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An fMRI investigation into the effect of preceding stimuli during visual oddball tasks

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HIGHLIGHTS

- We propose a new categorization of rare stimuli in the oddball task.
- BOLD signal throughout the brain is influenced by the sequence of preceding stimuli.
- We applied the new categorization successfully during visual oddball task examination.
- This presents a new method to explore attention, expectancy and decision-making mechanisms.

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ABSTRACT

Background: This study investigates the modulatory effect of stimulus sequence on neural responses to novel stimuli. A group of 34 healthy volunteers underwent event-related functional magnetic resonance imaging while performing a three-stimulus visual oddball task, involving randomly presented frequent stimuli and two types of infrequent stimuli – targets and distractors.
New method: We developed a modified categorization of rare stimuli that incorporated the type of preceding rare stimulus, and analyzed the event-related functional data according to this sequence categorization; specifically, we explored hemodynamic response modulation associated with increasing rare-to-rare stimulus interval.
Results: For two consecutive targets, a modulation of brain function was evident throughout posterior midline and lateral temporal cortex, while responses to targets preceded by distractors were modulated in a widely distributed fronto-parietal system. As for distractors that follow targets, brain function was modulated throughout a set of posterior brain structures. For two successive distractors, however, no significant modulation was observed, which is consistent with previous studies and our primary hypothesis.
Comparison with existing methods: The addition of the aforementioned technique extends the possibilities of conventional oddball task analysis, enabling researchers to explore the effects of the whole range of rare stimuli intervals.
Conclusion: This methodology can be applied to study a wide range of associated cognitive mechanisms, such as decision making, expectancy and attention.

1. Introduction

The oddball paradigm, in all its modifications, represents one of the most utilized experimental designs in cognitive neuroscience. It is based essentially on the random presentation of rare target stimuli among a train of frequent non-targets. In electroencephalographic recordings, target detection is associated with the P3 component of event-related potentials (ERPs; Sutton et al., 1965). When a second rare or "distractor" stimulus is introduced, another characteristic ERP is observed – the P3a waveform (Squires et al., 1975; Roman et al., 2005). In this three-stimulus form, the oddball task presents an opportunity to study a wide range of cognitive mechanisms, such as decision-making, attention, recognition, and memory update (Brazdil et al., 2005; Bledowski et al., 2004a;

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Halgren et al., 1995). Developments of functional magnetic resonance imaging (fMRI), intracranial EEG, and combined fMRI and ERP recordings have provided powerful tools that enable a more detailed identification of cerebral structures involved in rare target and distractor processing (Bledowski et al., 2004b; Clark et al., 2000).

In this study we designed an advanced categorization of stimuli that considers not only the type of actual rare stimulus, but also the type of the preceding rare stimulus (target or distractor) and the number of intervening frequent stimuli. This enabled us to identify brain regions in which the blood oxygen level-dependent (BOLD) response to rare stimuli is influenced by the preceding sequence. Such regions might play important roles in specific cognitive operations, such as expectancy (Esterman and Yantis, 2010), the need for cognitive closure (Kruglanski et al., 1991; Van Hiel and Mervielde, 2002), or working memory update (Stevens et al., 2005). Several studies have already investigated the modulatory influence of target-to-target interval (TTI) on hemodynamic responses (Horovitz et al., 2002; Stevens et al., 2005) and the P3 waveform (Steiner et al., 2013; Croft et al., 2003; Gonsalvez and Polich, 2002). This has shown a positive relationship between TTI and BOLD response amplitude, but no effect of distractor-to-distractor interval (DDI) on neural responses. In addition to aforementioned studies, our novel approach enabled to investigate hemodynamic modulation changes within the interval bounded by different types of rare stimuli – i.e. target-to-distractor (TDI) and distractor-to-target (DTI), respectively. The objective of the present study was to test our hypothesis, that increasing the number of frequent stimuli between two rare ones, changes the evoked hemodynamic response in specific brain regions, particularly those linked with expectancy and attention. We predicted that no such modulatory effect would be observed in the case of two subsequent distractors, because they are irrelevant for task accomplishment from the perspective of examined subject.

2. Materials and methods

2.1. Subjects

Recruited from undergraduate or doctoral students at the Medical Faculty of Masaryk University, Brno, the sample consisted of 34 right-handed healthy volunteers (22 males) with a mean age of 23.3 yrs (range = 20–29 yrs; SD = 2.4). All participants reported no history of neurological or psychiatric disorders, and all had normal or corrected-to-normal vision. Informed consent was obtained from all subjects before measurement, and the study was approved by the Ethics Committee of St. Anne's Hospital, Brno.

2.2. Task design

The experimental task comprised a three-stimulus visual oddball paradigm, divided into four sessions. Each session contained 84 stimuli presented pseudo randomly: 59 frequent, 12–13 target, and 12–13 distractor stimuli (i.e. 70% of frequents and 15% of targets and distractors, respectively). To avoid anticipation, the inter-stimulus interval (ISI) ranged between 4 and 6 s, and stimuli duration was constant at 500 ms. Stimuli consisted of yellow capital letters presented on a black background; targets were "X", frequents were "O," and distractors were various other letters. Stimuli were presented via a data projector and they were seen by the subjects through a mirror mounted on the radio-frequency head coil within the MR scanner. During the ISI, only the black background was projected. Participants were required to indicate when they detected a target stimulus by pressing a button placed in their dominant hand, as accurately and as quickly as possible.

2.3. Image acquisition

Images were acquired using a Siemens Symphony 1.5 T scanner. A total of 1024 functional volumes (256 per session) were obtained using T2*-weighted EPI sequence: flip angle = 80°, FOV = 250 × 250 mm, TR = 1660 ms, and TE = 45 ms. Each of 17 transverse slices had a matrix size of 64 × 64, and voxel dimensions were 3.44 × 3.44 × 6 mm (3 × 3 × 3 mm after spatial normalization). Anatomical T1-weighted high-resolution scans had a matrix size of 512 × 512 points, with voxel dimensions of 0.48 × 0.48 × 1.1 mm (1 mm isotropic voxel after spatial normalization).

2.4. Image processing and analysis

For image processing we used the SPM8 toolkit (Wellcome Department of Imaging Neuroscience, University College London, UK), running under MATLAB 7.5 computing environment (Mathworks Inc., Natick, MA). Results were visualized using the xjView toolbox (http://www.alivelearn.net/xjview). Pre-processing of the fMRI scans was performed for each session separately; this involved realignment and unwarping to suppress movement artifacts and field inhomogeneities, before the functional and anatomical images were coregistered. Spatial normalization then resampled both anatomical and functional scans into MNI stereotactic space, removing individual morphological differences and enabling a comparison of activation maps among subjects. Finally, functional images were spatially smoothed with a Gaussian kernel of FWHM = 8 mm, demonstrated to be optimal in terms of sensitivity (Mikl et al., 2008). High-pass filtering with a cut-off of 128 s was used to remove slow signal drifts.

Statistical analyses were performed with general linear modeling (GLM), with a canonical hemodynamic response function as a basis function. Statistical parametric maps were computed with *t*-statistics; the significance threshold was set to $p < 0.0001$ for conventional contrast and $p < 0.05$ for contrasts utilizing parametric modulation, both with correction for multiple comparisons with false discovery rate (FDR). To address our hypothesis, model specification involved parametric modulation and a more detailed categorization of stimuli. Specifically, every rare stimulus (target and distractor) was categorized according to the type of the previous rare stimulus, and the number of frequent stimuli between them. This provided us with 4 types of rare stimuli (4 regressors per session): target after target (TT; 23.45% of rare stimuli), target after distractor (DT; 26.45%), distractor after target (TD; 26.71%), and distractor after distractor (DD; 23.39%). We also implemented parametric modulators, defined as the interval between successive rare stimuli. Expressed as the number of frequents, this introduced yet another 4 regressors per session: Target-to-target interval (TTI; mean = 2.32, SD = 2.70, range = 0–26), distractor-to-target interval (DTI; mean = 2.04, SD = 2.41, range = 0–16), target-to-distractor interval (TDI; mean = 2.23, SD = 2.60, range = 0–17), and distractor-to-distractor interval (DDI; mean = 2.42, SD = 2.41, range = 0–20).

3. Results

3.1. Behavioral data

Overall, all subjects performed satisfactorily – all target stimuli were detected correctly, with only 0.73% of distractors and 0.27% of frequents falsely detected as a targets.

3.2. Conventional fMRI contrasts

To determine brain regions activated by certain categories of rare stimuli, first we performed data analysis using following fMRI contrasts: target > frequent ($T > F$), distractor > frequent ($D > F$), and