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An fMRI investigation into the neural mechanisms of spatial attentional selection in a location-based negative priming task

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ABSTRACT

Selective attention enables us to respond to objects and events that are relevant to our goals for adaptive interactions with the environment. Despite evidence from research addressing the selection of a target location, little is known about the neural mechanisms of attentional selection in situations in which the selection is biased in favor of the information in the irrelevant location. In this study, we combined event-related fMRI and a location-based negative priming paradigm with a prime–probe-trial design to investigate the neural mechanisms of spatial attentional selection. Participants were instructed to respond to the location of a pre-specified target while ignoring a distractor at an irrelevant location. The goal of this study was twofold. First, we identified brain regions that are linked to conflict resolution situations, in which the selection bias puts the irrelevant information in the probe trial on a selection advantage over the target. Second, we determined the mechanism of conflict resolution when the encoding conditions of stimuli are manipulated by presenting stimuli either abruptly (onset) or masked (no-onset). The results showed that the bottom-up-induced competition among stimuli in the target selection is stronger for onset than no-onset stimuli. The superior parietal lobule was sensitive to those changes in bottom-up-induced competition. Furthermore, the dorsolateral prefrontal cortex and inferior parietal lobe were activated to resolve the additional processing effort necessary to select the negatively biased target. In conclusion, the present study identified dissociable neural components needed to resolve the negative selection bias, which attentional modulation can be addressed in future studies by examining changes in the functional connectivity.

1. Introduction

In everyday life, successful survival requires us to effectively respond to locations containing relevant information and to ignore locations occupied with irrelevant information in the visual field. Attentional selection of task-relevant information for higher order processing is mediated by both bottom-up (sensory-driven) mechanisms, such as the salience of a stimulus or spatial proximity between target and distractor (Mounts and Tomaselli, 2005; Yantis, 2000), and top-down (feedback) mechanisms, such

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as advance knowledge or expectations (Eriksen and Hoffman, 1973; Posner et al., 1980).

Competition models of attentional selection propose that both excitatory and inhibitory processes mediate visual selection (Desimone and Duncan, 1995; Kastner and Pinsk, 2004; Reynolds and Desimone, 2003). Specifically, the stronger the bottom-up influence (or bias) induced by an irrelevant object in the visual field (e.g., high salience), the more difficult the selection process in determining the relevant location (Eltiti et al., 2005). For example, for a spatial selection task the effects of spatial inhibition can contribute to an efficient selection of target locations by actively preventing stimuli in irrelevant locations from gaining control of action (Fox, 1994; Tipper, 1985, 2001). In addition, a fronto-parietal network is assumed to play a putative role in directing attention with frontal components relating to control and target detection and posterior components related to representation of and orienting to spatial locations (Hopfinger et al., 2000; Nobre et al., 2004). Despite evidence addressing the selection of a target location, however, little is known about the neural mechanisms of attentional selection in situations in which the selection is biased in favor of the information in the irrelevant location.

A typical selective attention paradigm that has often been used to investigate inhibitory mechanisms of selective attention (as well as facilitatory mechanisms) is the negative priming (NP) paradigm (Botella et al., 2002; Wright et al., 2006). In a location-based version of the NP paradigm, participants respond to the location of a pre-specified target while ignoring a distractor at an irrelevant location. Because both target and distractor are competing for control of action, inhibitory mechanisms ensure the accurate selection of the target location. The condition of primary interest is when the target appears in a location that has been ignored as a distractor location in the previous trial (ignored repetition trial, IR). In the IR condition, responses are typically delayed compared to conditions of no location repetition (control condition, C). This delay in response time is defined as the NP effect.

In the literature, at least three different explanations have been proposed to account for the NP effect. The most prominent account is based on inhibitory processes involved in target selection in the preceding prime trial which are still active in the subsequent probe trial and need to be overcome (Tipper, 1985; Tipper and Cranston, 1985). Note that although it is assumed that inhibitory processes in the prime episode impair target processing when the prime distractor location becomes the target location, the specific feature that is subject to inhibition in the prime trial is still up to debate (Guy and Buckolz, 2007; Tipper, 2001). In so-called episodic retrieval accounts it is assumed that the irrelevant location in the prime trials receives a 'do-not-respond' tag that interferes with processing when the probe target appears in this exact location (e.g., Neill et al., 1992). A third account incorporates aspects from the previous two. Here, a probe episode is quickly classified as 'old' or 'new', which in both cases does not involve conflict. If the probe episode contains old and new aspects at the same time, an orienting system is required for processing and therefore, slows response times (Milliken et al., 1998). Although the exact mechanisms underlying negative priming are still subject to heavy debate, at least in location-based NP paradigms the involvement of inhibitory processes in the explanation of NP effects has received some recent support (Buckolz et al., 2002; Christie and Klein, 2001; Guy and Buckolz, 2007; Neill et al., 1994; Tipper, 2001; Tipper et al., 1990; Vink et al., 2005). Following this line of research, the focus of the present study is the investigation of inhibitory attentional processes using a location-based version of the NP paradigm.

Based on biased competition models, in the IR condition, an inhibited distractor location in the prime trial receives a negative bias that puts the distractor location in the subsequent probe trial at a competitive advantage over the target location. The probe trial selection is biased against the prime-trial distractor location, which is identical to the probe target location in the IR condition. Therefore, the selection process in the IR condition includes not only the 'usual' competition between target and distractor (that is also given in no location repetition), but also carries an additional source of conflict that requires resolution (Houghton and Tipper, 1994). Even though it appears quite logical that some additional processing might be involved to overcome such negative selection bias, the actual level of additional processing and the contribution of underlying neural networks are to date less understood.

In a recent fMRI study, Vink et al. (2005) used a size discrimination task in which participants were engaged in selecting a negatively biased location. Participants were asked to respond to one of four possible locations indicated by the larger of two circles. The IR condition included trials in which the irrelevant location of the smaller circle in the prime trials was occupied by the larger of the two circles in the subsequent probe trial. The authors argued that the additional processing effort in the IR compared to the C condition is due to a reduced activity in the superior parietal lobe and compensatory premotor activations (putamen and supplementary motor area). Such premotor activations are discussed in context of response selection (Milham et al., 2001).

It is unclear, however, whether these findings can also be generalized to other NP selection tasks (Wright et al., 2006). Note that such a discrimination task does not represent a typical selection task in a NP paradigm, which is usually based on the search of a pre-defined target item. In addition, recent electrophysiological studies provided evidence that the selection of a pre-specified target in a classical NP task involves conflict resolution at another level, namely at early sensory levels (Kathmann et al., 2006). In accordance to the inhibition account of NP, it has been shown by analyzing the parieto-occipital N1 that the location NP effect is related to early inhibition of sensory processing (Houghton and Tipper, 1994). Furthermore, two N2 components have been isolated by studying the mechanisms of attentional inhibition in NP that reflect aspects of a biased competition model for a distractor inhibition (Ruge and Naumann, 2006).

In this study, we used event-related fMRI to investigate whether the neural mechanisms of spatial attentional selection can be generalized to a location-based NP paradigm. The goal of this study was twofold. The first goal was to identify brain regions that were linked to conflict resolution situations, in which the selection bias (caused by prime trial inhibition) puts the irrelevant information in the probe trial on a selection advantage over the target. If the results by Vink et al. (2005) can be generalized to a more traditional location-based NP task, then premotor areas activations are expected to be involved in conflict resolution at the response level in the NP task. An alternative

Table 1 – Response times (RT), standard deviations (SD), and error rates (ER) for the prime- and probe-trials in onset and no-onset mode

Prime–Probe-Trial		Onset-mode		No-onset mode	
		RT ± SD (ms)	ER (%)	RT ± SD (ms)	ER (%)
Prime	Ignored repetition	574 ± 94	1.0	543 ± 85	0.0
	Control	580 ± 94	0.0	539 ± 73	0.0
Probe	Ignored repetition	609 ± 106	0.0	583 ± 87	0.0
	Control	594 ± 103	0.4	588 ± 84	0.4

explanation for the NP is the selective inhibition approach, which assumes that an additional processing effort is necessary to select a negatively biased location (Houghton and Tipper, 1994; Lavie and Fox, 2000). We hypothesized that the additional processing effort is related to bottom-up and top-down attentional control mechanisms in the fronto-parietal network (Hopfinger et al., 2000; Nobre et al., 2004) with a prefrontal cortex component (dorsolateral prefrontal cortex) involved in the top-down allocation of attentional resources (Fassbender et al., 2006; Milham et al., 2003; Miller and Cohen, 2001) and a parietal cortex component (inferior parietal lobule) involved in multiple functional modules such as target detection (Corbetta and Shulman, 2002; Pollmann et al., 2003), shift of attention (Corbetta and Shulman, 2002; Kelley et al., 2007), and translation of stimulus representations into response codes (Goodale and Milner, 1992).

The second goal was to investigate the mechanisms of conflict resolution when the encoding conditions of stimuli are manipulated in the participants' visual field (Fischer and Hagendorf, 2006). For this reason, target and distractor were presented either as onset (abruptly) or no-onset stimuli (masked). Studies demonstrated that onset stimuli trigger involuntary shifts of attention (Bacon and Egeth, 1994; Theeuwes, 1991) and salience is more influenced by onset stimuli than by no-onset stimuli (Eltiti et al., 2005). Based on those results we argue that the target selection is most efficient for no-onset stimuli. Due to their low salience, no-onset distractors will capture less attention and will interfere less with the target selection than onset distractors. This reduced impact of a prime distractor location on the selection of a target location will reduce the need for additional conflict resolution in processing of subsequent probe IR trials. We predict that control and ignored repetition conditions for the no-onset mode will not differ in their underlying cognitive processes. We hypothesize, therefore, a loss of the NP effect and no differences in activation pattern for both conditions.

2. Results

2.1. Behavioral results

Response times and error rates for the onset and no-onset conditions were used to determine NP effects (Table 1). NP effects of probe-trials were calculated by subtracting response times in the IR from the C condition. Participant performance was highly accurate during the experiment. Due to the low frequencies of errors (0.2%), no further error analysis was applied.

To determine the influence of the presentation mode, response times of probe-trials were submitted to a repeated-measure analysis of variance (ANOVA) with Priming (IR and C) and Mode (ON and NO) as within-subject factors. There were no significant main effects of Priming [$F(1,11)=0.82$, $P=0.386$] and Mode [$F(1,11)=1.25$, $P=0.288$]. Importantly, the interaction between Priming×Mode was significant [$F(1,11)=5.63$, $P<0.05$]. Planned follow-up paired t-tests revealed a significant negative PE for the onset mode [ON: −15 ms, $t(1,11)=2.72$, $P<0.05$] but not for the no-onset mode [NO: 5 ms, $t(1,11)=-0.54$, $P=0.599$]. Altogether, manipulating the presentation mode of the stimuli resulted in an elimination of the NP effect (Fig. 1).

2.2. Functional MRI results

Brain responses were obtained only for correct responses. Table 2 presents foci of group activations with anatomical region, Brodmann areas, Talairach coordinates, t- and P-values separated for all contrasts.

For the conjunction of RFX analysis, neural activity specific to inhibitory mechanisms that ensure accurate target selection during the competition between target and distractor was revealed. Brain activations were found in the right anterior cingulate cortex (ACC, BA 24), left superior parietal lobule (SPL, BA 7), left insula (BA 13), and postcentral gyrus (PCG, BA 3) (Table 2A). For the onset-priming contrast $(IR>C)_{ON}$, neural activity specific to the additional processing effort required to resolve the negative selection bias in the onset-mode was revealed. Activations were found in the right hemisphere of the inferior parietal lobule (IPL, BA 40) and dorsolateral prefrontal cortex (DLPFC, BA 8/9) (Table 2B; Fig. 2A). No activation was found for the no-onset priming contrast $(IR>C)_{NO}$. For the interaction contrast (Priming×Mode), neural activity specific to the variation in bottom-up-induced competition was revealed. Activations were observed in the right DLPFC (BA 8/9) and the left SPL (BA 7) (Table 2C; Fig. 2B).

To further explore the bottom-up-induced competition effect for the SPL region, a region of interest (ROI) analysis was employed. For each participant, parameter estimates (mean beta weights) for each predictor (IR_{ON}, C_{ON}, IR_{NO}, and C_{NO}) were derived from the SPL region after identifying the peak of activation and surrounding voxels encompassing 50 mm^3. A

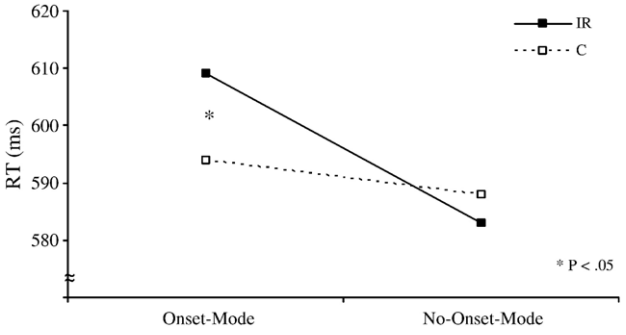

Fig. 1 – Response time of probe trials. Negative priming effects of probe-trials were calculated by subtracting response times in the IR from the C condition. A negative priming effect appeared only for the onset-mode but not for the no-onset mode.

Table 2 – Brain areas activated for the conjunction, onset priming, and priming × mode analysis

Regions of activation	Cluster size (voxel)	Laterality	Talairach coordinates			t-score *
			x	y	z	
(A) Conjunction analysis						
Anterior cingulate cortex (24)	20	R	1	12	31	4.32
Superior parietal lobule (7)	132	L	−4	−65	58	5.81
Insula (13)	21	L	−29	18	17	6.47
Postcentral gyrus (3)	84	L	−39	−24	60	5.46
(B) Onset priming analysis						
Inferior parietal lobule (40)	57	R	41	−41	39	4.53
Dorsolateral prefrontal cortex (8/9)	38	R	42	31	36	4.84
(C) Priming × Mode analysis						
Superior parietal lobule (7)	27	L	−13	−65	54	4.88
Dorsolateral prefrontal cortex (8/9)	21	R	40	28	36	5.02

Brodmann areas are depicted in parentheses. Cluster size (number of voxels), laterality (right and left hemisphere), and t-score are also given. The stereotaxic coordinates of the peak of the activation are given to Talairach space.
* $P<0.005$, 20 contiguous voxels.

repeated-measures ANOVA with Prime (IR and C) and Mode (ON and NO) as within-subject factors was performed. The main effects Priming [$F(1,11)=0.37$, $P=.557$] and Mode [$F(1,11)=0.27$, $P=.613$] were not significant. However, the interaction between Priming and Mode was significant [$F(1,11)=28.83$, $P<.001$] (Fig. 2C). This interaction provides support that the SPL is sensitive to the changes in bottom-up-induced competition. To explore the source of the interaction, we conducted ad hoc paired t-tests (Bonferroni-corrected) and found a significantly higher mean activation level for the IR compared to the C condition for the onset mode [$t(11)=-2.88$, $P<.05$] but not for the no-onset mode [$t(11)=2.42$, $P>.05$].

3. Discussion

In this study, we used event-related fMRI to investigate the neural mechanisms of spatial attentional selection in a location-based NP task. The first goal of the study was to determine regions that are linked to the conflict resolution in situations, in which the selection bias puts the irrelevant information in the probe trial on a selection advantage over the target. First, we performed a conjunction analysis to identify brain areas that were commonly involved in conflict mechanisms that ensure accurate target selection, because target and distractor capture visual attention and compete for control of action in both IR and C trials independently of the presentation mode. A distributed network was engaged consisting of SPL (BA 7), ACC (BA 24), PCG (BA 3), and insula (BA 13). The activation patterns are consistent with recent fMRI studies on visual target selection (Coull and Nobre, 1998; Hazeltine et al., 2000; Pollmann et al., 2003).

Second, for the onset mode, we determined brain regions that are linked to the conflict resolution in which the selection bias puts the irrelevant information in the probe trial on a selection advantage over the target. We found a NP effect caused by inhibitory processes that are involved in target selection in the preceding prime trial and are still active in the subsequent probe trial (Houghton and Tipper, 1994; Tipper, 1985; Tipper and Cranston, 1985). This result is consistent with findings from other behavioral location-based NP studies for onset stimuli (Fischer and Hagendorf, 2006; Ruge and Naumann, 2006; Tipper et al., 1994; Wright et al., 2005). In contrast, no reliable NP effects were found for the no-onset condition of stimulus presentation. This selective occurrence of NP is in accordance with results of previous NP studies (Fischer and Hagendorf, 2006; Frings and Wühr, 2007; Houghton et al., 1996). Further, we contrasted the C with IR condition to resolve brain activations associated with the additional processing effort required to overcome the negative selection bias. Based on the results of Vink et al. (2005) we expected increased activation in the premotor regions. Instead we found increased activation in the fronto-parietal network, especially in the right DLPFC and right IPL going along with the expectations derived from the inhibition approach.

We suggest that differences in activation patterns may result from differences in the applied NP paradigms. For their size discrimination task, Vink et al. (2005) asked their participants to respond to one of four possible locations indicated by the larger of two circles. The IR condition included situations in which the irrelevant location of the smaller circle in the prime trial was occupied by the larger of the two circles in the subsequent probe trial with both circles (smaller circle in prime trial and bigger circle in probe trial) of equivalent sizes. We argue that such a discrimination task (Which of the two circles is larger?) does not represent a typical selection task in a conventional NP paradigm, which is usually based on the search of a pre-defined target item according to the instructed control setting. This might be an important aspect because one cannot tell whether the compensatory processes in motor areas, apparently responsible to overcome the inhibition tagged to the probe target location or its link to response mechanisms, is solely bound to this specific task demand.

Furthermore, in a discrimination task (e.g., Vink et al., 2005) both target and distractor locations had to be attended and only a direct comparison of the size stimuli in these locations determines the target item. Therefore, an event episode is created via binding of the stimulus (target position and response) (Hommel, 2004). Such binding results in an integration of distractor position to an inhibited response according to the stimulus–response (S–R) rules. The selection bias towards initial processing of the two circles did not help in determining the

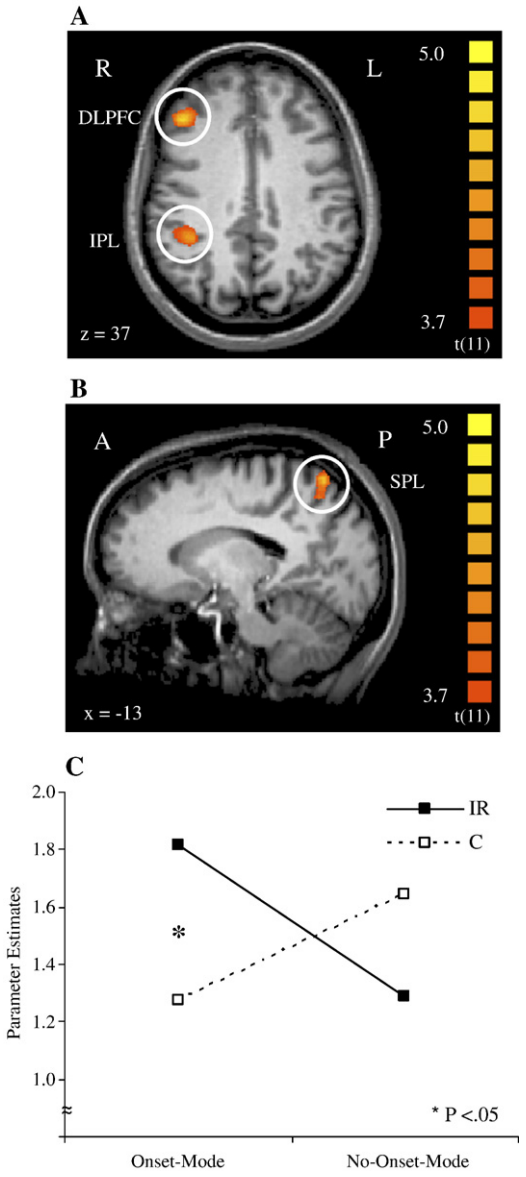

Fig. 2 – Activation map overlay on reference brain separated for (A) onset priming analysis and (B) interaction priming × mode analysis. (C) Parameter estimates (mean beta weights) for IR and C conditions derived from the functional region of interest of superior parietal lobule showed a significant interaction between the factor priming (IR and C) and Mode (onset and no-onset). IR, ignored repetition; C, control; DLPFC, dorsolateral PFC; IPL, inferior parietal lobule; SPL, superior parietal lobule.

appropriate response. Only the processing of the size information of both stimuli can lead to successful response selection. It is conceivable that in a task in which the identity of a target is revealed only through a direct comparison process, both potential response relevant items may be thoroughly processed and may eventually activate associated motor parameters. Therefore, the additional processing effort, required to overcome a negative bias, may indeed be located at the level of response code conflict which would predict the activation of premotor areas involved in preparing a response execution in the discrimination task.

For the onset priming contrast, two known sources of attentional control – the DLPFC and IPL – were activated to resolve the negative selection bias (Banich et al., 2001; Müller et al., 2003). In the IR condition, an inhibited distractor location in the prime trial obtains a negative bias that puts the distractor location in the subsequent probe trial at a competitive advantage over the target location. Therefore, besides the 'usual' competition between target and distractor, an additional source of conflict has to be resolved during the selection process in the IR condition (Houghton and Tipper, 1994). Based on the selection inhibition approach, additional processing effort is necessary to resolve the negative biased selection (Houghton and Tipper, 1994; Lavie and Fox, 2000; Tipper, 2001). Processing in early vision is driven by salience and only later in the processing top-down factors play a key role (Theeuwes, 1992). We argue that a shift of attention to the target location is required after attention was captured by the distractor location. Shifts of attention occur more consistently with onset than no-onset presentation (Wühr and Kunde, 2006), because onset stimuli elicit stronger competition through irrelevant locations (Simon effect) than no-onset stimuli. The priority of the shift in attention is coded into a 'salience map', which combines bottom-up and top-down signals (Eltiti et al., 2005; Theeuwes et al., 2001) and involves interacting bottom-up and top-down attentional control mechanisms in the fronto-parietal network (Corbetta and Shulman, 2002; Hopfinger et al., 2000; Nobre et al., 1997; Yantis et al., 2002). Specifically, we argue that the DLPFC serves as a top-down control needed to overcome the bias in selecting task-relevant information when task irrelevant information competes for priority in processing (Banich et al., 2000b; Banich et al., 2001; Hopfinger et al., 2000; Weissman et al., 2004). Such an increased PFC activity was also found in the location NP study by Wright et al. (2005). Moreover, Egner and Hirsch (2005) reported activity in the right DLPFC using an identity-based NP paradigm. The authors described the NP effect by an episodic memory retrieval mechanism and its neural localization (Henson et al., 1999; Neill et al., 1992). However, we linked the DLPFC activity to the source of attentional control, because the episodic memory retrieval cannot explain the additional activation in parietal cortex. Memory retrieval would have lead to a response competition in any condition that includes a target and distractor and parietal cortex activations would have been expected to initiate possible responses on the basis of learned stimulus–response associations (Bunge et al., 2002; Schumacher and D'Esposito, 2002; Sohn et al., 2003). However, since a response selection is oblique in both, the IR and C trials, we should not have found an IPL activation for the onset priming contrast.

Instead, we argue that the DLPFC modulates the activity within the IPL region to ensure task appropriate processing (Banich et al., 2000a; Milham et al., 2001). In particular, a meta analysis showed that the DLPFC is critically involved in top-down control of shifts in attention (Wager et al., 2004). We argue that the IPL was activated, because a shift in attention to the target location was required after attention was captured by the distractor location (Müller et al., 2003). Recent evidence supports our interpretation showing that the IPL is associated with redirecting attention after a stimulus is presented to a certain target location with a transient attention shift to locations in

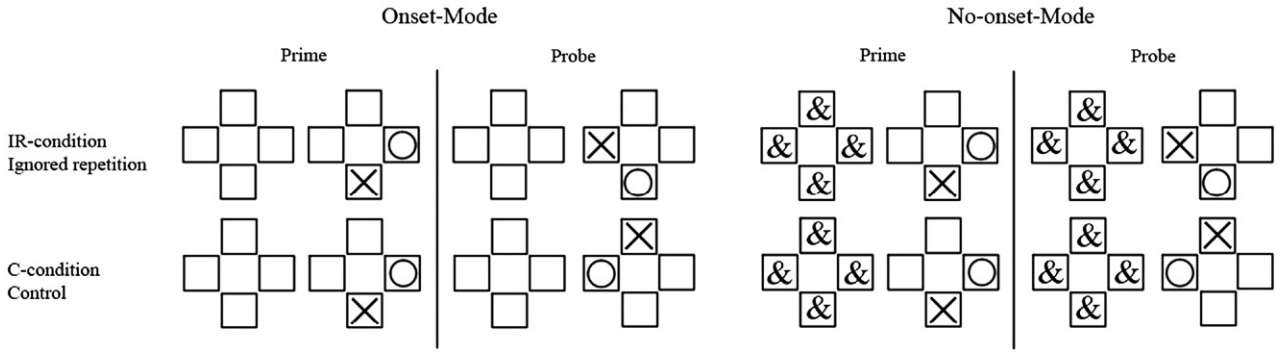

Fig. 3 – Graphical outline of the four conditions. In the ignored repetition (IR) condition, the position of the prime-distractor (X) is the position of the probe-target (O). In the control (C) condition, all stimuli change their position. IR and C condition appear either in onset or no-onset mode. The relevant response dimension was the location of the target.

space (Yantis et al., 2002). Further support is provided by a cueing study showing that the IPL activation is related to shifts of attention back to the target after attention is captured by distractors (Serences et al., 2004).

The second goal of the study was to demonstrate how the conflict resolution is affected by variation in bottom-up-induced competition. Therefore, target and distractor were presented either as onset or no-onset stimuli. Based on differences in attention control for onset and no-onset stimuli (Eltiti et al., 2005) we argued that the target selection is most efficient for no-onset stimuli (Fischer and Hagendorf, 2006). The NP effect disappeared in the no-onset mode and the behavioral results were supported by the imaging results. The C and IR conditions did not differ in their activation pattern, indicating that both conditions reflect the same underlying cognitive processes.

In our opinion, onset and no-onset stimuli differ in respect to the extent of bottom-up (stimulus-driven) competition involved in target selection. In the onset mode, target and distractor have a high salience and both stimuli capture visual attention automatically competing for target selection. In the no-onset mode, target and distractor have low salience and do not capture visual attention automatically. This leads to a reduced bottom-up competition, followed by reduced negative bias for the prime distractor location, and resulting in a reduced inhibitory mechanism for the target selection. Our results are in agreement with studies that have shown that onset stimuli trigger involuntary shifts of attention (Yantis and Hillstrom, 1994; Yantis and Nakama, 1998).

In addition, the interaction Priming × Mode analysis provided evidence that the SPL is sensitive to the changes in bottom-up-induced competition. Ad hoc paired *t*-tests indicated a significantly higher mean activation level for the IR compared to the C condition for the onset mode but not for the no-onset mode. Wojciulik and Kanwisher (1999) investigated general attentional mechanisms in posterior parietal cortex and proposed that posterior SPL is involved in the suppression of irrelevant distractors. Our data are in good agreement with this hypothesis that the SPL is specifically involved in suppression of distractors. We argue that such suppression is necessary for the conditions with onset stimuli because of the higher salience of the distractor. Further support for our interpretation is provided in a study by Pollmann et al. (2003), who showed that the function of the SPL is related to suppression of irrelevant distractors in visual marking. The authors reported an almost identical location in the SPL ($x=-7$, $y=-62$, $z=52$) to that which we found in the present study ($x=-13$, $y=-65$, $z=54$). Shomstein and Yantis (2004) have shown that SPL shows domain independent transient activity in top-down-regulated attentional processes during shifts of attention between locations, features, objects, and modalities. We suggest that SPL activity is related to forming the representation of an attentional priority map. This map indexes the current locus of attention. Additional experiments will be needed to further investigate this potential locally specific attentional modulation in parietal cortex (Serences and Yantis, 2007).

In conclusion, this study investigated the neural mechanism of spatial attention selection for onset and no-onset stimuli in a location-based NP task. We identified dissociable neural components needed to resolve the negative selection bias. The bottom-up-induced competition among stimuli in the target selection is stronger for onset than no-onset stimuli, and the superior parietal lobule was sensitive to the changes in bottom-up-induced competition. Moreover, the dorsolateral prefrontal cortex and inferior parietal lobe were activated to resolve the additional processing effort necessary to select the negatively biased target. Future comparative electrophysiological and human brain imaging studies may empirically address this potential locally specific attentional modulation in this fronto-parietal network by examining changes in the functional connectivity of its components.

4. Experimental procedures

4.1. *Subjects*

Participants consisted of twelve normal volunteers (mean ± SD, seven females, mean age 26.4 ± 4.1 years old, range 20–33) with graduate or postgraduate education level. Data from two additional participants had to be excluded prior to the statistical analysis ($N=1$, no response times recorded; $N=1$, head motion). All participants were strongly right-handed as determined from the Edinburgh Handedness Inventory (Oldfield, 1971). All volunteers had normal or corrected-to-normal vision, had no history of medical, psychiatric or neurological diagnoses, and were not taking medication. All participants gave informed consent and

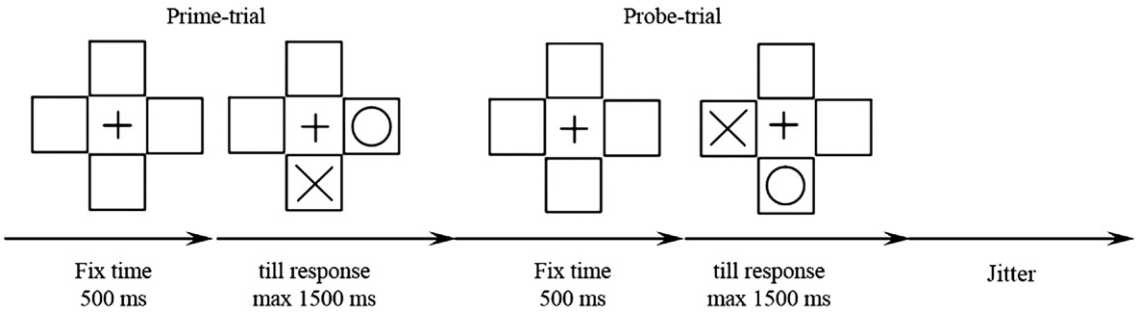

Fig. 4 – Task structure for a representative prime–probe-trial. Participants were asked to respond to the location of the prime- and probe-target with the corresponding button on the response pad.

the study was approved by the local research ethics committee at the Humboldt University, Campus Charité Mitte in Berlin, Germany.

4.2. *MRI*

Imaging was performed on a 1.5-T Siemens Vision whole-body scanner (Siemens, Erlangen, Germany) equipped with a standard circularly polarized head coil. Anatomical [T1-weighted 3D MP-RAGE (magnetization-prepared rapid acquisition gradient echo) sequence: TR, 9.7 ms; TE, 4.0 ms; flip angle, 12°; number of slices, 190; FOV, 256 mm; matrix size, 256×256; voxel size, 1×1×1 mm^3] and functional images [2D gradient EPI (echo-planar image) sequence: TR, 2 s; TE, 60 ms; flip angle, 90°; thickness, 5 mm; number of slices, 16; FOV, 210 mm; matrix size, 64×64] were acquired. During the experiment, 292 volume mosaic images were taken parallel to the anterior commissure–posterior commissure (AC–PC) line. The first four volumes were discarded to allow for T1 equilibration effects.

4.3. *Stimuli and activation tasks*

We employed a location-based NP paradigm with a prime–probe-trial design adapted from Tipper et al. (1994) (Fig. 3). Stimuli consisted of four black squared placeholders (side length 20 mm) equally placed around a fixation cross (left, right, bottom, top) in front of a gray background. In the squares, an 'O' and an 'X' in black color could appear. Participants were instructed to respond as quickly and as accurately as possible to the position of the target (O) and to ignore the distractor (X) at the same time. The four buttons on the response pad corresponded to the location of the placeholder (bottom, left, top, and right, respectively).

Four conditions were applied, defined through the type of stimuli and the location of the stimuli in a prime- and probe-trial. In the ignored repetition (IR) condition, the position of the prime-distractor became the position of the probe-target. In the control (C) condition, all stimuli changed their position, i.e., no relation exists between the targets and the distractors of the prime and probe trials. It served as a baseline that controlled for motor response and visual display. IR and C condition were displayed in two different modes. In the onset mode (ON), target and distractor appeared abruptly on the display. In the no-onset mode (NO), placeholders appeared in the beginning of a trial containing a mask (&) in each square. Prime–probe-trial combinations created trials that were presented in a pseudorandomized counterbalanced order. Stimuli in the prime and probe displays appeared in each of the four locations with equal probability. Altogether, the experiment consisted of 96 trials (24 per condition). The fMRI experiment lasted 12 min and response times and accuracy were recorded for each trial.

4.4. *Prime- and probe-trials*

Prior to scanning, participants were first trained on a separate set of stimuli to familiarize them with the experiment. Stimulus presentation was synchronized with the scanner pulses using the ERTS (Experimental Run Time System, Berisoft Cooperation, Germany, http://www.erts.de) software package running on an IBM computer. With a magnetically shielded LCD video projector, stimuli were back-projected onto a translucent screen. Participants viewed the screen by a mirror system attached to the head coil. Head motion was restricted using foam pads placed around the participants' head. Participants made finger-press responses on a hand-held fiber-optic response pad with their right index finger resting in the middle of the pad.

Each prime–probe-trial proceeded as follows (Fig. 4). Each trial lasted a maximum of 3000 ms. A fixation cross and four empty square placeholders appeared as potential locations of the prime-stimuli. After 500 ms target (O) and distractor (X) appeared within the squares. Participants had to respond to the location of the prime-target with the corresponding button on the response pad. Response to the prime-trial automatically started the probe-trial. Fixation cross and placeholders appeared again and after 500 ms the probe-stimuli were presented. Participants again had to respond to the location of the probe-trial. This timeline allowed us to connect prime- and probe-trials as closely as possible and to distinguish them as a separate trial-combination from the following ones. If participants exceeded the maximum response time of 1500 ms, the trial continued and was taken as an error trial for the further analysis. In the no-onset mode, placeholders contained the symbols '&' in each position. All '&' symbols were replaced by stimuli or blank space, respectively. Stimulus presentation was event-related and trials were separated by a randomly assigned jittered interstimulus interval of 4 s (range: 2 s to 6 s).

4.5. *Data analysis*

Behavioral data analysis was carried out using SPSS (SPSS Inc., Chicago, USA, http://www.spss.com). Alpha was set to $P<0.05$ for

all behavioral analyses. Image analyses were performed using Brain Voyager 2000 and Brain Voyager QX (Brain Innovation, Maastricht, The Netherlands, http://www.BrainVoyager.com). The following data pre-processing steps were applied: slice scan time correction (using a 'sinc' interpolation technique), linear trend removal, temporal high-pass filtering to remove low-frequency nonlinear drifts of 3 or fewer cycles per time course, spatial smoothing [8 mm full-width at half-maximum (FWHM)], and 3D motion correction to detect and correct for small head movements by spatial alignment of all participants to the first volume by rigid body transformation. Estimated translation and rotation parameters were inspected and never exceeded 3 mm or 3°. Functional slices were coregistered to the anatomical volume using position parameters from the scanner and manual adjustment to obtain optimal fit and transformed into Talairach space (Talairach and Tournoux, 1988). To transform the functional data into Talairach space, the functional time series data of each subject was first coregistered with the subject's 3D anatomical data set and resampled to 3×3×3 mm^3 isotropic voxels resulting in a normalized 4D volume time course ('VTC') data. The Talairach transformation included two steps: (1) rotation of 3D data sets of each participant to align with stereotaxic axes by specifying manually the location of the AC, PC and two rotation parameters for midsagittal alignment; and (2) specification of extreme points of the cerebrum and scaling the 3D data sets into the dimensions of the standard brain of the Talairach space by using extreme points together with AC and PC.

Multisubject analyses using multiple linear regressions of the blood oxygen level-dependent (BOLD) response time course in each voxel were applied and two general linear models (GLM) corrected for first-order serial correlation were performed. First, a single factor design matrix was designed for the following four predictors: (a) ignored repetition for onset mode (IR_{ON}), (b) control for onset mode (C_{ON}), (c) ignored repetition for no-onset mode (IR_{NO}), and (d) control for no-onset mode (C_{NO}). Statistical models were fit for three linear contrasts, indicating the following. (1) Conjunction contrast ($IR_{ON} \cap C_{ON} \cap IR_{NO} \cap C_{NO}$). Independently of the presentation mode, target and distractor capture visual attention and compete for control of action in IR and C trials. To identify areas that were commonly involved in inhibitory mechanisms ensuring accurate target selection a conjunction contrast was performed. (2) Onset priming contrast $(IR > C)_{ON}$. The additional processing effort required to overcome the negative selection bias can be elicited by contrasting C with IR in the onset representation. (3) No-onset priming contrast $(IR > C)_{NO}$. Competition for selection is assumed to be low in the no-onset presentation and both C and IR should evoke equal activation patterns. Differences between both conditions can be revealed by contrasting C with IR. Second, a 2×2 factorial design matrix with the first factor Priming (IR and C) and the second factor Mode (ON and NO) was created. To reveal neural activity specific to the variation in the bottom-up-induced competition the interaction effect Priming×Mode was calculated.

Predictor time courses were adjusted for the hemodynamic response delay by convolution with a hemodynamic response function (HRF, delta 2.5, tau 1.25) (Boynton et al., 1996). For each participant, contrasts were calculated at every voxel in the brain between regression coefficients where the average contrast value for the group as a whole (n=12 participants) differed significantly from zero (random-effects analysis). Activations are reported at an uncorrected $P<0.005$ with a cluster size threshold of 20. Statistical images were overlaid onto Brain Voyager's single subject canonical T1 image in Talairach space. Brodmann areas (BA) were determined by using the Talairach Daemon Client software (Research Imaging Center, San Antonio, TX, http://ric.uthscsa.edu/).

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