

Interference processing in dual tasks - the functional role of the lateral prefrontal cortex

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Abstract

Numerous studies indicate fundamental limitations in the human ability to do multiple things at the same time. Recent theories on dual-task processing postulate the involvement of cognitive control processes in the coordination of the processing stream of multiple tasks. The most prominent neuroanatomical structure associated with the control of goal-directed human behavior is the lateral prefrontal cortex (LPFC). It has been shown with functional Magnetic Resonance Imaging (fMRI) that the LPFC is also involved in the processing of dual tasks. However, the precise role of the LPFC for the control of dual-task processing and the neural mechanisms of dual-task coordination are still widely unknown. The three fMRI studies presented in this dissertation specify the functional role of the LPFC in interference processing in dual tasks. The results show (1) the generality of LPFC involvement across different types of dual-task situations, (2) the functional neuroanatomical dissociability of different dual-task relevant control processes in the LPFC, (3) the role of the interaction of the LPFC with posterior task-relevant brain regions for the control of dual-task processing

Keywords:

lateral prefrontal cortex

cognitive control

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dual tasks

fMRI

Zusammenfassung

Zahlreiche Untersuchungen belegen fundamentale Grenzen in der menschlichen Fähigkeit, mehrere Dinge gleichzeitig zu tun. Aktuelle Theorien zur Verarbeitung von Doppelaufgaben gehen davon aus, dass kognitive Kontrollprozesse den Verarbeitungsstrom mehrerer Aufgaben koordinieren. Funktionell-neuroanatomisch wird insbesondere der laterale Präfrontalcortex (IPFC) mit der Kontrolle zielgerichteten Verhaltens in Verbindung gebracht. Mittels funktioneller Magnetresonanztomographie (fMRT) wurde bereits eine Beteiligung des IPFC an der Verarbeitung von Doppelaufgaben nachgewiesen. Die neuronalen Mechanismen der Doppelaufgabenkoordination sind jedoch weitgehend ungeklärt. Die drei fMRT Studien der vorliegenden Dissertation spezifizieren die funktionelle Rolle des IPFC bei der Interferenzverarbeitung in Doppelaufgaben. Die Ergebnisse zeigen (1) die Allgemeinheit der IPFC-Beteiligung über verschiedenen Doppelaufgabensituationen hinweg, (2) die funktionell-neuroanatomische Dissoziierbarkeit verschiedener doppelaufgabenrelevanter Kontrollfunktionen im IPFC, (3) die Bedeutung der Interaktion des IPFC mit posterioren aufgabenrelevanten Regionen für die Kontrolle von Doppelaufgabenverarbeitung.

Schlagwörter:

lateraler Präfrontalcortex

kognitive Kontrolle

Interferenzverarbeitung

Doppelaufgaben

fMRT

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1 Introduction

Whether people talk to their co-driver while driving a car, browse the web while using other computer programs or cook a meal while monitoring their children's activities – humans are permanently confronted with a multitude of information streams and options to behave.

Multi-tasking seems to be part of the everyday life in most of us.

However, there exist fundamental limitations in our ability to do multiple things at the same time. In fact, there is strong evidence from experimental psychology that humans are generally not even able to do *two* simple things at the same time (Pashler, 1994; Welford, 1952). Even when trying to make two easy decisions simultaneously, severe performance costs emerge – that is, people are slower and make more errors as compared to a situation where both decisions are made sequentially. While this may be acceptable in some situations (e.g. being slower in browsing the web) it can have disastrous consequences in other situations (e.g. not braking in time for a child running on the street).

In any case, we need to control the temporal order of our actions in order to perform optimally and in accordance with our internal goals. Recent theories on dual-task processing assume that there exist control processes in the human cognitive system which coordinate the processing stream of multiple tasks and thus deal with the seemingly inherent multi-tasking deficit expressed in dual-task performance costs (Meyer & Kieras, 1997; Logan & Gordon, 2001; Sigman & Dehaene, 2006).

The most prominent neuroanatomical structure associated with the control of human behavior is the lateral prefrontal cortex (LPFC) (Duncan, 2001; Fuster, 2000; Miller & Cohen, 2001). The LPFC is known to be involved in the maintenance of information and the attentional selection and coordination of relevant and irrelevant information enabling goal-directed behavior.

It has been shown with functional Magnetic Resonance Imaging (fMRI) that the IPFC is also involved in the processing of dual tasks (D'Esposito et al., 1995; Erickson et al., 2005a; Schubert & Szameitat, 2003). These studies identified dual-task-related regions by comparing the processing of dual tasks with the processing of single tasks. Such a comparison, however, might reflect any difference between the two types of tasks. Only a few recent studies attempted to specify the type of interference and the control processes related to the dual-task-related activity in the IPFC (Dux, Ivanoff, & Marois, 2006; Herath, Klingberg, Young, Amunts, & Roland, 2001; Jiang, 2004; Szameitat, Schubert, Mueller, & von Cramon., 2002; Szameitat, Lepsien, von Cramon, Sterr, & Schubert, 2006). However, the precise functional role of the IPFC for the control of dual-task processing and the neural mechanism of dual-task coordination are still widely unknown. In particular, three important questions concerning the functional role of the IPFC in dual-task processing remain open. These questions concern:

- I. the **generality** of the IPFC involvement in dual-task processing across different tasks and different types of dual-task coordination
- II. the functional neuroanatomical **dissociability** of different control processes involved in dual-task processing in the IPFC
- III. the **interaction** of the IPFC with posterior task-relevant brain regions serving the control of the dual-task processing stream.

The three fMRI studies presented in this dissertation aim at specifying the functional role of the IPFC in interference processing in dual tasks with respect to these three issues. All three issues are of relevance not only for the understanding of the neural implementation of dual-task processing in the IPFC but also for the understanding of the functionality of the IPFC in general.

In the following section, first, a short background on cognitive theories on dual-task processing will be provided. Then, the functionality of the IPFC for cognitive control in general will be described in order to derive hypotheses about the functionality of the IPFC in

dual-task processing. After describing the methodological approaches used in the three studies of this dissertation, an overview of the research questions and the obtained results of these studies will be given. The obtained findings will then be summarised and some future directions will be outlined. Each study is presented in detail as original article.

2 Theoretical and empirical background

2.1 Interference processing in dual tasks

2.1.1 The dual-task paradigm

The limited ability to perform two tasks simultaneously has been extensively studied in cognitive psychology. The common principle of these studies is to present two tasks more or less simultaneously and to measure behavioral performance costs associated with dual-task processing. However, the applied paradigms also vary depending on the theoretical backgrounds and research questions of the respective authors. Baddeley (1998), for example, frequently used continuous secondary tasks like visual tracking to investigate the properties of assumed sub-systems in human working memory. Other authors like Kahnemann (1973) also mostly applied rather complex component tasks and investigated the resource allocation of their participants to these tasks in order to understand the dynamics of the assumed resource limitations.

The paradigm of the Psychological Refractory Period (PRP) was established by authors assuming a structural processing limitation in the cognitive system (Pashler, 1994; Welford, 1952). In comparison to the other dual-task paradigms, the PRP-paradigm has the advantage of being very precise with respect to the definition of the ongoing tasks and the underlying processing stages. As will be seen later, these properties also form the basis for the precise investigation of the neural mechanisms involved in dual-task processing.

In the PRP paradigm (see Figure 1), two stimuli (S1, S2) are presented with varying stimulus onset asynchronies (SOA) and participants are required to respond to both stimuli

with distinct motor responses (R1, R2). Usually, participants are required to respond to the stimuli according to the presentation order, thus giving priority to S1. The most important finding with the PRP-paradigm is that the processing times for the second of the two tasks (Task 2) increase with decreasing SOA while processing times for the first task (Task 1) are widely unaffected by the SOA manipulation. Telford (1931) first observed this behavioral effect and called it the effect of the Psychological Refractory Period, in analogy to the neural refractory period which relates to the inability of a neuron to elicit two action potentials in short succession.

This idea of the PRP was further specified by Welford (1952) and more recently by Pashler (1994). These authors related the PRP effect to a processing bottleneck inherent to the cognitive system. Assuming that information processing can be divided into several processing stages (Sternberg, 1969), the bottleneck assumption postulates that certain processing stages can proceed in parallel in two temporally overlapping tasks whereas other stages are capacity-limited and can only be processed serially. Accordingly, at high temporal

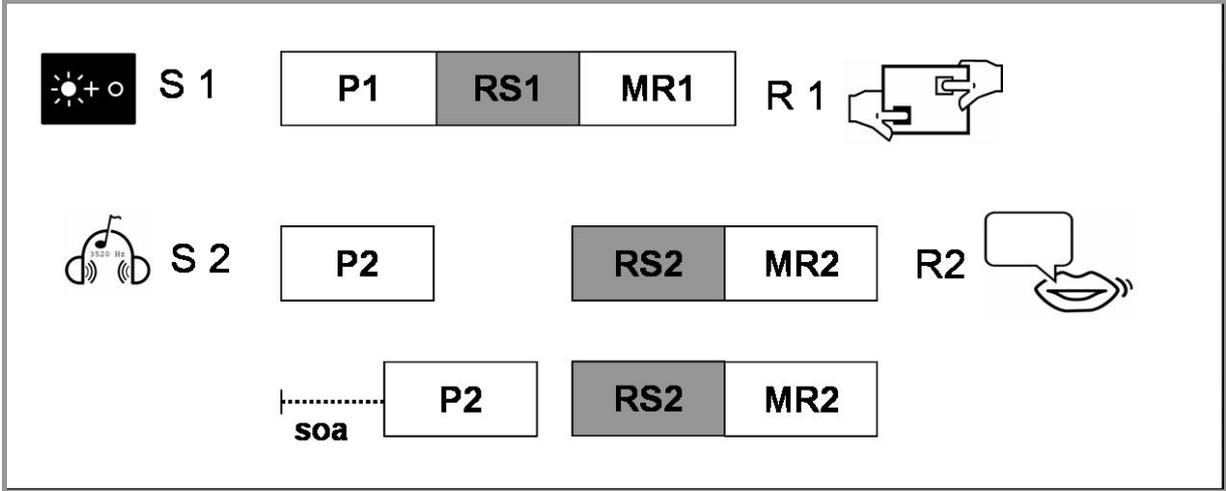


Figure 1. The central bottleneck model in the PRP paradigm (Pashler, 1994). Two stimuli (S1, S2) are presented with different temporal overlaps (stimulus onset asynchrony, SOA) and participants are required to respond with two motor responses (R1, R2). The central bottleneck model assumes that at short SOAs response selection (RS) is temporally interrupted in task 2 until task 1 has finished. Stimulus perception (P) and initiation of the motor response (MR) can be processed in parallel in both tasks.

overlap, the two tasks of a dual-task situation compete for access to these capacity-limited processing stages. This competition for attentional processing capacities at a putative processing bottleneck in dual-task situations is also called dual-task interference. The bottleneck model relates the increased reaction times in Task 2 (RT2) to a temporal interruption of Task 2 processing during the processing of the bottleneck stage in Task 1.

According to the so-called “first-come first-served” principle (Pashler, 1994), the task that reaches the capacity-limited processing stage first – usually Task 1 - gains access to this processing stage and the processing of the other task is delayed. Accordingly, RT1 is usually widely unaffected by the SOA manipulation whereas the duration of the interruption in Task 2 and the resulting RT2 depend on the temporal overlap of the two tasks.

Note that there exists an ongoing debate about the location and the robustness of the dual-task bottleneck within the information processing stream. The original central bottleneck model by Pashler (1994) postulated that the bottleneck is located at the response selection stage (McCann & Johnston, 1992; Pashler, 1994; Schubert, 1999). However, there is also some evidence for capacity limitations at a perceptual (Arnell & Duncan, 2002; Hein & Schubert, 2004; Marois & Ivanoff, 2005) or motor stage (Karlin & Kerstenbaum, 1968; Meyer & Kieras, 1997; Schumacher et al., 2001). Although the studies of the present dissertation do not aim at resolving this debate, evidence for the consistency of the response selection bottleneck may be drawn from all three presented studies.

Importantly, Pashler (1994) assumed that the transition from Task 1 bottleneck processing to Task 2 bottleneck processing is passive. That is, as soon as Task 1 has finished, Task 2 processing automatically continues without the recruitment of additional control processes. This assumption implies an important prediction for the neural implementation of dual-task processing. If no additional control processes are involved in dual-task processing, one might not expect additional brain regions to be involved in dual-task processing compared to the processing of the component single tasks. Previous empirical findings

regarding this prediction will be reviewed in chapter 2.2.3. In addition, the presence of dual-task-specific brain activity will also be tested empirically in Study 1 of this dissertation. As will be outlined in the next section, more recent dual-task models conquer this view of passive bottleneck processing. These models postulate the involvement of active cognitive control mechanisms that coordinate the dual-task processing stream.

2.1.2 Cognitive control in the dual-task paradigm

Recent dual-task models assume the involvement of additional processes related to the active control of the processing stream at and before the bottleneck (De Jong, 1995; Meyer & Kieras, 1997; Logan & Gordon, 2001; Sigman & Dehaene, 2006). This idea was initially formulated to explain for the finding that participants can voluntarily switch the processing order in a dual task and do not solely depend on the presentation order (De Jong, 1995, Meyer & Kieras, 1997). The influence of strategic and voluntary control in dual-task processing was then further investigated and tested in computational dual-task models.

According to these models, the control of the task order in a dual-task situation includes the planning and coordination of the appropriate sequence of actions in two tasks prior to stimulus presentation and during bottleneck processing itself. Recently, Sigman and Dehaene (2006) proposed a computational model for PRP situations where the serial processing of the two tasks at the bottleneck originates from several control mechanisms. First, an attentional task setting mechanism is involved in the planning and coordination of the appropriate action sequence. In addition, an attentional switching mechanism enables the task processes in the second task to proceed after the first task has passed the bottleneck. This is very similar to the conceptions by Logan and Gordon (2001) and also Meyer and Kieras (1997) proposed similar mechanisms in their production-rule-based EPIC (Executive-Process/Interactive Control) architecture (see also Luria & Meiran, 2003). Taken together, the

postulated control mechanisms serve the flexible, goal-directed behavior required to deal with the interference of two tasks in a dual-task situation.

Although the proposed computational models provide a detailed description of the involved control mechanism, there is only few direct evidence from cognitive psychology for such control processes (but see De Jong (1995) or Luria & Meiran (2003) for exceptions).

However, various neuroimaging studies tested the basic assumption of these active control models, namely that additional processing requirements are involved in dual-task situations compared to single-task ones. Additional processing requirements should be reflected in additional effort in the brain in dual-task situations compared to single-task situations. The finding of increased brain activity during dual-task processing would provide converging evidence for the involvement of additional active control processes in the processing of dual tasks and may be difficult to reconcile with the assumption of a passive processing bottleneck (Pashler, 1994). It would also provide the basis for more detailed investigations regarding the nature of these control mechanisms. A candidate brain region for the neural implementation of active control mechanisms in dual tasks may be the lateral prefrontal cortex which has been consistently associated with cognitive control mechanisms in single tasks (Miller & Cohen, 2001; Norman & Shallice, 1986; Passingham, 1993).

2.2 The functional role of the lateral prefrontal cortex (IPFC)

2.2.1 The IPFC and cognitive control

Several authors have argued that cognitive control mechanisms are the key function of the IPFC (Miller & Cohen, 2001; Norman & Shallice, 1986, Passingham, 1993; Petrides, 2000). Cognitive control describes the ability to coordinate thoughts and actions in accordance with internal goals in order to elicit coordinated and purposeful behavior (Fuster, 1989; Miller & Cohen, 2001; Koechlin, Ody, & Kouneiher, 2003; Norman & Shallice, 1986). As we are permanently confronted with multiple options for behavior, it is important that we control

which behaviors are executed in which order and which behaviors are not executed at all. On the one hand, we have to flexibly overcome reflexive and automatic behavior that interferes with intended goal-directed behavior. On the other hand, we also need to maintain and coordinate multiple relevant information streams according to our internal goal hierarchies. These two mechanisms – the inhibition of interfering prepotent response tendencies including the attentional re-focussing on relevant information as well as the maintenance and coordination of multiple relevant information streams as it is necessary in dual-task processing – both constitute important aspects of cognitive control.

The crucial role of the IPFC for cognitive control is supported by ample empirical evidence from single-cell recordings in monkeys, neuropsychological patients and neuroimaging studies (for the neuroanatomical landmarks of the IPFC, see Figure 2).

In single-cell recordings in monkeys, lateral prefrontal neurons have been shown to have the capability to maintain relevant information (de Pellegrino & Wise, 1991; Fuster & Alexander, 1971; Goldman-Rakic, 1987; Kubota & Niki, 1971), even in the face of distracting information (Miller, Erickson, & Desimone, 1996). At the same time, lateral prefrontal neurons are highly flexible and can adopt various task rules (Bunge, Kahn, Wallis, Miller, & Wagner, 2003; Muhammad, Wallis, & Miller, 2006; Wallis, Anderson, & Miller, 2001) even including contingencies on a higher-order level (Shima, Isoda, Mushiake, & Tanji, 2007). These properties of the lateral prefrontal neurons form the basis for flexible, goal-directed behavior.

In accordance with these findings in monkeys, human patients with lateral prefrontal lesions show severe deficits in daily-life behaviors and experimental paradigms involving cognitive control. This includes deficits in the maintenance of information against distractor

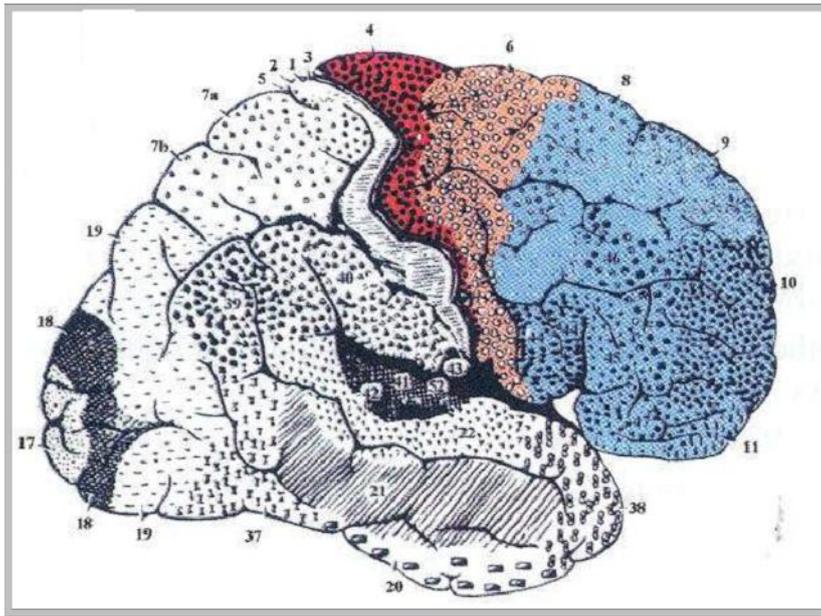


Figure 2: Cytoarchitectonic map by Brodmann (1909). Lateral view. Lateral frontal cortex is colored. red: motor cortex; orange: premotor cortex; blue: prefrontal cortex. Numbers refer to the Brodmann areas. (taken from Barbas, Ghashghaei, Rempel-Clower, & Xiao, 2002).

The lateral prefrontal cortex is part the frontal lobes which comprise the most anterior part of the cerebral hemispheres. Identification and classification of subregions within the frontal lobes are based on morphological features like surface landmarks and microscopic analyses of the constituent neurons resulting in cytoarchitectonic maps. The depicted cytoarchitectonic map by Brodmann (1909) is one of the most widely accepted. Three primary functional subregions of the frontal lobes can be identified on the caudal-to-rostral axis of the lateral frontal surface: motor cortex, premotor cortex and prefrontal cortex. In addition, medial frontal cortex has its own subdivisions, interacting strongly with the lateral frontal regions. The primary motor cortex (Brodmann's area (BA) 4) is the smallest and most homogeneous of these regions, mainly stretching along the central sulcus. Rostral to BA4, the lateral premotor cortex (BA 6) extends along the precentral sulcus and gyrus. Often, BA 8 (frontal eye fields) and BA44 (pars opercularis) are also counted to the lateral premotor cortex. All cortical regions anterior to the premotor cortex are called the prefrontal cortex (PFC). The PFC may be subdivided into several subregions: (1) dorsolateral PFC (dlPFC, BA 9/46), (2) ventrolateral PFC (vlPFC, BA 45/47), (3) anterior PFC (aPFC, BA 10), (4) orbitofrontal Cortex (OFC, BA 11/12/13/14/47), (5) medial PFC (mPFC, BA 24/32). The dlPFC and the vlPFC can be anatomically separated as the neural substrate dorsal and ventral to the inferior frontal sulcus (IFS), respectively. It will be referred to these two subregions stretching along the three frontal gyri (superior, middle and inferior frontal gyrus), when using the term "lateral prefrontal cortex".

interference (Chao & Knight, 1995) as well as the inability to flexibly switch between task representations (Aron, Monsell, Sahakian, & Robbins, 2004; Stuss, Floden, Alexander, Levine, & Katz, 2001). The latter is also exemplified in the Wisconsin Card Sorting Test (WCST; Grant and Berg, 1948), a prominent test for lateral prefrontal functioning. In the WCST, subjects are required to place the top card of a card deck under one of four target cards according to a sorting rule. The sorting rule, however, is only indicated implicitly by the experimenter's feedback about the correctness of the current response. After ten consecutive correct responses the sorting rule changes unbeknownst to the subject. Patients with lateral prefrontal damage are frequently unable to use the feedback of the experimenter in order to switch to the newly relevant sorting rule. They perseverate on the previous rule, unable to flexibly change their behavior according to the new context (Barceló & Knight, 2000; Stuss et al., 2000). Patient studies like this support the importance of lateral prefrontal regions for cognitive control. Note, however, that the WCST is a very complex task consisting of various cognitive components so that no direct inference about the functionality of the IPFC can be made solely based on such neuropsychological findings. Importantly, the involvement of the IPFC in specific components of the WCST was further specified in neuroimaging studies that showed increased IPFC activity particularly related to rule shifts in the WCST (Monchi, Petrides, Petre, Worsley, & Dagher, 2001; Konishi et al., 1998; Lie, Specht, Marshall, & Fink, 2006). Thus, the flexible switching between task rules seems to be the crucial component associated with the lateral prefrontal cortex in the WCST.

Similarly, a vast amount of fMRI studies showed that the IPFC is related to cognitive control in various task situations. In particular, this includes the maintenance of task rules in the face of distraction (de Fockert, Rees, Frith, & Lavie, 2001; Sakai & Passingham, 2003) and the control of interference processing in single tasks like the Stroop task (Banich et al., 2001; Zysset, Müller, Lohmann, & von Cramon, 2001), in task switching (Braver, Reynolds, & Donaldson, 2003; Dove, Pollmann, Schubert, Wiggins, & von Cramon, 2000), the Simon

Task (Fan, Flombaum, McCandliss, Thomas, & Posner, 2003; Liu, Banich, Jacobson, & Tanabe, 2004), the Flanker paradigm (Casey et al., 2000; Hazeltine, Poldrack, & Gabrieli, 2000) and incompatibly mapped choice reaction tasks (Schumacher & D'Esposito, 2002; Schumacher, Elston, & D'Esposito, 2003). Common to all these paradigms is the requirement to suppress prepotent response tendencies interfering with the required responses and thus flexibly switch to another stimulus dimension or stimulus-response mapping. Thus, all these paradigms tag cognitive control as defined above, supporting the view that the IPFC is crucially involved in cognitive control.

The neural mechanisms of cognitive control, in particular the roles of conflict monitoring (Botvinick, Braver, Barch, Carter, & Cohen, 2001) and top-down attentional control (Hopfinger, Buonocore, & Mangun, 2000) are recently debated. The role of the IPFC in cognitive control in such interference situations can be understood as the biasing of task processing in posterior brain regions to resolve interference (Badre & Wagner, 2004; Miller & Cohen 2001). Importantly, there exists recent evidence for the presence of conflict-contingent amplification of activity in task-relevant regions compared to task-irrelevant regions (Egner & Hirsch, 2005). Egner and Hirsch (2005) used a variant of the Stroop paradigm and compared so-called high-control compared to low-control situations. High-control situations were related to conflict adaptation effects (see also Kerns et al., 2004) for recent Stroop trials preceded by an incongruent Stroop trial (high control) compared to precedence by a congruent Stroop trial (low control). Reduced behavioral interference effects for incongruent trials in high-control situations was associated with cortical amplification of activity in task-relevant sensory brain regions. Even more importantly, reduced behavioral interference effects were also associated with increases in functional coupling between task-relevant regions and the IPFC. Accordingly, the top-down modulation of task-relevant regions exerted by the IPFC seems to be an important mechanism for dealing with interference between relevant and irrelevant task representations.

As outlined above, cognitive control is also important in dual tasks, controlling the processing associated with the putative bottleneck. In dual-task situations, however, two stimuli are both relevant for subsequent behavior within the same task trial. This renders the task situation more complex as both task representations are relevant and attention to the second stimulus must also be present to some degree so that the second task can still be performed correctly. Both task streams have to be maintained and coordinated so that they both can find expression in behavior. Although there is an emerging literature on the involvement of the IPFC in dual-task processing, only little is known about how general this involvement is and how exactly the IPFC exerts cognitive control in such dual-task situations. The specification of the functional role of the IPFC in cognitive control in dual tasks is the primary aim of this dissertation.

2.2.2 IPFC involvement in dual tasks - Is the whole more than the sum of its parts?

Early neuroimaging studies on dual-task processing in the IPFC (Adcock, Constable, Gore, & Goldman-Rakic, 2000; Bunge, Klingberg, Jacobsen, & Gabrieli, 2000; D'Esposito et al., 1995; Goldberg et al., 1998; Jaeggi et al., 2003; Just et al., 2001; Klingberg, 1998; Koechlin, Basso, Pietrini, Panzer, & Grafman, 1999; Smith et al., 2001) were mainly concerned with the question whether there exist regions in the IPFC related to additional processing requirements in dual tasks or not. In most of these studies, rather complex tasks like mental rotation, semantic categorization or the reading span test were administered either separately, as single tasks, or temporally overlapping, as dual tasks. The comparison of the activity changes in dual-task blocks with the sum of the single-task blocks was used as an indicator whether the “whole is more than the sum of its parts” (Duncan, 1979), that is, whether additional dual-task-specific activity is elicited in dual tasks or not. Whereas some of these studies did not find dual-task-specific activity in the IPFC (Adcock et al., 2000; Bunge et al., 2000; Klingberg, 1998; Smith et al., 2001) others found either increased dual-task activity in

the IPFC compared to the single tasks (Jaeggi et al., 2003) or even additional IPFC regions involved in dual-task blocks that were not involved supra-threshold in single-task blocks (D'Esposito et al., 1995; Koechlin et al., 1999).

These divergent results on the involvement of the IPFC in dual-task processing might have several reasons. Most likely, the complexity of the applied component tasks leaves many degrees of freedom in the way the dual task is performed by the participants in the different studies - with more or less additional processing requirements being involved. In addition, the rather complex component tasks in these studies might already involve cognitive control processes associated with IPFC regions that overlap with the potential dual-task-related control regions. Accordingly, no additional dual-task-related activity could show up in the comparison of the dual-task blocks with the single-task blocks.

More recent fMRI studies on the functional neuroanatomy of dual-task processing therefore applied better controlled dual tasks using the PRP paradigm (Collette et al., 2003; Erickson et al., 2005a; Schubert & Szameitat, 2003). As outlined above, the advantage of the PRP paradigm is that the applied choice reaction tasks are well-defined and that there exist precise assumptions regarding the underlying processing stream. When comparing the activity changes in the IPFC associated with two choice reaction tasks performed as single versus dual tasks, clear evidence for a dual-task-specific involvement of the IPFC was found (Schubert & Szameitat, 2003; Szameitat et al., 2002). The consistently activated dual-task-related regions were located in regions around the inferior frontal sulcus (IFS) and in regions of the middle frontal gyrus (MFG). Schubert & Szameitat (2003) related this activity to mechanisms of interference control in dual tasks. In addition, Erickson et al. (2005a) showed that dual-task-related regions in the IPFC are not just related to differences in task preparation between dual-task and single-task blocks. In their study, Erickson et al. (2005a) mixed dual-task and single-task trials within the same task blocks such that task preparation was identical for both task types. Still, increased activity in the IPFC, particularly in the left posterior IPFC and the

bilateral IFG was found in dual-task trials compared to single-task trials. Applying the well-controlled PRP paradigm, these studies show consistently that the IPFC is involved in dual-task processing.

However, for several reasons, no unequivocal inferences can be made from these studies with respect to the underlying cognitive mechanisms associated with the dual-task-related IPFC activity.

First, it remains unclear which type of interference is reflected in the additional activity in the IPFC. As outlined above, interference can emerge at different processing stages – related to perception, response selection or the motor response. The studies above do not provide unequivocal evidence that additional processing requirements reflected in the increased IPFC activity are related to the processing of a response selection bottleneck. These studies used either overlapping stimulus modalities (Erickson et al., 2005) or overlapping response modalities (Schubert & Szameitat, 2003). Therefore, the obtained dual-task-related activity changes in the IPFC might also be related to the resolution of perceptual or motor interference instead. In chapter 2.2.3, this possibility will be discussed in detail. In Study 1 of this dissertation, these alternative sources of dual-task-related activity in the IPFC will be eliminated by using component tasks without any overlap on a perceptual or motor level. The finding of dual-task-related activity in such a task situation could then be attributed to the processing associated with the response selection bottleneck.

Second, comparing dual-task blocks with single-task blocks may reflect any cognitive difference between these types of blocks. Besides the outlined mechanism of task order control, this may also include differences in working memory load¹ or divided attention which are clearly more demanding in dual-task blocks. In order to understand the functionality of the dual-task-related IPFC regions in more detail, the underlying cognitive mechanisms need to

¹ This is not the case for the Erickson et al. (2005) study

be identified. For this purpose, in all three studies of this dissertation, parametric fMRI designs are used (Braver et al., 1997). By manipulating the difficulty of specific cognitive functions within different dual-task blocks, specific hypotheses with respect to the functionality of the IPFC in dual-task processing can be tested (see also chapter 2.2.4). In addition, in Study 2 different control functions distinguishing dual tasks from single task were manipulated within the same experiment, giving the possibility to compare the localization of these functions within the IPFC.

Third, focusing exclusively on the IPFC when investigating the functional neuroanatomy of dual-task processing might provide an incomplete picture of the involved neural mechanisms. As outlined above, the IPFC interacts strongly with posterior regions to control task processing according to internal goals in single tasks. The investigation of the functional integration between IPFC and posterior task-relevant regions in dual-task situations is the aim of Study 3.

2.2.3 Types of interference processing in the IPFC (Study 1)

As outlined above, the studies reported so far do not indicate which type of interference is associated with the dual-task-related IPFC activity. The involvement of processing related to perceptual or motor interference cannot be excluded. Some more recent dual-task neuroimaging studies addressed this question (Dux et al., 2006; Herath et al., 2001; Jiang, 2004). Jiang (2004) and Herath et al. (2001) investigated this by using variants of the PRP paradigm to parametrically manipulate certain aspects of dual-task processing. Both studies found increased activity in high-interference dual-task situations at short SOAs compared to long SOAs in a region in the posterior IPFC (pIPFC). However, Jiang (2004) found the SOA effect exclusively for conditions with both stimuli presented in the periphery of a circular display, thus requiring the simultaneous allocation of attention in space. Accordingly, Jiang (2004) concluded that this region in the pIPFC is related to the resolution of perceptual

interference rather than to the resolution of cognitive bottleneck interference in dual tasks. In the study by Herath et al. (2001), however, stimuli in different perceptual modalities (visual, somatosensory) were presented. The finding of an SOA-related activation in the pIPFC in that study excludes the possibility that exclusively perceptual interference is related to pIPFC. In addition, it is rather unlikely that interference at a cognitive level is associated with the activity in that study, as simple detection tasks were used which seem not to require response selection and therefore do not interfere at a cognitive level of processing (Schubert, 1999). Consequently, Herath and colleagues associated this region with the processing of interference at a motor level. Although these studies excluded alternative accounts for dual-task-related IPFC activity due to their parametric manipulations of dual-task interference, no direct evidence for interference at a central response selection stage was provided so far. Only by excluding an overlap of stimulus- and response modalities of the component tasks, direct evidence for an association of dual-task-related IPFC activity to the processing of the response selection bottleneck can be obtained. Study 1 of this dissertation applied such an approach, using non-overlapping modality pairings for the component tasks². In addition, the degree to which these non-overlapping modality pairings are compatible with each other was

² Only recently, after the publication of Study 1 of this dissertation, additional evidence for the association of the pIPFC with the response selection bottleneck was provided by Dux et al. (2006). These authors also used non-overlapping modalities in their component task of a PRP paradigm applying rapid time-resolved fMRI acquisition. In particular, they tested the serial postponement prediction of the central bottleneck model (Pashler, 1994). Serial postponement relates to the idea that response selection in Task 2 is delayed at short SOAs as long as response selection is ongoing in Task 1. This delay is longer, the longer response selection takes in Task 1. In contrast, at long SOAs no such effect of the duration of response selection in Task 1 on RT2 should be present. Dux et al. measured signal latencies in pIPFC regions that were related to response selection at short and long SOAs. The comparison of trials with slow versus fast RT1 revealed a differential pattern at short compared to long SOA consistent with the serial postponement prediction. That is, pIPFC peak latency depended on RT1 speed at short SOA with prolonged activity for slow RT1. No similar effect was found at long SOA. This result further supports that the pIPFC is associated with the central processing bottleneck characterized by the inability to perform two decisional processes at the same time.

manipulated in Study 1. By comparing dual-tasks with modality-compatible (e.g. visual-manual and auditory vocal) and modality-incompatible (e.g. visual-vocal and auditory manual) tasks as component tasks, an additional manipulation of the degree of central task interference was introduced (Hazeltine, Ruthruff, & Remington, 2006). As shown by Hazeltine and colleagues (2006), different pairings of non-overlapping stimulus-response modality pairings may differ with respect to content-dependent interference. That is, although there is no overlap in perceptual or motor processing, interactions between the task-related central codes may differ. This would indicate that central interference is not generic, but depends on the task contents.

To investigate the neural effects of such a manipulation, we used individually determined regions of interest in the IFS, obtained from the dual-task vs. single-task-task contrast. In so far, Study 1 can provide crucial information regarding the question whether the processing of central bottleneck interference is associated with the IPFC during dual-task processing.

2.2.4 Neural implementation of dual-task-related cognitive control in the IPFC (Study 2)

Surprisingly little is known about the neural implementation of control processes that are involved in dual-task processing. As outlined above, recent dual-task models assume that active control processes are involved in the coordination of the dual-task stream by setting task priorities and switching between the two task streams (Logan & Gordon, 2001; Meyer & Kieras, 1997; Sigman & Dehaene, 2006). These mechanisms of task order control serve the optimal task performance despite of the involved bottleneck and may contribute essentially to the dual-task-specific IPFC activity that was found previously.

To my knowledge, only the two studies by Szameitat and colleagues (2002; 2006) addressed the question whether there are neural correlates of dual-task-related control

processes in the IPFC. Szameitat et al. (2002) used a version of the PRP paradigm and compared the fMRI signals between dual-task blocks with different demands on task order control. In their dual-task paradigm, participants performed a visual-manual and an auditory-manual choice reaction task in every trial. The two tasks were presented in dual-task blocks with either random temporal order of the two component tasks or in blocks with fixed order. Within random-order blocks, the task order of the two component tasks changed randomly from trial to trial. Accordingly, participants needed to re-arrange and control the processing order permanently in order to perform the dual tasks in the correct temporal order. The increased demands on the computational processes related to task order control led to increased reaction times and error rates in random-order compared to fixed-order blocks (see also De Jong, 1995; Luria & Meiran, 2003). Even more importantly, when comparing the activity changes in random-order and fixed-order blocks, Szameitat et al. (2002) found an extended fronto-parietal network with bilateral activation foci in the IPFC. The IPFC activation was mainly located in regions surrounding the left and right IFS extending from anterior to posterior portions of this sulcus and dorsally into the MFG. These activation foci overlapped closely with the activation foci obtained when subtracting the signal changes in single-task blocks from those in dual-task blocks as indicated in an additional analysis of the same study. Szameitat et al. (2002) concluded that these dual-task-related regions in the IPFC are associated with the control of the task order in dual-task situations.

Even stronger evidence for this conclusion comes from their event-related study (Szameitat et al., 2006), where task order control was manipulated within the same task blocks. In detail, Szameitat et al. (2006) compared the activity changes in so-called same-order and so-called different-order dual-task trials. While in same-order trials the processing order of the two component tasks in a given trial N (e.g., visual then auditory task) was identical to trial N-1, the order of the two component tasks was reversed between trial N and N-1 in different-order trials. According to the assumption that mechanisms of task order

control may rely on the episodic trace of the task order in the previous trial, task order control difficulty was expected to be increased in different-order compared to same-order trials (De Jong, 1995; Luria & Meiran, 2003). As expected, the processing times and the error rates were elevated in different- compared to same-order dual-task trials and, even more importantly, these differences were associated with two activation peaks in the IPFC. These were located in the right MFG and along the left IFS overlapping with the activity peaks from Szameitat et al. (2002). Thus, there is strong evidence that task order control is one cognitive mechanisms that is associated with dual-task-related regions in middle and posterior portions of the IPFC.

However, the attribution of dual-task-related IPFC activity to task order control processes was recently objected to by other authors (Jiang, Saxe, & Kanwisher., 2004). Jiang et al. (2004) noted that the demands to maintain additional task set components in working memory might cause the additional IPFC activity in dual-task compared to single-task situations. According to this argument, task order control might not be the only factor underlying dual-task-specific IPFC activity. The maintenance of additional task set components may also be crucial. If this is the case, it would be important to investigate whether both functions, task order control and task set maintenance, use overlapping or non overlapping neural substrate in the IPFC. In Study 2, we manipulated task order control and task set maintenance orthogonally to identify the contribution of both functions to IPFC activity during dual-task performance.

2.2.5 Interaction of the IPFC with other brain regions during dual-task processing (Study 3)

The understanding how the IPFC interacts with other task relevant regions is crucial for the understanding functionality of the IPFC in dual-task processing. As Miller & Cohen (2001)

stated, an essential function of the IPFC is the biasing of signals to other brain regions to guide the flow of activity along neural pathways in accordance with internal goals.

Of specific importance for the understanding of this top-down control is the pattern of connectivity of the IPFC subregions with the rest of the human brain (Barbas et al., 2002; Petrides & Pandya, 1999). All PFC regions, including the IPFC, have distinct patterns of cortical connectivity with other regions throughout the brain (see also Fuster, 1989 and Goldman-Rakic, 1987). These connections are mostly reciprocal and enable prefrontal regions to integrate various types of information and to exert a top-down influence on other regions in order to coordinate information processing across a wide range of the central nervous system (Desimone & Duncan, 1995; Miller & Desimone, 1994).

It was outlined above (chapter 2.2.1) that the top-down modulation of task-relevant regions has been shown to be an important mechanism for dealing with interference between relevant and irrelevant task representations in single-task situations (Egner & Hirsch, 2005). Other studies using measures of functional connectivity also support the importance of top-down control for flexible, goal-directed behavior (Abe et al., 2007; Erickson, Ringo Ho, Colcombe, & Kramer, 2005b; Gazzaley, Rissmann, & D'Esposito, 2004).

However, for dual tasks where two task representations are simultaneously relevant there is no evidence yet whether and how the IPFC interacts with task-relevant regions. According to the computational dual-task models by Sigman & Dehaene (2006) or Logan and Gordon (2002), so-called attentional task setting mechanisms might be crucial for the observed behavioral pattern present in the PRP-effect. In Study 3, the interactions of the IPFC with posterior task-relevant regions as well as the activity pattern in these task-relevant regions associated with the PRP effect were investigated. For this purpose a localizer approach (see chapter 3.2.2) and functional connectivity measures (see chapter 3.2.3) were applied in Study 3.

2.3 Summary

A predominant function of the IPFC is cognitive control – the ability to coordinate thoughts and actions in accordance with internal goals in order to elicit coordinated and purposeful behavior. Dual-task processing is unique in that sense, as two internal goals are simultaneously relevant and need to be coordinated in order to successfully perform both tasks. The reviewed literature shows (1) that the IPFC is involved dual-task processing, (2) that different types of dual-task interference are related to the IPFC and (3) that active mechanisms of task order control might underlie dual-task-related activity in the IPFC. However, there are several open questions with respect to the exact functional role of the IPFC in dual-task processing which will be addressed in the present dissertation. These concern the generality of previous findings, the dissociability of different control processes in the IPFC and the interaction of the IPFC with posterior task-relevant brain regions.

Before summarizing the specific research questions and results of the three studies of this dissertation, I will give a short overview on the applied methods in these studies.

3 General Method: Functional Magnetic Resonance Imaging (fMRI)

The advent of neuroimaging methods, in particular functional Magnetic Resonance Imaging (fMRI) opened the possibility to non-invasively map cognitive functions in the healthy human brain. The principle of fMRI is to measure task-evoked physiological changes in blood flow and local metabolism that correlate with the related neural activity. The underlying physiological and statistical procedures will be shortly summarized in the following sections.

3.1 The blood-oxygenation level dependent (BOLD) signal

What kind of physiological signal is measured with fMRI? Neural activity leads to an increased metabolism – the consumption of glucose and oxygen, which is needed to restore

concentration gradients in the neuron that are changed following neural activity. Metabolites are supplied by the vascular system with one essential aspect being the arterial blood supply of oxygenated hemoglobin. The increase in oxygenation usually exceeds the actual demand in the respective brain region. Early research on the MRI signal demonstrated that deoxygenated hemoglobin is paramagnetic while oxygenated hemoglobin is diamagnetic. The different ratio of oxygenated and deoxygenated blood after neural activity leads to temporal local field inhomogeneities that are reflected in the $T2^*$ decay time which crucially depends on the field homogeneity. It has been shown that these differences in magnetic properties after neural activity can be measured with MRI (Ogawa, Lee, Kay, & Tank, 1990). This effect was named the BOLD (blood-oxygenation-level-dependent) effect which was then applied to functional measurements with fMRI (Bandettini, Wong, Hix, Tikofsky, & Hyde, 1992; Kwong et al., 1992; Ogawa et al., 1992). Thus, the BOLD contrast describes the difference in MRI signal on $T2^*$ -weighed images as a function of the amount of deoxygenated hemoglobin.

The BOLD response to neural activity consists of a short onset delay, a rise to a peak after a few seconds, a return to baseline, and a prolonged undershoot. Usually, this takes about 5-12 seconds, excluding the undershoot (Aguirre, Zarahn, & D'Esposito, 1998; Friston, Frith, Turner, & Frackowiak, 1995a; Miezin, Maccotta, Ollinger, Petersen, & Buckner, 2000). This is also called the hemodynamic response function (HRF). Amplitude and latency of the HRF depend on the strength of the evoking stimulus on the one hand but also on the region where it is measured. In addition, high inter-individual variability in the shape of the function has been measured (Aguirre et al., 1998; Handwerker, Ollinger, & D'Esposito, 2004).

Depending on the specific research question, different experimental designs can be used to increase the signal-to-noise ratio in the task-evoked BOLD-signal. In blocked designs, the different experimental conditions are presented block-wise with high task frequency within one block. That way a very strong signal that develops over the course of the block can be measured. In event-related designs, single trials are presented within the same blocks with

longer inter-stimulus intervals (ISI). In event-related designs, the HRF can be determined for every task trial individually, giving the possibility to compare trials within one task block and to eliminate error trials. However, event-related designs have usually smaller detection power, e.g. the ability to detect an activation, than block designs. Study 1 and 2 of this dissertation used pure blocked experimental designs; Study 3 was measured in a mixed block and event-related design.

3.2 Statistical analysis

3.2.1 Data processing

As outlined above, the functional task-related measurements consist of T2* images that are acquired on a slice-by-slice basis in high temporal frequency (1.5- 2.2 seconds per brain volume in the present studies) in small 3-dimensional units (voxels) in the brain.

Before the actual statistical analysis of the task-related BOLD-signal changes in certain brain regions, a couple of preprocessing steps are performed on these time series data depending on the applied experimental design. Using the software SPM2 (<http://www.fil.ion.ucl.ac.uk/spm/>), in the present studies images were slice-time corrected to account for differences in acquisition time between slices (Study 3 only) and motion corrected (all studies) and unwarped (Study 3 only) to account for movement of the participants in the scanner. The images were then spatially normalized into the standard MNI atlas space using the high-resolution T1-weighted anatomical images of every participant and applying the normalization parameters to the functional images after having coregistered those to the anatomical images. Then, the functional data were smoothed with an 8-mm FWHM Gaussian kernel to suppress residual differences in functional and gyral anatomy during inter-subject averaging. In addition, a high-pass filter was applied during analysis to eliminate residual low-frequency noise. The data were statistically analysed using the general linear model (GLM) for serially auto-correlated data (Friston et al., 1995b). In the GLM the given

experimental design is correlated with the brain activity in every voxel in the brain. For that purpose the predictors (regressors) are convolved with a given HRF. The obtained parameter estimates (beta values) per voxel describe the degree to which this voxel correlates with the given experimental design. That way, voxels are identified that show increased BOLD-signal changes under certain task contexts. These signal increases are then tested for statistical significance in a second-level analysis across all participants, either in comparison to a baseline condition or to another task condition. Usually two task conditions are compared to eliminate specific cognitive processes (Braver et al., 1997). The resulting statistical maps can then be overlaid onto normalised anatomical images to locate the significant activities in the brain. That way, regions are identified on a whole-brain basis that are related to the manipulated cognitive processes.

3.2.2 Regions-of-interest (ROI) - Analysis and Localizer Technique

In addition to the statistical analyses on a whole-brain level, so-called regions-of-interest (ROI) analyses were applied in all three studies. The goal of an ROI-analysis is to test specific hypotheses about the pattern of task-related activity in a particular brain region. A-priori ROIs can be identified either as anatomical or/and as functional ROIs. For anatomical ROIs, usually, structural T1 images are used to draw the ROIs on specific sulci, gyri or other subcortical structures. The mean signal changes or the related parameter estimates from voxels included in these regions are then tested with respect to the formulated hypothesis.

Another powerful approach that was applied in the present studies to test the effects of the parametric manipulations is to use functional ROIs. The advantage of functional ROIs is that they can take functional subdivisions within anatomical regions into account. These ROIs are based on functional criteria such as the results of a whole-brain analysis. Some researchers use the group activity peaks from other studies as centers of ROI-masks for their analyses. Another way that takes inter-individual variabilities in functional neuroanatomy better into

account, is to use the individual ROIs determined within the participants who also perform the actual experiment. This approach was applied in the present three studies. It is also called the localizer technique. Either prior to the main experiment (Saxe, Brett, & Kanwisher, 2006) or based on another functional contrast within the main experiment (Friston, Rotshtein, Geng, Sterzer, & Henson, 2006), the functional ROIs are isolated from a contrast that eliminates the respective region of interest (see for example Nieto-Castanon, Ghosh, Tourville, & Guenther, 2003).

ROI-approaches have the advantage that the number of statistical comparisons is greatly reduced compared to the whole-brain analysis, thus minimizing the need for correction of multiple comparisons. Note however, that solely relying on an ROI-approach might prevent one from discovering other regions involved in the processes of interest. Therefore a combined whole-brain and ROI-approach is often a reasonable approach.

3.2.3 Psychophysiological Interactions (PPI)

Given that functional integration plays an important role in most cognitive processes, investigating the interaction of different brain regions during task performance is important to better understand the neural dynamics of cognitive processes. Different approaches to measure functional connectivity between brain regions have been proposed (Lee & Mechelli, 2003). PPI analysis is such a functional connectivity method which also takes the specific task context into account.

The aim of a PPI analysis is to explain neural responses in one brain region in terms of the interaction between the neural responses in another brain region and a specific psychological context (Friston et al., 1997). PPI analysis thus measures context-sensitive changes in functional connectivity between two regions. For example, PPI analysis can be used to investigate whether posterior brain region related to the perceptual processing of a

task are differentially coupled with lateral prefrontal regions under specific task conditions (Friston et al., 1997). This was done in Study 3 of this dissertation.

In general, the PPI analysis consists of a design matrix with three regressors: (1) the “psychological variable” representing two task contexts to be compared, (2) the physiological variable representing the neural response in a given brain region (“seed region”) and (3) the interaction of term (1) and (2). The corresponding subject-specific contrast images of the interaction term are then entered into a random effects analysis. The whole-brain analysis identifies voxels that show increased functional coupling with the according seed region under task context 1 compared to task context 2. To test specific hypotheses about certain brain regions, this approach can be combined with the ROI approach described above.

4 Summary of studies 1 – 3

Based on the outlined state of the art in the research on the functional neuroanatomy of dual-task processing, three basic questions concerning the functional role of the IPFC in interference processing in dual tasks remain open. These three questions concern:

- I. the **generality** of the IPFC involvement in dual-task processing across stimulus-response modality pairings and different types of dual-task coordination
- II. the **dissociability** of different control processes involved in dual-task processing in the IPFC
- III. the **interaction** of the IPFC with posterior task-relevant brain regions to deal with dual-task interference

These three issues form the starting point for the three fMRI studies that are presented in detail as original articles below. Each study focuses on one of these issues but also has implications for the other questions outlined above. Next, a short overview will be given on the specific research questions of the three articles and the obtained results will be shortly summarised.

4.1 Study 1: “The neural effect of stimulus-response modality compatibility on dual-task performance: an fMRI study (Stelzel et al., 2006)”

Research Question:

Study 1 aimed at investigating the generality of the IPFC involvement in dual-task processing on two levels. First, generality with respect to IPFC involvement across different types of interference and second, generality with respect to the type of dual-task coordination associated with dual-task-related activity in the IPFC.

As outlined above, some dual-task fMRI studies with the PRP paradigm tried to specify the *type* of dual-task interference related to IPFC activity. Whereas Jiang (2004) and Herath et al. (2001) found evidence for perceptual and motor interference, at the point of Study 1, no unambiguous evidence was present for central bottleneck interference in the IPFC. This is because all studies that compared dual-task-blocks with single-task-blocks used either overlapping perceptual or motor modalities in the component tasks. Therefore, the obtained dual-task-related activity changes in the IPFC might also be related to the resolution of perceptual or motor interference instead. Aim 1 of Study 1 was to exclude perceptual and motor interference and to investigate whether dual-task-related IPFC activity can also be found in situations with non-overlapping stimulus and response modalities. For that purpose tasks with visual and auditory stimuli and manual and vocal responses were combined to compare the BOLD-signal changes between dual-task and single-task blocks. The finding of dual-task-related activity in such a task situation would then be attributable to the processing associated with the response selection bottleneck.

Other dual-task studies (Szameitat et al., 2002; 2006) related the IPFC to the coordination of the temporal order of two tasks. Coordination, however, might also have other aspects. One important aspect is to coordinate the concurrent mapping of sensory information onto corresponding motor responses on an abstract level. When central task representations, like abstract verbal or spatial codes of two tasks, overlap, increased processing demands

might be related to the coordination of the concurrent processing of the two tasks. Additional coordinative demands might keep overlapping contents separated (Hazeltine et al., 2006). Aim 2 of Study 1 therefore was to investigate whether differences in IPFC activity can be found for two tasks with or without such central content overlap. For that purpose the stimulus-response modality compatibility between the two component tasks was manipulated. Importantly, modality incompatible tasks both required spatial coding and therefore are assumed involve the postulated processes of task coordination. In sum, modality compatibility offers the opportunity to manipulate the degree of central task overlap while keeping the applied stimuli and responses constant. Increased IPFC was expected for modality incompatible compared to modality compatible tasks.

Results & Discussion:

The comparison of dual-task and single-task blocks revealed dual-task-specific activity predominantly in lateral frontal and parietal regions. That is, even in dual-task situations without perceptual and motor overlap, lateral prefrontal regions surrounding the left inferior frontal sulcus showed increased dual-task-related activity. Thus, Study 1 supports the idea that the involvement of the IPFC in interference processing is rather general and that the IPFC is also related to the processing of central bottleneck interference. This complements previous findings by Herath et al. (2001) and Jiang (2004) and is also in accordance with later findings by Dux et al. (2006).

In addition, modality incompatible dual tasks that overlap with respect to central task representation revealed increased activity in the IFS compared with modality compatible task.

The effects in the IFS were investigated in individual ROIs based on the dual-task minus single-task contrast. That way inter-individual variability in the exact location of dual-task specific regions was taken into account. In addition, this effect was accompanied by strong behavioral effects of modality compatibility in the dual task conditions but not in the

single tasks. Importantly, modality compatible and incompatible dual tasks did not differ with respect to the timing of the two tasks as it was the case for the manipulation of task order in the studies by Szameitat et al. (2002; 2006). Hence, effects of dual-task coordination in the IPFC are not limited to situations of changing task order but can also be shown for coordination related to overlapping central contents.

4.2 Study 2: “Dissociable neural effects of task order control and task set maintenance during dual-task processing (Stelzel et al., in press)”

Research Question:

The aim of Study 2 was to dissociate the neural effects of different control functions associated with dual-task performance: task order control and task set maintenance. As summarized above, there is evidence for a consistent involvement of the IPFC in dual-task performance. Usually, this was measured by comparing BOLD-signal changes in dual-task blocks with single-task blocks (Schubert & Szameitat, 2003; Szameitat et al., 2002). The results of this subtraction method, however, may reflect any difference between dual tasks and single tasks. Although Szameitat et al. (2002; 2006) showed that one such difference between dual tasks and single tasks – the demand to control the task order – is related to activity changes in the IPFC, other differences between dual tasks and single tasks are conceivable. Jiang et al. (2004) argued that simply the requirement to maintain two task sets simultaneously may be the crucial factor underlying dual-task-related activity in the IPFC. In Study 2, the contribution of task order control and task set maintenance to activity changes in the IPFC was investigated while participants performed dual tasks. For that purpose, a parametrical manipulation of task order control and task set maintenance was realized in an integrated experimental design performed by one group of participants. Specifically, task order control was measured in the comparison of dual-task blocks with random and fixed temporal order of the component tasks. Task set maintenance was manipulated via the number

of relevant stimulus-response mappings per component task. Note that such an integrated design has the advantage that the corresponding activity changes can be compared directly within the same group of participants. Inferences about the overlap in functional localization of different control functions in the IPFC therefore exclude differences between participants, between the applied paradigms or scanning and analysis procedures as they may be present in the comparison of activity peaks between studies.

Results & Discussion:

The fMRI data revealed a functional-neuroanatomical dissociation of both factors in the IPFC (see Figure 3). Regions surrounding the inferior frontal sulcus and the middle frontal gyrus were exclusively associated with task order control but not with increased demands on task set maintenance during dual-task processing. The only IPFC region associated with task set maintenance was located in the left anterior insula. Outside the IPFC, there were dissociable regions for task order control and task set maintenance bilaterally in the premotor cortices

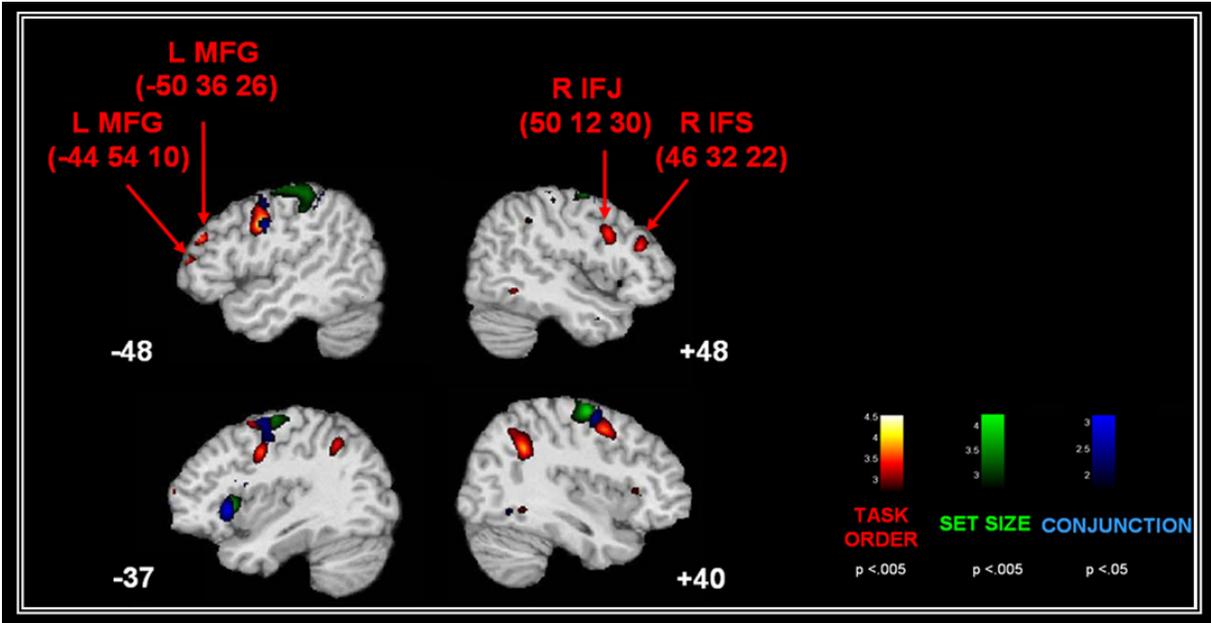


Figure 3: Results of Study 2. Whol-brain analysis for the comparison of dual-task blocks with random order and fixed order (red) and blocks with set sizes of 8 vs. 4 S-R mappings (green) as well as the conjunction of both factors (blue).

with more rostral premotor activity for task order control and more caudal premotor activity for task set maintenance. These data clearly contradict the assumption that IPFC activity during dual-task processing is simply related to the requirement to maintain the task sets of two tasks simultaneously (Jiang et al., 2004). Instead, the results of Study 2 suggest that task order control is a separable cognitive mechanism in dual-task situations that is related to activity changes in the IPFC and that can be dissociated from task set maintenance.

4.3 Study 3: “Neural mechanisms of attentional task setting in dual tasks (Stelzel et al., submitted for publication)”

Research Question:

While Studies 1 and 2 showed the involvement of the IPFC in the control of dual-task processing, they left open how exactly the IPFC controls the dual-task processing stream. Study 3 aimed at specifying the interaction of the IPFC with task-relevant sensory regions in order to better understand the neural dynamics involved in dual-task processing. The computational dual-task models described above suggest that control mechanisms like attentional task setting (Sigman & Dehaene, 2006) serve the coordination of two interfering tasks (see also Logan & Gordon, 2001; Meyer & Kieras, 1997). These models suggest that S1 processing is not affected by a secondary task because – due to its temporal precedence or because of the task instructions – its processing is attentionally more focused. At the same time, the PRP effect in S2 processing emerges due to delayed focussing on S2. Importantly, the assumption of attentional task setting implies different temporal dynamics for S1 and S2 processing with respect to the devoted attentional resources at different temporal overlaps. Due to the S1-related task setting mechanism, attentional focussing is assumed to be increased for S1 processing when there is temporal overlap with S2 compared to situations without such temporal overlap. Attentional focussing on S2, in contrast, should not depend on the temporal overlap.

Until now, the neural mechanism associated with these task setting mechanisms are not well understood. In Study 3, two plausible neural mechanisms that might reflect such attentional task setting with respect to S1 and S2 processing in a PRP situation were tested. First, task-relevant sensory regions were tested for a differential up-regulation in S1-relevant sensory regions in dual-task situations with high temporal overlap (see Egnér & Hirsch, 2005; but also Desimone & Duncan, 1995). Second, changes in functional connectivity of S1-relevant sensory regions with dual-task-related regions in the IPFC might represent a second neural mechanism reflecting attentional task setting in dual tasks. Functional coupling was assessed between IPFC regions related to dual-task control and task-relevant sensory regions in the Fusiform Face Area (FFA) for S1-processing and Visual Word Form Area (VWFA) for S2-processing. In particular, the functional coupling was measured for condition-specific contrasts between different SOAs in the PRP paradigm. To control for perceptual differences in the three SOA conditions (100, 300, 1000 ms), a control condition was included where the secondary stimulus was completely irrelevant for task performance (dual-task vs single-task blocks). High interference at short SOA was expected to be associated with increased functional coupling of dual-task-related IPFC regions and S1-relevant regions in the FFA compared to low or non-overlapping tasks. At the same time, deficient coupling of IPFC with S2-relevant regions in the VWFA was expected to be related to the performance costs in this secondary task.

Results & Discussion:

As a first result of Study 3, we replicated the behavioral PRP effect. The activity in S1-relevant regions in the FFA depended on the degree of temporal overlap of the two stimuli with signal increases at high and no temporal overlap. However, identical effects were found for DUAL TASKS and SINGLE TASKS, indicating that the SOA-effects did not solely reflect the PRP-effect or associated task setting mechanisms present in the DUAL-TASK

condition but rather perceptual effects of simultaneous stimulus presentation. S2-relevant activity in the VWFA was modulated by the task relevance of S2 with increased activity in situations where participants also responded to S2. This fits nicely to known top-down effects of sustained attention on activity in sensory regions (Desimone & Duncan, 1995).

For the dual-task-related regions in the pIPFC, we found effects of SOA and task relevance. However, there was no interaction of both factors. Again, this suggests that the activity differences between the SOAs in the pIPFC are not related to the PRP effect and attentional task setting in dual tasks only. Instead, effects related to the processing of the more or less simultaneously presented second stimulus seem to be a more plausible account for the obtained SOA effects in the pIPFC (see also Jiang et al., 2004).

Most importantly, in Study 3 significant differences in the functional coupling across SOAs were present between S1-relevant regions in the FFA and dual-task-related regions in the right IPFC. Functional coupling was strongest at SOA100 as expected from the theory of attentional task setting. In contrast, no SOA-related up-regulation of functional coupling with the IPFC was present for the VWFA.

In addition, the degree of functional coupling of the right pIPFC and the FFA was negatively correlated with the error rates in dual tasks but not in single tasks. That is, participants with increased functional coupling of pIPFC and FFA at short SOAs made generally less dual-task errors and were thus more efficient in dual-task processing.

Taken together, the results of Study 3 support the idea that the presence of transient changes in functional coupling of control regions in the pIPFC and S1-relevant regions together with the absence of such coupling for S2-relevant regions in situation of temporal overlap is associated with the PRP performance pattern.

5 General discussion and future directions

In sum, the results of the three fMRI studies presented in this dissertation contribute essentially to the understanding of the functional role of the lateral prefrontal cortex in interference processing in dual tasks.

Study 1 showed the **generality** of dual-task-related activity in the LPFC. The finding of dual-task-specific involvement of the LPFC was extended to stimulus-response pairings with non-overlapping stimulus- and response modalities, thus unambiguously relating dual-task-specific activity changes to the processing of central bottleneck interference. In addition, Study 1 revealed that not only the coordination of the temporal order in dual tasks is related to LPFC activity but also coordination with respect to overlapping central task representations. These findings show that the LPFC has a rather generic function for the processing of interference at different levels. Interference processing in single tasks is only one facet (Miller & Cohen, 2001). Perceptual (Jiang et al., 2004), motor (Herath et al., 2001) and, importantly, response selection interference in dual-task situations require the coordination and control of two relevant task streams according to internal priorities and goals. Study 1 has firstly shown unambiguously that the LPFC is involved in coordinating the processing of two decisional processes that that can not proceed in parallel.

In Study 2, the behavioral and neural **dissociability** of two control functions involved in dual-task processing in the LPFC was shown. Whereas the control of the task order in dual tasks was associated with LPFC activity, task set maintenance was mainly associated with lateral premotor activity. This result supports the idea that task order control is a separable control mechanism in the LPFC that deals with dual-task interference and that can be dissociated from simple task set maintenance. From a cognitive neuroscience perspective this result supports the conclusion that not all types of cognitive control mechanisms are located in overlapping regions within the LPFC (see also Hester, Murphy, and Garavan, 2004). Instead, it was shown that the specific localization of different cognitive control mechanisms can be

distinguished using appropriate experimental designs. In addition, this neural evidence for the involvement of task order control in dual-task processing clearly contradicts cognitive models that assume passive bottleneck processing (Pashler, 1994). Instead, direct evidence is provided for active control mechanism involved in dual-task processing (Logan & Gordon, 2001; Meyer & Kieras, 1997; Sigman & Dehaene, 2006).

The third study of this dissertation showed that the differential **interaction** of the IPFC with posterior task relevant regions (FFA, VWFA) is one crucial mechanism how the IPFC deals with dual-task interference. Functional coupling of the IPFC with regions relevant for S1- processing was increased at high temporal overlap with a secondary task. This is in accordance with the assumption that active task setting mechanisms focus attention on task 1 to prevent interference in this prioritized task. In contrast, task 2 performance costs might be related to the deficient functional coupling of regions relevant for S2 processing with the IPFC at high temporal overlap. This result greatly extends previous insights on the functional neuroanatomy of dual-task processing which was primarily investigated within the IPFC. Study 3 provides evidence that setting priorities between multiple relevant information streams takes place in interaction with those information streams. Study 3 showed that the integration of relevant sensory information with the internal information on priorities and goals is realised by functional coupling of sensory and prefrontal regions.

Taken together, the functional role of the IPFC in dual-task processing can be described within the framework of cognitive control: the IPFC coordinates multiple task-relevant information streams in accordance with our internal goal hierarchies. The IPFC does so by biasing the processing in posterior brain regions in order to set task priorities and to switch between relevant task representations (Koechlin et al., 2003; Miller & Cohen, 2001).

The finding that goal-oriented mechanisms of task order control can be separated from other dual-task related mechanism like task set maintenance also fits well to conceptions of a hierarchical organization of the frontal cortex (Fuster, 1989; 2001; Koechlin et al., 2003).

These models relate the premotor cortex to pure sensory-motor control and more rostral IPFC regions to the context-specific control and control related to specific episodes. Thus, the findings of the dissertation support existing models on cognitive control in the IPFC, providing extensive new empirical evidence for task situations with multiple relevant information streams.

The focus of all three studies presented here lay on the functional role of the IPFC in dual-task processing. Not surprisingly, in all three studies additional regions were involved as indicated in the respective whole brain analyses. The potential role of these regions will be shortly discussed at this point.

The medial prefrontal cortex was involved in the comparison of dual tasks and single tasks in Study 1 as well as in the SOA contrast in Study 3. The medial prefrontal cortex, including the pre-supplementary motor area (pre-SMA) and the anterior cingulate cortex (ACC), has been found to be involved in performance monitoring and the detection of errors and conflicting response tendencies (Botvinick et al., 2001; Ridderinkhof, Ullsperger, Crone, & Nieuwenhuis, 2004). Monitoring and detection of interference is another important aspect of cognitive control which is also present in the processing of dual-task interference, being necessary for the initiation of interference resolution. While the focus of the present studies was on control mechanism involved in the resolution of interference in the IPFC, the interactions of IPFC and medial PFC might also be of interest for future studies. This might also shed further light on the specific contributions of IPFC regions to the processing of different types of interference on the hand and to the resolution of this interference on the other hand. There may be dissociable regions in the IPFC related to the bottleneck itself (Study 1; Dux et al., 2006; Herath et al., 2001; Jiang, 2004) and regions related to the resolution of interference, e.g. the active control of bottleneck processing (Study 2 & 3, Szameitat et al., 2002; 2006), showing different interactions with the medial PFC. Note that effects of task order control in the present studies were always present in the pIPFC but also

more anteriorly in middle portions of the IFS. It may be that these regions have different functional roles in interference processing in dual task. For example, the inferior frontal junction region in the plPFC has been consistently associated with the updating of task representations as one aspect of cognitive control (Brass, Derrfuss, Forstmann, & von Cramon, 2005). However, additional analyses of Study 3 showed that also in mid-IFS regions, the effect of comparable SOA-effects related to dual-task and single-task processing was present as indicated by the whole-brain analysis testing for interaction effects. Thus, activity patterns of these regions related to a prototypical interference manipulation in dual tasks (SOA) do not reveal different functional roles of mid- and posterior IPFC. Future analyses might specifically test the connectivity patterns with medial PFC to elucidate the specific contributions of these IPFC regions to interference processing in dual tasks.

Furthermore, in the parietal cortex, in particular regions along the intraparietal sulcus (IPS) were consistently activated in the comparison of dual tasks and single tasks (Study 1) as well as in the contrasts for task order control (Study 2) and SOA (Study 3). This finding converges with findings of other studies suggesting a role of the parietal cortex in the spatial coordination and control of motor sequences as it is also present in dual-task situations (Andersen, Essick, & Siegel, 1987; Schubert, von Cramon, Niendorf, Pollmann, & Bublak, 1998; see Culham & Kanwisher, 2001 for a comprehensive review). Also, the IPS has been related to the actual implementation of attentional processes that are initiated by the IPFC (Corbetta & Shulman, 2002; Hopfinger et al. 2000). The specific contribution of the superior parietal cortex to efficient dual-task processing might be another topic for future studies.

On a more abstract level, the aPFC has been associated with the weighting and integration of information in the pursuit of higher behavioral goals (Christoff & Garbieli, 2000; Pollmann, 2001; Ramnani & Owen, 2004). A typical paradigm associated with the aPFC is the prospective memory paradigm where participants are required to perform a pre-defined action upon the presentation of a delayed cue presented within a continuous task

performance (Burgess, Veitch, de Lacy Costello, & Shallice, 2000; Burgess, Scott, & Frith, 2003). The prospective memory paradigm seems to be related to the dual-task paradigm with two tasks being performed more or less simultaneously. However, no consistent aPFC activity was found in the present studies which might be related to some fundamental differences between the prospective memory paradigm and the PRP paradigm. Most importantly, the information to be responded to in the PRP paradigm is always externally defined – that is perceivable stimuli that require a distinctive motor response in every task trial. Control mechanisms serve the coordination of this externally presented information. In contrast, carrying out an intended action upon the presentation of the prospective memory cue is more internally guided - it requires the consideration of multiple conditions for correct performance. Although there was no supra-threshold activity in the aPFC in the present studies, investigating the transition between the two types of goal-directed multi-tasking might be worth to be further investigated.

Altogether, the present dissertation contributes essentially to the understanding of how dual-task processing is realized by the human brain. Based on the obtained conclusions on the functional role of the IPFC in dual-task processing, further network-oriented approaches might help to elucidate the interplay of the IPFC with medial and anterior PFC and the superior parietal cortex. Besides effective connectivity measures, the high temporal resolution of evoked activity and the neuronal oscillatory synchronization as measured in electro- and magnet encephalography may further extend the gained insights by specifying the temporal dynamics of cognitive control in dual-task processing (see for example Swainson et al., 2003).

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6 Selbständigkeitserklärung

Hiermit erkläre ich, dass ich die vorliegende Arbeit ohne unzulässige Hilfe und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe. Die aus fremden Quellen direkt oder indirekt übernommenen Gedanken habe ich als solche kenntlich gemacht.

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