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Tracking the subprocesses of decision-based action in the human frontal lobes

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Situationally adaptive behavior relies on the identification of relevant target stimuli, the evaluation of these with respect to the current context and the selection of an appropriate action. We used functional magnetic resonance imaging (fMRI) to disentangle the neural networks underlying these processes within a single task. Our results show that activation of mid-ventrolateral prefrontal cortex (PFC) reflects the perceived presence of a target stimulus regardless of context, whereas context-appropriate evaluation is subserved by mid-dorsolateral PFC. Enhancing demands on response selection by means of response conflict activated a network of regions, all of which are directly connected to motor areas. On the midline, rostral anterior paracingulate cortex was found to link target detection and response selection by monitoring for the presence of behaviorally significant conditions.

In summary, we provide new evidence for process-specific functional dissociations in the frontal lobes. In target-centered processing, target detection in the VLPFC is separable from contextual evaluation in the DLPFC. Response-centered processing in motor-associated regions occurs partly in parallel to these processes, which may enhance behavioral efficiency, but it may also lead to reaction time increases when an irrelevant response tendency is elicited.

Keywords: Prefrontal cortex; Target detection; Contextual evaluation; Monitoring; Response conflict

Adequacy of human behavior is often defined by its situational context. Acting appropriately in changing contexts requires that no stimulus triggers an action automatically (Shallice, 1982). Even in the face of prepotent stimuli, the current situation as well as possible actions and their consequences need to be evaluated. The continuous situational evaluation that is required to adjust one's behavior involves at least three distinct processes: target detection, contextual evaluation and response selection.

First, the presence of a relevant target stimulus needs to be detected. The term 'target detection' refers to a process by means of which stimuli are classified as target or non-target as a result of a comparison between a set of relevant stimuli and the currently present stimulus. Context dependency requires that target detection is complemented by an evaluation of context information, so as to ensure that an action in response to the perceived target is appropriate in the current situation. Target detection and contextual evaluation are referred to here as 'target processing'. In addition to these processes, an action needs to be selected in accordance with the specific target and the current context, in order to carry out an adequate response.

The vast majority of studies on target processing have used the two-stimulus oddball task to elucidate fMRI activations or event-related potentials in both healthy participants and in many clinical populations (e.g., McCarthy et al., 1997; Clark et al., 2000; Kiehl et al., 2001; Huettel and McCarthy, 2004; for a review of ERP data, see Soltani and Knight, 2000). In this paradigm, a train of frequent so-called "standard" stimuli is randomly interspersed by rare target stimuli on which the participant has to react by button press or silent counting of the number of occurrences. Since the first functional MRI-based observation of frontal and parietal activation in the oddball task (McCarthy et al., 1997), converging evidence for a frontoparietal target processing network has accumulated (e.g., Jiang et al., 2000; Kiehl et al., 2001; Huettel and McCarthy, 2004; Huettel et al., 2002). Even though these studies implemented different paradigms such as the oddball task, item recognition in short-term memory, or expectation-based moment-to-moment change detection, they demonstrated similar activation patterns.

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In order to differentiate between the detection of task-relevant and task-irrelevant stimuli, the three-stimulus variant of the oddball task presents "novel" non-target stimuli at the same low level of frequency as the targets in a train of frequent standard stimuli (e.g., Bledowski et al., 2004). While targets and non-targets share the feature of infrequent presentation, non-targets are different in that they are irrelevant and do not require a response. Regions showing stronger activation to novel stimuli compared to targets are thought to subserve the filtering of irrelevant information. Even though fMRI investigations of these processes usually report activations of the frontal cortex, their localization is very inhomogeneous across studies, involving both mid-ventrolateral prefrontal cortex (VLPFC) and mid-dorsolateral prefrontal cortex (DLPFC) (Clark et al., 2000), DLPFC only (Kiehl et al., 2001) or involvement of PFC in targets, but not in novel stimuli (Kirino et al., 2000).

The filtering of irrelevant information as measured by the response to novel stimuli is an important aspect of target processing and might overlap with contextual evaluation. However, the core feature of contextual evaluation, the context-sensitive classification of information as relevant or irrelevant, is only partly examined by effects of novel stimuli, as these are always irrelevant, independent of context. Strictly, a paradigm would be needed in which the same stimulus has to be responded to or has to be ignored depending on task context.

Several theoretical conceptions of prefrontal cortex' functions agree that mid-DLPFC's place at the top of motor and the sensory hierarchies makes it an ideal structure to integrate and evaluate information from diverse sources (e.g., Petrides, 2000; Owen et al., 1996; Rowe et al., 2000; Miller and Cohen, 2001; Passingham and Toni, 2001). Such supramodal processing of information is indispensable for superordinate cognitive control and selection mechanisms such as contextual evaluation.

According to Owen's and Petrides' well-known view, mid-VLPFC is, in contrast to mid-DLPFC, much more concerned with 'low-level' control, such as active judgment of familiarity in memory encoding and retrieval, and active maintenance of information by biasing information processing in temporal and parietal sites (Owen et al., 1996, 1998, 1999; Petrides and Pandya, 2002a,b; Petrides et al., 2002).

Following this line of reasoning, we expected that target detection – relying on explicit judgments of familiarity – would activate VLPFC, whereas contextual evaluation – requiring integration of information – would be reflected in DLPFC activation.

However, VLPFC and DLPFC are not the only components of the target processing network; rather, the frontal part of this network additionally includes dorsal and ventral premotor cortex (PMC) on the lateral surface, pre-supplementary motor area (pSMA) and anterior cingulate cortex (ACC) on the medial wall. Also, its activation is not unique to target processing. Indeed, response selection has been found to activate a set of regions that closely resembles the frontal part of the target processing network across different paradigms (Duncan and Owen, 2000; Jiang and Kanwisher, 2003). Our second goal was therefore to disentangle target processing from response processing in these regions.

To summarize, we sought to achieve a fine-grained functional parcellation of frontal lobe regions by identifying the neural substrates of target detection, contextual evaluation and response selection.

In order to achieve the goal of dissociating target- and response-oriented processing, we combined a delayed-match-to-sample task with a response conflict paradigm. The task consisted of short block-like units each comprising an encoding phase, a short delay interval and an extended response phase (Fig. 1a). In the learning phase, participants encoded a set of two or four relevant target colors, each of which was associated with a specific response side (left vs. right mouse click), thereby gaining behavioral relevance. After a short delay period, in the response phase, a colored probe square was presented and had to be classified as target or non-target, depending on whether its color matched one of those presented during the learning phase. If so (target trials), the button on the associated side had to be pressed. In case of a non-matching color (non-target trials), the middle button was to be pressed.

Additionally, to introduce response conflict, the central probe square was surrounded by a larger 'flanker' square. Subjects had to focus on the small square in the central probe position while ignoring the color in the surrounding flanker position. To vary demands on response-centered processes, the color of the flanker square was varied: Either it was printed in the same color as the probe square so that only the response associated with this color should be activated. Or the color of the flanker square was associated with a different response than the one associated with the probe square, in which case the responses associated with both the target and the flanker color should automatically be activated. The presence of flanker stimuli demanding alternative responses elicits a response conflict as evidenced by prolonged reaction times and higher error rates (Eriksen and Eriksen, 1974; Casey et al., 2000; Hazeltine et al., 2000; van Veen et al., 2001).

Thus, target processing and response conflict were incorporated as two dimensions of a single task, allowing us to identify each function's neural underpinnings and their loci of interaction (Fig. 1b, left panel).

Approaching the goal of dissociating subprocesses of target processing mainly implied setting sharp criteria to discriminate

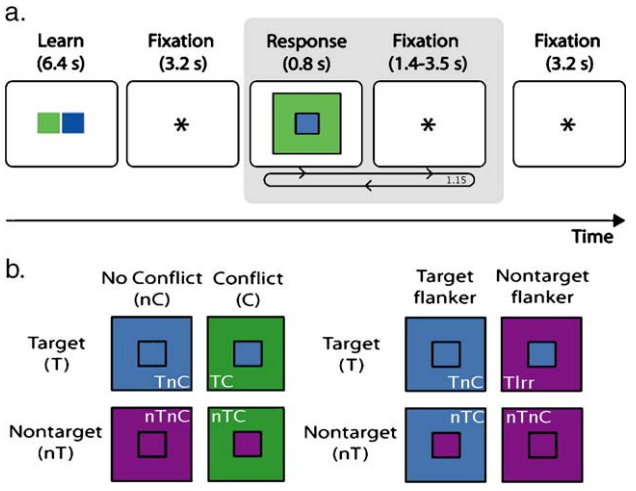

Fig. 1. (a) Schematic of the three task phases. After learning color-response associations and a short delay phase, in the response phase, a rapidly paced sequence of 15 probes was presented in a randomized order. For each probe, the subject had to decide whether the small central square matched any of the learned colors and respond accordingly. (b) Trial types. Left panel: Trial types used for the two dimensional main analysis of target set and response conflict. Right panel: Trial types used for analysis of target vs. non-target differences regarding the flanker position (left vs. right column) independent of the probe stimulus. nTnC = non-target trial without conflict; nTC = non-target trial with conflict; TnC = target trial without conflict; TC = target trial with conflict; Tirr = target trial with an irrelevant flanker.