Neural Correlates of the Interaction Between Transient and Sustained Processes: A Mixed Blocked/Event-Related fMRI Study

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Abstract: Complete understanding of the neural correlates of cognitive processes requires investigation of both event- and state-related correlates of cognitive performance as well as their interaction. Neuroimaging studies using blocked designs confound these two types of processes and studies using event-related designs focus exclusively on the detection of transient effects. Recent fMRI studies used mixed blocked/event-related designs and found that transient and sustained activity can be dissociated, but it is not yet known how event-related and state-related processing interact. Here we used a phonological categorization paradigm in a mixed blocked/event-related design to investigate where in the brain transient activity interacts with sustained activity. Task difficulty was parametrically manipulated based on individually determined categorization thresholds. We found an interaction effect of transient and sustained activity in the left precuneus. In this cortical structure transient activity increased with increasing task difficulty, while sustained neural activity decreased with increasing task difficulty. Our data suggest that sustained activity is enhanced during processing of an easy task, presumably because of ongoing internally cued endogenous processing, still allowing effortless processing of transient stimuli. During performance of a difficult task, sustained activity in the precuneus is reduced to provide resources for processing incoming stimuli. Processing of stimuli that are expected to be difficult elicits increased transient responses independent of the actual physical properties of the stimuli. In showing an interaction between transient and sustained activity in the precuneus, the present results accommodate seemingly diverging results from previous studies using event-related or blocked designs and expand the knowledge emerging from previous studies using mixed blocked/event-related designs. *Hum Brain Mapp 27:545–551, 2006.* © 2005 Wiley-Liss, Inc.

Key words: fMRI; mixed blocked/event-related design; task difficulty; transient and sustained activity; interaction; precuneus

INTRODUCTION

One of the main goals of cognitive neuroscience is to understand how cognitive processes are represented in the human brain. Functional magnetic resonance imaging (fMRI) studies have yielded important information about where in the brain specific processes are represented. However, recent developments in fMRI design allow not only to localize brain activity but also "to parse brain activity into its constituent parts" [Donaldson, 2004]. Thus, brain regions can be characterized based on the temporal dynamics of their neural activity.

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Recent neuroimaging studies suggest that cognitive operations involve at least two general types of processes occurring simultaneously, namely, event-related and state-related processes. Event-related processes are those involved in the specific processing of individual items and depend on the transient activation of cortical areas. In contrast, state-related processes are related to ongoing task demand [Donaldson et al., 2001]. Such sustained processes are thought to rely on continuous activation of cortical areas. A complete understanding of the neural correlates of cognitive processes requires investigation of both event- and state-related correlates of cognitive performance as well as their interaction.

Until recently, it was difficult to dissociate transient and sustained processes using standard neuroimaging techniques. Blocked experimental designs average neural activity over a series of events and thus confound these two types of processes, whereas event-related experimental designs focus exclusively on the detection of transient effects [Buckner and Braver, 1999]. Transient and sustained processes can only be identified simultaneously using designs that allow separating hemodynamic signals into event- and state-related components [Donaldson et al., 2001]. Several recent fMRI studies investigated these processes using so-called mixed blocked/event-related designs and demonstrated that transient and sustained processes can be detected, although they are temporally superimposed [Braver et al., 2003; Burgund et al., 2003; Donaldson et al., 2001; Laurienti et al., 2003; Otten et al., 2002; Velanova et al., 2003; Visscher et al., 2003]. Furthermore, neural correlates of transient and sustained processes can be dissociated using this approach. Transient and sustained neural activity were investigated during memory processes [Donaldson et al., 2001; Otten et al., 2002; Velanova et al., 2003], object-naming [Burgund et al., 2003], and task switching [Braver et al., 2003]. Laurienti et al. [2003] demonstrated the separability of these two types of processes using a mixed blocked/event-related paradigm with visual and auditory stimulation. Using simulated data Visscher et al. [2003] recently confirmed that a mixed blocked/event-related design can differentiate transient and sustained activity appropriately. Importantly, transient stimuli alone did not lead to spurious positive sustained responses and sustained stimuli alone produced only negligible spurious transient responses. A second experiment with actual fMRI data confirmed that mixed designs do not confound sustained and transient signals [Visscher et al., 2003]. The aforementioned studies found transient activations in regions specific for processing of the particular task, while sustained activity was inconsistently found in a variety of brain regions, predominantly in cingulate cortex and frontal areas.

In sum, previous studies showed the dissociability of transient and sustained processes and reported specific neural correlates for both types. However, it is not known how event-related processing is modulated by changes in state-related processing, or conversely, how state-related processing is modulated by changes in event-related processing. In other words, it is still unclear whether and where transient and sustained effects interact in the brain.

The goal of the present fMRI study was to investigate where in the brain event-related processes interact with state-related processes. To address this issue we used a mixed blocked/event-related design and parametrically modulated task demand in a phonological categorization paradigm by varying the difficulty of categorization.

SUBJECTS AND METHODS

Subjects

Seventeen right-handed, male, healthy subjects (age 27.0 ± 4.3 years; mean ± SD) participated in the experiment and were paid for participation. All subjects were native German speakers, reported normal hearing, had no history of any neurological or psychiatric disorder, and no structural brain abnormality. The study was approved by the local ethics committee and written consent was obtained from each subject prior to investigation.

Stimulus Material and Task

To manipulate task difficulty parametrically we used a phoneme categorization task. Subjects were presented with the syllables /da/ and /ta/. Differential perception of these syllables is influenced by durational parameters of the acoustic signal such as the interval between consonant onset and the start of rhythmic vocal-cord vibrations (voice onset time, VOT, of the consonants) [Lisker and Abramson, 1964]. By incrementally increasing the VOT of the syllable /da/ the percept shifts from the voiced (i.e., /da/) to the analogous unvoiced consonant (i.e., /ta/) at a VOT of approximately 35 ms [Ackermann et al., 1997]. We manipulated the difficulty of the categorization task by prolonging the VOT of a recorded syllable /da/, with VOTs ranging from 15 ms (prototypical /da/) to 60 ms (prototypical /ta/) [Steinschneider et al., 1999]. Stimuli with VOTs close to the threshold (i.e., ~35 ms) were most ambiguous. Stimuli resembling a prototypical syllable /da/ and /ta/ (i.e., VOT of 15 ms and 60 ms, respectively) were most unambiguous.

Stimuli were presented using a digital playback system and a high-frequency shielded transducer system including a piezoelectric loudspeaker. The MR-compatible headphones allowed unimpeded conduction of the stimuli with good suppression of ambient scanner noise by ~36 dB. We used noise-protection earplugs providing additional noise attenuation. This transmission system allowed auditory stimulation with relatively few distortions.

To account for between-subject differences, individual categorization thresholds were determined in the scanner. Syllables with VOTs ranging from 15–60 ms in incremental steps of 3 ms were presented 10 times each in random order (stimulus onset asynchrony, SOA, ranging from 3.3–5.1 s, mean 4.2 s). Participants had to judge whether the stimulus was a /da/ or a /ta/ and had to indicate their response with a right-hand forced choice button press.

Using a maximum likelihood estimation algorithm [Wichmann and Hill, 2001a,b] we fitted a logistic function to each

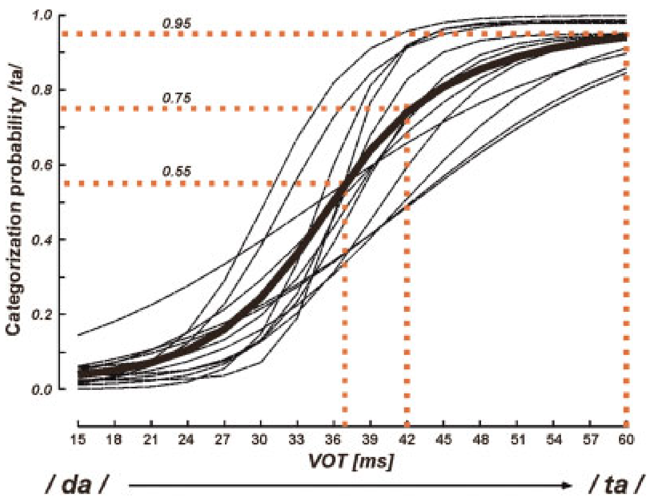

Figure 1.

Psychometric assessment of categorization probabilities. The individual fitted logistic psychometric functions for each subject's performance data in the scanner and mean psychometric function. Dashed lines indicate the categorization probabilities *P* of 0.95, 0.75, and 0.55 for the syllable /ta/. The corresponding individual VOTs were then used in the fMRI experiment. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

subject's performance data and determined the VOTs for individual categorization probabilities *P* of 0.95, 0.75, and 0.55, respectively, for /ta/ (Fig. 1). Thus, the voice onset durations for the stimuli in the easy, medium, and difficult blocks were determined based on each individual's psychometric function and were therefore adjusted to the individual's syllable discrimination ability. Syllables with the corresponding VOTs were then used in the following fMRI experiment, subsequently referred to as $/ta/_{95}$ ($P = 0.95$, i.e., easily categorized as a /ta/), $/ta/_{75}$ ($P = 0.75$, i.e., medium difficulty), and $/ta/_{55}$ ($P = 0.55$, i.e., difficult to categorize as a /ta/) (Fig. 1). For subjects who did not reach a categorization probability *P* of 0.95, /ta/ stimuli with a VOT of 60 ms were used for the easy condition ($/ta/_{95}$).

In the following fMRI experiment stimuli were presented in a mixed blocked/event-related design (Fig. 2A). There were three different conditions of phoneme categorization (easy, medium, and difficult). Four blocks per condition were presented. Each block contained 10 /ta/ and 10 /da/ as single events. Difficulty within each block was modulated via the /ta/ stimuli: $/ta/_{95}$ in easy blocks ($block_{easy}$), $/ta/_{75}$ in medium blocks ($block_{med}$), and $/ta/_{55}$ in difficult blocks ($block_{diff}$). Note that /da/ stimuli were identical in all blocks and had a VOT of 15 ms. Subsequently, we refer to /da/ stimuli in easy blocks as $/da/_{easy}$, in medium blocks as $/da/_{med}$, and in difficult blocks as $/da/_{diff}$. The subjects had to judge whether a syllable was a /da/ or a /ta/ in a two-alternative forced-choice manner. They were instructed to answer as quickly and correctly as possible by right-hand button press (/ta/ = index finger, /da/ = middle finger). The subjects were told that the blocks might differ with respect to task difficulty, but were not instructed which type of block was coming next. During the block periods stimuli were presented randomized and temporally jittered similar to an event-related design (SOA ranging from 3.2–5.1 s, mean 4.2 s). A pre-cue (100 ms) indicated the onset of a new block and was presented 4.2 s prior to each block. Each functional run consisted of a randomized sequence of an easy, a medium, and a difficult block, lasting 83.84 s each, alternating with resting periods (20.96 s). In total, each subject completed four runs, resulting in four repetitions per condition.

fMRI Scanning

A 1.5 T Siemens Magnetom Vision scanner (Erlangen, Germany) with a standard head coil was used to acquire echoplanar T_2*-weighted images. Head movement was minimized using a vacuum pad. We acquired a total of 352 volumes (88 per run, 20 per block, i.e., 80 per condition) with 22 slices approximately parallel to the bicommissural plane (ac–pc-plane) covering the entire brain (TR 4.192 s, TE 40 ms; flip angle 90°; field of view 256 × 256 mm; matrix 64 × 64; slice thickness 5 mm; interslice gap 1 mm; voxel size 4 × 4 × 6 mm; ascending acquisition of images). To avoid interference of the scanner noise with the auditory stimulation, a sparse temporal sampling method was used. Thus, the stimuli were presented during the 2,480-ms interscan intervals, one per interval. Stimuli were presented in temporal asynchrony to the scans to overcome a systematic bias in sampling over peristimulus time (jittered stimulus presentation) [Burock et al., 1998; Dale, 1999]. Afterwards, structural 3-D datasets were obtained using a T_1-weighted sequence (MP-RAGE; TR 9.7 ms; TE 4 ms; flip angle 12°; voxel size 1 mm^3).

Behavioral Data Analysis

We assessed reaction times and computed accuracy of response and the discriminability (d′) of the presented stimuli per block. We computed d′ for each of the three conditions (easy, medium, and difficult) as a ratio of hits and false alarms using standard psychometric methods. A hit was defined as responding "/ta/" when a /ta/ was presented. A false alarm was defined as responding "/ta/" when a /da/ was presented. To compare conditions regarding reaction times, accuracy of response, and d′, repeated-measures ANOVAs were calculated. The statistical analyses were conducted using SPSS (v. 11.0; SPSS, Cary, NC).

fMRI Data Analysis

Imaging data were preprocessed and then analyzed within the framework of the general linear model as implemented in SPM2 (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology, University College London, UK, http://www.fil.ion.ucl.ac.uk/spm). The first three volumes of each run were discarded to avoid non-steady-state effects due to T_1 saturation. Preprocessing included slice-time correction, realignment to correct for movement artifacts, normalization to the Montreal Neurological Institute (MNI) standard brain, and spatial smoothing with a 3-D Gaussian filter (full-width half-maximum = 8 × 8 × 8 mm) using standard SPM2 methods [Friston et al.,

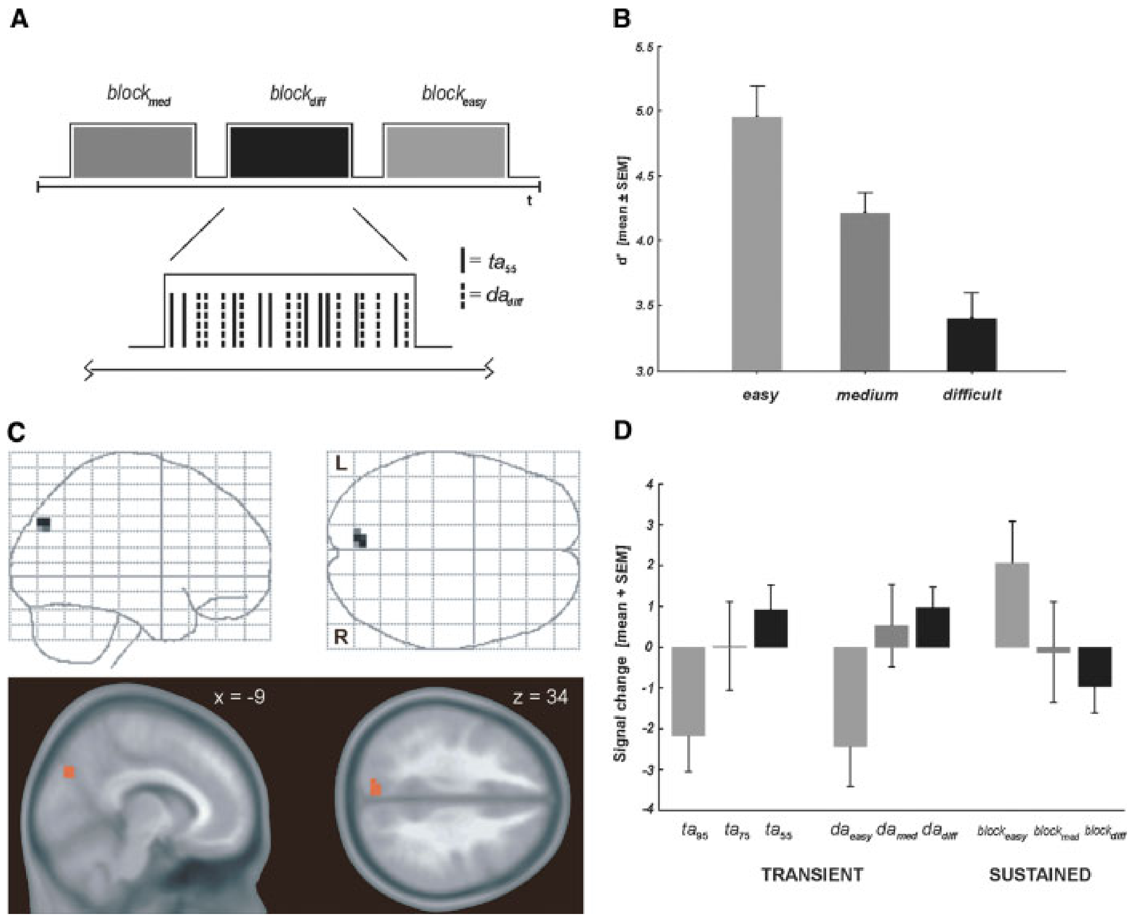

Figure 2.

A: Mixed blocked/event-related design during a single fMRI run. Top: Each run consisted of a randomized sequence of an easy, a medium, and a difficult block. There were resting periods both at the beginning and at the end of the run as well as between the blocks. Bottom: Within each block the respective /ta/ stimuli (i.e., /ta/$_{95}$, /ta/$_{75}$, /ta/$_{55}$) mixed with /da/ stimuli were presented in a randomized manner and temporally jittered. Note that /da/ stimuli were identical in all blocks. **B:** Psychophysical data acquired in the scanner. Discriminability (d′) as a function of task difficulty during functional scanning. Note that d′ significantly decreased with increasing block difficulty ($P = 0.001$). **C:** Interaction between transient and sustained activity. The precuneus showed an interaction of event-related activity with state-related activity. **D:** BOLD signal change in response to the different types of events in the precuneus. Note the increase in signal change for transient stimuli (/ta/$_{95}$, /ta/$_{75}$, /ta/$_{55}$, and /da/$_{easy}$, /da/$_{med}$, /da/$_{diff}$) and the decrease in signal change for sustained blocks (block$_{easy}$, block$_{med}$, block$_{diff}$) with increasing block difficulty. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

1995]. Global linear trends were minimized through high-pass filtering the data with a cutoff period of 128 s.

The mixed design was modeled using canonical hemodynamic response functions as regressors for each type of event (/ta/$_{95}$, /ta/$_{75}$, /ta/$_{55}$, /da/$_{easy}$, /da/$_{med}$, /da/$_{diff}$, and pre-cue) and boxcar functions convolved with the hemodynamic response function as regressors for each type of block (block$_{easy}$, block$_{med}$, and block$_{diff}$). Regressors for the easy, medium, and difficult conditions were modeled separately to determine the relationship of difficulty and amplitude of the hemodynamic response. An alternative approach would be to model the three conditions in one regressor. However, this kind of analysis introduces a bias because one would have to assume that the relationship between difficulty in this task and amplitude of the hemodynamic response is known (e.g., linear, exponential, polynomial). Derivatives of the resulting regressors were included to account for differences in timing of the hemodynamic response. The correlation between block and event regressors was kept relatively low through randomly varying the interval between the individual items within each block. The mean correlation coefficient between block and event regressors was 0.56. This level of correlation allows the dissociation and independent estimation of the two time courses of neural activity [cf. Otten et al., 2002]. Furthermore, we analyzed multicollinearity among the regressors by calculating the variance inflation factor (VIF). The VIF is computed using the multiple correlation coefficient (R) of a given re-

TABLE I. Modulation of sustained activity, transient activity and the interaction between sustained and transient activity

Region	Left/Right	BA	*t*	Peak MNI coordinates (x, y, z)
Modulation of sustained activity *block*				
Superior temporal gyrus	R	38	3.66	44, 0, −24
Middle temporal gyrus	R	21	3.61	56, −16, −20
Pons	R	n.d.	3.51	16, −36, −40
Modulation of transient activity /ta/				
Precuneus	L	7	3.41	−8, −80, 36
Modulation of transient activity /da/				
Precuneus	L	7	3.38	−8, −76, 36
Interaction between sustained and transient activity				
Precuneus	L	7	3.38	−4, −76, 36

Sustained activity: $block_{diff} - block_{easy}$; transient activity: $/ta/_{55} - /ta/_{95}$ and $/da/_{diff} - /da/_{easy}$; sustained and transient activity $(/da/_{diff} - /da/_{easy}) - (block_{diff} - block_{easy})$.
For each contrast the respective activated anatomical region, hemisphere, approximate BA, *t* value, and coordinates of the local maxima of significance within the MNI coordinate system are given.
$P < 0.005$ (mixed effects, uncorrected). Voxel extend threshold = 7 voxels.
BA, Brodmann area; MNI, Montreal Neurological Institute; n.d., not defined.

gressor fitted by the remaining regressors and should not exceed a value of 10, otherwise indexing the statistical results as unreliable [Chatterjee and Price, 1977]. To obtain the mean VIF for each regressor of interest ($/ta/_{95}$, $/ta/_{75}$, $/ta/_{55}$, $/da/_{easy}$, $/da/_{med}$, $/da/_{diff}$, $block_{easy}$, $block_{med}$, and $block_{diff}$), we extracted the respective regressors from the filtered and whitened design matrix for each run separately (temporal derivatives of the regressors were not included in this analysis). For each of these regressors the VIF was computed ($VIF = 1/(1-R^2)$) and then averaged across runs, resulting in six VIFs for the different event-related regressors and three VIFs for the block regressors for each subject. For the whole sample the mean event VIF was 5.19, the mean block VIF was 4.21, and the overall mean VIF was 4.86, indicating that a potential correlation between block and event regressors is not an issue in this study.

After computing contrast images for each condition and the contrasts of interest for each subject, group effects were computed using the contrast images in a mixed effects model treating subjects as random (one-sample *t*-tests, threshold $P < 0.005$, uncorrected, cluster-extent threshold of 7 voxels). Group analysis was performed to identify regions showing a modulation of sustained activity ($block_{diff} - block_{easy}$), transient activity ($/ta/_{55} - /ta/_{95}$ and $/da/_{diff} - /da/_{easy}$), and an interaction between sustained and transient effects ($(/da/_{diff} - /da/_{easy}) - (block_{diff} - block_{easy})$). An interaction is defined as the difference in response to one factor caused by another factor or processing demand. Therefore, we first assessed which voxels showed a linear parametric modulation of transient and sustained activity, respectively, during the easy, medium, and difficult conditions. We modeled this linear parametric modulation for transient and sustained activity, respectively, by weighting the corresponding regressors as [–1 0 1]. The interaction contrast then constitutes the difference in regression slopes of these parametric modulations ([–1 0 1] – [–1 0 1]), resulting in [–1 0 1 1 0 –1].

To confirm the interaction effect, we computed an additional ROI (region of interest) analysis based on the voxels found activated in the interaction contrast and averaged the signal magnitudes across these voxels for each subject. In analogy to the voxel-based analysis described above, we then performed a mixed-effects analysis using the resulting averaged signal magnitudes of the respective regressors in a one-way ANOVA.

MNI coordinates were converted to Talairach coordinates. Labels for activation foci were specified using the Talairach Daemon database [Lancaster et al., 2000].

RESULTS

Data from two subjects had to be excluded from further analysis because of uncorrectable motion artifacts and one subject aborted the measurement; the results are therefore reported for 14 subjects.

Behavioral Data

As expected, because hit rate and false alarm rate showed opposite changes with increasing ambiguity, d′ significantly decreased with increasing block difficulty (easy block: 4.94 ± 0.94, medium block: 4.20 ± 0.63, difficult block: 3.42 ± 0.70, $P = 0.001$, repeated-measures ANOVA) (Fig. 2B). There was a significant effect of difficulty for /ta/ (reaction time $P = 0.006$, accuracy of response $P = 0.001$, repeated-measures ANOVA) and no effect for /da/ (reaction time $P = 0.328$, accuracy of response $P = 0.484$, repeated-measures ANOVA).

fMRI Results

The mixed effects analysis revealed a modulation of sustained activity by task difficulty ($block_{diff} - block_{easy}$) in right middle temporal gyrus (BA 21), right superior temporal gyrus

(BA 38), and right pons (Table I). We found a modulation of transient activity by difficulty of categorization (/ta/$_{55}$ – /ta/$_{95}$) for /ta/ in the left precuneus (BA 7) (Table I). Similarly, the same area showed a modulation of transient activity for /da/ (/da/$_{diff}$ – /da/$_{easy}$, note that the /da/ were physically identical in all blocks) (Table I). The left precuneus showed an interaction between event-related activity and state-related activity (Fig. 2C; Table I). Figure 2D shows the signal change relative to the baseline in response to the different types of events in the precuneus (i.e., transient /ta/, transient /da/, sustained blocks). Note the increase in blood oxygenation level-dependent (BOLD) response for transient stimuli and the decrease in BOLD response for sustained blocks with increasing block difficulty. The additional mixed effects analysis with the signal magnitudes derived in an ROI analysis confirmed this interaction effect ($P = 0.001$).

DISCUSSION

To investigate the interaction between sustained activity elicited by state-related processes and transient activity elicited by event-related processes, we used a mixed blocked/event-related fMRI design and a phonological categorization task. The difficulty of the task was parametrically modulated by manipulating the categorizability of the syllables. As expected, discriminability significantly decreased and reaction times significantly increased with increasing stimulus ambiguity, indicating that the more ambiguous condition was more difficult. We found an interaction effect of transient and sustained activity in the left precuneus. Physically identical stimuli (/da/$_{easy}$, /da/$_{med}$, /da/$_{diff}$) elicited increasing changes in transient BOLD response with increasing block difficulty, whereas sustained activity (block$_{easy}$, block$_{med}$, block$_{diff}$) decreased with increasing block difficulty.

The increase of the transient BOLD signal with increasing task difficulty corroborates results from several previous event-related fMRI studies. Gould et al. [2003] used a visual paired-associates learning task with parametrically varied memory load to investigate the effect of task difficulty, while controlling for individual memory performance. They found a linear signal intensity increase in the precuneus with increasing task difficulty. A similar relationship of parametrically varied task difficulty and precuneus activation was also shown in another fMRI experiment using a spatial problem-solving task [van den Heuvel et al., 2003]. Because the noted studies used event-related designs to investigate the effect of task difficulty, these results can be attributed to transient processing. These results are potentially confounded by sustained processes, which cannot be detected using this experimental approach.

In contrast to transient activity, sustained activity in the precuneus decreased with increasing task difficulty in the present study. Previous blocked design studies reported a similar relationship between task difficulty and decreased activity [Mazoyer et al., 2002; McKiernan et al., 2003]. In a sustained attention task, activation in the precuneus was negatively correlated with reaction times. Considering reaction time as a proxy of task difficulty, activity in the precuneus thus decreased with increasing task difficulty [Mazoyer et al., 2002]. A decrease in activity during performance of an active task compared to a resting baseline was found in several cortical regions including the precuneus [McKiernan et al., 2003; Shulman et al., 1997a,b]. These deactivations occur across different tasks and stimulus modalities [Gusnard and Raichle, 2001; Mazoyer et al., 2001; McKiernan et al., 2003; Shulman et al., 1997b]. Gusnard and Raichle suggested that this kind of deactivation is related to an enhancement of neural activity during the resting state [Gusnard and Raichle, 2001; Raichle et al., 2001]. According to this theory, the resting brain is engaged in a number of internally cued endogenous processes such as monitoring the environment and one's internal state [Gusnard and Raichle, 2001], generating a representation of the world [Vogt et al., 1992], emotional processing [Maddock, 1999], as well as integrating emotional and cognitive processes [Greicius et al., 2003]. These processes are ongoing during rest and are posited to require attentional resources. When the brain switches from the resting baseline to performing an externally cued cognitive task, such as a semantic decision task, attentional resources have to be reallocated, resulting in decreased activity in the resting state network [Binder et al., 1999]. The precuneus is one of the structures in the brain with the highest level of glucose consumption in the resting state [Gusnard and Raichle, 2001], indicating a high level of information-processing during rest in this region, while activity is attenuated during demanding externally cued tasks. This implies that increasing task difficulty results in a decrease of the BOLD signal in the precuneus, because the task requires allocation of attention [McKiernan et al., 2003]. This corresponds with the pattern of decreased sustained activity found in this brain region in the present study. One should bear in mind that in the present study the sustained effect was not found by comparing active and passive states, but by comparing two active states, namely, difficult and easy blocks. This might indicate that the resting state network is not recruited by resting per se but that it is also activated during performance of easy tasks. Because the aforementioned studies that investigated the effect of task difficulty found the precuneus to be active using different tasks and modalities, and the present study showed the interaction of sustained and transient processes within the very same brain region, its activation might be considered to be relatively task-independent.

Because the studies discussed above used either blocked designs to investigate sustained activity or event-related designs to assess transient changes in activity, the interaction between transient processes and sustained processing has not yet been explored. Mixed blocked/event-related designs make it possible to investigate the interaction of sustained and transient processing. While an increase in task difficulty provoked a decrease of *sustained* activation in the precuneus, processing of identical stimuli (/da/$_{easy}$, /da/$_{med}$, /da/$_{diff}$) resulted in an enhanced *transient* hemodynamic signal with increasing task difficulty in the same structure. Similarly, stimuli with increased ambiguity (/ta/$_{95}$, /ta/$_{75}$, /ta/$_{55}$) induced an increased BOLD response in the precuneus. This similarity of the response patterns in the precuneus to /da/ and /ta/ stimuli indicates that the amount of transient activation does not depend on the actual physical properties of the stimuli, but on their expected difficulty.

A possible explanation of our results is that switching from internally cued processing to a difficult externally cued task requires reallocation of attention and thereby leads to reduced sustained activity in the precuneus. This reduction in baseline activity provides resources for processing incoming stimuli and leads to greater transient responses to stimuli that are expected to be difficult. During an easy task transient stimuli can be processed effortlessly, and the attentional resources are sufficient to still engage in internal imaginations and thoughts. In showing a decrease in sustained activity with increasing task difficulty and an increase in transient responses with increasing task difficulty in the precuneus, the results of the present study accommodate seemingly diverging findings from previous event-related and blocked design studies. This indicates that mixed blocked/event-related designs enable us to gain a more complete understanding of the cerebral organization of cognitive processes, because they allow the assessment of both event- and state-related correlates of cognitive performance, as well as their interaction.

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