblum & Stevens, 2002).

According to the theoretical framework of the dimensional overlap, it is possible to differentiate between various conflict effects. In the case of the Simon task, the response set and the irrelevant stimulus share a dimension: the location. As a consequence, this shared dimension primes the associated response.

In general, most conflict tasks juxtaposed with other tasks used in the neuroimaging literature show a basic principle. All are based on the notion that an irrelevant stimulus

dimension activates an associated response fast and automatically, whereas the relevant stimulus-response mapping proceeds much slower. The time-consuming process of overriding the incorrect response activation leads to the virtual cause of the Simon effect. The reason for the fact that subjects tend to commit more errors in the incompatible than in the compatible condition is exactly this automatic activation of the incorrect response. In this case, reaching of response thresholds leads to short error reaction times.

In support for this, evidences from LRP (lateralized readiness potential) and the more peripheral EMG (electromyography) recordings show that during incompatible trials the incorrect response is activated relatively early, followed by a later activation of the correct response (de Jong et al., 1988; Burle et al., 2002). Unlike other interference tasks, in the Simon task there is no conflict between the relevant and the irrelevant stimulus dimensions (Kornblum & Stevens, 2002).

An additional investigation (Two Simon tasks with different sources of conflict: an ERP study of motion- and location-based compatibility effects) was conducted with the same paradigm as first experiment, but compared the two Simon task variations by means of electroencephalography (EEG). Similarly to the functional MRI study reported here, there was a motion-based Simon task and a location-based Simon task.

In the motion-based Simon task, dots in the target shape were moving in a synchronized fashion either to the corresponding response side (compatible condition), to the side opposite to the correct response side (incompatible condition), or upwards, thereby inducing neither interference nor facilitation. During all trials, target stimuli appeared at the centre of the screen.

The location-based Simon task was constructed in a similar way. Accordingly, there were three experimental conditions, but in the location-based Simon task, interference was evoked by stimulus eccentricity. During compatible trials, target stimuli appeared in the hemifield corresponding to the correct response side while the dots in the target were moving upwards. In the incompatible condition, targets were presented in the hemifield opposite to the required response side comparable to task designs of regular Simon tasks.

It was concluded that the result of an interference effect in the motion-based Simon task in which all targets were presented centrally speak against an attention-shifting account as an explanation for the differences in behavioral data (prolonged reaction times and higher error rates) and event-related potentials (ERPs).

This study was published in Biological Psychology (in press, 2008) with Daniela Galashan as the first author. The results provided evidence for an amplitude reduction of a late positive deflection (P300) usually associated with recruitment of attentional processes during incompatible trials compared with compatible trials.

1.2 Error processing

While the first experiment (Comparison of two Simon tasks: Neuronal correlates of conflict resolution based on coherent motion perception; published in *Neuroimage* 32, 2006), aimed at comparing two Simon tasks only differing regarding to the source of spatial incompatibility, the second experiment investigates the influences that cognitive conflict on a specific trial might have on how errors are being processed (The influence of response conflict on error processing: evidence from event-related fMRI; published in *Brain Research* 1194, 2008).

The neural mechanisms underlying error processing have been the subject of various investigations (for a review, see Ridderinckhof et al., 2004). Error processing refers to the identification and correction of differences between an intended and an executed response. Such a kind of performance monitoring system in the human brain was firstly described and investigated by Rabbitt (1966) who discussed the importance of behavior adjustments in relation to a changing environment.

Since the early 1990s, there was an increasing interest in performance monitoring processes due to the fact that two independently working groups were able to observe correlating event-related potentials (ERPs). They discovered a negative electrical potential with a frontocentral maximum, approximately 50 to 100 ms after error commission (Falkenstein et al., 1990; Falkenstein et al., 1991; Gehring et al., 1993). Source localization studies (van Veen & Carter, 2002b; Herrmann et al., 2004; Mathewson et al., 2005) have suggested the anterior cingulate cortex (ACC) to be the main generator for this error-related negativity (ERN or N_E). This ERP-component seems to be independent of response modality

as it was described in the context of hand, foot, and eye movements (Holroyd et al., 1997; Van't Ent & Apkarian, 1999; Niewenhuis et al., 2001; Gehring & Fencsik, 2001).

Various attempts have been made to disentangle error-processing- from response-conflict-related activations. Kiehl and colleagues (2000) obtained neuroanatomical dissociations from a Go/ NoGo task where error-related rostral and caudal ACC activity stood in contrast to more dorsal frontomedian wall activity related to response conflict.

In the effort to understand error monitoring functions, the second experiment (The influence of response conflict on error processing: evidence from event-related fMRI) directly contrasted error-related activation during trials with high cognitive conflict (incompatible condition) to activation during trials without interfering spatial incompatibilities (compatible condition). Since task difficulty seems to be an unlikely reason for erroneous responses to compatible trials, the existence of specific brain networks associated with errors on compatible and incompatible trials was hypothesized.

1.3 Double conflict

In the incongruent condition in the Stroop task, there is a conflict between the relevant and irrelevant stimulus dimensions, above and beyond the conflict between the responses associated with these stimulus dimensions (MacLeod, 1991). Thus, in the attempt to combine different interference tasks to increase difficulty and to search for common underlying neuronal networks associated with conflict processing, there is still the problem of confounding different task attributes and response selection mechanisms and thus, differing sources of incompatibility.

For example, Fan and colleagues (2003) constructed a conflict task that was based upon the color-word Stroop task, the Simon task, and the Eriksen flanker task. By means of functional MRI, they found common as well as specific neural correlates of conflict monitoring.

By combining the conflicting sources of the two variations of the Simon task into a novel task design, the experimental setup of the third study (How the brain resolves high conflict situations: Double conflict involvement of dorsolateral prefrontal cortex; submitted on April 18th, 2008) raised the possibility to investigate behavioral and brain activation differences between conflict processing in response to one or two interfering sources. It elucidates the role of the dorsolateral prefrontal cortex when more conflicting information has to be suppressed to achieve appropriate response selection.

In experiment 3 subjects were presented a combination of the two Simon task variants resulting in an interference condition in which two conflicting information streams had to be ignored to accurately perform the task. In order to avoid the above mentioned problematic

confounds, this study investigated neural activations in response to two variants of the Simon task while both interfering information were based on spatial incompatibility.

The third investigation also aimed at shedding light on the effect of post-error activation as well as trial sequence modulation.

1.4 Post-error activity

Control is thought to be more strongly engaged on trials following erroneous responses. Subjects tend to react slower and with higher accuracy following error trials, an effect termed as post-error slowing (Kleiter & Schwarzenbacher, 1989; Laming 1979).

In respect to the current neuroimaging literature, activity related to post-error trials has been associated with increasing BOLD signal in the dorso-lateral prefrontal cortex (dlPFC) (Kerns, 2004). Botvinick and colleagues (2001) implemented the effect of post-error slowing in the context of their neural network model. They concluded that after an error has been made; the level of baseline activation of the response units is decreased, resulting in slower and more accurate performance on post-error trials.

1.5 Conflict adaption effect

Interference effects tend to be increased on trials following compatible trials, and reduced on trials following incompatible trials. Botvinick et al. (2001) proposed to call this phenomenon the *Gratton effect* because it was originally reported by Gratton, Coles, and Dochin (1992) in the context of a letter flanker task. In recent years, the term *conflict adaption effect* has become more common (Egner & Hirsch 2005; Mayr et al., 2003).

Based on computational modeling and neuroimaging findings, Botvinick and colleagues (2001) hypothesized that a cognitive control component associated with the dorso-lateral prefrontal cortex (dlPFC) is regulated on a trial-by-trial basis by a monitoring component associated with the anterior cingulate cortex (ACC). The ACC detects the amount of conflict that exists between active representations of processed information. This cognitive control system accomplishes interference resolution by increasing the processing of the task-relevant information and suppressing the processing of task-irrelevant information.

Especially in the context of Simon tasks, it was suggested that as a consequence of the ACC detecting conflict, it engages context representations in the dorsolateral prefrontal cortex (dlPFC). On the subsequent Simon trial, the increased dlPFC activation engages the relevant sensory representation more strongly, and inhibits the irrelevant information or the associated response, leading to a smaller susceptibility to the irrelevant stimulus dimension (Kerns, 2004; Egner, 2007b; van Veen, 2006).

Thus, the sequence of events as a function of the trial type is:

- cC. Compatible stimuli following a compatible stimulus are associated with fast responses.

- cI Incompatible stimuli following a compatible stimulus are associated with slow responses, resulting in a large current trial congruency effect.

- iI. The processing of incompatible stimuli following incompatible stimuli is better able to ignore the distracting information, consequently decreasing response conflict, and leading to relatively fast and accurate responses.

- iC. Similarly to the previous trial sequence, the processing of compatible trials preceded by an incompatible trial is less influenced by the irrelevant spatial information. However, the facilitating advantage is removed, since the current trial is compatible and the processing of irrelevant information is reduced, resulting in somewhat slower reaction times compared to cC.

Supportive evidence for the notion that response conflict reaches highest levels during cI-trials has been recently found in the analyses of behavioral data. Distributional analyses revealed that the increased error rates to cI-trials compared to iI-trails are specifically due to fast slips (Gratton et al., 1992; Stürmer et al., 2002).

In sum, the conflict adaption effect can be described as an interaction between previous and current trial congruency with smaller congruency effects following an incongruent stimulus than following congruent one.

The following chapters contain studies originally published or submitted for publication in international and peer-reviewed journals of neuroscientific research. The first author has developed the experimental design and recruited all participants. Additionally, he has done the functional measurements, has analyzed the data, and has interpreted and discussed the results. Many thanks go to the co-authors for helpful comments and for language editing.

2.0 COMPARISON OF TWO SIMON TASKS: NEURONAL CORRELATES OF CONFLICT RESOLUTION BASED ON COHERENT MOTION PERCEPTION

PUBLISHED IN *NEUROIMAGE*, 32 (2006)

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2.1 Introduction

The Simon task has been widely used to study conflict resolution in cognitive psychology (Simon, 1969). When stimulus and response sides (right/ left) do not correspond even though stimulus location is task-irrelevant the resulting increase in reaction time (RT) is referred to as the Simon effect. This robust phenomenon is interpreted as resulting from the automatic generation of a spatial code in response to stimulus location. Since the spatial code overlaps

with the relevant response code derived from the non-spatial dimension (e.g. shape), it interferes with the speed of correct response selection. The Dimensional Overlap (DO) model by Kornblum (e.g. Kornblum & Stevens, 2002) provides a theoretical framework to differentiate between the various conflict effects. It accounts for stimulus-stimulus (S-S) and stimulus-response (S-R) compatibility effects based on perceptual, conceptual or structural similarity between the relevant and the irrelevant stimulus dimensions on one side, and the response dimension of the task on the other side. According to the DO model, the Simon effect results from a direct stimulus-response conflict induced by a prepotent association between the stimulus and a response on the same side (Type-3 stimulus-response ensemble).

Although advances in neuroimaging methods over the past decade have opened new windows into human cognitive functions, the neural mechanism of cognitive control processes underlying experimental procedures such as the Simon, Stroop, or Eriksen flanker tasks, remains largely unexplained. Up to now only few studies compared in some detail neural networks activated by different conflict tasks within the same experimental session with event-related fMRI (Fan et al., 2003; Liu et al., 2004; Peterson et al., 2002; Wager et al., 2005). These studies reported numerous brain regions being activated during the conflict task condition as compared to the no-conflict task condition. Among these are the posterior frontomedian cortex (pFMC; in particular the anterior cingulate cortex (ACC), the pre-supplementary and the supplementary motor areas (pre-SMA/ SMA)), the middle frontal cortex, the anterior insula/ frontal operculum, anterior prefrontal, superior and inferior parietal cortices, as well as posterior areas. According to the conflict monitoring theory by Botvinick et al. (2004), it is the dorsal ACC (in particular the posterior rostral cingulate zone (rCZp) as defined by Picard and Strick (2001)) that responds to the occurrence of conflict. This area is

supposed to trigger strategic adjustments, which serve to reduce conflict in subsequent performance. Corroborating this issue, Barch et al. (2001) presented data from a meta-analysis that clearly demonstrated the posterior rostral cingulate zone (rCZp; 3, 19, 35) to be involved in conflict resolution.

In order to test the hypothesis of a common neural network of conflict resolution, some recent fMRI studies compared different conflict tasks, such as Simon, Stroop, and Eriksen flanker task. Peterson et al. (2002) reported remarkably similar activation patterns during interference resolution in both the Stroop and the Simon tasks which overlapped in the ACC, SMA, visual association cortex, dorsolateral prefrontal cortex (dlPFC), caudate nuclei, as well as in inferior temporal, parietal, and frontal cortex. Although extent and magnitude of regional activations across tasks varied slightly, Peterson and colleagues suggested that the underlying neural processes associated with conflict resolution are very similar, though obviously not identical with respect to differing stimulus features between tasks. This study, however, was criticized by Liu et al. (2004) stating that the experimental design implicated an overlap of relevant and irrelevant stimulus dimensions, which is the main feature discriminating between the Simon and Stroop effects (Kornblum & Stevens, 2002). In order to control for stimulus attributes, Liu et al. (2004) introduced an experimental procedure incorporating both types of Stroop and Simon tasks, and reported a common cluster of brain regions being activated by both tasks, but also task-specific brain regions.

Fan et al. (2003) conducted an fMRI experiment with three conflict tasks (color-word Stroop, Simon, and Ericksen flanker tasks) within the same group of participants in search for a common network for conflict resolution. They found significant activations in the ACC and left prefrontal cortex in all three conflict tasks, but also additional areas that were exclusively

activated in each task. Based on these data the authors stated that not a single unified network, but distinguishable task-specific networks might underlie conflict processing. All three tasks, however, consisted of very different stimuli: color words in the Stroop task, color drawings of generic cartoon characters or objects in the Simon task, and a row of arrows in the Ericksen flanker task. The neuronal activation pattern derived from that study, therefore, reflected a possible confound of different task attributes and response selection mechanisms.

The aim of the present study was to analyse conflict resolution induced by two Simon tasks which only differed with respect to the source of conflicting information and thus avoiding individually differing recruitments of brain mechanisms of interference resolution due to different tasks. In order to comply with this experimental precondition we introduced a task design where subjects had to identify shapes on the basis of form-from-motion perception (FFMo) within a randomly moving dot field, while (1) motion direction (motion-based Simon) or (2) stimulus location (location-based Simon) had to be ignored. Forms were defined only by coherent dot motion against stochastic background motion, without any static form cues. Most recently, Bosbach et al. (2004a, b) investigated the relation between high-level motion perception and action by conducting experiments in which the direction of motion was the irrelevant dimension while the position of the stimuli was constant over time. The authors reported that (1) motion detection and motion processing may be independent of spatial position, and (2) a significant Simon effect might be induced by dynamic stimuli that do not allow for relative position coding. If a single neural network is engaged in conflict resolution based on the two variants of a type 3 stimulus-response ensembles (Kornblum & Stevens, 2002), then the activation patterns of response conflict induced by both motion

direction and stimulus location should only differ with respect to the specific demands related to the processing of different types of incompatible information.

2.2 Materials and Methods

2.2.1 Subjects

Twenty healthy subjects (3 male, range 21 – 31 years, mean age: 25.5 years) participated in the study. None of the participants had a history of neurological or psychiatric disorders nor substance abuse or dependence. Each subject gave informed and written consent and was paid 10 € for participation. The study was approved by the local ethics committee.

2.2.2 Experimental procedure: stimuli and tasks

Subjects had to detect and identify form-from-motion stimuli in two different experiments which were conducted within one session. The stimuli consisted of either a triangle or a square containing approximately 200 coherently moving bright dots on a dark screen against a randomly moving background of a total of 4000 dots. Both stimuli comprised the same area and number of dots. At the start of each trial both a red fixation point and the stimulus were presented for a fixed period of 700 ms. Each press of the response button changed the color of the fixation point from red to white, thus providing a feedback signal that a response had been registered. During an interstimulus interval which was randomly jittered between 700 and 1300 ms, only a red fixation point remained on a homogeneous dark background.

2.2.2.1 Motion-based Simon task The motion-based Simon task contained three conditions: (1) compatible trials (COMP) consisted of dots moving coherently to the side corresponding to a correct response (e.g., a triangle requires a right-hand button press and all dots within the triangle were moving to the right), (2) in incompatible trials (INCOMP) dots within the triangle or square were moving coherently in a direction opposite to the correct side (e.g. the correct response to a square was to press the left-hand button but the target-dots were moving to the right), and (3) during neutral trials (NEU) dots were moving upwards, therefore evoking neither interference nor facilitation. In 25 percent of all trials the stimulus was either INCOMP or NEU which has been demonstrated as a prerequisite of inducing interference effects (Braver et al., 2001). The stimuli always appeared at the center of the screen, subtending an area of 2.8° of visual angle.

Subjects had to press the left-hand button as fast and correct as possible if coherently moving dots formed a square and the right-hand button if a triangle was presented. The experiment was run in two sessions with a short break in-between runs, and consisted of a total number of 500 stimuli. The sequence of trials was presented in a pseudo-randomized order, eliminating two consecutive incompatible trials. Left-hand responses and right-hand responses were counterbalanced.

2.2.2.2 Location-based Simon task Stimulus location was the task-irrelevant dimension in this Simon task. The design of the task again included three conditions: (1) on COMP trials, stimuli appeared in the hemifield corresponding to the required response, (2), on

INCOMP trials, subjects had to respond to stimuli that appeared on the side opposite to the correct response button (e.g., a square right of the fixation which required a left-hand key press), while (3) in the NEU condition stimuli were shown at the center of the screen (see Fig. 1). Movement direction of the coherently moving dots in the NEU condition led to neither interference nor facilitation because the dots were moving upwards in all trials. All other parameters were identical to the motion-based Simon task, apart from the fact that stimuli appeared not centrally but at a 6° eccentricity to the left or to the right of the fixation point.

The order of the two Simon tasks was counterbalanced across subjects.

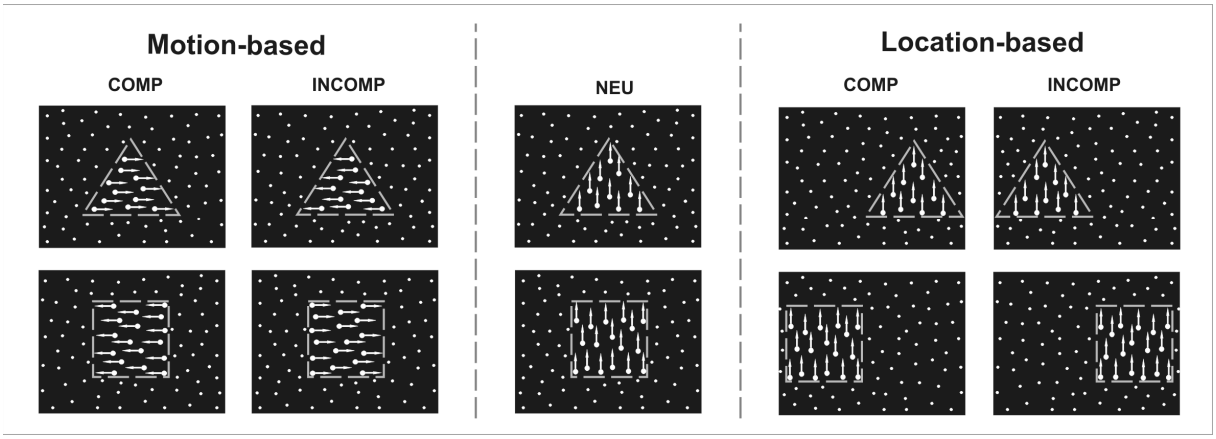

Figure 1: Schematic diagram depicting stimuli and task of the study. Subjects had to press the right hand button after occurrence of a triangle and the left button following a square. The task-irrelevant but conflict-inducing feature was the motion direction of dots within the form in the motion-based Simon task, whereas the form's position was task-irrelevant in the location-based Simon task. The neutral condition consisted of either a triangle or a square formed by upwards moving dots which were presented at the center of the screen. This condition was the same for both tasks.

2.2.3 MRI data acquisition

MRI data were acquired on a 3-T SIEMENS Magnetom Allegra system (Siemens, Erlangen, Germany) equipped with a standard quadrature head coil. Changes in blood oxygenation level-dependent (BOLD) T2*-weighted MR signal were measured using a gradient echo-planar imaging (EPI) sequence (38 slices, slice-thickness: 3 mm with a 0.3 mm gap, TR = 2.5 s, TE = 30 ms, flip angle = 90°, 64 x 64 matrix, FOV 192 x 192, interleaved acquisition). After two preceding dummy scans to allow for magnetic saturation effects, 180 volumes were scanned for each run, resulting in a total of 720 whole-brain volumes oriented along the AC-PC plane. Each run lasted around 7 minutes. During a one minute delay between runs subjects were given time to rest.

Subjects wore foam earplugs and were positioned on a scanner couch in a dimly illuminated room. Stimuli were presented via a JVC video projector onto a projection screen positioned at the rear end of the scanner. The viewing distance was 100 cm. A T1-weighted image (MPRAGE, 160 slices, TR = 2.3 s, TE = 4.38 ms, flip angle = 8°, TI = 900 ms, FOV 296 X 296, 1 mm^3 voxels) was obtained after subjects had completed the task. The acquisition of the structural scan took 9 minutes 50 seconds. The orientation of this 3D volume was identical to the functional slices.

2.2.4 Image analysis

Statistical analysis was performed using statistical parametric mapping software (SPM2; Welcome Department of Cognitive Neurology, London, UK). Parameter estimates were calculated using Marsbar toolbox (http://marsbar.sourceforge.net). After image conversion

from DICOM (Digital Imaging and Communications in Medicine) to Analyze format, slice-time correction, motion estimation, and realignment (to the tenth scan of each run) were performed. Realigned images were segmented (grey matter, white matter, cerebrospinal fluid and scalp), and the grey-white matter border was used to co-register structural and functional images. Images were normalized to the Montreal Neurological Institute (MNI) stereotaxic template (12 linear affine parameters for brain size and position, 16 non-linear iterations and 2 x 2 x 2 nonlinear basis functions for subtle morphological differences). During normalization, voxels were re-sampled to 2x2x2 mm. Statistical analyses were calculated on smoothed data using a 8 mm isotropic Gaussian kernel. The presentation of each stimulus was modelled by a canonical hemodynamic response function and its time derivative, thus allowing for different delays across brain regions. The data were high-pass filtered (128 seconds) to remove low-frequency signal drifts and were rescaled to the global mean. For the first-level analyses, ten regressors were entered into a regression model including COMP, INCOMP, NEU conditions, all erroneous responses, as well as six realignment parameters (x, y, z, and the three rotation angles) as effects of no interest.

To achieve our goal of detecting common and distinct conflict-related brain regions between the two Simon tasks, we entered the resulting parameter estimates for each regressor at each voxel into a second-level random effects analysis, where each subject served as a random effect in a one-way within-subject ANOVA. Unless otherwise noted, a statistical threshold of $p < 0.05$ corrected for multiple comparisons by controlling the false discovery rate (FDR) was used to identify regions of activation within the whole brain (Genovese et al., 2002). This correction ensures that on average no more than 5 % of activated voxels for each contrast are expected to be false positive results. Additionally, a cluster size of 3 voxels was

applied. A conjunction analysis was performed for the purpose of identifying regions commonly activated across tasks. We computed an analysis which tests the global null hypothesis that both Simon tasks do not activate the voxel against the alternative that one or the other activates the voxel (Nichols et al., 2005). Thus, the conjunction analysis removed all voxels showing significant differences between the specified contrasts. The criterion of significant conjunction activation was defined using a joint probability threshold of $p = 0.0005$ (minimum t value 3.57) uncorrected for multiple comparisons and an extent of $k = 3$ voxels. In a disjunction analysis, unique areas were determined by masking one contrast exclusively with the other. We specified the mask at an uncorrected p-value of 0.05 and the main contrast at FDR-corrected p-value of 0.05 (with an additional extent threshold of $k = 5$ voxels). To confirm these distinctly activated regions, we additionally performed an interaction analysis by directly contrasting the task main effects (minimum t value 3.57). Conjunction, disjunction, and interaction analyses were conducted at the whole brain level. Coordinates of activation were converted from MNI templates to Talairach space (Talairach & Tournoux, 1988) by using the mni2tal-transformation developed by Matthew Brett (www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html). The Talairach atlas as implemented by the Talairach Daemon (Lancaster et al., 2000; www.ric.uthscsa.edu/projects/talairachdaemon.html) was used as reference template to identify the corresponding Brodmann areas.

2.3 Results

2.3.1 Behavioral data

Both motion-based and location-based Simon tasks resulted in highly significant interference inductions when reaction time (RT) and correct responses were compared across all trial types. A repeated-measures analysis of variance (ANOVA) for RTs (based on correct trials only) with the factors condition and run showed a significant main effect of condition (motion-based Simon task: $F[1.31, 24.9] = 52.646$, $p<.0001$ (effect size, $r = 0.74$); location-based Simon task: $F[2, 38] = 175.474$, $p<.0001$ (effect size, $r = 0.9$)) but no main effect of runs ($F[1, 19] = 0.083$, $p<.776$; $F[2, 38] = 3.145$, $p<.092$). For the location-based Simon task, an interaction effect of condition and run ($F [2, 38] = 4.227$, $p<.022$) indicated slightly faster responses on incompatible and neutral trials in the second run whereas no interaction of main effects was found for the motion-based Simon task (see Fig. 2).

During the motion-based Simon task, subjects showed significantly slower responses to INCOMP compared to COMP trials (536 ms vs. 486 ms; $t [19] = 7.73$, $p<.0001$), and to neutral trials (503 ms; $t [19] = 7.34$, $p<.0001$). Pair-wise comparisons of all three conditions for the location-based Simon task revealed an even more pronounced interference induction (INCOMP trials: 638 ms vs. COMP trials: 564 ms; $t [19] = 16.28$, $p<.0001$). RTs were also significantly faster on NEU trials (INCOMP trials: 638 ms vs. NEU trials: 540 ms; $t [19] = 16.18$, $p<.0001$). A Friedman's ANOVA showed significantly different error-rates for the conditions of the motion-based Simon task ($\chi2(2) = 25.595$; $p<.0001$). Post-hoc Wilcoxon tests revealed significantly more errors in the INCOMP than in the COMP condition ($t [20] = -3.883$; $p=.0001$), and a higher error-rate in the INCOMP condition compared to the NEU condition ($t [20] = -3.659$; $p=.0001$). Furthermore, the COMP condition resulted in

significantly fewer errors than the NEU condition (t [19] = -2.777; p=.005). In the same way, Friedman's ANOVA for the location-based Simon task revealed a significant effect for error-rates ($\chi 2(2) = 30.9$; p<.0001). Wilcoxon tests showed significantly more errors in the INCOMP than in the COMP condition (t [20] = -3.92; p=.0001), and a higher error-rate in the INCOMP condition compared to the NEU condition (t [20] = -3.92; p=.0001). Accuracy in the COMP condition did not significantly differ from the NEU condition (t [20] = -1.344; p=.179).

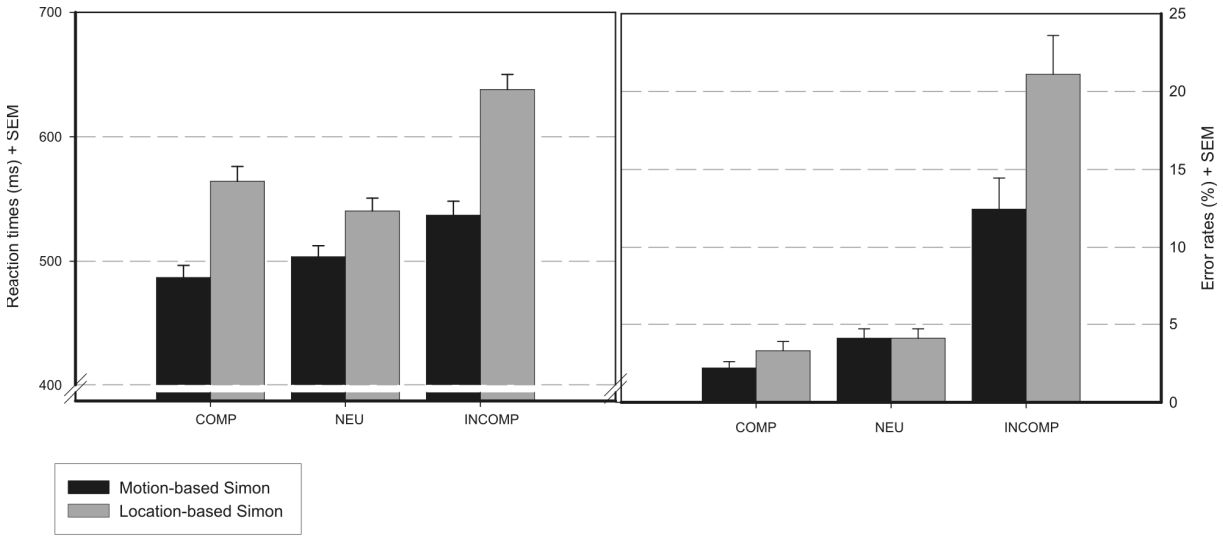

Figure 2: Behavioral data. Left: mean RTs of all three conditions averaged across subjects. Right: mean error rates. Error bars indicate SEM.

2.3.2 Imaging results

In a first analysis, we specified the conflict-related areas by contrasting INCOMP versus COMP conditions for both the motion-based and location-based Simon task. All analyses for the motion-

based task revealed activations in the posterior frontomedian cortex (pFMC) (supplementary motor area (SMA) and pre-SMA) as well as in the posterior portion of the rostral cingulate zone (rCZp). In addition, we found left-sided superior and inferior parietal activations as well as left superior temporal gyrus, right postcentral gyrus, and occipital signal enhancement (cuneus, lingual gyrus). The conflict-related activation pattern for the location-based Simon task comprised areas in the cerebellum, fusiform gyrus, and lingual gyrus as well as SMA/pre-SMA, bilateral middle frontal gyrus, right inferior parietal and temporal gyrus (see Table 1).

Table 1
Brain regions showing greater activation for incompatible than compatible trials

Regions	Right/Left	Brodmann's area	*Z* score local maximum	Cluster size (voxels)	Talairach coordinates (*x*, *y*, *z*)		
Motion-based: INCOMP > COMP							
SMA	L	6	4.88	206	0	−1	63
Pre-SMA	R	6	4.39		2	7	53
ACC	L	32	4.09		−2	14	42
SPL	L	7	4.87	83	−14	−61	58
Cuneus	L	30	4.54	132	0	−66	7
Lingual gyrus	L	NA	4.10		−6	−79	4
IPL	L	40	4.50	70	−59	−31	46
STG	L	42	4.13	56	−65	−21	12
Postcentral gyrus	R	43	3.77	4	71	−20	18
Cuneus	R	17	3.76	9	8	−83	4
Location-based: INCOMP > COMP							
Fusiform gyrus	L	19	5.31	272	−36	−65	−15
Cerebellum	L	NA	4.88		−28	−59	−17
Lingual gyrus	R	17	4.28	118	12	−82	1
Cuneus	L	18	4.14	83	−6	−87	17
Rostral PMd	R	6	3.94	12	30	−5	56
Rostral PMd	L	6	3.91	16	24	−9	61
Inf. temporal gyrus	R	19	3.92	16	50	−64	−2
IPL	R	40	3.91	5	36	−40	55
SMA	R	6	3.79	7	−6	−1	55
Cuneus	R	19	3.76	7	30	−76	28

The spatial extent threshold was $k > 3$ voxels and a FDR of 0.05 was used to correct for multiple comparisons. List of abbreviations: ACC, anterior cingulate cortex; SMA, supplementary motor area; Pre-SMA, pre-supplementary motor area; PMd, dorsal premotor cortex; rCZp, posterior rostral cingulate zone; rCZa, anterior rostral cingulate zone; pFMC, posterior frontomedian cortex; dlPFC, dorsolateral prefrontal cortex; STG, superior temporal gyrus; IPL, inferior parietal lobule; SPL, superior parietal lobule; COMP, compatible experimental condition; INCOMP, incompatible experimental condition; NEU, neutral experimental condition.

The conjunction analysis of conflict resolution of both motion- and location-based Simon tasks revealed a common activation cluster in the mesial BA 6 (pre-SMA), left SPL, and bilateral striate as well as extrastriate regions (see Table 2).

Table 2
Common and distinct regions showing increases in neural activity during conflict processing

Regions	Right/Left	Brodmann's area	*Z* score local maximum	Cluster size (voxels)	Talairach Coordinates (*x*, *y*, *z*)		
Conjunction: common activity of INCOMP > COMP of both Simon tasks							
Cuneus	R	17	3.76	49	8	−83	4
	L	17	3.44		−2	−81	8
Lingual gyrus	R	18	3.42		4	−74	4
Pre-SMA	L	6	3.52	6	−4	1	55
Pre-SMA	R	6	3.39	4	2	8	53
SPL	L	7	3.36	3	−16	−57	56
Specific conflict-related activity of the motion-based Simon							
Cuneus	L	30	4.54	29	0	−66	7
IPL	L	40	4.50	51	−59	−31	46
Pre-SMA	R	6	4.39	10	2	1	63
STG	**L**	**42**	**4.13**	**56**	**−65**	**−21**	**12**
ACC	L	32	4.09	21	−2	14	42
Specific conflict-related activity of the location-based Simon							
Fusiform gyrus/Cerebellum	**L**	**19**	**5.31**	**211**	**−36**	**−65**	**−15**
Cerebellum	L	NA	4.88		−28	−59	−17
Cuneus	L	18	4.14	64	−6	−87	17
Rostral PMd	L	6	3.91	16	−24	−9	61
Middle occipital gyrus	R	37	3.81	7	48	−64	−4
Cuneus	R	19	3.76	7	30	−76	28
Fusiform gyrus	R	19	3.75	9	40	−65	−19

The spatial extent threshold was $k > 3$ voxels and a FDR of 0.05 was used to correct for multiple comparisons. Bold regions indicate significant interaction effects (uncorrected $P > 0.0005$, $k < 3$ voxels). Abbreviations: see Table 1.

Areas activated by the motion-based Simon task only were right cuneus, IPL, right SMA, anterior cingulate cortex (rCZp), and superior temporal gyrus. In contrast, conflict resolution induced by the location-based Simon task revealed areas in the occipital lobe (left cuneus, bilateral fusiform gyrus, and ventral intraparietal sulcus), in the cerebellum, left middle frontal gyrus, and left SMA. The results of an interaction analysis conducted on whole brain level demonstrated that only left superior temporal gyrus (STG) (motion-based), and left fusiform gyrus/ cerebellum (location-based) survived the statistical threshold (see Fig. 3).

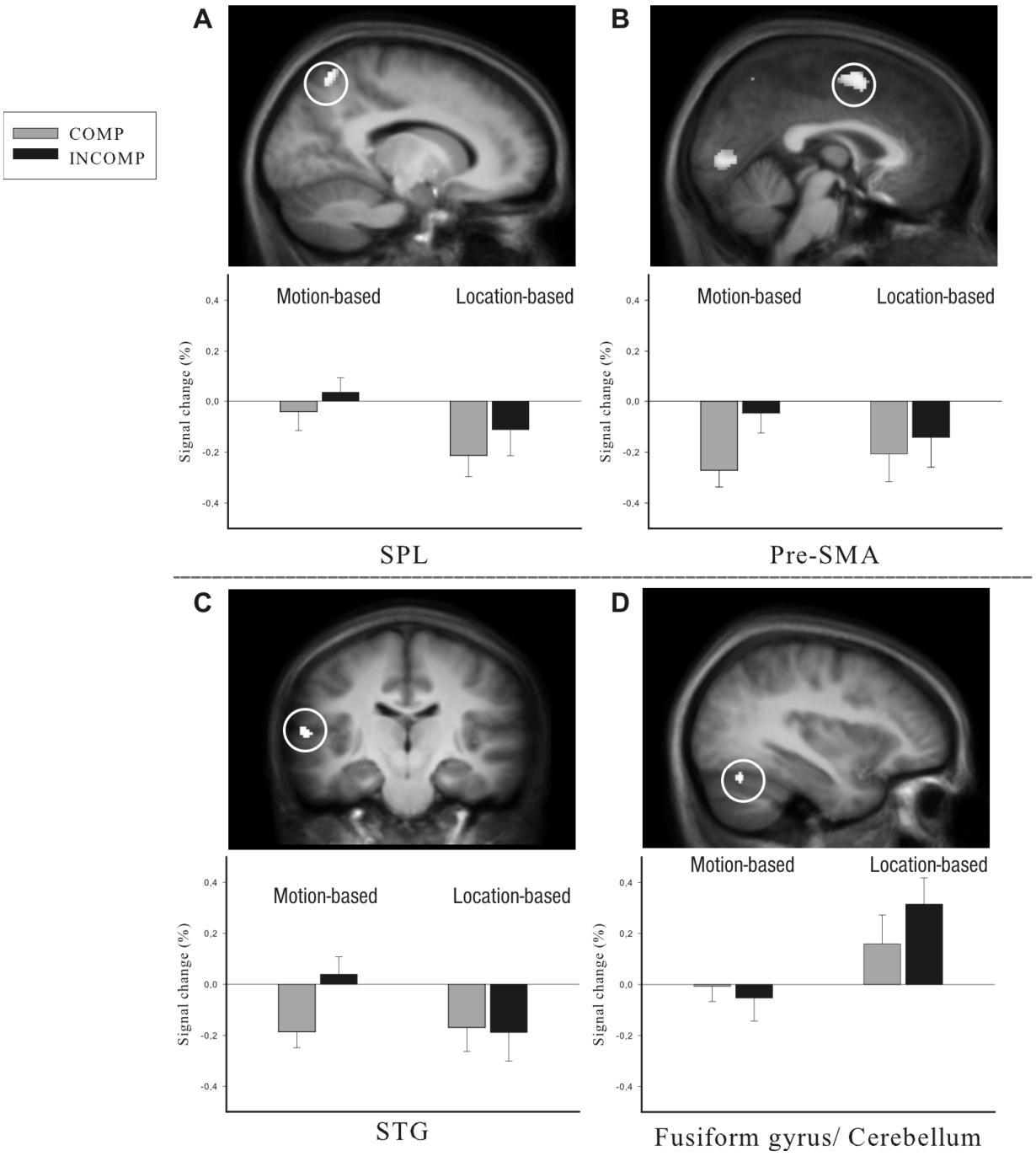

Figure 3: Activations of both conjunction and interaction effects. The figure illustrates peak conjunction activations in (A) superior parietal lobule [-16, -57, 56], (B) pre-SMA [2, 8, 53]; and specific activations revealed by interactions analyses in (C) superior temporal gyrus [-65, -21, 12], and (D) fusiform gyrus [-36, -65, -15]. The view of the brain shown in each panel is indicated by the relevant Talairach coordinate. Activation clusters are superimposed on an average T_1-weighted MR image of all subjects. Bar graphs of the circled clusters illustrate mean percentage signal changes (+/- 1 SEM).

2.4 Discussion

The aim of the present study was to investigate the neural correlates underlying two variants of a Simon task based on coherent motion perception. Both behavioural and fMRI results indicate that not only stimulus location but also motion direction per se directly affect response selection. Responses were significantly faster when the perceived motion direction corresponded to the response side, indicating that motion information activates corresponding motor responses. Task resolution in the present study was based on the subject's ability to recover structure-from-motion. This ability is a high-level representation of motion-direction and probably a prerequisite for the occurrence of a Simon effect in this context (Bosbach et al., 2004a).

Interestingly, we found faster RTs in the NEU condition as compared to the COMP condition in the location-based Simon task. Behavioral data of the motion-based Simon task showed the fastest RTs in the COMP condition. The NEU conditions were identical in both paradigms. Hence, when subjects were orienting towards the periphery, with simultaneous structure-from-motion processing, reaction times in the COMP condition of the location-based Simon task showed an increase. Additionally, we found higher error rates on INCOMP trials in both tasks which indicate that the overall conflict led to a frequent collapse of the brain's response selection system. The relationship between RT and performance accuracy yet remains elusive, as many studies were not able to show response conflict in both parameters. Taken together, we found highly significant RT differences in both tasks indicating that motion-based as well as location-based Simon tasks were able to generate robust conflict effects.

At first, fMRI data analysis was based on the question of whether there are brain regions commonly activated in both tasks during interference resolution. Both Simon tasks showed very similar activation patterns. (Please note that the only difference of the stimulus attributes between the two Simon tasks was the different source of the task-irrelevant information. Otherwise, stimuli were physically identical and the relevant stimulus attribute was the same in both tasks). The present fMRI data indicate a network responsible for the resolution of response conflict associated with different variations of the Simon paradigm that comprised the pre-SMA and the superior parietal lobule (SPL) as well as striate and extrastriate areas. This finding is corroborated by other fMRI studies investigating interference resolution (Sylvester et al., 2003; Brass et al., 2005). The present results are also consistent with the activation patterns reported by Liu et al. (2004). The resolution of the Simon interference seems to engage brain areas sensitive to the detection of response conflict, response planning and selection (pre-SMA) as well as visuospatial-motor association (SPL).

The activation of the SPL seems to reflect engagement of a neuronal visuo-spatial-motor circuitry regulating the conflict in the Simon task which is caused by a possibly hard-wired association between the same side (or motion-directed) visuospatial perception and the acquired motor response (Liu et al., 2004). The SPL might be viewed as serving as the source of an attentional control signal to shift attentive states (Behrmann et al., 2004) and SPL activation during compatibility manipulations has been frequently reported (Iacoboni et al., 1996; Hopfinger et al, 2000; Dassonville et al., 2001; Merriam et al., 2001; Milham et al., 2001; van Veen et al., 2001; Schumacher & D'Esposito, 2002). We assume that the overlap of posterior processing regions that were activated in both Simon tasks do reflect the effect of top-down modulation of attentional selection. The fact that this process activates areas such as

V1 and V2 (cuneus and lingual gyrus) in the visual pathway might be another indication of top-down influence on early visual processing.

Activation of the pFMC region (which includes the pre-SMA) is widely reported in studies on conflict processing. The pFMC is supposed to detect response conflict by triggering other brain areas involved in monitoring correct response selection.

However, there is still an ongoing debate on the precise anatomical localisation of response conflict. In particular, the dorsal anterior cingulate cortex (dACC) which is located more ventrally than the pre-SMA seems to be frequently involved in conflict resolution (e.g. Barch et al., 2001; Botvinick et al, 2004), whereas the rostral portion of the pre-SMA has recently been associated with the generation of spontaneous actions (Lau et al., 2006).

Regarding functional subdivisions of the pFMC, the present data corroborate the hypothesis that it is mainly the pre-SMA and not the anterior cingulate cortex (ACC) which triggers conflict resolution (Ullsperger & von Cramon, 2001; Nachev et al., 2005). Common peak activations could be assigned to the pre-SMA, although applying more liberal thresholds ($p < 0.05$, uncorrected) would extend this midline activation dorsally into nearby portions of the SMA, and ventrally into the dACC (rCZp). This line of argumentation is supported by the following notions: (1) since precise localisation within the ACC is affected by a high intersubject variability in the patterns of the major sulci (Paus et al., 1996; Vogt et al., 1995), pre-SMA activation may have been erroneously mapped to the cingulate cortex; and (2) results of a recent loss-of-function study (Fellows & Farah, 2005) cast doubt on the importance of the ACC in conflict processing. Patients suffering from damage to the ACC did not present impairments of cognitive control processing when compared to normal controls, even in cases of extensive bilateral lesions. Furthermore, a study of conflict monitoring in

macaque monkey failed to show any conflict-related signal enhancement in the ACC although behavioral data and physiological measures pointed to conflict processing (Nakamura et al., 2004).

Comparisons of different types of conflict tasks, however, complicate this issue. We assume that conflict resolution mechanisms during different Simon tasks may engage anatomically different portions of the pFMC compared to response selection during Stroop or Eriksen flanker tasks. This view is supported by Wager et al. (2005) who reported evidence for common and distinct activations across three interference tasks. The brain activation patterns resulting from these cognitive conflict tasks (Go/ no-go; Eriksen flanker; Stimulus response compatibility task) were supposed to reflect a common network of brain areas engaged in conflict resolution, which however was individually different across tasks and hence led to low correlations among performance scores.

Apart from an activation pattern reflecting conflict resolution in both types of Simon tasks, the present study demonstrated specific brain areas engaged in either the motion-based or the location-based Simon task only. Contrasting INCOMP versus COMP events showed a left IPL, left superior temporal and right postcentral activation in the motion-based Simon task and a distinct signal enhancement in the fusiform gyrus / cerebellum and the SMA in the location-based Simon task. IPL activation was associated with biasing conflict processing toward the task-relevant attribute, and the IPL was interpreted as the source of top-down modulatory influences on motion processing areas (Büchel et al., 1998). The IPL was also supposed to be involved in the specification of visuomotor transformation rules or motor attention (Rushworth et al., 2001).

It was hypothesized by Ridderinkhof (2002), that in the case of the Simon task, the task-irrelevant stimulus dimension (position) automatically activates the ipsilateral response through a direct route, whereas the task-relevant stimulus dimension (form) activates the correct response via a controlled route. To respond correctly, subjects must actively suppress the incorrect (and more or less automatically triggered) response. Results of EMG recordings suggest that even in correct trials, minimal EMG activation in muscles associated with the incorrect response could be detected (Burle et al., 2002). In the present study, the inhibition of a prepotent response behavior in the location-based Simon task suggests an involvement of SMA and cerebellar structures. Activity of these regions may reflect different motor inhibition processes due to (1) stimulus eccentricity (compared to foveally presented stimulus material in the motion-based task), and (2) a higher overall conflict level as indicated by a significantly higher ratio of incompatible to compatible RTs.

ANOVA interaction analysis showed that only the left STG (motion-based), and the left fusiform gyrus (location-based) remained as significantly activated areas during the processing of task-irrelevant information. In particular, the left STG was supposed to form a link between dorsal motion-processing areas and temporal-lobe processing areas related to object identification (Braddick et al., 2001). The particular role of the STG in the motion-based Simon task seems plausible since the this task requires the resolution of a strong prepotent association between the same side visuospatial perception and motor response (dot motion) to favour correct performance regarding the task-relevant attribute (shape identification). In contrast, in the incompatible condition of the location-based Simon task, not motion perception but stimulus eccentricity generated response conflict. Therefore, activation of posterior regions (fusiform gyrus) related to object identification (induced by coherent

motion perception) will be increased (Pernet et al., 2004; Murray et al., 2003; Zeki et al., 2003). These data may contribute some further information to the discussion on the neuronal mechanisms of cognitive control. Task-specific activations in both Simon tasks seem to reflect the respective demands needed for successful task performance. Banich et al. (2000) compared the activation patterns of a color-word and a color-object Stroop task which (similar to our present study) only differed in the task-irrelevant stimulus dimension. They also found activation in posterior brain regions which were interpreted to reflect the processing of the task-irrelevant dimension. In a most recent study, Herd and co-workers (2006) presented an integrative model of Stroop task performance: since there is a learned connection between task-relevant and task-irrelevant stimulus dimensions on a conceptual level (color), increased activation of areas involved in the processing of the "to-be-ignored feature" will also be observed during incompatible trials. The results of our present study suggest that (similar to Stroop tasks), posterior brain regions were modulated by the processing of task-irrelevant information in Simon tasks as well (although there was no direct stimulus-stimulus conflict). In a broader sense, the task-specific regions are most likely to detect the relationship between task-relevant and task-irrelevant information.

Although there was no significant interaction effect regarding the pFMC, lowering the threshold ($p < 0.005$, uncorrected) indicated that even our conceptually comparable Simon tasks may in fact engage different portions of the frontal midline areas. Interference resolution induced by the location-based Simon task mainly caused signal enhancement in the SMA, whereas the mesial prefrontal activity in the motion-based Simon task extended into the dorsal ACC (rCZp). Since we examined the same group of subjects within the same sessions, differences of activation foci are unlikely to be evoked by anatomical variability. SMA

activation has been frequently reported in conflict tasks based on a Simon effect (Peterson et al., 2002; Liu et al., 2004), and was previously discussed in the framework of a dorsal/ventral dissociation of irrelevant stimulus processing (Banich et al., 2000).

Some concern may arise as to whether we investigated two variants of 'pure' Simon tasks. In both paradigms, all stimuli were composed of three dimensions: location, motion, and shape. For the location-based Simon task, location and motion were task-irrelevant, while only shape was task-relevant. We cannot exclude some Stroop-like interference induced by motion and shape at a perceptual or semantic level even though motion direction (upward) was orthogonal to the response location (left or right). This possible confound, however, would affect all conditions in the location-based Simon task and, thus, eliminated by contrasting the task conditions. The experimental paradigm of the present study offered a number of critical advantages which were specifically designed to study variants of two Simon tasks within one session in the same group of volunteers. The task-relevant feature was always the shape which subjects had to respond to. Thus, location-based and motion-based Simon tasks, respectively, differed only in the source of task-interfering information.

2.5 Conclusion

In conclusion, the present data derived from two Simon tasks based on coherent motion perception indicate that both stimulus location and motion direction induce strong interference effects. Both types of conflict resolution resulted in shared activation as well as in task-specific activation patterns. Although both tasks were classified as Type-3 stimulus-response ensembles (Kornblum & Stevens, 2002), brain activation patterns in response to events that

compete for activation with strong alternatives revealed differences between the two tasks. Despite conceptual similarities of task design, the observed activation patterns significantly differ probably related to the source of task-irrelevant information, thus indicating the existence of different task-specific networks of conflict resolution.

3.0 THE INFLUENCE OF RESPONSE CONFLICT ON ERROR PROCESSING: EVIDENCE FROM EVENT-RELATED FMRI

PUBLISHED IN *BRAIN RESEARCH*, 1194 (2008)

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3.1 Introduction

Cumulating evidence suggests that performance monitoring comprises several sub-processes: on the one hand processes associated with the monitoring of pre-response conflict and uncertainty as well as control of cognitive conflict and on the other hand processes which are related to the detection of post-response errors. However, while detection of pre-response conflict implies the possibility to improve control, still providing the option of a correct

response, this is obviously not the case after detection of an erroneous response. Response behavior could only be improved in subsequent trials. Recently, there has been growing interest in both investigating the neuronal basis of the brain's ability to concentrate on task-relevant information, and on the mechanisms underlying the detection and processing of errors. Functional MRI studies corroborate the view that a specific error-detection system exists in the human brain which generates error-specific signals. Based on a variety of neuroimaging studies which show that frontal and parietal brain regions are both involved in cognitive control (Brass et al., 2005), further findings suggest that error-related brain activity differs from activity related to cognitive control processes, irrespective of the particular paradigm used to generate response conflict (Carter et al., 1998; Kiehl et al., 2000; Braver et al., 2001; Menon et al., 2001; Ullsperger and von Cramon, 2001; Garavan et al., 2002; Rubia et al., 2003, Bechtereva et al., 2005). Studies investigating different groups of patients demonstrated altered abilities to monitor erroneous responses in these patients, improving our understanding of the underlying functional processes of specific disorders (Johannes et al., 2002; Laurens et al., 2003; Kerns et al., 2005; Fitzgerald et al., 2005; Pizzagalli et al., 2006).

An important anatomical region associated with error processing is the posterior frontomedian cortex (pFMC), a term suggested by Ullsperger and von Cramon (2004). The pFMC denotes several areas in the frontomedian wall of the human brain and is comprised of the pre-supplementary motor area (pre-SMA; BA 6), mesial BA 8, and part of the anterior cingulate cortex (ACC; BA32). While these areas are subsumed under the term pFMC, they are subject to rather large interindividual variability, and the accuracy in determining their borders based on cytoarchitectonic features in anatomical MR images is still rather poor (Paus et al., 1996; Yücel et al., 2001; Fornito et al., 2004). Several studies (Carter, et al., 1998;

Kiehl et al., 2000; Braver et al., 2001; Ullsperger and von Cramon, 2001; Garavan et al., 2002; see also Swick and Turken, 2002) tried to disentangle brain activity related to errors from brain activity related to high-conflict and were able to differentiate subdivisions of the pFMC. The focus of response conflict-related activation was found in the mesial BA 8, whereas error processing engaged a region more ventrally and anterior, in the rostral anterior cingulate cortex (rACC). Interestingly, the pre-SMA (BA 6) and adjoining dorsal ACC (dACC) areas showed activation during both processes (Ullsperger and von Cramon, 2001). Corroborating this finding of a subregional dissociation in the superior-inferior direction, Ullsperger and von Cramon (2004) reviewed main activation coordinates related to conflict and error processing from fourteen neuroimaging studies. Although response conflict seems to engage a more dorsal region of the frontomedian wall when compared to error processing, some overlap of activation was found between conditions. Thus, it remains unresolved whether these data reflect a strict functional specialization or rather a different degree of engagement of the above mentioned midline structures. The contribution of these different brain regions to cognitive control and error processing is still under debate. In particular, while the conflict monitoring hypothesis proposes the view of the dACC as a conflict detector which alerts regulative processes subserved by lateral prefrontal regions, a recent study demonstrated that the dACC might be engaged in regulation processes itself (Roelofs et al., 2006). These authors observed dACC activation not only on incongruent but also on neutral trials in which no conflicting response alternatives occur.

The results by Dosenbach and collegues (2006) even indicate that the dACC along with operculo-insular areas might form a core system implementing goal-directed task sets. These regions showed reliable start-cue and sustained activation across different tasks. Interestingly,

these areas carried the most reliable error-related signal increase in a subset of tasks indicating their role in a general regulating system in response to conflict and errors. In sum, these data broaden the view of the functional role of the dACC from pure conflict detection to performance regulation per se.

Behavioral data from different types of conflict tasks consistently show that errors are made more frequently on trials in which task-irrelevant information generates a strong tendency towards the incorrect response. Nevertheless, subjects do occasionally make errors also during events which are meant to facilitate the correct response. In the present study we investigated the differential brain activation patterns for errors committed in response to compatible versus in response to incompatible events.

We used a previously developed Simon task based on coherent motion perception which induced strong and persistent conflict effects (Bosbach et al., 2004; Wittfoth et al., 2006). The Simon effect (Simon, 1969) is a robust phenomenon which arises if stimulus and response location do not correspond, albeit stimulus location is task-irrelevant.

By comparing errors committed by high-conflict trials to errors committed by non-conflicting trials (in the absence of pre-response conflict) we try to shed light on a possible influence of cognitive conflict and cognitive facilitation on error processing. Based on recent findings that error-related activity differs from conflict-related activity, we further hypothesize that the present experimental task should result in significantly different activation when contrasting error trials with correct trials. Since errors made on trials which facilitate the appropriate response are unlikely to be caused by task difficulty, a specific recruitment of brain regions should be observed by analyzing the interaction of compatible

and incompatible errors. In line with the above mentioned meta-analysis (Ullsperger and von Cramon, 2004) we expect a regional dissociation of conflict- and error-related areas.

3.2 Experimental Procedure

3.2.1 Participants

Twenty right-handed healthy subjects (3 male, range 21 – 31 years, mean age: 25.5 years) with no history of neurological or psychiatric disorder participated in the study. Experimental design and study procedure were approved by the local ethics committee. All participants had normal or corrected to normal vision. Subjects were paid € 10 for participation after signing the written informed consent documents.

3.2.2 Design and Procedure

In the present experiment participants had to detect and identify form-from-motion targets. These targets consisted of either a triangle or a square containing approximately 200 coherently moving white dots on a black screen against a background of a total of 4000 randomly moving dots. The overall position of stimuli was constant over time, and both shapes consisted of the same area and number of dots (see Wittfoth et al., 2006).

At the beginning of each trial, a red fixation point and the stimulus were presented for a fixed period of 700 ms. After each press of the response button the fixation point changed its color from red to white, thus providing a feedback signal indicating that the response had

been registered. The purpose of this feedback signals was to maintain subject's attention on the task, and not to inform subjects about the accuracy of their responses. During a 1000 ms interstimulus interval whose duration was randomly jittered (+/- 300 ms), a red fixation point remained on a homogenous dark background.

Subjects were instructed to press the left-hand button if the coherent dot motion forms a square and the right-hand button if perceiving a triangle while carefully maintaining fixation. All subjects were instructed to react as fast and as correctly as possible. There were three possible conditions: on compatible trials (COMP), dots were coherently moving to the side on which subjects had to press for a correct response (e.g. a triangle required a right-hand button press, all dots in the triangle were moving to the right). On incompatible trials (INCOMP), dots were moving coherently to the opposite side (e.g. target-dots were moving to the right while the appropriate response to a presented square was a left button press), and during neutral trials (NEU), dots were moving upwards, evoking neither interference nor facilitation. In 20 percent of all trials incompatible stimuli were presented. Neutral trials had the same probability of occurrence. The absolute number of trials for the three experimental conditions was 300 COMP trials, 100 INCOMP trials, and 100 NEU trials, respectively. The stimuli always appeared at the center of the screen, subtending an area of 2.8° of visual angle. Subjects had to complete two runs with 250 stimuli each which were separated by a short pause. The sequence of trials was presented in a pseudo-randomized order avoiding repetition priming effects by not presenting incompatible trials in succession (Mayr et al., 2003). Furthermore, the experiment consisted of an equal number of right and left hand responses.

3.2.3 Data acquisition

MRI data were acquired on a 3-T SIEMENS Magnetom Allegra system (Siemens, Erlangen, Germany) equipped with a standard quadrature head coil. Subjects wore foam earplugs and were positioned on a scanner couch in a dimly illuminated room. Stimuli were presented via a JVC video projector onto a projection screen positioned at the rear end of the scanner's core. A T1-weighted structural 3D-image of the brain was obtained using the MPRAGE-sequence as provided by the manufacturer with the following parameters: TR = 2.3 s, TE = 4.38 ms, TI = 900 ms, flip angle = 8°, FOV = 256 x 256 x 160 mm, spatial resolution = 1 mm3/voxel). Functional images optimized for blood oxygenation level-dependent (BOLD) contrast at 3 Tesla were acquired using a T2*-weighted echo-planar imaging sequence with the following parameters: TR/TE = 2500/30 ms, flip angle = 90°, 38 slices, slice-thickness: 3 mm with a 0.3 mm gap, 64 x 64 matrix, in plane resolution = 3 x 3 mm, interleaved acquisition order. Prior to data acquisition, two dummy scans were performed. The experimental procedure consisted of two runs with a one minute pause in-between. For each run, 180 volumes were acquired in about 7 minutes.

3.2.4 Image analysis

Data from five subjects were excluded from further analysis due to insufficient number of errors (< 10 during COMP errors or INCOMP errors). Statistical parametric mapping software (SPM2; www.fil.ion.ucl.ac.uk/spm/spm2.html) was used for pre-processing and subsequent statistical analyses on a Matlab platform (Matlab 6.5.1, Mathworks Inc., Sherborn, MA). Data were converted from DICOM (Digital Imaging and Communications in Medicine)

to Analyze format. After slice-time correction, motion parameters were estimated, and images were realigned to the tenth scan of each run. Realigned images were segmented (grey matter, white matter, CSF and scalp), in order to coregister the structural and functional images based on grey-white matter information. Voxels were resampled to 2 x 2 x 2 mm during normalization to the Montreal Neurological Institute (MNI) stereotaxic template, which was conducted with 12 linear affine parameters for brain size and position, 16 non-linear iterations and 7 x 9 x 7 nonlinear basis functions for subtle morphological differences. Data were subjected to statistical analyses after smoothing with a Gaussian filter (full-width half maximum 8 mm).

Voxel-wise differences in BOLD contrast within the smoothed normalized images engendered by the different task conditions and trial types were examined using SPM2. A first-level analysis was performed individually for each subject based on the general linear model. The presentation of each stimulus was modeled by the canonical hemodynamic response function (HRF) and its time derivative as implemented in SPM2, providing the possibility to model BOLD responses with different delays across brain regions. A high-pass filter of 128 seconds was applied to remove low-frequency signal drifts. Data were low-pass filtered by rescaling them to the global mean. Twelve regressors were entered into a regression model including those for the COMP, INCOMP and NEU conditions (which included only correct trials), three separate regressors for errors on compatible (ERR_{COMP}), errors on incompatible (ERR_{INCOMP}), and errors on neutral trials including trials during which no response had been made (misses), as well as six realignment parameters (x, y, z, and the three rotation angles) as covariates of no interest to remove brain motion artifacts. Contrasts between INCOMP vs. COMP were calculated. In order to obtain specific error-related

activation, each subject contributed two additional contrasts: ERR_{COMP} vs. COMP (correct trials only), and ERR_{INCOMP} vs. INCOMP (correct trials only).

For group analyses of each main contrast, the resulting images of all participants were subjected to a second-level random effects model (one-sample t-test) which was used to determine voxel-wise t-statistics contrasting specific conditions of interest. Resulting statistical parametric maps were thresholded at $p < 0.05$ using a false discovery rate (FDR) correction (Genovese et al., 2002), with a minimal cluster size of 50 contiguous voxels.

One might argue that our analysis included a very low number of COMP errors which might affect the validity of the reported activation patterns. However, all subjects in the present study committed errors of both types, (i.e., there was no subject without errors in compatible trials (ERR_{COMP})); and furthermore, the number of COMP errors was statistically sufficient to obtain stable and reproducible SPMs based on random effects analyses (see supplementary material: Figures 4 and 5; and Table 4). The small number of error trials is in line with the data of other investigations on error processing (e.g. Braver et al., 2001). The validity of the present approach is also substantiated by the fact that the use of FDR-corrected thresholds resulted in an error-related activity pattern that is corroborated by a number of other studies on the topic. What still holds true is the fact that results might be false negative, i.e. additional activation may be observed by increasing the number of errors.

For a region to be identified as showing conjunct activation during error trials as well as during conflict resolution on high-conflict trials, we conducted a random effects one-way within-subject ANOVA which consisted of the three main effects (ERR_{COMP}, ERR_{INCOMP}, and conflict activity). In particular, three first level contrasts were submitted to a second-level group analysis (ERR_{COMP} > COMP, ERR_{INCOMP} > INCOMP, INCOMP > COMP). We used

interaction analyses performed at the whole brain level ($p < 0.001$, uncorrected, $k > 50$) to identify brain regions showing greater activation in INCOMP errors over COMP errors, and showing greater activation in COMP errors over INCOMP errors.

We were interested in whether a set of brain responses showed activation across all main effects and their possible combinations. To achieve this goal, we computed an analysis testing the conjunction null hypothesis that both high- and low-conflict errors do not activate a voxel against the alternative that one or the other activates a voxel (Nichols et al., 2005). Thus, conjunction analyses were performed using SPMs of the minimum T-statistic over the two orthogonal main contrasts. The criterion of significant conjunction activation was defined using a height threshold of $p = 0.05$ and an extent of 50 voxels which has been used in previous studies (Fan et al., 2003; Wager et al., 2005).

Coordinates of activation were converted from Montreal Neurological Institute to Talairach space (Talairach and Tournoux, 1988) by using the mni2tal-transform developed by Matthew Brett (www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html). The Talairach atlas as implemented by the Talairach Daemon (Lancaster et al., 2000; www.ric.uthscsa.edu/projects/talairachdaemon.html) was used as a reference to identify the corresponding Brodmann areas (BA).

3.3 Results

3.3.1. Behavioral data

Fifteen out of twenty subjects were included in the following analyses. The coherent motion based Simon task resulted in a highly significant interference induction when reaction times (RTs) and number of correct responses were compared across all trial types (see Fig. 1). A repeated-measures analysis of variance (ANOVA) for RTs (based on correct trials only) with factors condition x run showed a significant main effect of condition ($F [2, 28] = 74.539$, $p < .0001$) but no main effect of run ($p < .996$), and no interaction of main effects ($p < .117$).

Subjects' reaction times showed a response cost on incompatible trials and facilitation on compatible trials (538 ms vs. 482 ms; $t [14] = 9.72$, $p < .0001$). An additional significant difference was observed between incompatible and neutral trials (538 ms vs. 500 ms; $t [14] = 9.54$, $p < .0001$), thus demonstrating conflict induction. Subjects were also significantly slower on neutral compared to compatible trials ($t [14] = 4.37$, $p < .001$).

The results of a Friedman's ANOVA showed significantly different error-rates for the three task conditions ($\chi 2(2) = 24{,}1$; $p < .0001$; see Fig. 1). Post-hoc Wilcoxon tests revealed significantly more errors in the incompatible (mean number = 12.9, range 10-29) than in the compatible (mean number = 12.2, range 10-17) condition ($t [15] = -3.422$; $p = .001$), and a higher error-rate in the incompatible condition compared to the neutral condition ($t [15] = -3.415$; $p = .001$). The comparison of the compatible condition and the neutral condition resulted in no significant difference ($t [15] = -0.89$; $p = .37$).

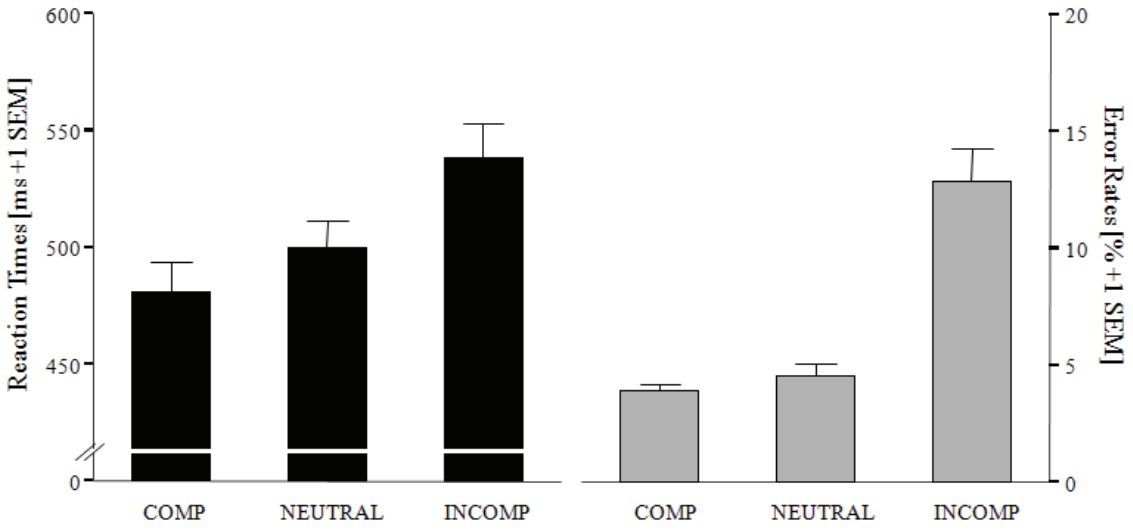


Figure 4: Behavioral data

Left axis, black bars: mean RTs (msec) in the compatible (COMP), neutral and incompatible (INCOMP) conditions; right axis, grey bars: mean number (percent) of incorrect responses. Error bars indicate standard errors of mean.

3.3.2 Imaging Data

3.3.2.1 Conflict-related activity Five participants were excluded from analysis due to low error rates (less than 10 errors in each condition) or perfect accuracy. Significance threshold for activation maps related to conflict activity were set to an uncorrected threshold of $p < 0.001$, because no voxels survived the corrected threshold. Enhanced activity associated with conflict resolution on INCOMP compared to COMP trials was found in the left superior parietal and left inferior parietal lobules (see Table 1), a large cluster in the right inferior/ middle frontal gyrus (BA 9/45), left postcentral gyrus (BA 43), as well as in the right fusiform

gyrus and in the posterior cingulate cortex. By setting a slightly lower threshold of $p < 0.002$, medial wall activity in the msFC (BA 6) was observed.

Table 3: Areas activated during conflict resolution and error processing

Regions	Right/left	Brodmann's area	Z score local maximum	Cluster size (voxels)	Talairach coordinates		
					X	Y	Z
Conflict-related activation (INCOMP>COMP)							
Frontal lobe							
Inferior frontal gyrus	R	9	3.98	286	50	11	25
	R	45	3.74		53	26	19
Middle frontal gyrus	R	46	3.20		51	34	24
Temporal lobe							
Superior temporal gyrus	R	38	4.14	51	59	15	−7
	R	22	3.33		65	12	−1
Fusiform gyrus	R	37	3.54	56	46	−45	−16
	R	37	3.53		48	−55	−12
Parietal lobe							
Superior parietal lobule	L	7	4.69	180	−16	−59	60
Inferior parietal lobule	L	40	3.76	249	−40	−44	54
	L	40	3.47		−49	−44	56
	L	40	3.39		−59	−31	49
	R	30	3.85	93	44	−40	50
Occipital lobe							
Inferior occipital gyrus	L	19	4.11	52	−36	−74	−8
	L	19	3.58		−42	−78	−5
Activation related to COMP errors (ERR_{COMP}>COMP)							
Frontal lobe							
Inferior frontal gyrus	R	9	4.79	82	55	11	29
	R	47	4.40	127	32	25	−3
	R	47	3.74		42	19	1
msFC/dACC	R	8	4.32	474	6	24	45
	L	8	4.25		−2	25	39
	R	32	4.10		6	19	30
Superior frontal gyrus	R	6	4.09	52	14	7	66
Parietal lobe							
Inferior parietal lobule	R	40	4.28	79	65	−37	33
Activation related to INCOMP errors (ERR_{INCOMP}>INCOMP)							
Frontal lobe							
dACC	L	32	4.85	2504	−2	38	13
rACC	L	32	4.65		−2	25	26
	R	32	4.58		2	32	26
Midcingulate cortex	L	23	4.78	204	0	−18	30
Inferior frontal gyrus	R	47	3.99	158	32	17	−14
Insula	L	13	4.05	118	−40	9	−6
Parietal lobe							
Precuneus	L	7	4.06	409	−10	−66	35
	R	7	3.99		10	−66	35
	R	7	3.60		4	−63	55
Subcortical							
Mesencephalon		NA	3.95	56	0	−14	−13
Mammillary body	R	NA	3.30		2	−14	−13
Thalamus	L	NA	3.73	91	−8	−7	6
	L	NA	3.54		−4	−23	5
	R	NA	3.41		6	−23	5

3.3.2.2 Error-related activity The analysis of errors committed in response to COMP trials (when contrasted with correct responses to COMP trials) showed several brain regions comprising large clusters in right inferior frontal gyrus, dorsal anterior cingulate cortex/ medial superior frontal cortex (dACC/ msFC), right superior frontal gyrus (BA 6), and right inferior parietal lobule (BA 40). Because of the relatively small number of errors on compatible trials, we used a random effects model, which estimates the statistical variance across subjects. This procedure ensured that only brain areas consistently activated across subjects would emerge as significant second-level activations. Murphy and Garavan (2004) reported that even a surprisingly small number of errors were able to alter activation maps if data were analyzed by treating error responses as if they were correct. This consistent distribution of error-related activation across subjects corroborates the data reported by Menon et al. (2001).

Brain activation related to INCOMP errors (ERR_{INCOMP} > INCOMP) comprised areas of the right inferior frontal cortex (BA 47), left insula, dACC/ msFC, rostral ACC, and mid-cingulate cortex (BA 23). Parietal activity was observed in the precuneus (BA 7).

Table 4: Areas specifically related to the processing of COMP and INCOMP errors

Regions	Right/ left	Brodmann's area	Z score local maximum	Cluster size (voxels)	Talairach coordinates		
					X	Y	Z
Interaction analysis ($(ERR_{COMP} > COMP) > (ERR_{INCOMP} > INCOMP)$)							
Frontal lobe							
Inferior frontal gyrus	R	9	4.30	431	55	13	27
	R	45	4.01		57	18	19
Parietal lobe							
Postcentral gyrus/inferior parietal lobule	R	2	4.30	383	53	−27	42
	R	40	3.61		59	−27	39
	R	40	3.24		48	−39	41
Postcentral gyrus	R	2	3.80	66	46	−34	59
Inferior parietal lobule	L	40	3.70	92	−59	−38	46
	L	40	3.21		−51	−33	42
Postcentral gyrus	L	2	3.54	79	−63	−18	21
	L	2	3.24		−57	−24	21
Temporal lobe							
Inferior temporal gyrus	L	37	4.99	319	−57	−61	−9
Inferior occipital gyrus	L	18	4.63		−40	−78	−6
Middle temporal gyrus	R	37	3.78	143	53	−62	0
Fusiform gyrus	L	37	3.51	88	−46	−41	−13
	L	37	3.41		−40	−48	−25
Cerebellum		NA	3.95	92	0	−71	−23
Interaction analysis ($(ERR_{INCOMP} > INCOMP) > (ERR_{COMP} > COMP)$)							
Frontal lobe							
msFC/dACC	L	9	4.50	1120	−14	41	35
	L	32	4.04		−14	39	4
	L	24	3.97		−6	34	11
Middle frontal gyrus	L	6	4.28	78	−34	6	42
Superior frontal gyrus	R	8	3.76	163	12	47	38
	R	9	3.73		22	36	28
rACC	L	32	3.75	324	−6	33	−10
Medial frontal gyrus	L	11	3.69		4	34	−12
Temporal lobe							
Inferior temporal gyrus	L	21	4.13	165	−65	−12	−15
Middle temporal gyrus	L	21	3.17		61	3	−22
Middle temporal gyrus	R			88	61	3	−22
Parahippocampal gyrus	L	NA	4.27	131	−24	−14	−16
Parietal lobe							
Precuneus	R	31	4.63	1355	12	−51	32
	L	31	4.02		−12	−51	27
Posterior cingulate gyrus	L	31	4.25		−4	−45	30
Precuneus	L	39	3.62	87	−40	−64	36

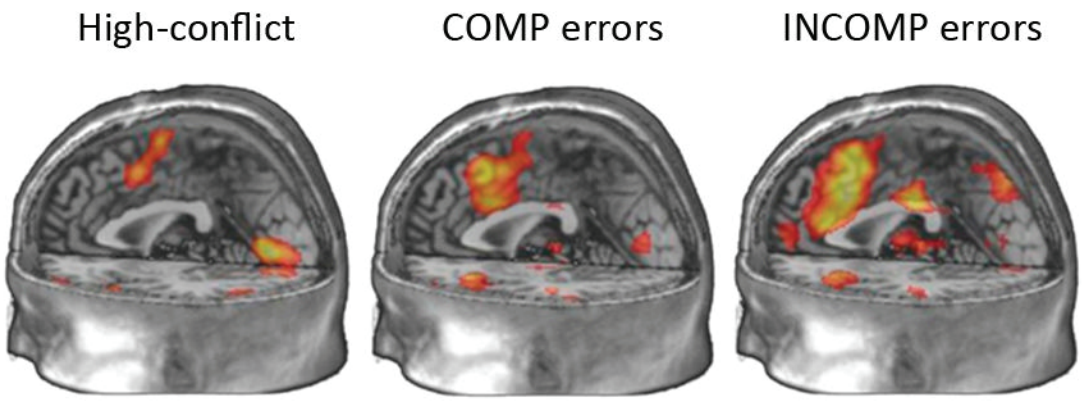


Figure 5: Conflict and error activation. Midline activity during high-conflict trials (left), COMP errors (middle), and INCOMP errors (right) overlaid onto the Colin template brain ($p > 0.005$ for visualization purposes).

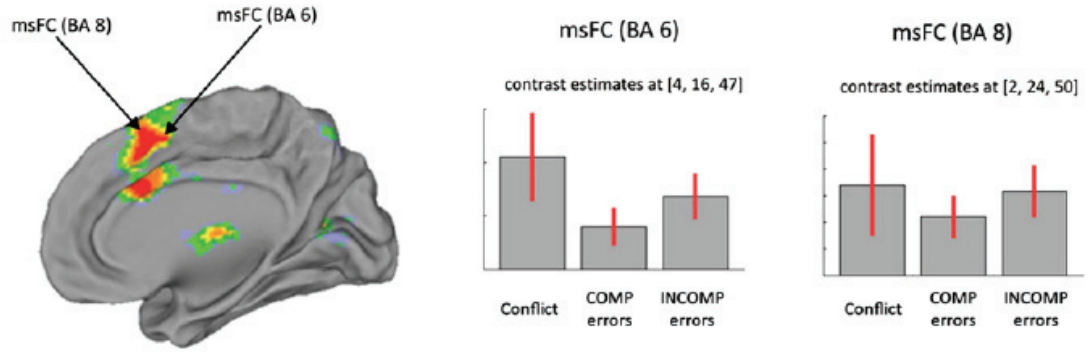
By means of an interaction analysis, we found areas specifically activated during COMP and INCOMP errors respectively (see Table 2). COMP errors were shown to lead to specific signal enhancement in the right inferior frontal gyrus, bilateral in the inferior parietal lobe/ postcentral gyrus, in the right middle and left inferior temporal gyrus, and the left fusiform gyrus gyrus, as well as in the cerebellum. Areas specifically activated by INCOMP errors comprised dACC/ msFC, rACC extending to the medial frontal gyrus (BA 11), bilateral precuneus/ posterior cingulate, the left inferior temporal (BA 21), the right middle temporal gyrus (BA 21), and the left parahippocampal gyrus.

Table 5: Common regions of main effects

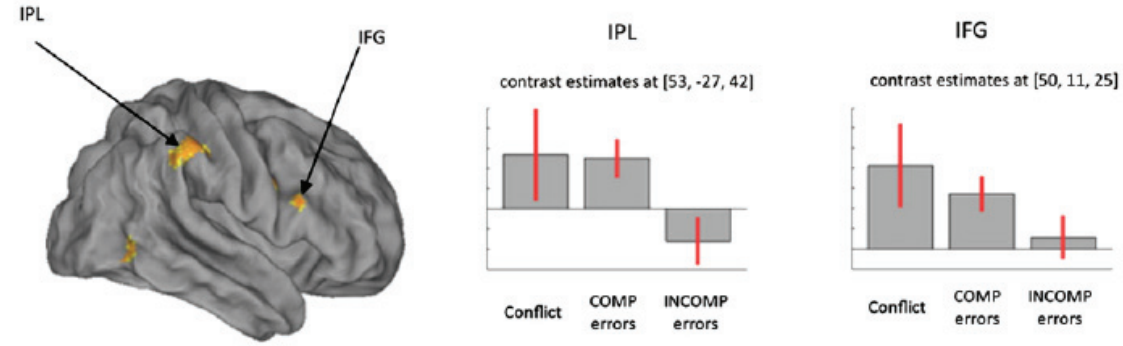
Regions	Talairach coordinates (x, y, z)		
Conjunction ((ERR$_{COMP}$ > COMP) + (ERR$_{INCOMP}$ > INCOMP))			
dACC/msFC	2	24	50
R inferior frontal gyrus/insula	32	21	−8
L inferior frontal gyrus/insula	−44	9	−6
Conjunction ((ERR$_{COMP}$ > COMP) + (INCOMP > COMP))			
msFC	4	10	52
R inferior frontal gyrus	56	10	30
L inferior parietal lobule	−58	−42	52
R inferior parietal lobule	58	−38	40
Conjunction ((ERR$_{INCOMP}$ > INCOMP) + (INCOMP > COMP))			
msFC	4	10	52
R inferior frontal gyrus	56	20	−2
L inferior frontal gyrus	−44	16	−6

3.3.2.3 Conjunction of conflict and error processing In order to find common activations between COMP/ INCOMP errors and high-conflict trials, we conducted conjunction tests (see Methods section) which showed (besides common msFC activation) right inferior frontal gyrus and the bilateral inferior parietal lobule (BA 40) as areas being recruited during both the resolution of conflict and the processing of COMP errors. Common regions of INCOMP errors and conflict processing were msFC and small clusters in bilateral inferior frontal gyrus.

Conjunction of error conditions



Specific activation of COMP errors



Specific activation of INCOMP errors

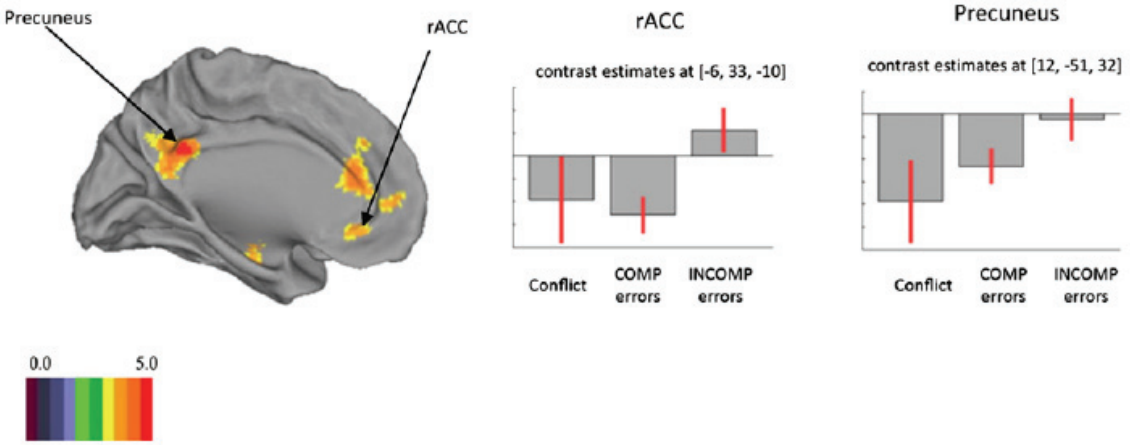


Figure 6: Cortical Regions related to conjunct and specific error activation. Activations are displayed on a human PALS SPM2 template using the CARET program (Van Essen et al., 2001).

Upper row: Conjunction of regions showing both greater activity during errors compared to correct trials displayed on the right medial surface (ERR_{COMP} > COMP) + (ERR_{INCOMP} > INCOMP), thresholded at $p < 0.05$, uncorrected for multiple comparisons; and an additional extend threshold of 50 voxels. In the msFC (BA 8), BOLD responses were increased for conjunct activity for errors, whereas in msFC (BA 6) peak activation was found during all main conditions (ERR_{COMP} > COMP) + (ERR_{INCOMP} > INCOMP) + (INCOMP > COMP). Contrast estimates of the three main contrasts (conflict, COMP errors, and INCOMP errors) for the corresponding voxels are in arbitrary units with SEMs.

Middle row: Specific activation of COMP errors displayed on the right lateral surface (ERR_{COMP} > COMP) > (ERR_{INCOMP} > INCOMP), thresholded at $p < 0.001$, uncorrected for multiple comparisons; and an additional extend threshold of 50 voxels. Contrast estimates for the right inferior parietal lobule and the right inferior frontal gyrus indicate that these areas were specifically activated during COMP errors as well as during high-conflict trials.

Lower row: Specific activation of INCOMP errors displayed on the left medial surface (ERR_{INCOMP} > INCOMP) > (ERR_{COMP} > COMP) thresholded at $p < 0.001$, uncorrected for multiple comparisons; and an additional extend threshold of 50 voxels. Contrast estimates for the left precuneus and the left rostral anterior cingulate cortex indicate that these areas were specifically activated during INCOMP errors.

3.4 Discussion

3.4.1 Conflict-related activity

Behavioral data indicate a clear response conflict with significantly prolonged reaction times and lower accuracy in the incompatible response condition. Although the conflicting information was not based on the stimulus location as in typical Simon tasks but on the motion direction of dots, our results demonstrate that centrally presented stimuli consisting of coherently moving dots against the background of a random dot field generate a strong stimulus-response incompatibility effect. While holding the position of the stimuli constant

over time, motion direction within the target (task-irrelevant information) does successfully influence ongoing task execution, and leads to poorer performance in the conflict case (Wittfoth et al., 2006; Bosbach et al., 2004).

The present data indicate that high-conflict trials - when contrasted with trials providing a facilitation of the correct response - were associated with a brain activation pattern consisting of dACC, bilateral inferior frontal gyrus, left superior temporal gyrus, superior and inferior parietal lobes, as well as extrastriate areas. These data are in line with the results of previous studies reporting similar brain regions as being engaged in cognitive conflict resolution induced by Simon tasks (Iacoboni et al., 1996; Peterson et al., 2002; Fan et al., 2003; Liu et al., 2004). The prevailing conflict detection hypothesis proposes that the functional neuroanatomy of attentional control comprises dissociable subprocesses of conflict monitoring and cognitive control. While the dACC is engaged during continuous monitoring of potential response conflicts generated by interference of different information processing streams, the lateral frontal cortex (LFC) implements cognitive control processing (Botvinick et al., 2001; MacDonald et al., 2000). If a high conflict situation is detected, the lateral prefrontal cortex is involved in resolving conflict by biasing information processing towards task-relevant properties (Botvinick et al., 2004; Ridderinkhof et al., 2004; Egner and Hirsch, 2005).

3.4.2 Error-related activity

In the present study we tried to differentiate error-related brain activation patterns associated with COMP and INCOMP errors. Thus, the present study provides an analysis of brain activation patterns for error-related processes without confounding pre-response conflict. We identified a common error processing network by comparing brain activity

associated with both errors on COMP and INCOMP events versus correct responses in both conditions. In particular, conjunction analysis demonstrated error-related activation in medial superior frontal cortex (msFC), dorsal ACC, right inferior frontal gyrus, and left insula. This finding is consistent with previous studies that examined error-related activation in cognitive tasks (Carter et al., 1998; Kiehl et al., 2000; Braver et al., 2001; Menon et al., 2001; Ullsperger and von Cramon, 2001; Garavan et al., 2002), and also supports the view that error-related activation patterns are quite robust despite the use of a variety of diverging cognitive paradigms (Hester et al., 2004).

There is an ongoing controversy regarding the existence of a specific error detection network and whether the anterior cingulate cortex is involved in error processing per se rather than in conflict monitoring (Ullsperger and von Cramon, 2004; Stemmer et al., 2003). Two prominent models of performance monitoring based on the functional significance of the error-related negativity (ERN) propose a theoretical framework for error processing:

(1) According to the reinforcement-learning theory of the ERN (Holroyd and Coles, 2002), error signals are produced by a response-monitoring system located in the basal ganglia which activates the mesencephalic dopamine system and the ERN is evoked by the impact of dopamine activity on the anterior cingulate cortex. At the same time, a monitoring system in the basal ganglia is thought to predict the outcome of the response, on the basis of information received from both the external environment and an 'efference copy' of the response. Hence, the detection of errors is based on the non-occurrence of an anticipated reward. According to this model, the ERN is coded as phasic increases and decreases of dopaminergic input originating in the ventral tegmental area (VTA) of the midbrain. In particular, the ERN originates when a phasic decrease in activity of mesencephalic

dopaminergic neurons disinhibits the apical dendrites of motor neurons in the dACC following error commission.

(2) The conflict monitoring theory proposes the ERN to reflect the activation of a system which monitors conflict following the commission of an error (Botvinick et al., 2004). This system is located in the anterior cingulate cortex and is functionally related to the occurrence of response conflict. Whenever incompatible response channels are simultaneously activated, the ACC conveys this information to brain regions involved in attentional control, such as lateral prefrontal cortex.

The observation of dACC activity in response to errors on COMP trials in which there is in fact no pre-response conflict indicates that this midline area might instead detect an outcome worse than the desired one (see also Brown and Braver, 2005). Although, peak activations of the dACC during COMP errors and during high-conflict processing were located in close vicinity (4, 10, 47; -4, 14, 42) within the human homologue of the monkey rostral cingulate motor area (rCMA; Picard and Strick, 2001), our data also show distinct areas. Nevertheless, the interpretation of functionally separate areas for these processes must be taken with caution. Future investigations regarding these brain mechanisms might provide additional support for this finding.

Since results of conjunct activation during high-conflict and INCOMP error trials revealed a cluster of common activation in the msFC, we suppose that conflict monitoring and error processing during the occurrence of conflict activate additional functionally different regions - at least in the context of the Simon conflict task. This functional dissociation is corroborated by the data of fMRI studies investigating both error processing and response conflict within one experimental setup (Carter et al., 1998; Kiehl et al., 2000; Ullsperger and von Cramon,

2001; Garavan et al., 2002; Garavan et al., 2003; Hester et al., 2004). Additionally, evidence for this theory comes from human ERP studies (Swick and Turken, 2002) and from research in non-human primates showing that different neurons clustered within specific pFMC regions may play specific roles during performance monitoring (Gemba et al., 1986; Shidara et al., 2002; Ito et al., 2003).

Our results on the overlap of thresholded statistical maps for both error types are in line with recent findings (Carter et al., 1998; Kiehl et al., 2000; Braver et al., 2001; Menon et al., 2001; Ullsperger and von Cramon, 2001; Garavan et al., 2002; Rubia et al., 2003, Bechtereva et al., 2005; Dosenbach et al., 2006). When COMP and INCOMP errors were conjointly analyzed, our data showed dACC/ msFC and bilateral operculo-insular activation which might belong to a core task-set system. It is proposed that this core system shows also reliable start-cue and sustained activations (Dosenbach et al., 2006). In a larger context, this error-processing network shows an interesting similarity with activations related to pain processing (Tracey, 2005; Vogt, 2005); a finding which might point to the notion of both error- and pain-related processes representing a detection of negative outcomes as the basis for a reconfiguration of behavior. While there was conflict-related activation in a dorsal region of the ACC, the error-related midline activation included more rostral and caudal cingulate areas.

Our results showing dACC activity on erroneous compatible trials together with findings of other studies which support the view of the dACC as the generator of the ERN (van Veen and Carter, 2002), point to a recruitment of this midline region during the detection of performance errors. The present data emphasize a functional differentiation of error-related activation during COMP and INCOMP errors despite a large overlap of conjunct activity.

While errors committed to INCOMP events lead to specific activation in the rostral ACC (Polli et al., 2005), errors in response to COMP trials revealed a specific activation pattern comprising the right inferior frontal and bilateral inferior parietal lobules. These findings indicate that error processing is implemented in an extended network of brain regions, and that the dACC is just one of them. This is supported by a study (Stemmer et al., 2003) which described five cognitively impaired patients with lesions encompassing the anterior communicating artery and thus including the ACC, the medial prefrontal cortex and other related subcortical areas. Although, they were able to detect their error on an experimental task, they were not able to produce an ERN.

In the present study we were able to disentangle error processing on trials with high pre-response conflict versus trials with no pre-response conflict. Error-related dorsal ACC activity in the absence of simultaneously interfering processing streams (as in the case of COMP errors) seems to favor the assumption that the ACC acts as a detector of erroneous motor responses, instead of being a pure conflict monitoring system. Our data may also reflect a post-response on COMP error trials thus indicating that erroneous responses to compatible trials induce strong post-conflict effects. This at first glance counterintuitive assumption was first presented by Yeung et al. (2004). These authors demonstrated on simulated data that the post-response conflict on erroneous compatible trials is even larger than the post-response conflict on incompatible trials. The conflict arises in the period following an error as a consequence of the continued processing of the compatible stimulus and the incorrect response just committed.

But what is the difference in processing between INCOMP and COMP errors? And how does this difference relate to the specific activation observed? The presence of rostral anterior

cingulate activity during INCOMP errors may reflect subject's different attribution of significance to both types of errors. Although it seems reasonable to propose that activation in the emotional division of the ACC is related to the emotional valence of errors (Whalen et al., 1998; Bush et al., 2002), a comprehensive perspective challenges the functional dichotomy of anterior cingulate cortex into a cognitive and an emotional division. By taking into account not only cognitive and affective task paradigms (Bush et al., 2000), but also studies investigating pain-related processes, the cognitive-affective dichotomy becomes doubtful and insufficient because numerous studies reliably showed an association between the emotional distress of pain with the dACC rather than the rACC (Rainville et al., 1997; Peyron et al., 2000). Etkin and colleagues (2006) showed that even during the monitoring of emotional conflict dACC signal enhancement could be observed. Therefore, the rACC activation might reflect not a distinction of emotional versus non-emotional stimulus processing but rather processes of autonomic arousal and parasympathetic modulation (Matthews et al., 2004; Critchley, 2004; Critchley et al., 2005; Davis et al., 2005) which might be crucial for assessing the presence of potentially relevant motivational and emotional consequences (Davidson et al., 2002).

Activation in the precuneus and posterior cingulate cortex in response to errors has also been reported in previous studies (Menon et al., 2001; Fassbender et al., 2003). Based on differing cytoarchitectonic structures anatomically separating this brain area from adjacent precuneus, the medial parietal cortex has been proposed to be a cortical transition zone (Cavanna and Trimble, 2006). Our data support the view of an important role for these areas during the processing of INCOMP errors. Activity in the precuneus and in the medial parietal cortex adjoining the posterior cingulate cortex might reflect evaluative functions such as

monitoring behavior (Vogt et al., 1992) or the self-relevance of the underlying evaluation processes (Maddock et al., 2001; Vogeley and Fink, 2003; Vogeley et al., 2004; Nunez et al., 2005; Northoff and Bermpohl, 2004).

While the brain activation pattern of INCOMP error trials (ERR_{INCOMP} > INCOMP) corroborates the results of recent fMRI studies on error processing, it is still unknown why subjects commit errors in response to compatible trials. In contrast to incompatible events which generate coactivation of mutually incompatible responses and therefore increase response tendencies towards the erroneous alternative, compatible events are comparatively easy to execute. Both information streams of the present task, the shape of the target and the direction of dot motion, facilitate the subjects' correct response. On the background of our data, it seems plausible that a temporary "fading of attentional activation level" led to these errors. The activation pattern of COMP errors (ERR_{COMP} > COMP) with distinct right prefrontal and inferior parietal cortex activation suggests that this type of error led to the recruitment of additional areas linked to the attentional network (Corbetta and Shulman., 2002) in order to prevent further error commitment. This hypothesis has already been discussed by Rubia et al. (2003) who described bilateral inferior parietal cortex activity in addition to the ACC activity in the context of inhibitory failure. The peak activations as revealed in the present study support the hypothesis that these fronto-parietal brain regions might possibly be linked to the implementation of cognitive control without an additional engagement of emotional or motivational arousal (Critchley et al., 2005).

However, one concern with these analyses is that the differential brain activities between the two error types (ERR_{COMP}, ERR_{INCOMP}) could reflect neural activation not specifically related to error processing. In particular, the right inferior frontal cortex is active during

conflict-related activity (INCOMP > COMP) as well as during error commission on compatible trials (ERR_{COMP} > COMP). In order to resolve this issue, we conducted additional analyses. We exclusively masked brain activation maps of COMP errors and of INCOMP errors with conflict-related activity. Although, there was no altering of specific error-related activity during INCOMP errors, we found that only right parietal activity remains as specific for COMP errors when masking out conflict-related activation. Thus, it seems plausible that the right inferior frontal activity during COMP errors and incompatible correct trials does not reflect solely error-specific processes. Right inferior frontal cortex function is commonly associated with inhibitory processes, in particular during control of task sets (Aron et al., 2004), interference resolution (Herrmann et al., 2001); and patients with damage in this region show elevated impairment of inhibition (Michael et al., 2006; Clark et al., 2006). The increased BOLD response might reflect greater inhibitory efforts or even a greater amount of inhibitory failure during these trials. More work is needed to improve our understanding of the underlying mechanisms during COMP errors and to raise alternative interpretations of the right IFG function, since this area is also frequently activated in fMRI studies that do not have an obvious inhibitory component (Duncan & Owen, 2000).

Until now, these specific kinds of errors did not attract much interest, presumably because subjects tend to make only a small number of erroneous responses to compatible events. But our results might contribute to a better understanding of these special types of errors without pre-response conflict and their underlying brain processes.

3.5 Conclusion

To summarize, our observations of specific error-related activations depending on the occurrence of conflict information support the idea of a more widespread error detection system in the human brain. Moreover, in contrast to recent investigations disentangling neural correlates of aware and unaware errors (Hester et al., 2005; Klein et al., 2007a), the present findings emphasize functionally specific activation patterns in response to errors related to compatible and incompatible events. While the dACC/ msFC and operculo-insular frontal cortices may serve as a common error-processing network, functionally specific regions contribute to the processing of errors in regard to whether these erroneous responses were made after the presentation of high- or low-conflict trials.

4.0 HOW THE BRAIN RESOLVES HIGH CONFLICT SITUATIONS: DOUBLE CONFLICT INVOLVEMENT OF DORSOLATERAL PREFRONTAL CORTEX

SUBMITTED TO *SCIENCE* IN APRIL 2008

BY

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4.1 Introduction

Common conflict tasks require subjects to respond to one stimulus dimension while ignoring another conflicting dimension. The most commonly used conflict tasks are the Stroop task (MacLeod, 1991), the Eriksen Flanker task (Eriksen & Eriksen, 1974), and the Simon task (Simon, 1969; Simon & Berbaum, 1990). In the case of the Simon task, the costs

in reaction time and accuracy are due to an incompatibility between stimulus location and response side. Although stimulus location is irrelevant for the task, subjects are faster and make fewer errors when stimulus and response location correspond (compatible condition) than when the stimulus is presented opposite to the response side (incompatible condition). The most common interpretation of the Simon effect refers to a conflict between an indirect and a direct route of response selection (Kornblum et al., 1990). The indirect route provides the correct response on the basis of the relevant stimulus feature; and in parallel the direct route triggers an automatic response tendency towards the spatial position of the stimulus.

In an earlier study variants of the Simon task based on form-from-motion induced strong conflict effects (Wittfoth et al., 2006). Brain areas such as the medial frontal gyrus and superior parietal lobule (SPL) play major roles monitoring different types of conflict. We introduced two different but comparable types of conflicts. In a location-based Simon task stimulus position served as conflicting information, while in a motion-based Simon task the direction of dot motion had to be ignored. In the latter variant, stimuli were always presented at the centre of the screen and a Simon effect was observed although stimulus location was irrelevant for task solution.

Based on these findings, we investigated possible influences of two simultaneous and conflicting information streams. While several functional MRI studies of cognitive conflict resolution pointed to an extensive network of brain areas (particularly the medial prefrontal, anterior cingulate cortex (ACC), lateral prefrontal and parietal regions (Peterson et al., 2002; Liu et al., 2004)), there has been no investigation of double conflict resolution so far. Only Fan and colleagues (2003) provided behavioral data of a task in which incongruent flankers were merged with a spatial incompatibility task.

A variety of studies provided evidence of differing neural strategies for resolving conflict. While in the Stroop task incompatible stimulus features generate conflict that arises from task-relevant versus task-irrelevant stimulus processing (Desimore & Duncan, 1995), it is the inhibition by task-irrelevant information on motor output that serves as a mechanism to overcome conflict in the Simon task (Stuermer et al., 2002; Nieuwenhuis & Yeung, 2005). Hence, comparing conflict tasks there are basic confounds of qualitatively different conflict resolution strategies due to different sources of interfering information. Recent data suggest that these control mechanisms are executed in an independent and parallel fashion (Egner et al., 2007).

The advantage of the present experimental design is that both conflicting information are based on spatial incompatibility thus avoiding confounds derived from the fact that processing of stimulus-stimulus conflicts might engage different networks than stimulus-response conflicts (Kornblum & Stevens, 2002). Based on previous studies on cognitive conflict activity in stimulus-response compatibility tasks (Merriam et al., 2001; Schumacher & D'Esposito, 2002) we expect parietal as well as lateral prefrontal brain regions to be additionally recruited during double conflict processing. Lateral prefrontal areas are known to implement performance adjustments in a variety of tasks, while the ACC monitors ongoing performance and signals the need for higher control in conflicting trials (Ridderinkhof et al., 2004; Botvinick et al. 2004).

We expect a double conflict condition with two interfering information streams to require additional cognitive resources in order to maintain appropriate response behavior when compared to two single conflict conditions (location-based and motion-based Simon tasks).

Higher ACC activation following double conflict trials may indicate that this area also reflects additional response conflict.

Moreover, recent findings regarding the conflict adaption effect may be replicated in the present investigation. The conflict adaption effect reflects the phenomenon that prior context situations influence the interference effects in subsequent trials. Especially the Simon effect is reduced or even absent when a high-conflict incompatible trial is followed by another incompatible trial compared to a task situation where the preceding trial is compatible (Wuhr & Ansorge, 2005). The conflict monitoring hypothesis (Botvinick et al., 2001) interprets these performance adjustments as an adaption of conflict control areas after conflict has been detected in the preceding trial. In essence, we compared brain activity induced by incompatible trials which were preceded by a compatible trial providing a high amount of cognitive conflict with incompatible trials preceded by another incompatible trial resulting in low cognitive conflict. However, conflict resolution processes are also likely in trials following incorrect responses. Subjects tend to react slower after error commission (Kleiter & Schwarzenbacher, 1989; Kerns et al., 2004) indicating a high degree of response conflict on post-error trials.

Thus, we investigated brain activation patterns associated with different mechanisms of cognitive control by separating brain activation in conflict and error detection on one side and high-conflict resolution processes (incompatible trial after incompatible trial) and error resolution after error commitment (post-error trials) on the other side.

4.2 Methods

4.2.1 Subjects

Fourteen right handed, 22- to-30-year-old volunteers (mean age 25 (SD 2.6); 2 males) with no history of neurologic or psychiatric disease participated in the study. All subjects had normal or corrected-to-normal vision. Written informed consent was obtained from all participants prior to scanning and the study was approved by the local ethics committee. Subjects were paid € 10 for participation.

4.2.2 Experimental procedure: stimuli and tasks

The experimental setup consisted of a Simon task based on form-from-motion target which was evaluated during a previous study (Wittfoth et al., 2006). On each trial, subjects were presented with coherently moving dots which popped-out from a of randomly moving background pattern forming either a triangle or a square. The triangular or square target shapes consisted of approximately 200 white dots subtending 2.8° of visual space and were surrounded by approximately 4000 randomly moving dots. The overall position of stimuli was constant over time, and both shapes consisted of the same area and number of dots. Subjects were instructed to press a right-hand response button for a triangle and a left-hand button for a square while ignoring both the location of the target and the direction of the coherently moving dots. After a verbal instruction emphasizing both speed and accuracy, a short 30-trial practice session was administered to make sure that subjects understood the task

properly before proceeding into the scanner. A red fixation point along with the stimulus was presented at the start of each trial for 700 ms. After button press the fixation point changed its color from red to white, providing a feedback signal which indicated that the response had been registered. The feedback signal provided no information about the correctness of the response. Trial duration was 1000 ms with a jitter of ±300 ms.

Cognitive conflict was induced either by motion direction of target dots (IM), by stimulus eccentricity (IL; i.e. location 6° to the left or the right of a fixation point), or by both simultaneously interfering information (II). Thus, the experimental protocol included three interference inducing incompatible conditions. In the IM (motion-based interference task) condition, subjects were presented with a target shape which appeared in the requested hemifield but which was composed of dots coherently moving to the opposite direction. In the IL (location-based interference task) condition, subjects were shown a target shape in the hemifield opposite to the side of the requested button press but dots were moving to the correct direction. The double incompatible condition (II) consisted of both a target symbol located in the hemifield opposite to the required button press and composed by dots moving to the opposite direction. In the compatible condition (C), stimuli provided facilitating information with both stimulus location and motion direction pointing to the correct response side. In addition, we introduced a neutral condition (N) consisting of targets which were presented at the centre of the screen and which were composed of upwards moving dots, thus providing no conflicting or facilitating information.

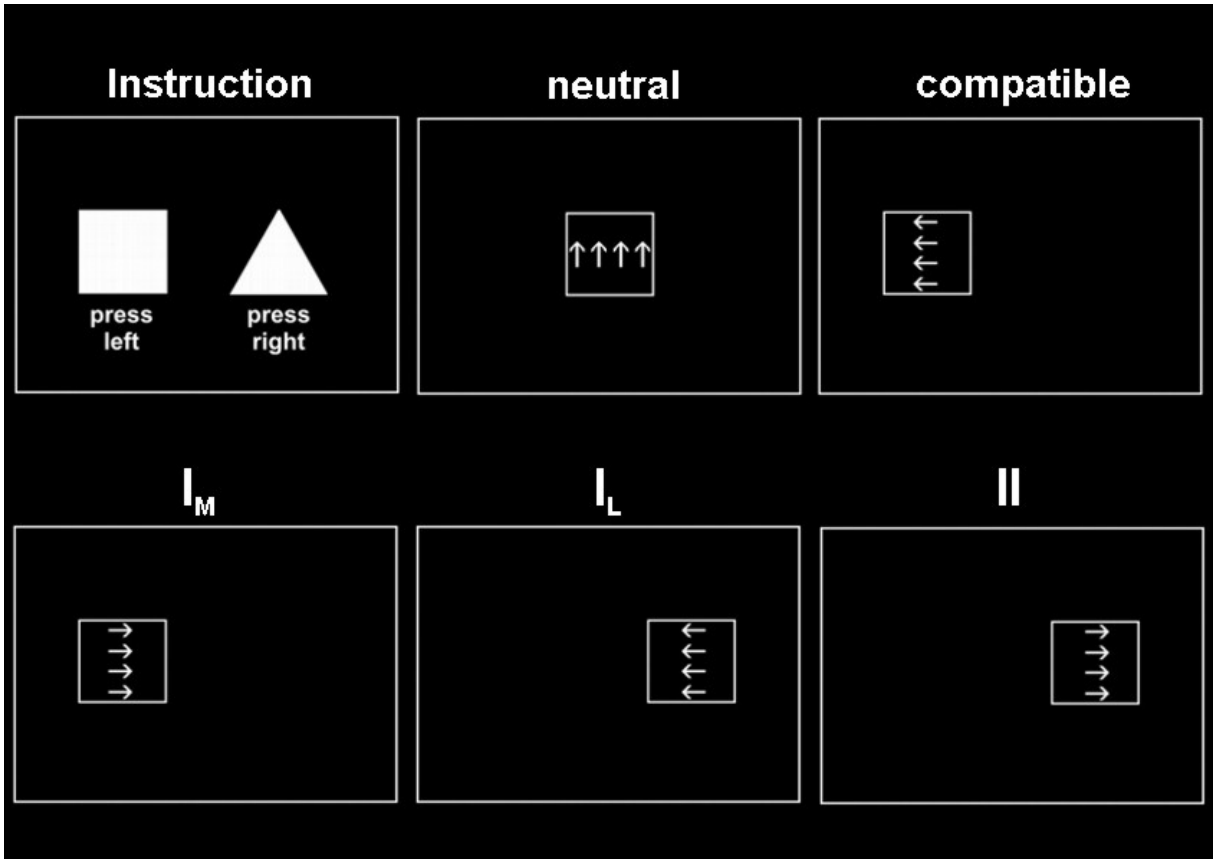

Figure 7: Schematic illustration of the experimental setup.

Subjects had to press a right-hand button for a triangle and a left-hand button for a square. The figure shows a square which 'pops-out' by coherent motion of approximately 200 white dots within a randomly moving dot kinematogram (4000 dots). Arrows show the movement direction of dots composing the stimulus target. In the compatible condition, for example, subjects were presented a square in the left hemifield which consisted of leftwards moving dots, thus facilitating the correct response. In the motion-based incompatible condition (I_M) the target appeared on the side corresponding to the correct response side, but coherent dot motion direction was opposite to the response side. In the location-based incompatible condition (I_L) coherent dot motion was towards the correct response, but stimulus target was located in the opposite hemifield. In the double incompatible condition (II), both spatial and dynamic stimulus features were opposite to the correct response side. The neutral condition consisted of symbols presented in the centre of the screen and composed of upwards moving dots.

In three consecutive runs, subjects were presented with a total of 700 pseudo-randomized trials (300 compatible, 300 incompatible (100 of each incompatible condition), and 100

neutral events) with an equal number of right and left hand button presses (see Supplementary material). The duration of each run was approximately 7 min, resulting in a length of 21 min for the entire functional investigation.

4.2.3 Data Acquisition

Scanning was performed on a 3-T SIEMENS Magnetom Allegra® system (Siemens, Erlangen, Germany) equipped with a standard quadrature head coil. Subjects wore foam earplugs and were positioned on a scanner couch in a dimly illuminated room. Stimuli were presented via a JVC video projector onto a projection screen positioned at the rear end of the scanner's core.

Prior to the functional runs, a T1-weighted structural 3D-image of the brain was obtained using the MPRAGE-sequence as provided by the manufacturer (TR = 2.3 s, TE = 4.38 ms, TI = 900 ms, flip angle = 8°, FOV = 256 x 256 x 160 mm, spatial resolution = 1 mm^3/ voxel). Functional data were collected with a T2*-weighted echo-planar imaging sequence (TR/TE = 2500/30 ms, flip angle = 90°, 38 slices, slice-thickness: 3 mm with a 0.3 mm gap, 64 x 64 matrix, in plane resolution = 3 x 3 mm, interleaved acquisition order). Prior to data acquisition, two dummy scans were performed.

4.2.4 Data Analysis

Pre-processing of functional MRI data, including slice timing, realignment, normalisation on the basis of the co-registered high-resolution structural image, and smoothing with an 8-mm full-width at half-maximum Gaussian kernel, was performed with SPM5 software

(Wellcome Department of Cognitive Neurology, London, UK; see http//www.fil.ion.ucl.ac.uk/spm). Data on the first- and second level were analyzed using a general linear model (GLM) approach. Thirteen regressors were modelled for each single subject using a standard hemodynamic response function (please see supplementary material for a complete list of all conditions): compatible trial preceded by a compatible trial (**CC**), compatible trial preceded by a neutral trial (N**C**), all neutral trials (Neut), compatible trial preceded by an incompatible trial (i**C**), double conflict trial preceded by a compatible trial (C**II**), double conflict trial preceded by a neutral trial (N**II**), location-based incompatible trial preceded by a compatible trial (C$\mathbf{I_L}$), location-based incompatible trial preceded by a neutral trial (N$\mathbf{I_L}$), motion-based incompatible trial preceded by a compatible trial (C$\mathbf{I_M}$), motion-based incompatible trial preceded by a neutral trial (N$\mathbf{I_M}$), incompatible trial preceded by an incompatible trial (HCR), error trials (Err), and correct trials after an error commission (Posterr). Movement parameters from realignment correction were entered as additional covariates of no interest to account for residual movement artefacts after realignment. To remove low-frequency signal drifts, data were high-pass filtered (128 s). An autoregressive function (AR-1) was employed to estimate temporal autocorrelations in the data and to correct the degrees of freedom accordingly.

For the purpose of group analyses, the resulting parameter estimates for each regressor at each voxel were then entered into a second-level analysis of variance (ANOVA). In order to obtain specific activation related to the double incompatible condition we tested for the contrast (C**II** > C$\mathbf{I_L}$ + C$\mathbf{I_M}$). Similarly, we obtained common activations of all three incompatible condition compared to the compatible condition with the contrast (C**II** + C$\mathbf{I_L}$ + C$\mathbf{I_M}$ > **CC**).

Data analyses were further on based on specifying separate a priori anatomical ROIs within MNI atlas space using automated anatomical labelling and WFU pickatlas software (Maldjian et al., 2003; Tzourio-Mazoyer et al., 2002) for analyses of data from bilateral superior and inferior parietal lobules, the dorsolateral prefrontal Cortex (dlPFC, mask was created by combining prefrontal regions as described in Eippert et al., 2007), and medial frontal/ anterior cingulate cortex. To examine signal changes during high-conflict resolution (incompatible trials preceded by another incompatible trial) as well as during error commission and error resolution three further analyses were performed. We contrasted HCR > C**II** + C$\mathbf{I}_{\mathbf{L}}$ + C$\mathbf{I}_{\mathbf{M}}$, Err > correct trials, and Posterr > all other conditions except error trials. The results were thresholded with an uncorrected $p > 0.001$ and an extension threshold of 10 voxels. The statistical criterion was selected on the basis of similar criteria used for the examination of a priori ROIs in other neuroimaging studies with random effects models.

Coordinates of activation were converted from Montreal Neurological Institute to Talairach space (Talairach and Tournoux, 1988) by using the mni2tal-transform developed by Matthew Brett (www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html). Anatomical labels are based on the Talairach Daemon database (www.ric.uthscsa.edu/projects/talairachdaemon.html).

4.3 Results

4.3.1 Behavioral data

Subjects' responses in all incompatible conditions (C**II**, C$\mathbf{I_L}$, and C$\mathbf{I_M}$) were significantly prolonged compared to reaction times to compatible trials (**CC**), thus indicating conflict processing (see Table 1). For the incompatible conditions, only C**II** and C$\mathbf{I_L}$ trials differed not significantly ($p > 0.72$) by showing both longer reaction times compared to C$\mathbf{I_M}$. Additionally, responses to incompatible trials preceded by another incompatible trial of a different condition (e.g. I_L-**II**) were significantly slower than incompatible trial sequences with an exact condition repetition ($p > 0.004$). Within the different type of compatible trials (II**C**, I_L**C**, I_M**C**), we found that subjects reacted significantly longer on a compatible trial if it was preceded by an incompatible trial with the exception of I_M**C** ($p > 0.93$). Post-error trials showed no significant differences towards a slowing of reaction times compared to error trials ($p < 0.29$), although by inspecting data of single subjects in nine of fourteen participants a post-error slowing could be observed.

Subjects committed significantly more errors on incompatible trials (C**II**, C$\mathbf{I_L}$, and C$\mathbf{I_M}$) than on compatible trials (**CC**). For the incompatible conditions, there were significant differences between C$\mathbf{I_L}$ and C$\mathbf{I_M}$) ($p < 0.04$) and C**II** and C$\mathbf{I_M}$ ($p < 0.0019$). Interestingly, we found a significant difference even for C**II** and C$\mathbf{I_L}$ ($p < 0.03$), indicating that subjects had the lowest accuracy rate in response to double incompatible trials. When a compatible trial was preceded by II or I_L, subjects committed significantly more errors compared to **CC**.

Table 6: Descriptive statistics of behavioral data. Mean reaction times and SDs. The current trial is printed in bold.

	Mean	Std.Dev.
	(ms)	
Err	579	81
Posterr	593	66
C**C**	553	75
N**C**	574	72
C**N**	532	57
N**N**	478	56
II**C**	590	73
I_L**C**	581	67
I_M**C**	553	73
II**N**	531	50
I_L**N**	536	60
I_M**N**	534	54
C**II**	635	73
N**II**	630	75
C$\mathbf{I_L}$	631	79
N$\mathbf{I_L}$	639	87
C$\mathbf{I_M}$	582	73
N$\mathbf{I_M}$	587	75
HCR-equal	545	69
HCR-different	626	82

Table 7: Mean error rates and SDs. The current trial is printed in bold.

	Valid N	% Errors	Std.Dev.
C**C**	14	1.9	3.0
N**C**	14	2.4	3.9
C**N**	14	2.4	2.7
N**N**	14	5.9	9.3
II**C**	14	4.9	5.5
I_L**C**	14	5.0	4.7
I_M**C**	14	1.9	2.2
II**N**	14	1.9	3.4
I_L**N**	14	3.1	4.4
I_M**N**	14	2.8	5.0
C**II**	14	17.2	13.4
N**II**	14	16.2	12.2
C$\mathbf{I_L}$	14	10.2	8.8
N$\mathbf{I_L}$	14	7.9	8.2
C$\mathbf{I_M}$	14	4.6	4.5
N$\mathbf{I_M}$	14	2.2	3.3
HCR-equal	7	7.4	6.2
HCR-different	14	8.6	6.9

4.3.2 Imaging data

Table 8 shows activated clusters observed for specific double conflict-related activity and for common activity of all incompatible conditions. A significant increase in BOLD activation of the double incompatible condition compared to both simple conflict conditions (I_M; I_L) was found in the left dlPFC (BA 9). Common conflict-related activations for all interference conditions were observed in right inferior frontal gyrus (BA 9) and left IFG/ precentral gyrus (BA 6/ 9), bilateral inferior parietal lobule (BA 40), and in the medial prefrontal cortex (BA 8).

Table 8: Activation peaks for different conflict conditions. All coordinates are given according to the Talairach and Tournoux space together with their Z scores. Significance threshold $p < 0.001$ (uncorrected) with an additional extended cluster threshold of $k > 10$ voxels which yielded an equivalent correction for multiple comparisons and enriched for larger activation clusters. ROIs: bilateral dlPFC, ACC, medial frontal, superior and inferior parietal lobules.

	Side	Brodmann`s Area	Z score local maximum	Cluster Size (Voxels)	Talairach Coordinates		
					X	Y	Z
Double conflict-related activation ($cII > (cI_L + cI_M)$)							
DLPFC	L	9	3.64	27	-32	38	31
Common conflict-related activation ($cII + cI_L + cI_M > cC$)							
Inferior Frontal Gyrus	R	9	4.57	117	67	9	24
Inferior Frontal Gyrus/ Precentral Gyrus	L	9/ 6	4.09	216	-59	3	27
Inferior Parietal Lobule	R	40	3.90	51	36	-35	48
Inferior Parietal Lobule	L	40	3.51	29	-42	-33	42
Superior Frontal Gyrus	R	8	3.53	49	8	30	46
HCR > ($cII + cI_L + cI_M$)							
rostral ACC	L	32	3.67	28	-4	27	-8
Error > correct							
Putamen/ Insula	L	NA/ 13	6.79	3154	-22	10	1
Putamen/ Insula/ IFG	R	NA/ 13/47	7.44	2126	20	12	-1
Medial Frontal Gyrus	L	6	5.63	1880	-6	16	42
Inferior Parietal Lobule	L	40	3.58	83	-42	-42	46
Post-Err > correct							
ACC	R	32	3.74	96	6	30	22
Superior Frontal Gyrus	R	10	3.65	89	26	48	25
Inferior Frontal Gyrus	R	47	3.42	13	55	17	-6

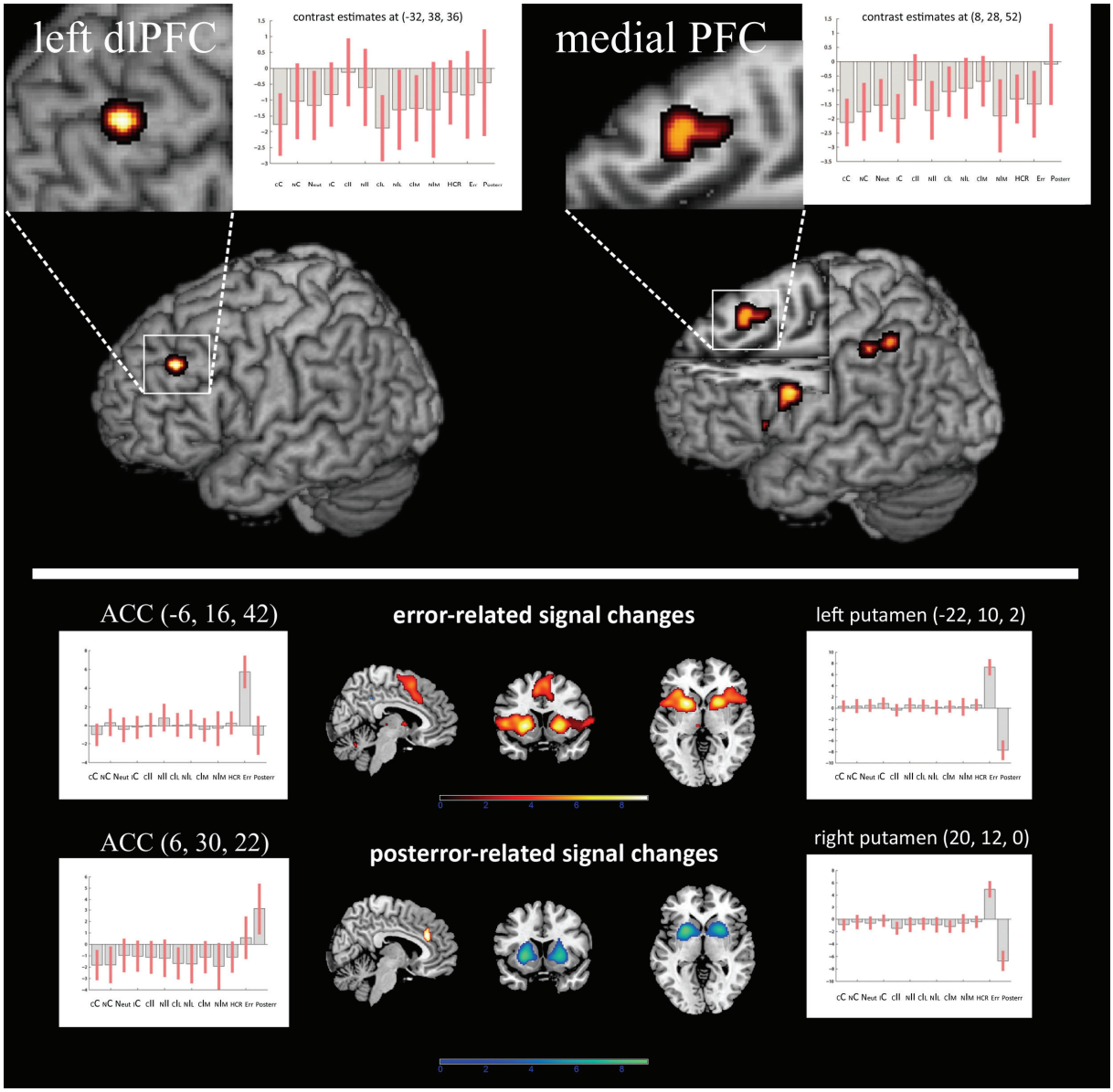

Figure 8: Activation of brain areas in different cognitive control conditions

Upper left: A region associated with specific double conflict processing was identified in the left DLPFC. Contrast estimates (with s.e.m.) for this specific area displayed for all regressors. Upper right: Common regions associated with cognitive control irrespective of the conflicting information. Contrast estimates (with s.e.m.) for medial wall activity (8, 28, 52).

Lower figure: Error- and post-error-related signal changes. Activity maps are superimposed on the Colin brain template (neurological convention) and show increases and decreases in BOLD signal when participants committed an error relative to correct trials. Lower activations maps show increases and decreases in BOLD signal in response to post-error trials. Additionally, contrast estimates (with s.e.m.) of relative BOLD signal changes for all regressors in selected regions of the ACC and bilateral basal ganglia (putamen). Note, that the parameter estimates were not normalized to the overall mean.

Abbreviations from left to right: C**C**: compatible trial preceded by a compatible trial; N**C**: compatible trial preceded by a neutral trial; Neut: neutral trials, i**C**: compatible trial preceded by an incompatible trial; **CII**: double conflict trial preceded by a compatible trial; N**II**: double conflict trial preceded by a neutral trial; C$\mathbf{I_L}$: location-based incompatible trial preceded by a compatible trial, N$\mathbf{I_L}$: location-based incompatible trial preceded by a neutral trial; C$\mathbf{I_M}$: motion-based incompatible trial preceded by a compatible trial; N$\mathbf{I_M}$: motion-based incompatible trial preceded by a neutral trial, HCR: incompatible trial preceded by an incompatible trial, Err: error trials; Posterr: correct trials after an error commission.

A priori regions of interest analysis for the high-conflict resolution trials revealed an activation cluster in the rostral ACC. Error trials were associated with a bilateral network comprising putamen, insula, and inferior frontal gyrus. Additionally, during error processing a signal increase in the pre-SMA extending into dorsal ACC was observed.

Post-error trials (error resolution) were significantly associated with activity in right inferior frontal gyrus (BA 47) and superior frontal gyrus (BA 10), and with activity in the ACC. In addition to these priori regions we found error resolution to be consistently associated with a significant decrease of BOLD response in bilateral putamen (see Figure 8).

4.4 Discussion

The major aim of our study was to investigate the specific neuronal correlates of conflict monitoring when two interfering information streams are presented simultaneously. We found the left dlPFC to be recruited in case of increasing task difficulty in addition to those areas known to be involved in conflict monitoring. Interestingly, no increased medial wall activity (medial prefrontal cortex or ACC) was observed in additional task demands when compared to single conflict conditions.

According to the conflict monitoring hypothesis (Botvinick et al., 2004), ACC activity usually reflects the detection of a response conflict. When conflicting response alternatives are activated, the ACC signals the need for conflict resolution. In the present study we observed conjunct right lateral prefrontal (dlPFC) activation in all three incompatible conditions during conflict detection. This finding seems to partially contradict the results of other studies that found dlPFC activity to be associated with conflict resolution, rather than monitoring (Egner & Hirsch, 2005a, 2005b; MacDonald et al., 2000). But since recent studies reported dlPFC activity also during task switching, high working memory loads, and incompatible Stroop condition (Derrfuss et al., 2005; Duncan & Owen, 2000; Wager et al., 2004), the detailed contribution of dlPFC to conflict mechanisms remains subject of future investigations.

Adaption effects in Simon tasks were shown in various studies (Stuermer et al., 2002; Wuhr, 2005; Wuhr & Ansorge, 2005; Kerns, 2004; Stoffels, 1996; Praamstra et al., 1999). Here we tried to differentiate these sequential trial effects based on a trial-by-trial analysis. It is well known that the degree of task-irrelevant interference during the processing of task-relevant information varies with the conflict level of the preceding trial (Egner, 2007). Less

behavioural conflict is observed in incompatible trials preceded by another incompatible trial (high-conflict resolution); and thus the finding of increasing reaction time on incompatible trials preceded by a compatible trial reflects high conflict but less conflict resolution resources. Although sequential modulations have been attributed to low-level priming effects, namely stimulus-response repetitions in successive trials (Mayr et al., 2003), several recent studies controlling these repetitions still showed differences in compensatory adjustments of cognitive control (Kerns et al,., 2004; Ullsperger et al., 2005). The present data add important new aspects to this debate. The behavioural data indicate that the decrease of interference in subsequent incompatible trials might only hold true for incompatible trials that contain the same type of conflicting information. When subjects had to process incompatible information from different conditions successively, they even showed a slight increase of reaction time. This observation argues for the hypothesis that despite of the common source of interfering information (spatial incompatibility) different neuronal sub-processes come into play.

The increased BOLD response during HCR trials in rostral anterior cingulate cortex (rACC) is in line with the data of Etkin et al. (2006) who found this region to be associated with conflict resolution within an emotional conflict task. During HCR trials activity increased not only in our regions of interest but also in the middle temporal area (MT+) which has been associated with motion processing (Born & Bradley, 2005). This observation points to a higher processing demand of the perceptual dimension during cognitive conflict resolution compatible with the fact that this conflict was partially based on motion processing.

Recent work on error monitoring has identified activation clusters in the medial prefrontal cortex as well as in other regions including bilateral anterior insula and inferior operculum as core regions for error-related activity (Dosenbach et al., 2006; Hester et al., 2004). Although

our findings corroborate part of the existing literature, the peak signal change in bilateral basal ganglia (putamen) in the present task allows additional insight in the neuronal activity underlying error processing. In the present investigation, however, we did not differentiate errors committed to the incompatible, compatible, or neutral task condition, and thus, we can only speculate that basal ganglia activation is associated with the specific demands of double conflict resolution, since subjects made most errors during that condition. This limitation holds also true for error commission and error resolution.

But even taking into consideration these limitations, the present data clearly indicate that different functional mechanisms separate post-conflict versus post-error compensatory adjustments of performance. Error resolution was associated with signal changes in lateral and medial prefrontal cortex that were distinct from the rACC activation during conflict resolution. Masking post-error activity with conflict-related activity for all incompatible conditions resulted in no change of activated brain areas. This finding suggests that the regions associated with error resolution are specifically related to this process and do not reflect overall conflict-related activity. These data also contradict the hypothesis that conflict resolution and error resolution are based on the same functional mechanism (di Pellegrino et al., 2007).

The increase of basal ganglia activity during error commission was contrasted by a decrease of BOLD signal after error resolution. The involvement of the basal ganglia in conflict resolution and error control has been highlighted before (Ullsperger & von Cramon, 2006); and has been associated with dopaminergic modulations due to the absence of an anticipated reward during error detection and with compensatory adjustments in the post-error trial. However, as far as we know the strong dissociation between BOLD responses in basal

ganglia during error commission and post-error resolution has never been reported before. We assume that the decrease of activation in the putamen is associated with inhibition processes that try to regain control by shifting the system to a more cautious and conservative response strategy. This assumption is line with computational models that assign to the basal ganglia a dynamic gating mechanisms driving action selection based on reinforcement learning (Frank et al., 2004; Hazy et al., 2007).

4.5. Conclusion

In conclusion, we found that left dlPFC is activated when two task-irrelevant information streams generate a strong tendency towards the task-irrelevant response. Our results moreover highlight the functional difference between conflict resolution and error resolution processes. Conflict resolution was associated with rACC activity whereas error resolution was associated with specific prefrontal regions. The basal ganglia seem to play an important role during error processing by increasing activity during error commission and decreasing it during post-error trials.

5.0 Cognitive Control and Error Processing in the Human Brain: Evidence from fMRI

PUBLISHED IN TOPICS IN ADVANCED IMAGING (2007)

(EDS. MANFRED HERRMANN & CHRISTIANE M. THIEL)

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5.1 Introduction

Cumulating evidence suggests that performance monitoring comprises several sub-processes: on the one hand processes associated with the monitoring of pre-response conflict and uncertainty as well as control of cognitive conflict and on the other hand processes which are related to the detection of post-response errors. By using two variants of the Simon task

which has been widely used to study conflict resolution in cognitive psychology, the present study was aimed to analyse conflict resolution induced by two interference tasks which only differed with respect to the source of conflicting information (Motion direction/ stimulus location). The Simon effect is a robust phenomenon which arises if stimulus and response location do not correspond, albeit stimulus location is task-irrelevant. This effect is interpreted as resulting from the automatic generation of a spatial code in response to stimulus location. Since the spatial code overlaps with the relevant response code derived from the non-spatial dimension (e.g. shape), it interferes with the speed of correct response selection. If a single neural network is engaged in conflict resolution then the activation patterns of response conflict induced by both motion direction and stimulus location should only differ with respect to the specific demands related to the processing of different types of incompatible information. Additionally, by comparing errors committed by high-conflict trials (which are forced due to task interference) to unforced errors committed by non-conflicting trials (in the absence of pre-response conflict) in the motion-based Simon task, we try to shed light on a possible influence of cognitive conflict and cognitive facilitation on error processing.

5.2 Methods

Twenty healthy subjects (3 male, range 21 – 31 years, mean age: 25.5 years) participated in the study. Subjects had to detect and identify form-from-motion stimuli in two different experiments which were conducted within one session. The stimuli consisted of either a

triangle or a square containing approximately 200 coherently moving bright dots on a dark screen against a randomly moving background of a total of 4000 dots. The motion-based Simon task contained three conditions: (1) compatible trials (COMP) consisted of dots moving coherently to the side corresponding to a correct response (e.g., a triangle requires a right-hand button press and all dots within the triangle were moving to the right), (2) in incompatible trials (INCOMP) dots within the triangle or square were moving coherently in a direction opposite to the correct side (e.g. the correct response to a square was to press the left-hand button but the target-dots were moving to the right), and (3) during neutral trials (NEU) dots were moving upwards, therefore evoking neither interference nor facilitation. In 20 percent of all trials incompatible stimuli were presented. Neutral trials had the same probability of occurrence. This has been demonstrated as a prerequisite of inducing interference effects (Braver et al., 2001). Subjects had to press the left-hand button as fast and correct as possible if coherently moving dots formed a square and the right-hand button if a triangle was presented. Stimulus location was the task-irrelevant dimension in the second variant (location-based Simon task). The design of this task again included three conditions. Movement direction of the coherently moving dots in the NEU condition led to neither interference nor facilitation because the dots were moving upwards in all trials. All other parameters were identical to the motion-based Simon task, apart from the fact that stimuli appeared not centrally but at a 6° eccentricity to the left or to the right of the fixation point. The order of the two Simon tasks was counterbalanced across subjects. MRI data were acquired on a 3-T SIEMENS Magnetom Allegra system (Siemens, Erlangen, Germany) equipped with a standard quadrature head coil. Changes in blood oxygenation level-dependent (BOLD) T2*-weighted MR signal were measured using a gradient echo-planar imaging (EPI) sequence (38 slices, slice-thickness: 3 mm with a 0.3 mm gap, TR = 2.5 s, TE = 30 ms, flip

angle = 90°, 64 x 64 matrix, FOV 192 x 192, interleaved acquisition). Data analysis was performed with SPM2 (Wellcome Department of Cognitive Neurology, London).

5.3 Results

Behavioral data revealed that both types of Simon tasks induced highly significant interference effects. Using event-related fMRI we could demonstrate that both tasks share a common cluster of activated brain regions during conflict resolution (pre-supplementary motor area (pre-SMA), superior parietal lobule (SPL), and cuneus) but also show task-specific activation patterns (left superior temporal cortex in the motion-based, and the left fusiform gyrus in the location-based Simon task).

For the analysis of error-related activation (which was limited to the motion-based Simon task), five participants were excluded due to low error rates (< 5 errors in each condition) or perfect accuracy. While errors related to incompatible trials (forced errors) were mainly associated with activation of the rostral anterior cingulate cortex (rACC) and the precuneus / posterior cingulate, errors related to trials without pre-response conflict (unforced errors) showed peak activation in right inferior frontal gyrus. In order to find common activations between unforced/ forced errors and high-conflict trials, we conducted conjunction tests which showed right inferior frontal gyrus and the bilateral inferior parietal lobule (BA 40) as areas being recruited during both the resolution of conflict and the processing of unforced errors. Common regions of forced errors and conflict processing were medial superior frontal cortex and small clusters in bilateral inferior frontal gyrus (see Figure 10).

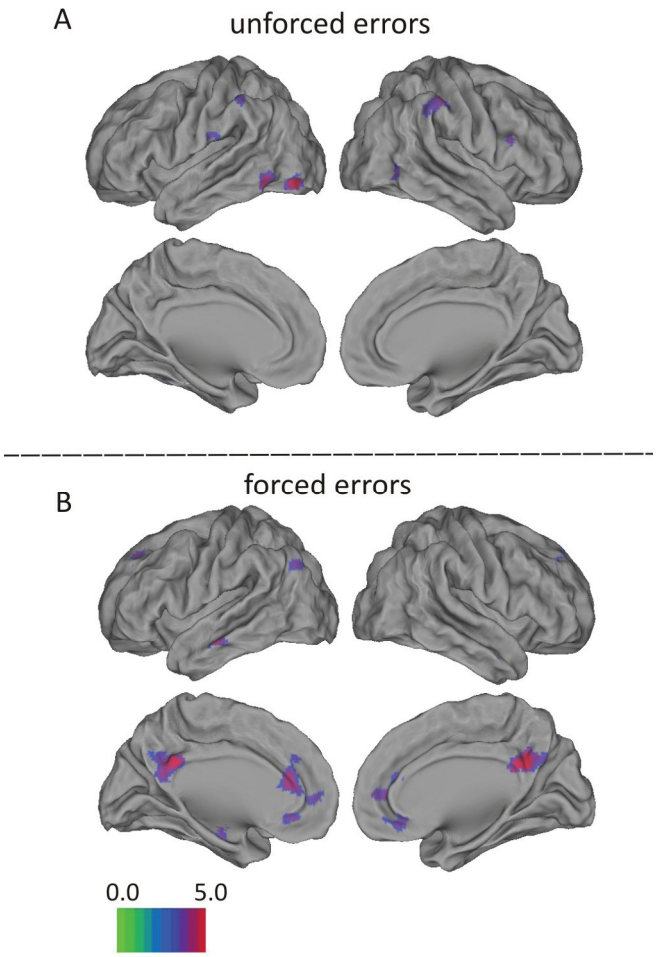

Figure 9: Specific brain activation related to (A) errors on compatible trials (unforced errors), and (B) errors on incompatible trials (forced errors) overlaid on a human PALS SPM2 template.

5.4 Discussion

The present data derived from two Simon tasks based on coherent motion perception indicate that both stimulus location and motion direction induce strong interference effects. Both types of conflict resolution resulted in shared activation as well as in task-specific activation patterns. Regarding functional subdivisions of the medial wall, the present data

corroborate the hypothesis that it is mainly the pre-SMA and not the anterior cingulate cortex (ACC) which triggers conflict resolution (Ullsperger & von Cramon, 2001; Nachev et al., 2005). Despite conceptual similarities of task design, the observed activation patterns significantly differ probably related to the source of task-irrelevant information, thus indicating the existence of different task-specific networks of conflict resolution (Wittfoth et al., 2006). The present findings regarding error-related activity emphasize functionally specific activation patterns in response to errors related to compatible and incompatible events. While the dorsal ACC/ medial superior frontal cortex and operculo-insular frontal cortices may serve as a common error-processing network, functionally specific regions contribute to the processing of errors in regard to whether these erroneous responses were made after the presentation of high- or low-conflict trials. Specifically, error-related dorsal ACC activity in the absence of simultaneously interfering processing streams (as in the case of unforced errors) seems to favor the assumption that the ACC acts as a detector of erroneous motor responses, instead of being a pure conflict monitoring system (Wittfoth et al., 2008).

6.0 GENERAL OUTLOOK

The past years of research into the neural mechanisms of performance monitoring and error processing have yielded a rich, rapidly growing field of converging studies which have focused in general on the classic types of conflict tasks, such as the color-word Stroop task, the Eriksen Flanker task, the Simon task, and last but not least Go/NoGo paradigms. In regard to the neural correlates of error detection and resolution, one can find a huge amount of EKP-studies which findings convincingly point to the ERN (N_E). The discovery of this important deflection has provided a better understanding of the mechanisms underlying error processing in different contexts. Source localization as well as neuroimaging studies suggested a primary contribution from the dorsal ACC/ msFC, as one of the key nodes in this process, along with lateral PFC and rostral ACC. Outside these areas, there is only little trusted knowledge about the roles of the bilateral anterior insula or the parietal regions frequently activated in some, but not all, studies. And still, no one can be sure how conscious detection of a committed error influences the brain processes compared to situations in which subjects do not realize that they act incorrect regarding task goals.

Results of the present work contribute to the research of performance monitoring and error processing from a different point of view compared to the majority of neuroimaging studies. By presenting moving stimuli instead of static forms, several advantages derived from this experimental setup. One of the most interesting features of this paradigm is the possibility present two interfering sources. And in contrast to other investigations which merged different

conflict tasks together, the information which induces cognitive conflict is based spatial incompatibility throughout.

The brains ability to detect and process error of commission has been the subject of many investigations. However, despite of the fact that cognitive conflict tasks usually imply a compatible as well as an incompatible condition, examination of the data was carried out in a way that only incompatible errors were contrasted with correct incompatible events. The second experiment of the present work can take credit for the evidence of a difference between error processing of events containing high or no conflict, respectively.

Future work will have to show how these results may contribute a better understanding of conflict and error monitoring in healthy subjects. Nevertheless, with the utmost probability, even the comprehension of pathological conditions that manifest in aberrant monitoring behavior will be increased.

Bibliography

Aron, A.R., Monsell, S., Sahakian, B.J., & Robbins, T.W. (2004). A componential analysis of task switching deficits associated with lesions of left and right frontal cortex. Brain 127, 1561-1573.

Banich, M.T., Milham, M.P., Atchley, R., Cohen, N.J., Webb, A., Wszalek, T., Kramer, A.F., Liang, Z.-P., Wright, A., Shenker, J., & Magin, R. (2000). fMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. Journal of Cognitive Neuroscience, 12, 988-1000.

Barch, D.M., Braver, T.S., Akbudak, E., Conturo, T., Ollinger, J., & Snyder, A. (2001). Anterior cingulate cortex and response conflict: effects of response modality and processing domain. Cerebral Cortex, 11, 837-848.

Baumgartner, T., Lutz, K., Schmidt, C.F., & Jäncke, L. (2006). The emotional power of music: How music enhances the feeling of affective pictures. Brain Research, 1075, 151-164.

Bechtereva, N.P., Shemyakina, N.V., Strachenko, M.G., Danko, S.G., & Medvedev, S.V. (2005). Error detection mechanisms of the brain: background and prospects. International Journal of Psychophysiology 58, 227-234.

Behrmann, M., Geng, J.J., & Shomstein, S. (2004). Parietal cortex and attention. Current opinion in Neurobiology, 14, 212-217.

Born, R.T. & Bradley, D.C. (2005). Structure and function of visual area MT. Annual review of neuroscience, Vol., 28, 157-189.

Bosbach, S., Prinz, W., & Kerzel, D. (2004a). A Simon effect with stationary moving stimuli. Journal of Experimental Psychology: Human Perception and Performance, 30, 39-55.

Bosbach, S., Prinz, W., & Kerzel, D. (2004b). Is direction position? Position- and direction-based correspondence effects in tasks with moving stimuli. The Quarterly Journal of Experimental Psychology, 57 A, 1-40.

Botvinick, M.M, Nystrom, L.E., Fissell, K., Carter, C.S., & Cohen, J.D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. Nature, 402, 179-181.

Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., & Cohen, J.D. (2001). Conflict monitoring and cognitive control. Psychological Review 108, 624-652.

Botvinick, M.M., Cohen, J.D., & Carter, C.S. (2004). Conflict monitoring and anterior cingulate cortex: an update. Trends in Cognitive Sciences, 8, 539-546.

Braddick, O.J., O'Brian, J.M.D., Wattam-Bell, J., Atkinson, J., Hartley, T., & Turner, R. (2001). Brain areas sensitive to coherent visual motion. Perception, 30, 61-72.

Brass, M., Derrfuss, J., & von Cramon, D.Y. (2005a). The inhibition of imitative and overlearned responses: a functional double dissociation. Neuropsychologia, 43, 89-98.

Brass, M., Ullsperger, M., Knoesche, T.R., von Cramon, D.Y., & Phillips, N.A. (2005b). Who comes first? The role of the prefrontal and parietal cortex in cognitive control. Journal of Cognitive Neuroscience 17, 1367-1375.

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

Brown, J.W., & Braver, T.S. (2005). Learned predictions of error likelihood in the anterior cingulate cortex. Science 307, 1118-1121.

Büchel, C., Josephs, O., Rees. G., Turner, R., Frith, C.D., & Friston, K.J. (1998). The functional anatomy of attention to visual motion. Brain, 121, 1281-1294.

Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., & Gabrieli, J.D.E. (2002). Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. Neuron, 33, 301-311.

Burle, B., Possamai, C.A., Vidal, F., Bonnet, M., Hasbroucq, T. (2002). Executive control in the Simon effect: An electromyographic and distributional analysis. Psychological Research, 66, 324-336.

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

Bush, G., Vogt, G.A., Holmes, J., Dale, A.M., Greve, D., Jenike, M.A. et al. (2002). Dorsal anterior cingulate cortex: A role in reward-based decision making. Proceedings of the National Academy of Sciences of the U.S.A. 99, 523-528.

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

Cavanna, A.E., & Trimble, M.R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. Brain 129, 564-583.

Clark, L., Blackwell, A.D., Aron, A.R., Turner, D.C., Dowson, J., Robbins, T.W., & Sahakian, B.J. (2006). Association between response inhibition and working memory in adult ADHD: a link to right frontal cortex pathology? Biol Psychiatry 61, 1396-1401.

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

Critchley, H.D. (2004). The human cortex responds to an interoceptive challenge. Proceeding of the National Academy of Sciences of the U.S.A. 101, 6333-6334.

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

Dassonville, P., Lewis, S.M., Zhu, X.-H., Ugurbil, K., Kim, S.-G., & Ashe, J. (2001). The effect of stimulus-response compatibility on cortical motor activation. NeuroImage, 13, 1-14.

Davidson, R.J., Pizzagalli, D., Nitschke, J.B., & Putnam, K. (2002). Depression: perspectives from affective neuroscience. Annual Review of Psychology 53, 545-574.

Davis, K.D., Taylor, K.S., Hutchinson, W.D., Dostrovsky, J.O., McAndrews, M.P., Richter, E.O., & Lozano, A.M. (2005). Human anterior cingulate cortex neurons encode cognitive and emotional demands. Journal of Neuroscience 25, 8402-8406.

De Jong, R., Wierda, M., Mulder, G. & Mulder, L.J. (1988). Use of partial stimulus information in response processing. J. Exp. Psychol. Hum. Percept. Perform., 14, 682-692.

Derrfuss, J., Brass, M., Neumann, J., & von Cramon (2005). Involvement of the inferior frontal junction in cognitive control: meta-analyses of switching and Stroop studies. Human Brain Mapping, 25, 22-34.

Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. Annual Review of Neuroscience, 18, 193-222.

Di Pellegrino, G., Ciaramelli, E., & Ladavas, E. (2007). The regulation of cognitive control following rostral anterior cingulate cortex lesion in humans. Journal of Cognitive Neuroscience, 19, 275-286.

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

Duncan, J., & Owen, A.M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. Trends Neurosci, 26, 475-483.

Egner, T., & Hirsch, J. (2005a). Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information. Nature Neuroscience 8, 1784-1790.

Egner, T., & Hirsch, J. (2005b). The neural correlates and functional integration of cognitive control in a Stroop task. NeuroImage, 24, 539-547.

Egner, T., Delano, M., & Hirsch, J. (2007a). Separate conflict-specific cognitive control mechanisms in the human brain. NeuroImage, 35, 940-948.

Egner, T (2007b). Congruency sequence effects and cognitive control. Cognitive, Affective, & Behavioral Neuroscience, 7, 380-390.

Eippert, F., Veit, V., Weiskopf, N., Erb, M., Bierbaumer, N., & Anders, S. (2007). Regulation of emotional responses elicited by threat-related stimuli. Human Brain Mapping, 28, 409.423.

Eriksen, B.A. & Eriksen, C.W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. Perceptions and Psychophysics, 16, 143-149.

Etkin, A., Egner, T., Peraza, D.M., Kandel, E.R., & Hirsch, J. (2006). Resolving emotional conflict: a role for the rostral anterior cingulate cortex in modulating activity in the amygdala. Neuron 51, 871-882.

Falkenstein, M., Hohnsbein, J., Hoormann, J., Blanke, L. (1990). Effect of errors in choice reaction tasks on the ERP under focused and divided attention. In: Brunia, C.H.M., Gaillard, A.W.K., & Kok, A. (Eds.). Psychophysiological Brain Research. Tilburg, Tilburg Universitiy Press, pp. 192-195.

Falkenstein, M., Hohnsbein, J., Hoormann, J., Blanke, L. (1991). Effects of crossmodal divided attention on late ERP components: II. Error processing in choice reaction tasks. Electroencephalogr Clin Neurophysiol, 78, 447-455.

Fan, J., Flombaum, J.I., McCandliss, B.D., Thomas, K.M., & Posner, M.I. (2003). Cognitive and brain consequences of conflict. NeuroImage, 18, 42-57.

Fassbender, C., Murphy, K., Foxe, J.J., Wylie, G.R., Javitt, D.C., Robertson, I.H., & Garavan, H. (2003). A topography of executive functions and their interactions revealed by functional magnetic resonance imaging. Cognitive Brain Research 20, 132-143.

Fellows, L.K., & Farah, M.J. (2005). Is anterior cingulate cortex necessary for cognitive control? Brain, 128, 788-796.

Fitzgerald, K.D., Welsh, R.C., Gehring, W.J., Abelson, J.L., Himle, J.A., Liberzon, I., & Taylor, S.F. (2005). Error-related hyperactivity of the anterior cingulate cortex in obsessive-compulsive disorder. Biological Psychiatry 57, 287-294.

Fornito, A., Yücel, M., Wood, S., Stuart, G.W., Buchanan, J-A., Proffitt, T., Anderson, V., Velakoulis, D., & Pantelis, C. (2004). Individual differences in anterior cingulate/ paracingulate morphology are related to executive functions in healthy males. Cerebral Cortex 14, 424-431.

Frank, M.J., Seeberger, L.C., & O'Reilly, R.C. (2004). By carrot or by stick: cognitive reinforcement learning in Parkinsonism. Science, 306, 1940-1943.

Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.B., Frith, C.D., & Frackowiak, R.S. (1995). Statistical parametric maps in functional imaging: a general linear model approach. Human Brain Mapping, 2, 189-210.

Forman, S.D., Cohen, J.D., Fitzgerald, M., Eddy, W.F., Mintun, M.A., & Noll, D.C. (1995). Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a clustersize threshold. Magn. Reson. Med., 33, 636-647.

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

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

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

Gehring, W.J., & Fencsik, D.E. (2001). Functions of the medial frontal cortex in the processing of conflict and errors. Journal of Neuroscience, 21, 9430-9437.

Gemba, H., Sasaki, K., & Brooks, V.B. (1986). 'Error' potentials in limbic cortex (anterior cingulate area 24) of monkeys during motor learning. Neuroscience Letters 70, 223-227.

Genovese, C.R., Lazar, N.A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. NeuroImage, 15, 870-878.

Grandy, D.K. & Kruzich, P.J. (2004) in Cognitive Neuroscience of Attention (ed. Posner, M.I.). Guilford, New York, pp 260-268.

Gratton, G., Coles, M.G.H., & Donchin, E. (1992). Optimizing the use of information: strategic control of activation and responses. Journal of Experimental Psychology: General 4, 480–506.

Hamann, S., & Mao, H. (2002). Positive and negative emotional verbal stimuli elicit activity in the left amygdala. Neuroreport, 13, 15-19.

Hazy, T.E., Frank, M.J., & O'Reilly, R.C. (2007). Towards an executive without a homunculus: computational models of the prefrontal cortex/ basal ganglia system. Phil. Trans. R. Soc. B, 29; 362(1485): 1521–1529.

Herd, S.A., Banich, M.T., & O'Reilly, R.C. (2006). Neural mechanisms of cognitive control: an integrative model of Stroop task performance and fMRI data. Journal of Cognitive Neuroscience, 18, 22-32.

Herrmann, M., Rotte, M., Grubich, C., Ebert, A.D., Schiltz, K., Münte, T.F., & Heinze, H.J. (2001). Control of semantic interference in episodic memory retrieval is associated with an anterior cingulated-prefrontal activation pattern. Human Brain Mapping 13, 94-103.

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

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

Hester, R., Foxe, J.J., Molholm, S., Shpaner, M., & Garavan, H. (2005). Neural mechanisms involved in error processing: A comparison of errors made with and without awareness. NeuroImage 27, 602-608.

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

Holroyd, C.B., & Coles, M.G.H. (2002). The neural basis of human error processing: Reinforcement learning, dopamine, and the error-related negativity. Psychological Review 109, 679-709.

Hopfinger, J.B., Buonocore, M.H., & Mangun, G.R. (2000). The neural mechanism of top-down attentional control. Nature Neuroscience, 3, 284-291.

Iacoboni, M., Woods, R.P., & Mazziotta, J.C. (1996). Brain-behavior relationships: evidence from practice effects in spatial stimulus-response compatibility. Journal of Neurophysiology, 71, 321-331.

Ito, S., Stuphorn, V., Brown, J.W., & Schall, J.D. (2003). Performance monitoring by the anterior cingulate cortex during saccade countermanding. Science 302, 120-122.

James, W. (1890). The principles of psychology. New York: Holt.

Johannes, S., Wieringa, B.M., Nager, W., Muller-Vahl, K.R., Dengler, R., & Münte, T.F., (2002). Excessive action monitoring in Tourette syndrome. Journal of Neurol. 249, 961-966.

Kastner, S., & Ungerleider, L.G. (2000). Mechanisms of visual attention in the human cortex. Annual Review of Neuroscience, 23, 315-431.

Kerns, J.G., Cohen, J.D., MacDonald III, A.W., Cho, R.Y., Stenger, V.A., & Carter, C.S. (2004). Anterior cingulate conflict monitoring and adjustments in control. Science, 303, 1023-1026.

Kerns, J.G., Cohen, J.D., MacDonald, A.W., Johnson, M.K., Stenger, V.A., Aizenstein, H., & Carter, C.S. (2005). Decreased conflict- and error-related activity in the anterior cingulate cortex in subjects with schizophrenia. American Journal of Psychiatry 162, 1833-1839.

Kerzel, D., Hommel, B., & Bekkering, H. (2001). A Simon effect induced by induced motion and location: Evidence for a direct linkage of cognitive and motor maps. Perception & Psychophysics 63, 862–874.

Kiehl, K.A., Liddle, P.F., & Hopfinger, J.B. (2000). Error processing and the rostral anterior cingulate: an event-related fMRI study. Psychophysiology 37, 216-223.

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

Klein, T.A., Neumann, J., Reuter, M., Hennig, J., von Cramon, D.Y., & Ullsperger, M. (2007b). Genetically determined differences in learning from errors. Science, 318, 1642-1645.

Kleiter, G.D., & Schwarzenbacher, K. (1989). Beyond the answer: Post-error processes. Cognition, 32(3), 255-277.

Konrad, K. et al., (2005). Development of attentional networks: an fMRI study with children and adults. NeuroImage, 28, 429-439.

Kornblum, S., Hasbroucq, T., & Osman, A. (1990). Dimensional overlap: Cognitive basis for stimulus-reponse compatibility – A model and taxanomy. Psychological Review, 97,253-270.

Kornblum, S., & Stevens, G. (2002). Sequential effects of dimensional overlap: findings and issues. In: Prinz, W., Hommel., B. (Eds.), Common mechanism in perception and action. Oxford University Press, Oxford, pp. 9-54.

Laming, D.R.J. (1968). Information theory in choice-reaction times. London: Academic Press.

Laming, D.R.J. (1979). Choice reaction performance following an error. Acta Psychologica, 43, 199-224.

Lancaster, J.L., Woldorff, M.G., Parsons, L.M., Liotti, M., Freitas, C.S., Rainey, L., et al. (2000). Automated Talairach atlas labels for functional brain mapping. Human Brain Mapping 10, 120-131.

Lau, H., Rogers, R.D., & Passingham, R.E. (2006). Dissociating response selection and conflict in the medial frontal surface. NeuroImage, 29, 446-451.

Laurens, K.R., Ngan, E.T.C., Bates, A.T., Kiehl, K.A., & Liddle, P.F. (2003). Rostral anterior cingulate cortex dysfunction during error processing in schizophrenia. Brain 126, 610-622.

Liu, X., Banich, M.T., Jacobson, B.L., & Tanabe, J.L. (2004). Common and distinct neural substrates of attentional control in an intergrated Simon and spatial Stroop task as assessed by event-related fMRI. NeuroImage, 22, 1097-1106.

MacDonald, A.W., Cohen, J.D., Stenger, V.A., & Carter, C.S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288, 1835-1838.

MacDonald, A.W, Becker, T.M., & Carter, C.S. (2006). Functional Magnetic Resonance Imaging Study of Cognitive Control in the Healthy Relatives of Schizophrenia Patients. Biological Psychiatry, 60 (11), 1241-1249.

MacLeod, C.M. (1991). Half a century of research on the Stroop effect: an integrative review. Psychol. Bull., 109, 163-203.

Maddock, R.J., Garrett, A.S., & Buonocore, M.H. (2001). Remembering familiar people: the posterior cingulate cortex and autobiographical memory retrieval. Neuroscience 104, 667-676.

Maldjian, J.A., Laurienti, P.J., Burdette, J.B., & Kraft, R.A. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. NeuroImage, 19, 1233-1239.

Mathewson, K.J., Dywan, J., & Segalowitz, S.J. (2005). Brain bases of error-related ERPs as influenced by age and task. Biological Psychology, 70, 88-104.

Matthews, S.C., Paulus, M.P., Simmons, A.N., Nelesen, R.A., & Dimsdale, J.E. (2004). Functional subdivisions within anteriror cingulate cortex and their relationship to autonomic nervous system functions. NeuroImage 22, 1151-1156.

Mayr, U., Awh, E., & Laurey, P. (2003). Conflict adaptation effects in the absence of executive control. Nature Neuroscience 6, 450-452.

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

Merriam, E.P., Colby, C.L., Thulborn, K.R., Luna, B., Olson, C.R., & Sweeney, J.A. (2001). Stimulus-response incompatibility activates cortex proximate to three eye fields. NeuroImage, 13, 794-800.

Michael, G.A., Garcia, S., Fernandez, D., Sellal, F., & Boucart, M. (2006). The ventral premotor cortex (vPM) and resistance to interference. Behav Neuroscience 120, 447-462.

Milham, M.P., Banich, M.T., Webb, A., Barad, V., Cohen, N.J., Wszalek, T., & Kramer, A.F. (2001). The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. Cognitive Brain Research, 12, 467-473.

Murphy, K., & Garavan, H. (2004). Artifactual fMRI group and condition differences driven by performance confounds. NeuroImage 21, 219-228.

Murray, S.O., Olshausen, B.A., & Woods, D.L. (2003). Processing shape, motion, and three-dimensional shape-from-motion in the human cortex. Cerebral Cortex, 13, 508-516

Nachev, P., Rees, G., Parton, A., Kennard, C., & Husain, M. (2005). Volition and conflict in human medial frontal cortex. Current Biology, 15, 122-128.

Nakamura, K., Roesch, M.R., & Olson, C.R. (2004). Neuronal activity in macaque SEF and ACC during performance of tasks involving conflict. Journal of Neurophysiology, 93, 884-908.

Nichols, T., Brett, M., Anderson. J., Wager, T., & Poline, J.-B. (2005). Valid conjunction inference with the minimum statistic. NeuroImage, 25, 653-660.

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

Nieuwenhuis, S., & Yeung, N. (2005). Neural mechanisms of attention and control: losing our inhibitions? Nature Neuroscience, 8, 1631-1633.

Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. Trends in Cognitive Sciences 8, 102-107.

Nunez, J.M., Casey, B.J., Egner, T., Hare, T., & Hirsch, J. (2005). Intentional false responding shares neural substrates with response conflict and cognitive control. NeuroImage 25, 267-277.

Opgen-Rhein, C., Neuhaus, A.H., Urbanek, C., Hahn, E., Sander, T., & Dettling, M. (2008). Executive Attention in Schizophrenic Males and the Impact of COMT Val108/158Met Genotype on Performance on the Attention Network Test. Schizophrenia Bulletin, in press.

Pagonabarraga, J., García-Sánchez, C., Llebaria, G., Pascual-Sedano, B., Gironell, A., & Kulisevsky, J. (2007). Controlled study of decision-making and cognitive impairment in Parkinson's disease. Movement disorders, 22(10), 1430-1435.

Paus, T., Okay, N., Caramanos, Z., MacDonald, D., Zijbendos, A., D'Avirro, D., Gutmans, D., Holmes, C., Tomaiuolo, F., & Evans, A.C. (1996a). In vivo morphometry of the intrasulcal grey matter in the human cingulate, paracingulate, and superior-rostral sulci: hemispheric asymmetries, gender differences and probability maps. Journal of Comparative Neurology, 376, 664-673.

Paus, T., Tomaiuolo, F., Otaky, N., MacDonald, D., Petrides, M., Atlas, J., Morris, R., & Evans, A.C. (1996b). Human cingulate and paracingulate sulci: pattern, variability, asymmetry, and probabilistic map. Cerebral Cortex 6, 207-214.

Pernet, C., Franceries, X., Basan, S., Cassol, E., Dermonet, J.F., & Celsis, P. (2004). Anatomy and time course of discrimination and categorization processes in vision: an fMRI study. NeuroImage, 22, 1563-1577.

Peterson, B.S., Kane, M.J., Alexander, G.M., Lacadie, C., Skudlarski, P., Leung, H-C., May, J., & Gore, J.C. (2002). An event-related functional MRI study comparing interference effects in the Simon and Stroop tasks. Cognitive Brain Research, 13, 427-440.

Peyron, R., Laurent, B., & Garcia-Larrea, L. (2000). Functional imaging of brain responses to pain. A review and meta-analysis. Clinical Neurophysiology 30, 263-288.

Picard, N., & Strick, P.L. (2001). Imaging the premotor areas. Current opinion in Neurobiology, 11, 663-672.

Pizzagalli, D.A., Peccoralo, L.A., Davidson, R.J., & Cohen, J.D. (2006). Resting anterior cingulate activity and abnormal response to errors in subjects with elevated depressive symptoms: a 128-channel EEG study. Human Brain Mapping 27, 185-201.

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

Posner, M.I., & Rothbart, M.K. (2007). Research on attention networks as a model fort he integration of psycholgical science. Annual Review of Psychol., 58, 1-23.

Praamstra, P., Kleine, B.U., & Schnitzler, A. (1999). Magnetic stimulation of the dorsal premotor cortex modulates the Simon effect. Neuroreport, 10, 3671-3674.

Rabbitt, P.M.A. (1966). Errors and error correction in choice response tasks. Journal of Experimental Psychology, 71, 264-272.

Rainville, P., Duncan, G.H., Price, D.D., Carrier, B., & Bushnell, M.D. (1997). Pain affect encoded in human anterior cingulate but not somatosensory cortex. Science 277, 968-971.

Ridderinkhof, K.R (2002). Activation and suppression in conflict tasks: Empirical clarification through distributional analyses. In: Prinz, W., Hommel., B. (Eds.), Common mechanism in perception and action. Oxford University Press, Oxford, pp. 494-519.

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

Ridderinkhof, K.R., van den Wildenberg, W.P., Segalowitz S.J., & Carter C.S. (2004b). Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. Brain and Cognition, 56, 129-140.

Roelofs, A., van Turennout, M., & Coles, M.G.H. (2006). Anterior cingulated cortex activity can be independent of response conflict in Stroop-like tasks. Proceedings of the National Academy of Sciences of the U.S.A. 103, 13884-13889.

Rosano, C. et al. (2005). Functional neuroimaging indicators of successful executive control in the oldest old. NeuroImage, 28, 881-889.

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

Rushworth, M.F., Paus, T., & Sipila, P.K. (2001). Attention systems and the organization of the human parietal cortex. Journal of Neuroscience, 21, 5262-5271.

Schumacher, E.H., & D'Esposito, M. (2002). Neural implementation of response selection in humans as revealed by localized effects of stimulus-response compatibility on brain activation. Human Brain Mapping, 17, 193-201.

Shidara, M., & Richmond, B. (2002). Anterior cingulate: single neuronal signals related to degree of reward expectancy. Science 296, 1709.

Simon, J.R. (1969). Reactions toward the source of stimulation. Journal of Experimental Psychology, 81, 174-176.

Simon, J.R. & Berbaum, K. (1990). Effect of conflicting cues on information-processing – the Stroop effect vs. the Simon effect. Acta Psychol, 73, 159-170.

Stemmer, B., Segalowitz, S.J., Witzke, W., & Schönle, P.W. (2003). Error detection in patients with lesions to the medial prefrontal cortex: an ERP study. Neuropsychologia 42, 118-130.

Stoffels, E.J. (1996). On stage robustness and response selection: further evidence. Acta Psychol., 91, 67-88.

Stroop, J.R. (1935). Studies of interference in serial verbal reactions. J. Exp. Psychol., 18, 643-662.

Stuermer, B., Leuthold, H., Soetens, E., Schroter, H., & Sommer, W. (2002). Control over location-based response activation in the Simon task: behavioural and electrophysiological evidence. J. Exp. Psychol. Hum. Percept. Perform., 28, 1345-1363.

Stuermer, B. &, Leuthold, H. (2003). Control over response priming in visuomotor processing: a lateralized event-related potential study. Exp. Brain Res., 153, 35-44.

Swick, D., & Turken, A.U. (2002). Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex. Proceedings of the National Academy of Sciences of the U.S.A. 99, 16354-16359.

Sylvester, C.-Y.C., Wager, T.D., Lacey, S.C., Hernandez, L., Nichols, T.E., Smith, E.E., & Jonides, J. (2003). Switching attention and resolving interference: fMRI measures of executive functions. Neuropsychologia, 41, 357-370.

Talairach, J., Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain. Georg Thieme Verlag, Stuttgart, Germany.

Tracey, I. (2005). Nociceptive processing in the human brain. Current Opinion in Neurobiology 15, 478-487.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., & Joliot, M. (2002). Automated anatomical labelling of activations in SPM

using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage, 15, 273-289.

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

Ullsperger, M., & von Cramon, D.Y. (2004). Neuroimaging of performance monitoring: error detection and beyond. Cortex 40, 593-604.

Ullsperger M., Bylsma, L.M., & Botvinick, M.M. (2005). The conflict adaption effect: It's not just priming. Cognitive, Affective & Behavioral Neuroscience, 5, 467-472.

Ullsperger, M., & von Cramon, D.Y. (2006). The role of intact frontostriatal circuits in error processing. Journal of Cognitive Neuroscience, 18, 651-664.

Van Essen, D.C., Dickson, J., Harwell, J., Hanlon, D., Anderson, C.H., & Drury, H.A. (2001). An integrated software suite for surface-based analyses of cerebral cortex. J Am. Med. Inform. Assoc. 41, 1359-1378.

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

Van Veen, V., & Carter, C. S. (2002b). The anterior cingulate as a conflict monitor: fMRI and ERP studies. Physiology & Behavior, 77(4-5), 477-482.

Van Veen, V. (2006). A neuroimaging approach to the relationship between attention and speed-accuracy tradeoff. Unpublished dissertation.

Van't Ent, D., & Apkarian, P. (1999). Motoric response inhibition in finger movement and saccadic eye movement: A comparative study. Clinical Neurophysiology, 110, 1058-1072.

Vogeley, K., & Fink, G.R. (2003). Neural correlates of the first-person-perspective. Trends in Cognitive Sciences 7, 38-42.

Vogeley, K., May, M., Ritzl, A., Falkai, P., Zilles, K., & Fink, G.R. (2004). Neural correlates of first-person perspective as one constituent of human self-consciousness. Journal of Cognitive Neuroscience 16, 817-827.

Vogt, B.A., Finch, D.M., & Olson, C.R. (1992). Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. Cerebral Cortex 2, 435-443.

Vogt, B.A., Nimchinsky, E.A., Vogt, L.J., & Hof, P.R. (1995). Human cingulate cortex: surface features, flat maps, and cytoarchitecture. Journal of Comparative Neurology, 359, 490-506.

Vogt, B.A. (2005). Pain and emotion interactions in subregions of the cingulate gyrus. Nature Reviews Neuroscience 6, 533-544.

Wager, T.D., Jonides, J., & Reading, S. (2004). Neuroimaging studies of shifting attention: a meta-analysis. NeuroImage, 22, 1679-1693.

Wager, T.D., Sylvester, C.-Y.C., Lacey, S.C., Nee, D.E., Franklin, M., & Jonides, J. (2005). Common and unique components of response inhibition revealed by fMRI. NeuroImage, 27, 323-340.

Whalen, P.J., Bush, G., McNally, R.J., Wilhelm, S., McInerney, S.C., Jenike, M.A., & Rauch, S.L. (1998). The emotional counting Stroop paradigm: a functional magnetic resonance imaging probe of the anterior cingulate affective division. Biological Psychiatry 44, 1219-1228.

Wilson, R.A., & Keil, F.C. (Eds.) (1999). The MIT encyclopedia of the cognitive sciences, Cambridge, Massachusetts: Bradford.

Wittfoth, M., Buck, D., Fahle, M., & Herrmann, M. (2006). Comparison of two Simon tasks: neuronal correlates of conflict resolution based on coherent motion perception. NeuroImage, 32, 921-929.

Wittfoth, M., Küstermann, E., Fahle, M., & Herrmann, M. (2008). The influence of response conflict on error processing: Evidence from event-related fMRI. Brain Research, 1194, 118-129.

Wuhr, P. (2005). Evidence for gating of direct response activation in the Simon task. Psychon. Bull. Rev., 12, 282-288.

Wuhr, P., & Ansorge, U. (2005). Exporing trial-by-trial modulations of the Simon effect. Q. J. Exp. Psychol. A., 58, 705-731.

Yeung, N., Botvinick, M.M., & Cohen, J.D. (2004). The neural basis of error detection: conflict monitoring and the error-related negativity. Psychological Review 111, 931-959.

Yücel, M., Stuart, G.W., Maruff, P., Velakoulis, D., Crowe, S.F., Savage, G., & Pantelis, C. (2001). Hemispheric and gender-related differences in the gross morphology of the anterior cingulate cortex/ paracingulate cortex in normal volunteers: an MRI morphometric study. Cerebral Cortex 11, 17-25.

Zeki, S., Perry, R.J., & Bartels, A. (2003). The processing of kinetic contours in the brain. Cerebral Cortex, 13, 189-202.