Violation of Expectation: Neural Correlates Reflect Bases of Prediction

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Abstract

■ Setting perceptual expectations can be based on different sources of information that determine which functional networks will be involved in implementing preparatory top–down influences and dealing with situations in which expectations are violated. The goal of the present study was to investigate and directly compare brain activations triggered by violating expectations within two different task contexts. In the serial prediction task, participants monitored ordered perceptual sequences for predefined sequential deviants. In contrast, the target detection task entailed a presentation of stimuli which had to be monitored for predefined nonsequential deviants. Detection of sequential deviants triggered an increase of activity in premotor and cerebellar components of the ''standard'' sequencing network and activations in additional frontal areas initially not involved in sequencing. This pattern of activity reflects the detection of a mismatch between the expected and presented stimuli, updating of the underlying sequence representation (i.e., forward model), and elaboration of the violation. In contrast, target detection elicited activations in posterior temporal and parietal areas, reflecting an increase in perceptual processing evoked by the nonsequential deviant. The obtained results suggest that distinct functional networks involved in detecting deviants in different contexts reflect the origin and the nature of expectations being violated. ■

INTRODUCTION

In an attempt to understand general principles of brain functioning, researchers have, in recent years, presented numerous findings which support the general concept of a predictive brain (Bar, 2007; Raichle & Gusnard, 2005). In contrast to the classical view of the brain waiting for sensory input which it then processes and ultimately channels into action, the active account assumes that the brain is constantly predicting future events and comparing these predictions to outcomes regardless whether they occur in the sensory, cognitive, or motor domain. The benefits of anticipation have long been established in perception by numerous studies showing that it can, by preparing relevant sensory cortices for the expected stimulus, improve speed and accuracy of subsequent information processing and performance (Gómez, Vaquero, & Vázquez-Marrufo, 2004; Brunia, 1999). On the other hand, sequential organization of behavior, such as planning and executing either a sequence of movements (Tanji & Shima, 1994) or tasks (Koechlin, Corrado, Pietrini, & Grafman, 2000), as well as general planning ability, working memory, and other executive functions (Fuster, 2001; LaBerge, 1995), requires anticipatory processing. In a wider sense, our decisions and overall behavior are determined by ''prospection,'' an ability to simulate future events and their hedonistic and emotional consequences (Gilbert & Wilson, 2007; Herwig et al., 2007). Because anticipatory processing is inherent to many different levels and types of processes, it is not surprising that it is reflected in neural activity of different brain networks, for example, in changes of neuronal threshold in sensory cortices (Gómez et al., 2004) or in the existence of preparatory-set cells in the prefrontal cortex (Quintana & Fuster, 1999).

Numerous studies of sequential processing in both the motor (Ashe, Lungu, Basford, & Lu, 2006; Keele, Ivry, Mayr, Hazeltine, & Heuer, 2002) and perceptual (Hoen, Pachot-Clouard, Segebarth, & Dominey, 2006; Remillard, 2003; Rüsseler & Rösler, 2000) domains show that prediction greatly facilitates processing of temporally structured events characterized by a certain degree of regularity as indexed by, for instance, repetitive patterns of such events, predictability of their end state or observers' previous experience. Recent studies specifically addressing the neural correlates of active processing of attended perceptual sequences have shown that this process relies on the premotor and connecting parietal areas (Schubotz & von Cramon, 2002a, 2002b, 2002c, 2003) whose role can be compared to that in sequential motor planning. Because it is the task of the subject and not the nature of the stimuli which determines the involvement of the

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premotor system, Schubotz and von Cramon (2003) recently proposed that, just as in the domain of motor control, the role of this system in perceptual prediction reflects the establishment of forward models.

This view assumes that prediction is common to both motor and perceptual processes in which the brain can emulate expected events, regardless of whether these constitute sensory consequences of one's own actions in motor planning or expected sensory stimuli in perceptual prediction. This emulation is enabled by creation of internal models which, in their most general form, act as models of the body and environment (Grush, 2004). More specifically, it is supported by a class of internal models, namely, forward models which can use the collected knowledge from the environment, such as a trajectory of some already-moving object, for predicting its future behavior (Wolpert & Kawato, 1998; Miall & Wolpert, 1996). The correctness of predictions can be evaluated by comparing the incoming bottom–up information with top–down expectations following the presentation of stimuli, allowing the successfully predicted stimulus to be perceived more efficiently. On the other hand, presentation of an event violating expectations triggers a cascade of processes which have not been previously investigated in the context of forward models in perception. Although previous studies have investigated violation detection in the perceptual domain, they have mainly focused on detecting events which violate perceptual expectations related to individual stimuli that are not embedded in a temporally structured pattern, as for example within the classical oddball paradigm (Sutton, Braren, & Zubin, 1965).

Because no systematic comparison between the effects of deviant detection in different contexts has previously been conducted, the present study attempted to address this issue. Our main goal was to test whether detecting violations in different contexts recruits a common network reflecting similar processing or whether different task contexts lead to involvement of different brain areas which reflect bases of underlying predictive processes. Two task contexts chosen for this comparison induced different types of anticipatory processing on the basis of either the relations between the stimuli in the sequential task or the perceptual context of the trial in the nonsequential task. Using functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), we presented participants with visual sequences based on which they could form perceptual expectations about the upcoming stimuli. Participants' task was to indicate whether the second presentation of a sequence constituted an ordered repetition or not. Sequencing in this so-called serial prediction task (Schubotz, 1999) was explicit, purely perceptual, and based on the relational structure between the stimuli. Additionally, we used a target detection task in which participants were presented with random sets of six stimuli which needed to be monitored for predefined target stimuli defined by color (size no longer being a relevant dimension). Trials within this task contained the same amount of physical information as in the sequencing task, but did not require extraction and prediction of order of stimuli within the trial, making the relation between the stimuli irrelevant. Within both tasks, participants were occasionally presented with events that deviated from the standard context of the trial, either a violation of sequential order (''sequential deviant'') or a stimulus distinct from standard events in the trial (''nonsequential deviant'').

Thus, both tasks included the presentation of equivalently organized trials and required participants to attend during the stimulus presentation in order to be able to detect the potential deviant (for discussion about preattentional deviance detection, cf. Näätänen, Jacobsen, & Winkler, 2005; Escera, Alho, Schröger, & Winkler, 2000). However, because the nature and specificity of expectations within the two contexts were clearly different, we expected the involvement of rather distinct networks with only limited overlap in detecting different types of deviants. In particular, processing of sequential deviants was expected to engage some components of the ''standard'' sequencing network, primarily the medial and lateral premotor cortex, which is normally involved in processing temporally ordered, to-be-predicted perceptual events, with additional recruitment of areas reflecting increased attentional and working memory demands following deviation presentation. In contrast, we expected the presentation of a target stimulus to evoke activity in posterior temporal and parietal brain areas, which would be comparable to the pattern of results commonly reported in the oddball paradigm. This hypothesis was based on the similarity between the target detection task used within this study and the classical oddball paradigm, both of which include frequent presentation of standard stimuli among which occasional predefined targets are embedded (Sutton et al., 1965).

METHODS

Participants

Fifteen right-handed, healthy volunteers (8 men, 7 women; age = 22–31 years; mean age = 26.6 years) participated in the study. Their average laterality quotient (LQ) as assessed using the *Edinburgh Handedness Inventory* (Oldfield, 1971) was 94.9. All subjects gave informed consent for participating, after being informed about potential risks, and were screened by the physician of the institution. The experimental standards were approved by the local ethics committee of the University of Leipzig. Collected data were handled anonymously.

Procedure

Participants were instructed and underwent a training session before the main experiment. Because continuous

EEG data were simultaneously collected during the experiment, before the MRI session, the participants were mounted with electrode caps with sintered Ag/AgCl ring electrodes containing built-in 5 kΩ resistors. A high-input impedance amplifier, designed for recording in high magnetic fields (Brain Amps MR plus, Brain Products, Munich, Germany), was used for collecting the EEG data and was fixated beside the head coil. A rechargeable power pack placed outside the scanner bore was used to power the amplifier. More details regarding the EEG recording will not be supplied because the EEG data are outside the scope of this article.

During the main experiment, participants were lying supine on the scanner bed, with their right and middle fingers positioned on the response buttons. In order to prevent postural adjustments, the subjects' arms and hands were carefully stabilized by tape. In addition, arm, hand, and head motion was prevented by using form-fitting cushions. In order to attenuate scanner noise, participants were provided with earplugs.

Stimuli and Task

The stimulus material used in this study consisted of 12 circles with diameters ranging from 0.6° to 2.8° visual angle. Each trial included successive presentation of six stimuli with the duration of 500 msec without temporal gaps, preceded by a task cue with the duration of 500 msec and followed by a 1500-msec response period. During all other periods in the experiment, a fixation cross was presented at the center of the screen. Overall trial duration was 7 sec and, in order to improve temporal resolution, each trial occurred at four different offset points (0, 500, 1000, and 1500 msec) in relation to fMRI data acquisition (Josephs, Turner, & Friston, 1997). During the course of the experiment, the stimulus trials were interspersed with 32 empty trials, during which only a fixation cross was presented and no task was given to the participants. Stimuli were presented using Presentation 9.9 (Neurobehavioral Systems, San Francisco, CA).

Serial prediction (sequencing) and target detection tasks were presented in a mixed-trial design. At the beginning of each trial, subjects were informed about the upcoming task by a cue (blue square for the serial prediction and red square for the target detection task) preceding the stimuli. In the sequencing task, participants were instructed to attend to the size of the presented stimuli in order to extract and predict the repetitive pattern contained within them. The first three stimuli of each trial formed a sequence that the participants were instructed to remember, whereas the last three could represent either a full repetition or a violation of the original three-stimulus sequence. The pattern of violation was always the same and included reversal in the order of the second and third element of the original sequence. The participants' task was to indicate, in a forced-choice mode, whether a sequential violation occurred or not.

In the target detection task, participants were instructed to attend to a random set of six stimuli in order to find a predefined target stimulus among them. Target stimuli were defined by color (stimuli with a lighter color than either the main circle or its outer rim) and participants' task was to indicate, in a forced-choice mode, whether a target was presented within the trial or not. Target stimuli could be presented in any position within the trial so that each position had the same probability of containing the target stimulus. This manipulation assured that the participants would attend to all stimuli during the target detection trials, which was accomplished by the nature of the task in the serial prediction trials.

Across all trials, the order of stimuli was pseudorandomized. The probability of each stimulus and that of transitions between stimuli was balanced with an additional constraint stating that two neighboring stimuli within each trial always had to be dissimilar in size (separated by at least two intermediate circle sizes). This constraint was added on the basis of results from a behavioral pilot study, which showed differences in task difficulty with nonrestricted randomization.

In order to avoid any motor contributions to the tasks, participants' response was always required after the end of each sequence. The deviant events (sequential or nonsequential) within the context of each task were presented in 50% of all trials. No feedback was given after the trials. Overall, four types of trials could be differentiated within the experiment: *ordered sequences*, *violated sequences*, *no-target trials*, and *target trials* (Figure 1). Eighty trials of each type were used which, together with the 32 empty trials, amounted to a total of 352 trials presented in the course of the experiment.

Data Acquisition

Imaging was performed at 3 T on a Siemens Trio system (Erlangen, Germany) equipped with a standard bird-cage coil. Immediately prior to the functional experiment, a set of two-dimensional anatomical images was acquired for each subject using an MDEFT sequence (256 × 256 pixel matrix) (Norris, 2000; Ugurbil et al., 1993). Additionally, in order to improve the localization of activation foci, high-resolution whole-brain images using a T1-weighted, three-dimensional segmented MDEFT sequence were acquired for the participants in a separate session. This volume dataset with 160 slices and 1 mm slice thickness was standardized to the Talairach and Tournoux (1988) stereotactic space. Functional images in-plane with the anatomical images were acquired using a gradient-echo, echo-planar imaging (EPI) sequence with an echo time (TE) of 30 msec, a flip angle of 90°, and a repetition time (TR) of 2000 msec. Twenty-six functional slices were

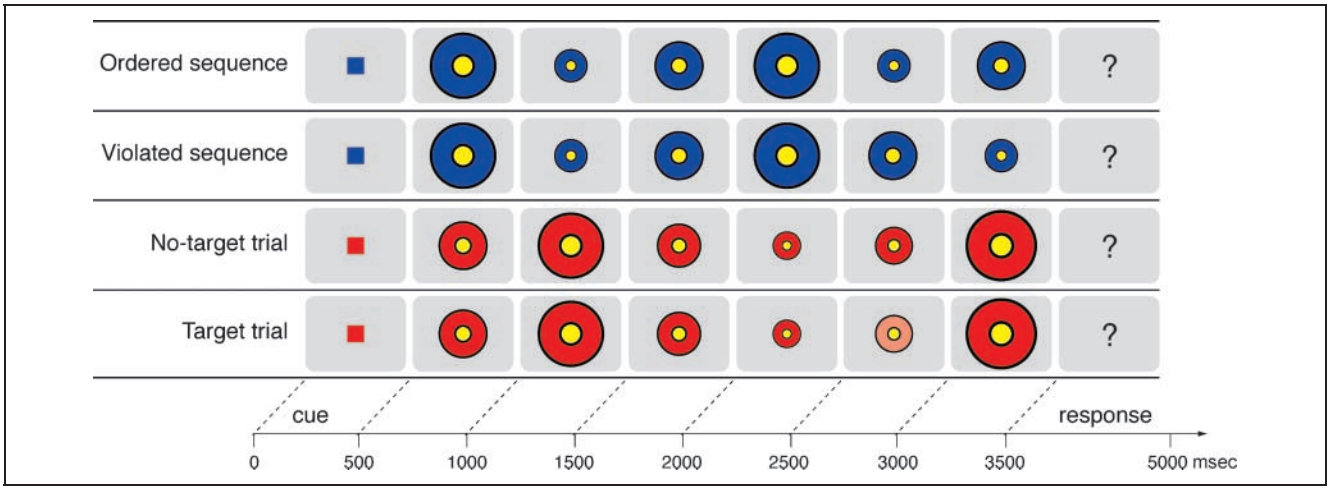

Figure 1. Schematic examples of four types of trials. Each trial started with a cue and was followed by six stimuli, all presented successively with the duration of 500 msec and without a temporal gap. The response was given at the end of each trial. In *ordered sequences*, the first three stimuli represented a sequence which was then correctly repeated. *Violated sequences* also started with the sequence of three stimuli which was followed by the presentation of a sequential deviant (reversed order of second and third stimuli of the original sequence). *No-target trials* included the presentation of six standard stimuli of the same color and randomly varied size. *Target trials* included presentation of five standard stimuli among which one nonsequential deviant was embedded (here a circle with lighter red color when compared to the standard circles presented at the fifth position within the trial).

acquired parallel to the bicommissural plane (AC–PC) (thickness = 4 mm, interslice gap = 0.4 mm) covering the whole brain. In order to visually monitor the simultaneously recorded EEG signal, acquisition of slices within the TR was arranged so that the slices were all rapidly acquired during the first 1800 msec, followed by a 200-msec period of no acquisition to complete the TR. The matrix acquired was 64 × 64 with a field of view of 192 mm, resulting in an in-plane resolution of 3 × 3 mm. A total of 1247 volumes was acquired.

Data Analysis

MR data processing was performed using the software package LIPSIA (Lohmann et al., 2001), which contains tools for preprocessing, coregistration, statistical evaluation, and visualization of fMRI data. Functional data were motion-corrected off-line with the Siemens motion correction protocol (Siemens, Erlangen, Germany). To correct for the temporal offset between the slices acquired in one scan, a cubic-spline interpolation was applied. A temporal high-pass filter with a cutoff frequency of 1/70 Hz was used for baseline correction, removing low-frequency drifts in an fMRI time series (frequencies due to global signal changes). Spatial Gaussian smoothing was applied using a Gaussian filter with 5.65 mm full width at half maximum.

To align the functional data slices with a 3-D stereotactic coordinate system, a rigid linear registration with six degrees of freedom (3 translational and 3 rotational parameters) was performed. The parameters were acquired on the basis on MDEFT and EPI-T1 slices to achieve an optimal match between these slices and the individual 3-D reference dataset. Each transformation matrix was subsequently transformed to a standard Talairach brain size (x = 135, y = 175, z = 120 mm; Talairach & Tournoux, 1988) by applying linear scaling. Finally, the normalized transformation matrices were applied to the acquired functional slices in order to align them with the stereotactic coordinate system. Transformation was performed using trilinear interpolation, thus generating data with a spatial resolution of 3 × 3 × 3 (27 mm^3).

The statistical evaluation was based on a least-squares estimation using the general linear model for serially autocorrelated observations (random effects model). In the first stage, autocorrelation parameters were estimated from the least squares residuals using the Yule–Walker equations and were used to ''whiten'' the data and the design matrix. In the second stage, the linear model was re-estimated using least squares on the whitened data to produce estimates of effects and their standard errors (Worsley et al., 2002). Two separate design matrices were used for modeling the data, both consisting of onset vectors for correct trials within each of four different sequence types, with additional vectors for response periods and empty trials. In order to address the process of deviant detection within trials, design matrix with events time-locked to the presentation of the deviant was used: In the serial prediction task, this was always the fifth element within a trial, whereas in the target detection task, the exact position of the target was identified for each individual trial and then used for setting the event onset (for both target and no-target trials all positions within the trial were

equally often used for setting the event onsets in order to parallel the two conditions). Additionally, in order to explore the process of recognizing and predicting the sequential patterns of perceptual stimuli, design matrix with events time-locked to the presentation of the first stimulus within each sequence was used. Within both types of matrices, the events related to each sequence type were modeled with the same duration. The design matrices were generated using a synthetic hemodynamic response function (Friston et al., 1998; Josephs et al., 1997) and its first derivative. Contrast images, namely, estimates of the raw score differences between specified conditions, were generated for each subject. Single-participant contrast images were entered into a second-level random effects analysis for each of the contrasts. The group analysis consisted of one-sample *t* tests across the contrast images of all subjects that indicated whether observed differences between conditions were significantly different from zero ($z > 3.09$, $p < .001$, uncorrected) (Holmes & Friston, 1998). In order to ensure an overall image-wise false-positive rate of $p < .05$, in direct contrasts between conditions, a region was considered significant only if it contained a cluster of 15 or more contiguous voxels (McAvoy, Ollinger, & Buckner, 2001; Forman et al., 1995).

RESULTS

Behavioral Performance

Behavioral performance was assessed primarily by error rates. One participant was excluded from further analysis due to below-chance level performance in the sequencing task and all subsequent analysis were performed on the data from 14 subjects. A repeated measures analysis of variance, with 2 two-level factors *task* (sequencing, target detection) and *deviant* (deviant present, deviant absent), was used in order to compare the performance in different tasks. The results revealed no statistically significant main or interaction effects [Task: $F(1, 13) = 0.34$, $p = .57$; Deviant: $F(1, 13) = 1.26$, $p = .28$; Task × Deviant: $F(1, 13) = 0.01$, $p = .98$], which suggests no differences in difficulty between the tasks (average error rates for different trial types were 9–14%).

Because the response was given only at the end of each trial, the reaction time measures could not be unequivocally interpreted and were calculated only as a secondary indicator of participants' performance. Average reaction time was 512 ± 26.5 msec for *ordered sequences*, 538 ± 23.6 msec for *violated sequences*, 590 ± 28.3 msec for *no-target trials*, and 536 ± 23.3 msec for *target trials*. Further analysis of reaction time data revealed a statistically significant main effect of task [$F(1, 13) = 6.85$, $p = .02$] and the interaction Task × Deviant [$F(1, 13) = 25.7$, $p < .001$], whereas the main effect of deviant was not significant [$F(1, 13) = 1.16$, $p = .30$].

MRI Data

Effects of Serial Prediction

Brain areas with significantly higher blood oxygenation level-dependent (BOLD) response during the serial prediction task in comparison to the target detection task are listed in Table 1. Only sequences without deviant stimuli that were correctly responded to by participants were used for this comparison (contrast ordered sequence vs. no-target trial). Activations were distributed bilaterally, with a somewhat more pronounced left bias, and included an activation encompassing the superior portion of the ventral premotor cortex (supPMv) and the frontal operculum (FOP). Further activations included the dorsal part of the premotor cortex (PMd), encompassing frontal eye fields (FEF) and the supplementary motor area (SMA). Furthermore, the inferior and superior parietal lobules (IPL and SPL) and the left paramedian portion of the posterior cerebellum were activated (Figure 3A).

Effects of Detecting Sequential Deviants

Brain areas with significantly higher BOLD response during the presentation of sequential deviants in comparison to the presentation of sequence repetitions are listed in Table 2 (contrast violated sequence vs. ordered sequence). The majority of activations were distributed dominantly within the right hemisphere, encompassing several lateral premotor and prefrontal areas. Additional strong foci of activations included the right frontal opercular cortex, the pre-SMA, and bilateral paramedian and lateral portions of the posterior cerebellum (Figure 2A, Figure 3A).

Effects of Detecting Nonsequential Deviants

Brain areas with significantly higher BOLD response during presentation of nonsequential deviants in comparison with trials containing only standard stimuli in the target detection task are listed in Table 2 (contrast target trial vs. no-target trial). Although distributed bilaterally, activations were somewhat more pronounced in the left hemisphere, with the exception of frontal activations which showed a right bias. The majority of activations were located within parietal and temporal lobes, encompassing the middle and inferior temporal gyri (bilateral MTG and ITG), the left IPL, the neighboring supramarginal gyrus (left SMG), and the bilateral SPL, with some additional medial, frontal and subcortical activation foci (Figure 2B).

Comparison between Sequential Violation and Target Detection Process

A conjunction analysis of contrasts revealing the specific activations related to deviant detection in the two tasks

Table 1. Anatomical Brain Area, Talairach Coordinates (x, y, z), Maximal Z-Score, and Size of Significant Activations

		Talairach Coordinates				
Brain Region (BA)	*Hem*	x	y	z	*Max Z-Score*	mm^3
Ordered Sequence vs. No-target Trial						
SMA	L	−2	−6	54	3.38	621
PMd	L	−38	−6	48	4.12	2970
	R	25	−12	60	3.71	2295
MFG (8)	R	31	12	48	4.72	
PMv	R	49	0	24	3.53	810
IFG (44)	R	40	12	15	4.02	
PMv	L	−44	3	26	3.11	
IFG (44)	L	−50	6	15	4.02	2538
IFG (45/47)	L	−53	18	0	3.59	
FOP	L	−41	0	3	4.14	
IPL (39/40)	R	43	−48	54	3.82	3051
	L	−50	−36	48	4.23	7398
SPL (7)	R	16	−69	57	3.95	
SPL/PCU (7)	R	10	−66	57	3.93	4077
	L	−8	−57	54	3.77	
OGs (19)	R	37	−75	33	4.25	675
MTG (21/37)	R	46	−51	9	4.19	1080
ITG (37)	R	55	−48	−9	4.43	432
CU (18)	L	−2	−96	15	4.00	945
CE	L	−17	−69	−21	3.43	432
GP	R	16	−6	15	4.01	567

PMd = dorsolateral premotor cortex; PMv = ventrolateral premotor cortex; SMA = supplementary motor area; MFG = middle frontal gyrus; IFG = inferior frontal gyrus; FOP = frontal operculum; IPL = inferior parietal lobule; SPL = superior parietal lobule; MTG = middle temporal gyrus; ITG = inferior temporal gyrus; PCU = precuneus; CU = cuneus; OGs = superior occipital gyrus; CE = cerebellum; GP = globus pallidus; BA = Brodmann's area.

(violated vs. ordered sequence and target trial vs. no-target trial) was performed in order to identify whether any common brain areas would be involved in both types of deviant detection. The results from this analysis indicate common engagement of the superior frontal gyrus (Brodmann's area [BA] 8; coordinates: $x = 7$, $y = 24$, $z = 57$; max Z-score: 3.39) in detecting both types of deviants (Figure 3B).

DISCUSSION

The present study explored and compared brain correlates of processing violations in ordered stimulus sequences (sequential deviants) and predefined targets in unordered stimulus sequences (nonsequential deviants), with the attention of participants always being directed to the presented stimuli. The obtained results suggest that these two types of processes are quite distinct as they show very limited overlap in the underlying brain activations. Detection of sequential deviants triggered activations dominated by right lateralized premotor and prefrontal areas, whereas target detection evoked primarily bilateral responses within parietal and temporal cortices. This pattern of results can be related to the differences between the characteristics of the expectations (relational vs. nonrelational) formed within the two tasks and the nature of the deviants presented within them.

Detecting Sequential Violations: Enhancement in Components of the Standard Sequencing Network

Presenting sequential violations triggered an increase of activation in the lateral and medial premotor cortex and the cerebellum, a subset of brain areas classically

Table 2. Anatomical Brain Area, Talairach Coordinates (x, y, z), Maximal Z-Score, and Size of Significant Activations

		Talairach Coordinates				
Brain Region (BA)	*Hem*	*x*	*y*	*z*	*Max Z-Score*	*mm³*
Violated vs. Ordered Sequence						
Pre-SMA	R	4	15	48	4.63	2403
PMv	R	43	3	39	4.78	
IFG (44)	R	46	18	21	4.17	7425
MFG (9/46)	R	49	21	36	4.84	
	R	46	36	18	4.23	
IFG (47)	R	46	36	−6	3.33	405
MFG (8/9)	L	−38	24	42	3.98	675
FOP	R	34	24	−3	4.34	1566
CE	L	−20	−75	−18	4.31	2997
	R	22	−75	−21	4.72	2214
THA (MDN)	L	−5	−15	3	3.61	702
	R	4	−6	6	3.14	
Target-trial vs. No-target Trial						
SFG (10)	R	16	54	18	4.23	486
SFG (8)	R	4	27	54	4.48	1890
pCG (31)	R	7	−36	39	4.34	567
SPL (7)	L	−11	−72	54	3.71	459
	R	10	−66	57	4.53	4752
IPL (40)	L	−50	−39	48	4.05	
SMG (39/40)	L	−53	−48	36	4.75	12231
MTG (21/37)	L	−53	−57	6	4.28	
ITG (21/37)	L	−50	−42	−9	4.34	
MTG (21/37)	R	49	−48	0	4.24	4185
ITG (37)	R	52	−39	−15	4.98	
PUT	L	−29	9	3	3.95	1863
GP	R	19	−3	−3	4.12	1215

pre-SMA = presupplementary motor area; THA = thalamus; MDN = medial dorsal nucleus; SFG = superior frontal gyrus; SMG = supramarginal gyrus; pCG = posterior cingulate gyrus; PUT = putamen; for other abbreviations, see Table 1.

considered sensorimotor (Wise, 1985), which have in recent years also been implicated in a much wider scope of cognitive processes (Chung, Han, Jeong, & Jack, 2005; Blackwood et al., 2004; Schubotz & von Cramon, 2003; Rizzolatti, Fogassi, & Gallese, 2002; Jordan, Heinze, Lutz, Kanowski, & Jäncke, 2001). As evident from former studies and replicated in the present study when contrasting sequencing and target detection task, these areas also support regular sequence processing (for an overview, see Schubotz & von Cramon, 2003). Generally, sequence processing can be taken to reflect a number of different subprocesses, including the acquisition and storage of the sequence representation (i.e., forward model in computational terms) as well as the comparison of expected and presented stimuli. As the premotor–parietal network is known to subserve sensorimotor integration, it is plausible to suggest a similar division of functions within different components of this network in both motor planning and perceptual prediction (Schubotz, 2007). The interplay between these areas could be compared to the dynamics of parietal–premotor interactions which have been suggested to reflect maintenance of connections

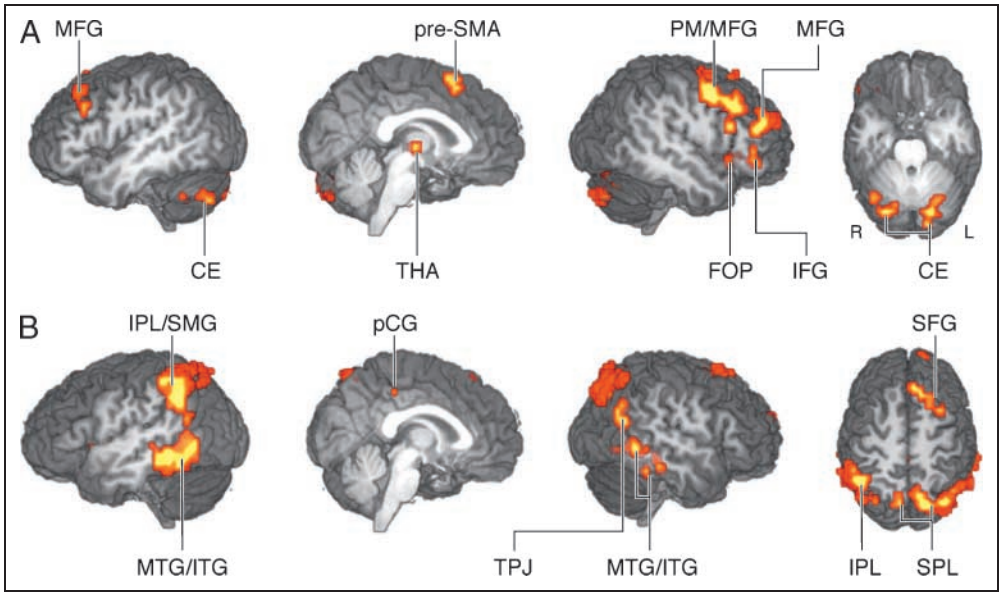

Figure 2. (A) Brain correlates of detecting sequential deviants (violated vs. ordered sequence). From left to right: left hemisphere from parasagittal section ($x = -46$); right hemisphere from sagittal midline section ($x = 0$) and parasagittal section ($x = 46$); axial section seen from below ($z = -22$; because of the changed view, left and right sides of the images are flipped and marked correspondingly). (B) Brain correlates of detecting nonsequential deviants (target trial vs. no-target trial). From left to right: left hemisphere from parasagittal section ($x = -52$); right hemisphere from sagittal midline section ($x = 0$) and parasagittal section ($x = 52$); axial section seen from above ($z = 53$). (A and B) Group-averaged statistical maps ($n = 14$) are superimposed onto an individual brain which was chosen for being the most similar to the average brain of all subjects participating in the experiment and scaled to the standard Talairach brain size (Talairach & Tournoux, 1988). For abbreviations of activated brain regions, see Tables 1 and 2.

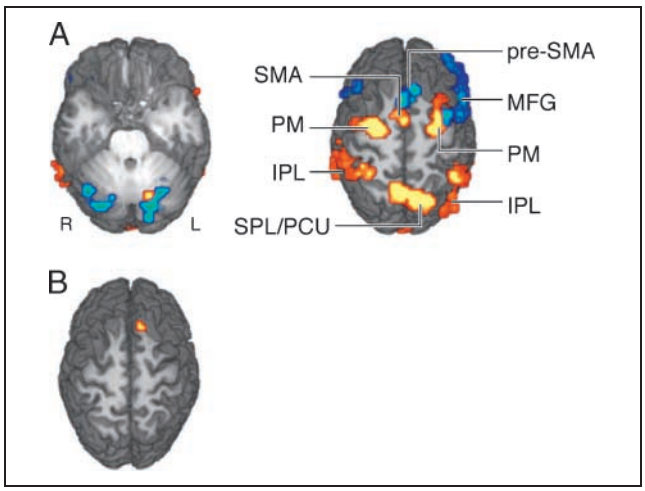

Figure 3. (A) The comparison of brain activations supporting regular sequence processing (red) and detection of sequential deviants (blue). Both processes engage parts of lateral and mesial premotor areas and the cerebellum. Left figure shows cerebellar activations in an axial sections seen from below ($z = -23$; because of the changed view, left and right sides of the images are flipped and marked correspondingly) and right figure shows axial section seen from above ($z = 56$). (B) Common brain activations supporting detection of sequential and nonsequential deviants revealed by the conjunction of contrasts violated versus ordered sequence and target trial versus no-target trial. Figure shows activation within the SFG seen from an axial section ($z = 57$). (A and B) Group-averaged statistical maps ($n = 14$) are superimposed onto an individual brain which was chosen for being the most similar to the average brain of all subjects participating in the experiment and scaled to the standard Talairach brain size (Talairach & Tournoux, 1988). For abbreviations of activated brain regions, see Tables 1 and 2.

between appropriate affordances and chosen movements in primate control of grasping (Fagg & Arbib, 1998) and visuomotor transformations in human grasping circuits (Jeannerod, Arbib, Rizzolatti, & Sakata, 1995).

Following this view, we suggest that the engagement of the lateral premotor cortex in perceptual prediction reflects establishment of a forward model upon which predictions about the upcoming stimuli in subsequent repetitions are formed and compared to the presented stimuli. This process is enabled by the constant interchange of information between lateral premotor and parietal areas, which have access to the perceptual input provided by visual cortical areas (Ungerleider & Haxby, 1994). Providing a description of all available stimulus features, the parietal cortex supports a complex stimulus representation which can be selected by the lateral premotor cortex for specific purposes, as determined by the current goal or task setting (Fogassi et al., 2005; Rizzolatti & Luppino, 2001; Fagg & Arbib, 1998; Rizzolatti, Fogassi, & Gallese, 1997). Therefore, because perceptual prediction relies on a single, task-relevant stimulus dimension (size), lateral premotor areas extract only this information and exert a top–down modulatory influence on the parietal areas, which become specifically tuned to that stimulus dimension.

The simulation of perceptual sequences needs to be coordinated and constantly updated by triggering the next entry in the forward model. This function can be subserved by the SMA and implemented by different types of neuronal activity supporting serial processing, which have been identified in the monkey medial

premotor cortex (Shima & Tanji, 2000). Although in the present study the engagement of SMA was sufficient for supporting ordered sequence processing, a mismatch between expected and presented stimuli, triggered by the presentation of a sequential deviant, additionally recruited the pre-SMA (cf. Picard & Strick, 1996, 2001). The activation of the pre-SMA has, in contrast to the SMA, previously been reported in more complex aspects of hierarchical processing, including sequence updating and switching (Bapi, Miyapuram, Graydon, & Doya, 2006; Kennerley, Sakai, & Rushworth, 2004; Jäncke, Himmelbach, Shah, & Zilles, 2000). It is thus plausible to suggest that the involvement of pre-SMA in processing sequential deviants in the present study reflects restructuring of the original forward model triggered by the mismatch between expected and presented stimuli. This restructuring was possible because the violation always included the reversal of order of the two last stimuli within the sequence, so the observers could have, after detecting the deviant, changed the underlying forward model and correctly predicted the last stimulus in the trial.

Both regular sequence processing and detecting sequential deviants additionally activated mainly the paramedian and also the lateral portions of the posterior cerebellum. The relevance of paramedian cerebellar areas, previously identified in supporting somatotopical representations of motor effectors (Grodd, Hülsmann, Lotze, Wildgruber, & Erb, 2001) in different aspects of perceptual prediction, can be related to the similar pattern of somatotopically organized premotor and connecting parietal activations, as suggested by the Habitual Pragmatic Event Map (HAPEM) account (cf. Schubotz, 2007). This involvement is in accordance with views suggesting an important role of the cerebellum in supporting fast, accurate, and rigid pairs of forward and inverse models and providing shortcut circuits or look-up tables for mappings initially developed by cerebral unsupervised learning modules (Kawato et al., 2003; Miall & Wolpert, 1996). Although this function is primarily crucial for motor control, the computational specificity of the cerebellum (Ramnani, 2006; Doya, 2000) suggests that it may also be exploited for cognitive functions to a certain extent. Indeed, lateral and mesial portions of the cerebellar cortex have been implicated in cognitive and motor tasks, respectively (Immamizu, Kuroda, Miyauchi, Yoshioka, & Kawato, 2003), and connectivity studies in primates show distinct patterns of connections between motor and prefrontal areas with cerebellar nuclei (Middleton & Strick, 2000), as well as different parts of the cerebellar cortex (Kelly & Strick, 2003). Following the internal model account which was introduced earlier, we suggest that the cerebellar activation in perceptual prediction reflects generating a prediction about the change in sensory input (i.e., corollary discharge or expected reafference) on the basis of the information provided by the pre-SMA (i.e., efference copy). Therefore, the cerebellum mediates the top–down influences from the pre-SMA into specific perceptual and proprioceptive expectations within the parietal cortex. Additionally, it is possible that the proposed cerebellar role could be restricted to conditions in which expectations can be strictly specified at the level of individual stimuli, similar to the conditions in which the cerebellum is exploited as a ''motor trainer'' (Davidson & Wolpert, 2005).

In interpreting the engagement of components of the ''sequencing network'' in detecting sequential deviants, we have repeatedly referred to the internal model account, primarily because it provides the most complete account of the obtained results. This framework has previously been suggested for the motor domain in which an internal (forward) model is used to predict the sensory consequences of movements on the basis of the motor command (Blakemore, Wolpert, & Frith, 2000). However, in line with the suggestion that there is ''no theoretical reason to drag a conceptual distinction between anticipating a perceptual event or planning an action'' (Hommel, Müsseler, Aschersleben, & Prinz, 2001, p. 860), we suggest that the prediction of temporally structured events is equivalently organized regardless whether these occur in the perceptual or the motor domain. It needs to be emphasized, however, that the conducted experiment did not compare different proposed models for either sequence processing or detection of sequential violations, and so the proposed interpretations are partly speculative.

Detecting Sequential Violations: Engagement of Additional Areas

In addition to increasing the activity within areas supporting regular perceptual prediction, presentation of sequential deviants also evoked activations within brain areas outside the ''standard'' sequencing network. This primarily included the dorsolateral prefrontal cortex (dlPFC, lateral BA 9 and 46), a region which is implicated in working memory tasks, which require monitoring and manipulation (and not the pure maintenance) of information (Petrides, 2005). The obtained results also indicate involvement of the ventrolateral prefrontal cortex, namely, the inferior frontal gyrus (BA 44 and 47), which is suggested to support active selection, comparison, and judgment of memorized information (Petrides, 2005). In accordance with these suggestions, the joint activation of lateral prefrontal areas in the present study may reflect a controlled process of verification of sequence regularity and active rearrangement of stimuli constituting the sequence following violation detection. In contrast, such manipulation of information was not required in regular sequence processing, which could therefore be subserved by the parietal–premotor network. Note that this does not imply that the representation of the sequence is initially stored within the dlPFC because it could be provided through connections between this

area and the lateral premotor cortex or the pre-SMA (Lu, Preston, & Strick, 1994). The involvement of lateral prefrontal areas in violation detection primarily reflects the need for cognitive control (Wood & Grafman, 2003) and is not, like the contribution of the pre-SMA, the lateral premotor cortex, and the cerebellum, an extension of the initial involvement in supporting regular sequence processing.

Processing sequential deviants additionally activated the right anterior FOP, an area whose coactivation with the dlPFC has previously been related to memory retrieval (cf. Lepage, Ghaffar, Nyberg, & Tulving, 2000). We suggest that the engagement of the FOP in the present study signals the occurrence of a mismatch between perception and expectations. This is in line with results showing the activation of this area in processing violations of expectations related to one's own performance (Klein et al., 2007; Ullsperger & von Cramon, 2001) or to rule-defined events within the context of artificial grammar (Friederici, Bahlmann, Heim, Schubotz, & Anwander, 2006). However, a more detailed specification of this functional contribution cannot be provided by the current data and needs to be explored in further studies.

Most activations evoked by sequential violation detection were strongly right lateralized, which can be related to previous results showing a right hemispheric bias in target or violation detection (Bledowski et al., 2004; Huettel, Mack, & McCarthy, 2002). Tervaniemi et al. (2000) suggested that right dominance may be specific to short-term violations of complex patterns requiring substantial need for information retrieval, which has also been suggested to be more lateralized to the right cerebral hemisphere (Krause et al., 1999; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994). Furthermore, numerous studies have shown that increasing processing load within a task often triggers an increase in activity within the right hemisphere, in contrast to the left which is more important in supporting the initial processing requirements (e.g., Dräger et al., 2004; Slotnick, Moo, Tesoro, & Hart, 2001).

Detecting Target Stimuli

The target detection task, as designed within the present study, is similar, but not completely equivalent, to a classical oddball paradigm which entails a presentation of a train of frequent, standard stimuli in which randomly distributed infrequent events are embedded (Sutton et al., 1965). The similarity of the requirements within two tasks was reflected in the underlying brain activations. The majority of activations obtained in contrasting target (i.e., nonsequential deviant) with no-target trials were bilateral within parietal and temporal lobes, particularly encompassing the MTG and ITG, the temporoparietal junction (TPJ), the IPL, the SMG, and the SPL.

This network is highly similar to that identified by studies which used the classical oddball task and consistently reported that successful target detection requires the involvement of parietal (Brázdil et al., 2005; Bledowski et al., 2004; Mulert et al., 2004; Ardekani et al., 2002; Clark, Fannon, Lai, Benson, & Bauer, 2000; McCarthy, Luby, Gore, & Goldman-Rakic, 1997) and temporal areas (Stevens, Calhoun, & Kiehl, 2005; Kiehl, Laurens, Duty, Forster, & Liddle, 2001; Stevens, Skudlarski, Gatenby, & Gore, 2000; Linden et al., 1999; Opitz, Mecklinger, Friederici, & von Cramon, 1999; Yoshiura et al., 1999). In an attempt to provide a functional account of these findings, Stevens et al. (2000) suggested that bilateral SMG and IPL activations may reflect an amodal target detection network involved in early working memory processing. Alternatively, the regions in the parietal cortex around the intraparietal sulcus, in the SPL, the IPL, and the precuneus, have been related to directing attention either to spatial locations or toward visual features or objects (Nobre, 2001). This functional interpretation is in line with processing requirements in the current study. In particular, elaborate perceptual processing of the predefined targets was needed as they were not perceptually salient or identical across all trials in the experiment. A very pronounced involvement of bilateral posterior parieto-temporal areas in this context can be related to the suggestion from Kiehl et al. (2001), who argued that the involvement of posterior brain regions in detecting predefined targets is usually less pronounced when compared to the detection of novel stimuli, which require more visuospatial processing by areas supporting object recognition, spatial attention, color, and form processing. Although the targets defined within the present study were clearly task relevant, they were, at least to some degree, perceptually novel which is reflected in the obtained findings.

In addition to the posterior cortical areas, our results indicate engagement of the dlPFC, mostly in the right superior frontal gyrus (SFG) with smaller contribution of the middle frontal gyrus (MFG), which is in line with results from previous studies (Casey et al., 2001; Stevens et al., 2000). The lateral prefrontal areas have often been reported in target detection studies and suggested to reflect semantic processing of identified deviants (Opitz et al., 1999) or orientation to rare stimuli (Kiehl et al., 2001). However, although the involvement of these areas in target detection is rather consistent, the extent of their activation is highly dependent on task demands (Kiehl et al., 2001), the degree of stimulus novelty (Kirino, Belger, Goldman-Rakic, & McCarthy, 2000), target probability (Casey et al., 2001), or degree of postdetection elaboration of the stimulus (Opitz et al., 1999).

Comparison between Different Types of Expectation Violations

The results of the presented study indicate involvement of distinct networks in detecting different types of

events deviating from a standard context defined by stability or continuity of presented events. While requiring comparable perceptual and attentional engagement, the two tasks differently defined the standard context, basing it on structural/relational properties of the stimuli in the sequencing task in contrast to their perceptual similarity in the target detection task. The expectations regarding the incoming stimuli in the sequencing task could be very clearly defined and restricted to a specific stimulus which, according to the underlying internal model, was expected to continue the perceptual sequence. In contrast, the expectations in the target detection task, which primarily reflect priming of the standard stimuli enhanced by their frequent presentation, did not have the same degree of specificity because the stimuli were defined as targets or standards on the basis of one stimulus feature and not identity. Thus, although both types of expectations reflect top–down tuning of the perceptual areas waiting for the most probable stimulus within the predefined context, they differ in their specificity, type, and origin. These differences are reflected in the obtained results showing that the violation of different types of expectations evoked different brain responses. This pattern of results was additionally corroborated by a limited overlap of brain areas, which participated in both processes as revealed by the conjunction analysis of the activations evoked by sequential and nonsequential deviants. This overlap was restricted to the medial portion of the SFG and probably reflected increased uncertainty triggered by the unexpected deviant or attentional shift following deviant detection. Previous studies showing the involvement of this area in processing events under uncertainty and error evaluation (Volz, Schubotz, & von Cramon, 2003, 2006) provide support for this interpretation.

Concluding Remarks

The obtained results suggest that brain correlates of detecting different types of deviants reflect the nature of expectations being violated (relational expectations on the basis of a forward model vs. nonrelational expectations set by context of standard stimuli), which are closely related to the nature of the deviant (sequential vs. nonsequential). Sequential deviants triggered an increase in activity of certain components of the sequencing network which we suggest to reflect detection of a mismatch in the comparison between the expectations based upon the underlying forward model and the presented stimuli followed by restructuring of the model. Additional engagement of areas not supporting serial prediction, primarily the lateral prefrontal areas, reflects subsequent elaboration of the violation, which required more cognitive control in contrast to sequence repetition. In contrast, bilateral, dominantly posterior responses of parietal and temporal cortices triggered by the presentation of nonsequential deviants reflect a need for more attentional and perceptual processing required to correctly identify the deviant. These findings reveal that detection of sequential violations cannot, in any way, be reduced to a simple target detection process, and suggest that processing sequentially embedded and nonembedded stimuli is, even when these are comparable in their perceptual characteristics, supported by distinct functional networks.

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