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Motor foundations of higher cognition: similarities and differences in processing regular and violated perceptual sequences of different specificity

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Abstract

Processing perceptual sequences relies on the motor system, which is able to simulate the dynamics of the environment by developing internal representations of external events and using them to predict the incoming stimuli. Although it has previously been demonstrated that such models may incorporate predictions based on exact stimulus properties and single stimulus dimensions, it is not known whether they can also support abstract predictions pertaining to the level of stimulus categories. This issue was investigated within the present event-related functional magnetic resonance imaging study, which compared the processing of perceptual sequences of different specificity, namely those in which the sequential structure was based on the order of presentation of individual stimuli (token), and those in which such structure was defined by stimulus categories (type). The results obtained indicate a comparable engagement of the basic premotor–parietal network in processing both specific and categorical perceptual sequences. However, type sequences additionally elicited activations within the lateral prefrontal, occipital and posterior temporal regions that supported categorization in this task context. Introducing sequential deviants into token sequences activated parietotemporal and ventrolateral frontal cortices, whereas a less pronounced overall response, dominated by lateral prefrontal activation, was elicited by violations introduced into type sequences. Overall, the findings obtained suggest that, although forward models in perception may be able to incorporate expectations of lower specificity when compared to the motor domain, such processing is crucially dependent on additional contributions from lateral prefrontal as well as inferior occipital and temporal cortices that support categorization occurring in such a dynamic context.

Introduction

It has long been accepted that fast and accurate execution of movements is supported by different classes of internal models, among which the crucial role of simulating the executed actions and their outcomes is attributed to the so-called forward models (Wolpert & Miall, 1996; Wolpert & Kawato, 1998). Extending this view, in recent years it has been proposed that forward models can also be used for modeling the structure of the external environment and predicting incoming perceptual events (Wolpert & Kawato, 1998; Grush, 2004). Support for this proposal comes from studies showing that prediction of purely perceptual events relies on different parts of the motor system, primarily the premotor cortex and its parietal projection areas (Schubotz & von Cramon, 2003), regardless of whether participants predict an upcoming stimulus with regard to all of its properties (Schubotz & von Cramon, 2002a,b) or to only one of its features, for example form or color (Schubotz & von Cramon, 2001; Schubotz *et al.*, 2003). On the basis of previous findings, it is not possible to say whether a higher class of abstraction, namely a categorical one based on an arbitrary rule-based conjunction of stimulus features, would be represented in a similar fashion. Naturally, similarity in this case would not imply equivalence, as categorizing exemplars would always require an additional processing step when compared to recognizing events whose identity is defined by immediately available physical features. However, it is possible to suggest that processing dynamic events of higher abstraction may still be somewhat comparable to processing those of higher specificity, given that our judgements and reactions to external events often presuppose automatic abstraction and categorization processes, for example when moving away from cars driving towards us, regardless of their exact features.

Motivated by such a suggestion, the present event-related functional magnetic resonance imaging (fMRI) study investigated and mutually compared the processing of perceptual sequences. In addition, the process of detecting sequential (associative) deviants embedded within the two classes of perceptual sequences was explored. Both classes of

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sequences included equivalently organized trials, containing an initial presentation of a three-element stimulus pattern, which was repeated with stimuli either of the same identity (token sequences) or from the same category (type sequences) as those from the initial pattern. While it was hypothesized that processing token sequences would engage the premotor–parietai network previously identified in this context (Schubotz & von Cramon, 2003), introducing categorical information within the more abstract type sequencing task was expected to elicit the activations within lateral prefrontal as well as posterior temporal and occipital cortices (Ashby & Ell, 2001; Martin, 2007). However, it was also hypothesized that the engagement of these areas would not replace or attenuate the contributions from the premotor–parietal network when compared to a control, non-sequencing task (Schubotz & von Cramon, 2003). Specifically, although categorization itself could not be subserved by this network, it was assumed that it could still support perceptual sequencing organized on a more abstract level, given that such processing in natural settings may often benefit from abstracting over different category exemplars.

Materials and methods

Participants

Twenty-two right-handed, healthy volunteers (11 male, 11 female; age 22–32 years, mean age 26.4 years) participated in the study. The measurement of one participant was interrupted at the participant's request, and this partially acquired data set was excluded from any further analysis. Furthermore, two participants were later excluded from further analysis, one because of movement during the experiment, and one because of poor behavioral performance, so all subsequent analyses were performed on the data from 18 subjects. All subjects gave informed consent after being informed about potential risks and screened by the physician of the institution. The study was performed in accordance with the Declaration of Helsinki and approved by the local ethics committee of the University of Leipzig. The collected data were handled anonymously.

Procedure

Participants were given instructions and underwent a 45-min behavioral training session one day before the measurement. They were initially familiarized with all three tasks used within the experiment (tasks described below) by a 5-min general training session, and this was followed by specific training with the type sequencing task (25 min) and the control serial-match-to-sample task (10 min). On the day of the measurement and before the main experiment, they were additionally presented with the instruction and given a 5-min training session that included all three tasks. During the main experiment, participants were 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 and headphones.

Stimuli and task

The stimulus material used in this study included 24 different stimuli, all consisting of two basic shapes, circle and quadrangle, presented in different sizes and positions within the picture. Four categories of stimuli were created on the basis of an arbitrary criterion which was determined by the relationship of two basic shapes: the two shapes could be partly overlapping; the two shapes could be not touching each other at all; or one shape could be contained within the other (quadrangle in circle or circle in quadrangle). Thus, each category of stimuli included six exemplars that all shared the general relative layout of the two basic shapes and differed in terms of their exact position and size within the pictures.

Two different versions of the sequencing task, also known as the serial prediction task (SPT) (Schubotz, 1999), and a control serial-match-to-sample task of equivalent trial organization were presented in a mixed trial design. Each trial included successive presentation of nine stimuli with a duration of 700 ms without temporal gaps, preceded by a task cue with a duration of 700 ms, and followed by a 1500 ms response period and 500 ms of feedback on the accuracy of their response. During the course of the experiment, additional shorter trials containing only six stimuli were presented in order to ensure that the attention of the participant was directed at the task during the whole course of a trial ('catch trials'). During all other periods in the experiment, a fixation cross was presented at the center of the screen. The overall trial duration was 12 s and, in order to improve temporal resolution, each trial occurred at four different offset points (0, 500, 1000 and 1500 ms) in relation to fMRI data acquisition (Josephs *et al.*, 1997). During the course of the experiment, the stimulus trials were interspersed with empty trials during which only a fixation cross was presented and no task was given to the participants. Stimuli were presented using Presentation 11.7 (Neurobehavioral Systems, San Francisco, CA, USA).

At the beginning of each trial, subjects were informed about the upcoming task by a cue preceding the stimuli. In both versions of the sequencing task, participants were instructed to attend to the order of presented stimuli in order to extract and predict the repetitive pattern contained within them. The first three stimuli of each trial formed a sequential pattern that the participants were instructed to remember, and the second part of the trial entailed either two full repetitions or one repetition and one violation of the original three-stimulus pattern. The pattern of violation included reversal in the order of the first and second, or the second and third, elements of the original pattern. Sequencing catch trials included only an original pattern and one repetition or violation. In one version of the SPT (token SPT), the participants were instructed to remember the exact stimuli of the original three-stimulus sequential pattern, which were then repeated in the second part of the trial. In the second version of the SPT (type SPT), participants had to attend to the categories of stimuli of the initial pattern, as its repetitions in the second part of the trial entailed different exemplars from the same category of the previously presented stimuli. Thus, the serial prediction type task could be described as a categorical version of the serial prediction token task. In both versions of the SPT, the participants' task was to indicate, in a forced-choice mode, whether a sequential deviant occurred or not. In the control, serial-match-to-sample task, participants were instructed to memorize the first stimulus within the trial and attend to the remaining stimuli in order to determine whether the category of the first stimulus was later repeated. Participants' task was to indicate, in a forced-choice manner, whether the repetition occurred in any position within the trial or not.

The parameters of the three tasks were tested and chosen on the basis of several behavioral pilot studies conducted before the experiment, in which the timing of stimulus presentation, stimulus categories and exemplars, as well as the amount of training prior to the experimental session, were varied. As all participants initially showed significantly higher performance in the token sequencing task, the

performance level across the three tasks was balanced by providing previously described training sessions.

Across all trials in the experiment, the order of stimuli was pseudo-randomized. The probability of each stimulus and stimulus category and that of transitions between stimuli were balanced across different positions within the trial. In order to avoid any motor contributions to the tasks, the participant's response was always required after the end of each trial. The sequential violations in sequencing tasks and repetitions of the first stimulus in the control task were presented in 50% of all trials. Overall, six types of trials could be differentiated within the experiment: ordered token sequences; violated token sequences; ordered type sequences; violated type sequences; control trials without a repetition (non-match trials); and control trials with a repetition (match trials) (Fig. 1). Twenty-seven trials of each type were used, which, together with the 18 catch and 18 empty trials, amounted to the total of 198 trials presented in the course of the experiment.

Data acquisition

The experiment was carried out on a 3T scanner (Medspec S300; Bruker, Ettlingen, 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 a MDEFT sequence (256 × 256-pixel matrix) (Ugurbil *et al.*, 1993; Norris, 2000). Additionally, in order to improve the localization of activation foci, high-resolution whole-brain images were acquired for the participants in a separate session, using a T1-weighted three-dimensional segmented MDEFT sequence. This volume data set, with 160 slices and 1-mm slice thickness, was standardized to the Talairach stereotactic space (Talairach & Tournoux, 1988). Functional images in plane with the anatomical images were acquired using a gradient-echo echo planar imaging sequence with an echo time of 30 ms, a flip angle of 90°, and a repetition time of 2000 ms. Twenty-six functional slices were acquired parallel to the bicommissural plane (AC–PC) (thickness, 4 mm; interslice gap, 1 mm), covering the whole brain. 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 1192 volumes were acquired.

Data analysis

Functional data were motion-corrected off-line using the SPM5 motion correction protocol (http://www.fil.ion.ucl.ac.uk/), and the rest of the magnetic resonance data processing was performed using the software package LIPSIA (Lohmann *et al.*, 2001), which contains tools for pre-processing, co-registration, statistical evaluation and visualization of fMRI data. 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 cut-off frequency of 1/120 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 3D stereotactic coordinate system, a rigid linear registration with six degrees of freedom (three translational and three rotational parameters) was performed. The parameters were acquired on the basis of MDEFT and echo planar imaging T1 slices to achieve an optimal match between these slices and the individual 3D reference data set. Each transformation matrix was subsequently transformed to a standard Talairach brain size (x = 135, y = 175 and 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 mm (27 mm^3).

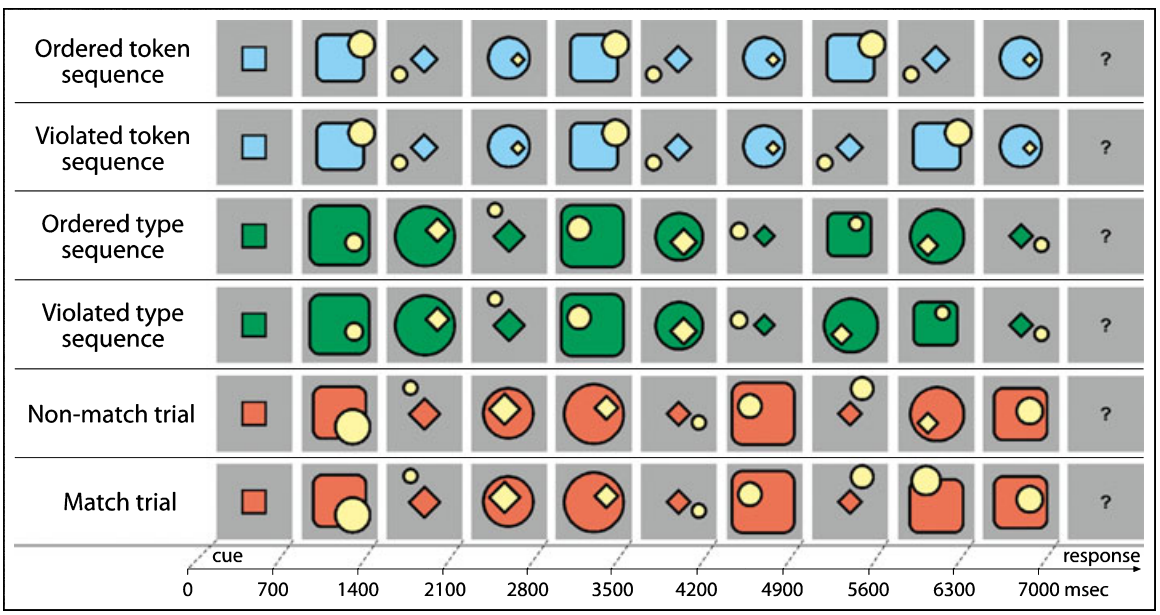

FIG. 1. Schematic examples of six types of trials. Each trial started with a cue and was followed by nine stimuli, all presented successively with a duration of 700 ms and without a temporal gap. The response was given at the end of each trial. In ordered sequences, the first three stimuli represented a sequential pattern, which was then correctly repeated, either with identical stimuli (ordered token sequence), or with other exemplars from the same category (ordered type sequence). Violated token and type sequences also started with a three-stimulus pattern, which was followed by one ordered repetition and one sequential deviant (here, the order of the first and second stimuli is reversed from the original pattern). The control task included the presentation of nine stimuli, among which the category of the first stimulus was either repeated, here in the eighth position within the trial (match trial) or not repeated (non-match trial) before the end of the trial.

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 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). Data were modeled using two design matrices: one consisting of onset vectors with events time-locked to the presentation of the first stimulus for trials within each of six different stimulus trial types, and another with events time-locked to the presentation of the violating stimulus (or the stimulus on the corresponding position within the trial for non-violated trials), with additional vectors for responses and the remaining parts of stimulation, including incorrectly responded trials. The design matrices were generated using a synthetic hemodynamic response function (Josephs *et al.*, 1997; Friston *et al.*, 1998) and its first derivative for the second matrix. 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 ($Z > 3.09$, $P < 0.001$, uncorrected) (Holmes & Friston, 1998). To correct for false-positive results, in the second step the results were corrected using cluster-size and cluster-value thresholds obtained by Monte Carlo simulations at a significance level of $P = 0.005$; that is, the reported activations are significantly activated at $P < 0.005$, corrected for multiple comparisons at the cluster level. Additionally, a conjunction analysis of the calculated contrasts (Nichols *et al.*, 2005) and a paired *t*-test were calculated in order to identify common regions supporting the two conditions of interest as well as those preferentially involved in processing one of them.

Results

Behavioral performance

Response accuracy and response times were used as indicators of behavioral performance, and were analysed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Response accuracy was calculated as the primary indicator of the participants' behavioral performance. Average accuracy, expressed as the proportion of correct responses, was 0.98 ± 0.004 for ordered token sequences, 0.98 ± 0.010 for violated token sequences, 0.97 ± 0.014 for ordered type sequences, 0.96 ± 0.013 for violated type sequences, 0.97 ± 0.009 for control trials without a repetition, and 0.99 ± 0.007 for control trials with a repetition. A repeated-measures ANOVA with two within-subject factors, namely one three-level factor 'task' (SPT token, SPT type, control) and one two-level factor 'response' (violation/repetition present, violation/repetition absent), was used in order to compare the response accuracy in different tasks. The results revealed no statistically significant main or interaction effects (task, $F_{2,34} = 2.468$, $P = 0.10$; response, $F_{1,17} = 0.039$, $P = 0.845$; task × response interaction, $F_{2,34} = 1.585$, $P = 0.22$), which suggests no differences in difficulty between the tasks.

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. The average reaction times were 431 ± 26.8 ms for ordered token sequences, 384 ± 24.6 ms for violated token sequences, 421 ± 26.3 ms for ordered type sequences, 403 ± 23.2 ms for violated type sequences, 593 ± 26.3 ms for control trials without a repetition, and 481 ± 15.8 ms for control trials with a repetition. Further analysis of reaction time data revealed statistically significant main effects of task ($F_{2,34} = 110.767$, $P < 0.001$), response ($F_{1,17} = 45.262$, $P < 0.001$), and the task × response interaction ($F_{2,34} = 22.039$, $P < 0.001$). *Post hoc* pairwise comparisons for the main effect of task showed that the responses within the control task were significantly longer than those in the type and token SPTs, which did not mutually differ. Furthermore, the responses made to the violation and match trials within all three tasks were significantly faster, which is in line with the fact that the decision in these trials could have been made earlier than in the ordered and non-match trials. Therefore, both accuracy and reaction time behavioral measures indicate equivalent behavioral performance in the two SPT tasks.

fMRI data

Effects of serial prediction across different levels of abstraction

Brain areas with significantly higher blood oxygen level-dependent responses during both type and token sequences were identified by a conjunction analysis of contrasts comparing each of the sequencing tasks with the control task (token sequences vs. control, and type sequences vs. control), and are listed in Table 1. Activations were distributed bilaterally, and included an activation encompassing dorsal

TABLE 1. Anatomical brain area, hemisphere, coordinates, *Z*-score and size of significant activations (token sequences vs. control, and type sequences vs. control)

Area (BA)	Hemisphere*	Talairach coordinates *x*	*y*	*z*	Maximal *Z*-score	Activated volume (mm^3)*
Type and token sequences (conjunction analysis)						
PMd	R[a]	25	−8	48	5.25	21 951[a]
PMv	R[a]	46	4	24	4.94	–
IFG (44)	R[a]	49	7	6	3.99	–
MFG (9)	R[a]	52	16	33	4.84	–
SMA	L[b]	−5	−5	51	4.58	17 388[b]
PMd	L[b]	−23	−5	48	5.25	–
PMv	L[b]	−50	1	27	5.07	–
IFG (44)	L[b]	−56	7	0	3.81	–
SPL/PCU (40/7)	L[c]	−41	−44	54	5.70	68 499[c]
IPL (39/40)	L[c]	−44	−38	45	5.47	–
STGp (22)	L[c]	−50	−38	18	3.89	–
PCU (7)	R[c]	−2	−53	60	3.51	–
CE	L[d]	−32	−59	−24	5.21	39 015[d]
CE	R[d]	25	−65	−21	4.79	–
BG	L[e]	−20	1	9	4.64	4266[e]
BG	R[f]	19	4	12	4.19	5238[f]
MTG (21)	L[g]	−47	−56	9	3.57	378[g]
Type vs. token sequences (paired *t*-test)						
IFS/iPrCS	L[h]	−41	7	27	4.24	3321[h]
OGm/OGi (19)	L[i]	−44	−77	0	4.99	7992[i]
FG/LG (18)	L[i]	−23	−86	−3	4.79	–
FG (19/37)	R[j]	34	−56	−9	4.39	4860[j]
FG (19/37)	R[j]	34	−65	−6	4.29	–
FG (36)	R[j]	34	−38	−21	4.03	–

BA, Brodmann area; BG, basal ganglia; CE, cerebellum; FG, fusiform gyrus; IFG, inferior frontal gyrus; IFS, inferior frontal sulcus; IPL, inferior parietal lobule; iPrCS, inferior precentral sulcus; LG, lingual gyrus; MFG, middle frontal gyrus; MTG, middle temporal gyrus; OGi, inferior occipital gyrus; OGm, middle occipital gyrus; PCU, precuneus; PMd, dorsolateral premotor cortex; PMv, ventrolateral premotor cortex, SMA: supplementary motor area; SPL, superior parietal lobule; STGp, posterior superior temporal gyrus. *Superscript letters indicate which areas were combined for the volume data.

and ventral portions of the premotor cortex, reaching Brodmann area (BA) 44 in the inferior frontal gyrus, and extending further along the inferior frontal sulcus into BA 9 in the right hemisphere. Further activations included the supplementary motor area and the inferior and superior parietal lobules. In addition to these, the cerebellum, putamen, globus palidus and a small portion of the middle temporal gyrus were activated in sequence processing (Table 1).

Brain areas that were more engaged in supporting type than supporting token sequences were revealed by comparing the type sequences vs. control and token sequences vs. control contrasts using a paired *t*-test. The activations included bilateral ventral and inferior temporal areas encompassing parts of the lingual, fusiform and occipital gyri, and the left inferior frontal sulcus encompassing the inferior frontal junction (IFJ) (Table 1; Fig. 2). A conjunction analysis of contrasts comparing the two categorical tasks with the non-categorical token SPT (type sequences vs. token sequences, and control task vs. token sequences) revealed no activations that would be exclusively shared by the two tasks requiring categorization of different complexity.

Deviant detection in sequences of different specificity

Brain areas with significantly higher blood oxygen level-dependent responses during the presentation of sequential deviants in the two classes of SPT as revealed through the comparison of violated and ordered sequence trials (contrasts: violated token sequences vs. ordered token sequences, and violated type sequences vs. ordered type sequences), as well as the conjunction between these two contrasts, are listed in Table 2. Presentation of deviants in the token SPT was characterized by an increase in the activity of mainly right-lateralized lateral prefrontal areas, mostly neighboring the inferior frontal gyrus as well as the bilateral inferior parietal lobule (IPL). In comparison, bilateral frontal activations that supported the processing of sequential deviants in the type SPT were less extended, and were restricted primarily to the areas surrounding the IFJ (Fig. 3). Additionally, the right IPL was also activated in processing of deviants in the type task context. Conjunction between the two contrasts revealed common activation of the right IPL (BA 39/40) ($x = 52$, $y = -47$, $z = 33$; maximum $z = 3.9$; size of activation 1404 mm^3) in processing of sequential deviants in the token and type SPT.

TABLE 2. Anatomical brain area, hemisphere, coordinates, *Z*-score and size of significant activations (violated vs. ordered token sequences, and violated vs. ordered type sequences)

Area (BA)	Hemisphere*	Talairach coordinates			Maximal *Z*-score	Activated volume (mm^3)*
		x	*y*	*z*		
Violated vs. ordered token sequence						
IFG (47)	R[a]	40	34	0	5.00	6480[a]
IFG (44/45)	R[a]	55	16	6	3.68	–
IFG (44)	R[a]	49	13	15	4.78	–
MFG (9)	R[a]	46	19	27	3.37	–
IFG (47)	L[b]	−38	28	0	4.73	2889[b]
IPL (39/40)	R[c]	55	−50	27	4.08	5400[c]
MTG (21)	R[d]	55	−38	0	5.06	4752[d]
IPL (39/40)	L[e]	−47	−56	27	4.40	4320[e]
Violated vs. ordered type sequence						
PMC	R[f]	37	1	27	4.22	1242[f]
IFG (44)	R[f]	46	10	21	3.67	–
MFG (8)	L[g]	−41	19	33	3.61	4158[g]
IFG (44)	L[g]	−44	16	21	4.50	–
PMC	L[g]	−41	1	36	4.12	–
IPL/STS (39/40)	R[h]	49	−44	30	4.25	1890[h]
IPL/STS (39/40)	R[h]	52	−53	21	4.08	–

IFG, inferior frontal gyrus; IPL, inferior parietal lobule; MFG, middle frontal gyrus; MTG, middle temporal gyrus; PMC, premotor cortex; STS, superior temporal sulcus. *Superscript letters indicate which areas were combined for the volume data.

Discussion

The present study compared the neural correlates of processing perceptual sequences of different specificity, namely token sequences in which the sequential structure was defined by the order of specific individual stimuli, with type sequences in which the order of stimulus categories determined the sequential structure. The results obtained show that both sequence classes are supported by an equivalent contribution from the premotor–parietal network, previously identified in perceptual sequencing (Schubotz & von Cramon, 2003). Additional engagement of prefrontal, occipital and posterior temporal areas previously associated with categorization (Ashby & Ell, 2001; Grill-Spector & Malach, 2004; Martin, 2007) differentiated the processing of token and type perceptual sequences. Introducing deviant events in these two classes of sequences evoked activations from middle and inferior portions of the lateral prefrontal cortex as well as the inferior parietal regions, such that those elicited by violations within token sequences were much more pronounced and widespread than those within type sequences. As it has previously been suggested that the processing as evoked by the serial prediction task is, by nature, predictive and can be conceptualized in a forward model framework

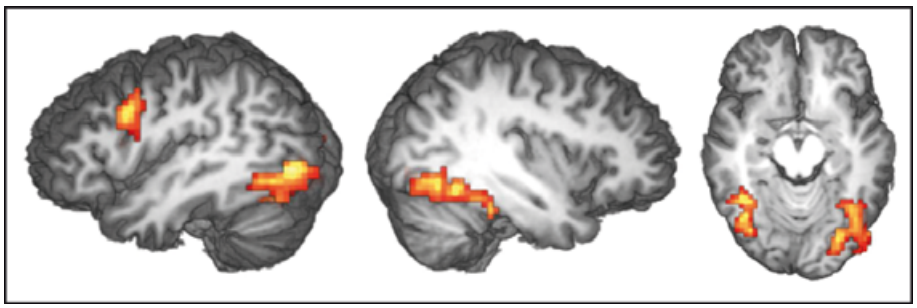

FIG. 2. Brain activations more engaged in supporting type than in supporting token sequences, revealed by the paired *t*-test of the following contrasts: type sequences vs. control, and token sequences vs. control. From left to right: left hemisphere from parasaggital section ($x = -40$); right hemisphere from parasaggital section ($x = 37$); and axial section seen from below ($z = -10$). Group-averaged statistical maps ($N = 18$) are superimposed onto an individual brain, which was chosen as 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).

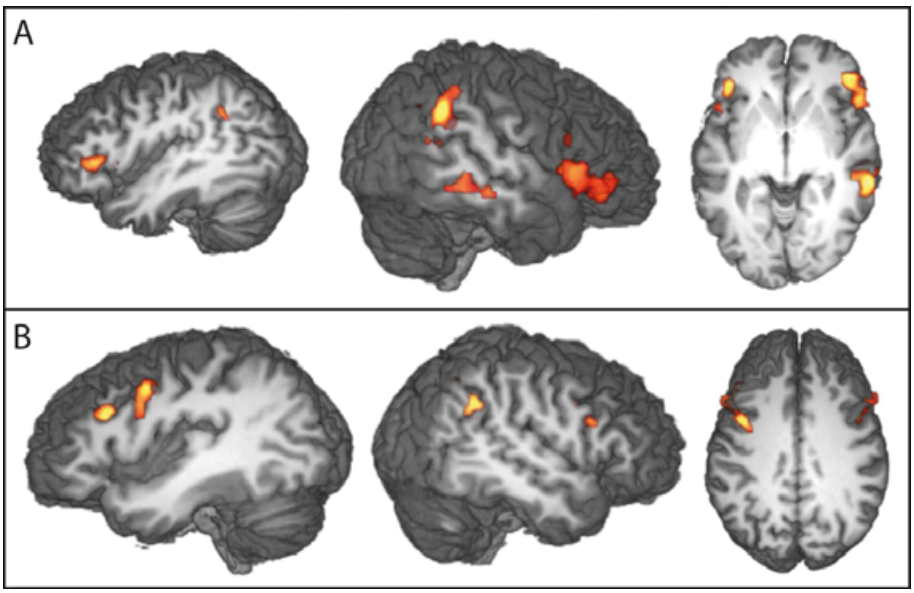

FIG. 3. (A) Brain correlates of detecting sequential deviants in token serial prediction task (SPT) (violated vs. ordered token sequence). From left to right: left hemisphere from parasaggital section (x = –40); right hemisphere from parasaggital section (x = 55); and axial section seen from above (z = 0). (B) Brain correlates of detecting sequential deviants in type SPT (violated vs. ordered type sequence). From left to right: left hemisphere from parasaggital section (x = –40); right hemisphere from parasaggital section (x = 49); and axial section seen from above (z = 35). (A and B) Group-averaged statistical maps (N = 18) are superimposed onto an individual brain, which was chosen as 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).

(Schubotz, 2007), the results of the current study will be interpreted in line with this framework.

Processing sequences of different levels of specificity

Processing of both token and type sequences engaged an extended network of areas, including the bilateral lateral and mesial premotor cortex, connecting parietal areas, the cerebellum, and the basal ganglia. Whereas the involvement of this network in token sequences replicates previous findings (Schubotz & von Cramon, 2002a,b,c), its equivalent contribution to processing type sequences extends current knowledge by showing that it can also contribute to processing more abstract dynamic events defined by arbitrary rules. However, processing categorical sequences in the present study additionally engaged occipital and inferior temporal regions encompassing the fusiform gyrus and the lateral occipital cortex [for anatomical connectivity, see Catani *et al.* (2002) and Schmahmann *et al.* (2007)], regions that have previously been shown to be involved in processing both familiar and non-familiar, as well as nonsense objects (Malach *et al.*, 1995; Grill-Spector *et al.*, 2001; Martin, 2007). Involvement of these posterior areas has previously been related to the categorization itself (Koida & Komatsu, 2007; Li *et al.*, 2007), as well as discrimination of exemplars within a category (Eger *et al.*, 2008). Additionally, an increase of activity in inferior temporal regions has been identified in situations with increased need for perceptual differentiation (Gerlach *et al.*, 1999), which would be complemented by the involvement of fusiform and inferior occipital gyri in binding elements to more elaborate shape configurations (Gerlach *et al.*, 2006). Processing type sequences included precisely such requirements, as a more detailed analysis of individual features and their integration was required in order to successfully accomplish the task.

In addition to occipital and temporal areas, processing of type sequences triggered an activation within the left inferior frontal sulcus encompassing the IFJ, a region located at the crossing of the inferior frontal and precentral sulcus (Derrfuss *et al.*, 2009). In line with the hypothesis of Derrfuss *et al.* (2004), who proposed a role of IFJ in maintaining task-relevant information used for biasing posterior brain systems, the involvement of this region in the present study could reflect the representation of rules that are important for defining stimulus categories in the type sequencing task. Specifically, in addition to having one relevant task rule that needed to be applied in each task, type sequences also required processing of subordinate rules defining category memberships. As the use of rule-based strategies for categorization was not only possible, but was also promoted by explicitly informing the participants about the rules defining stimulus categories (Medin *et al.*, 1993; Smith *et al.*, 1998), it could be assumed that the observed IFJ activation reflects the representation of subordinate rules. However, if the IFJ contributed to the static maintenance of categorization rules, its engagement should also be identified when the control task is compared with the token sequencing task, as this task also required a certain degree of categorization. Given that this was not the case, it is plausible to assume that the role of the IFJ in this experiment did not simply involve sustained maintenance of category rules or making category judgements (Thorpe & Fabre-Thorpe, 2001). If category specific, its role would be related to the constant updating of categorical representations that was required in the type sequencing, but not in the control task, in which only one rule needed to be maintained during the trial. This suggestion would be in line with the reported involvement of the IFJ in updating working memory representations (Roth *et al.*, 2006) as well as in activating novel task representations, as required in task-switching experiments (Brass & von Cramon, 2004; Brass *et al.*, 2005). Alternatively, the role of the IFJ could reflect a less specific role in representing any type of rule (not necessarily those pertaining to categorization) or guiding retrieval and post-retrieval selection of relevant information (Gerlach *et al.*, 1999; Martin, 2007). Overall, the additional involvement of lateral prefrontal regions in a task with a higher level of abstraction, requiring more cognitive control, is in line with suggestions

regarding the hierarchical organization of the lateral prefrontal cortex along the anterior–posterior dimension (Koechlin & Summerfield, 2007; Badre, 2008).

However, although providing necessary support for processing categorical sequences, the prefrontal cortex, which is more flexible in applying abstract rules pertaining to perceptual categorization (Muhammad *et al.*, 2006), did not completely take over this processing, as illustrated by the equivalent engagement of the premotor–parietal cortex in the token and type SPTs. It has previously been suggested that processing within this network, as required in the serial prediction task, is by nature predictive, and can be conceptualized in a forward model framework (Schubotz, 2007). Although previous results have indicted that such task-relevant information can pertain to stimulus identity and relevant stimulus features (Schubotz & von Cramon, 2001, 2002a,b; Schubotz *et al.*, 2003), findings from the present study indicate that these may also include arbitrarily defined categorical properties. However, this finding leaves open the question about the mechanisms underlying such processing. Principally, prediction on a categorical level could be accomplished either by concurrently running several forward models and matching derived alternative predictions with the incoming stimuli, or by flexibly tuning the level of specificity of a single forward model on the basis of the available stimulus information. The former account would be in line with the idea of a modular architecture housing multiple pairs of forward and inverse models (Wolpert & Kawato, 1998; Haruno *et al.*, 2001), which could be quite beneficial in ambiguous contexts (Blakemore *et al.*, 1998). The latter suggestion may signify that the specificity of perceptual forward models is context-dependent or, alternatively, that these models are always less specific than the extremely precise motor ones (Blakemore *et al.*, 1998; Miall, 2003). High precision in perception may be either unnecessary, because accurate prediction can often rely only on relational properties of external events, or even disadvantageous, because it occurs in a noisy system and environment. On the basis of the data of the present study, it is not possible to decide which of these options is more plausible or to suggest how the processing of multiple forward models or tuning of individual ones could be computationally achieved. In addition, the fact that overlapping parts of the premotor–parietal network were identified for both types of sequence does not necessarily imply that the same neural populations subserved the processing within two tasks. This suggestion is motivated by studies that investigated the neural mechanisms of categorization in nonhuman primates, and showed that diverse populations of neurons coding for stimulus features and different types of categories can coexist within the same cortical areas (Freedman *et al.*, 2002). Similarly, different populations within the premotor cortex could be involved in processing different types of forward models, an issue that should be addressed in future studies.

Detecting sequential deviants within sequences of different specificity

Introducing deviant events into token and type perceptual sequences evoked activations of middle and inferior portions of the lateral prefrontal cortex as well as the IPL. The activation of a wide portion of the inferior frontal gyrus was especially present in the token SPT, whereas deviants introduced into type SPT elicited a much more restricted activation focused around the IFJ, which may reflect the increased need for updating of categorical representations required in the type sequences following the presentation of a deviant. The widespread, mainly ventral prefrontal, activation in detecting token deviants may reflect controlled retrieval of the sequencing structure needed for the verification of sequence regularity. This suggestion would be in line with findings showing the involvement of this area in active selection, comparison and judgement of memorized information (Petrides, 2005). The activation of the inferior parietal and temporal cortices, encompassing the temporoparietal junction, which was especially pronounced following the presentation of violations in the token sequences, can, on the other hand, be related to findings indicating the involvement of this region in detecting salient and novel events, regardless of whether or not this salience is related to the current behavioral context (Downar *et al.*, 2002).

On a more general level, an overall stronger pattern of activation was identified by comparing violated and ordered sequence trials in the token task, where the expectations were more restricted and focused on the specific level of stimulus identity. These results might suggest that larger prediction errors or violations of very specific expectations are processed more elaborately than those of less specific ones (Friston *et al.*, 2006). This would suggest that deviant stimuli do not just generally trigger more elaborate processing, in contrast to attenuated standards (Blakemore *et al.*, 1998; Corbetta & Shulman, 2002), but that the level of such processing is related to the type and strength of the encountered deviance. If correct, this hypothesis would most probably be relevant for a subset of regions involved in deviant detection, and could not uniformly explain the effects across all levels of processing. The present experiment was not designed to directly test this possibility, as this would require a somewhat different experimental design, as well as more systematic investigations of all regions involved in deviant detection. However, the present data do not contradict this hypothesis either. It will be important to further address this issue in the future, as it raises interesting questions about potential sources of differences that might lead to the suggested pattern of results. Specifically, it is not clear whether violations of expectations of different specificities would differ in terms of processing or its final output. The first alternative, suggesting mutually different processing, may mean that comparing expectations of higher specificity to the incoming stimuli is more demanding, as it includes more features that need to be taken into account and mutually compared. Therefore, processing of sequential deviants within the token SPT would simply be more elaborate, and therefore elicit a stronger response. Alternatively, the source of the difference could be related to the outcome of such a comparison. In this case, the comparison itself would be computationally equivalent (although not based on exactly the same features), but the mismatch resulting from violating more specific expectations would elicit a higher prediction error. In other words, violating specific predictions might simply represent a larger mismatch or a greater surprise than violating less specific expectations, and consequently lead to the more pronounced activation pattern underlying the detection of such deviants.

In summary, the results obtained in the present study indicate that processing perceptual sequences of different specificity elicits a comparable engagement of the premotor–parietal network, which has previously been suggested to support perceptual predictive processing, providing an additional engagement of prefrontal and posterior cortices in the more abstract task context. Such additional activations supporting basic categorization processes are crucial for enabling the premotor–parietal network to support the suggested anticipatory transformations, which are often exemplar-unspecific and, therefore, similar in contexts of different specificity. However, although partly comparable, predictions of different specificity also differ, which is indicated by a more pronounced response following mismatches that violated more restricted, specific expectations, as postulated in the context of token sequences.

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Abbreviations

BA, Brodmann area; fMRI, functional magnetic resonance imaging; IFJ, inferior frontal junction; IPL, inferior parietal lobule; SPT, serial prediction task.

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