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MODALITY EFFECTS IN PACED SERIAL ADDITION TASK: DIFFERENTIAL RESPONSES TO AUDITORY AND VISUAL STIMULI

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Abstract—Paced Auditory Serial-Addition Task (PASAT) is a complex task commonly used to examine patients with diffuse brain damage. A visual version of the neuropsychological test (Paced Visual Serial-Addition Task, PVSAT) has also been introduced to clinical practice, and both versions were adapted to be used in neuroimaging, namely functional magnetic resonance imaging (fMRI). The aim of our work was direct comparison of auditory and visual versions of the paced serial addition test (PASAT/PVSAT) in a within-subject and within-session study and description of the commonalities and differences in both activated and deactivated brain regions. Twenty young adult right-handed healthy volunteers participated in the study and underwent whole-brain fMRI examination during PASAT and PVSAT performance. Higher-level statistical analysis was performed to generate group mean activation and deactivation maps for both tasks, their conjunctions and differences across modalities. In PASAT/PVSAT activation conjunction analysis, we confirmed the existence of a modality-independent neural network similar to working memory tasks and to previous PASAT or PVSAT studies. In PASAT/PVSAT deactivation conjunction analysis, we observed a rather symmetrical extensive pattern of deactivated regions, overlapping the default mode network. Significant differences between PASAT and PVSAT were found in the right frontal eye field (FEF) and bilaterally in the striate and extrastriate cortices. Activation in one task and deactivation in the other jointly contributed to significant differences in all occipital and occipitotemporal regions. Both tasks activated right FEF, but activation during PASAT was significantly stronger than during PVSAT. Between-modality differences should be considered when preparing and interpreting neuroimaging experiments.

Key words: fMRI, deactivation, default mode network, PASAT, PVSAT, verbal working memory.

INTRODUCTION

Functional magnetic resonance imaging (fMRI) has been widely used in cognitive neuroscience research. Patients with diffuse brain damage, e.g., patients after traumatic brain injury or suffering from multiple sclerosis have been often neuropsychologically examined with the Paced Auditory Serial-Addition Task (PASAT), that was introduced in the late 1970's. In the original format, the PASAT test consisted of 60 random digits which were sequentially presented by an investigator or from a tape. The subject was instructed to add the last digit to the preceding one, for every number supplied. The resulting sum had to be vocalized before the next digit was presented. Different presentation rates have been used (typically 2 or 3 s/digit) (Gronwall, 1977). The test was later included in standard cognitive testing of multiple sclerosis patients, e.g., the brief repeatable battery of neuropsychological tests in multiple sclerosis (BRBMS) (Cutter et al., 1999) or Multiple-Sclerosis Functional Composite (MSFC) score (Fischer et al., 1999). PASAT became popular in diseases with underlying diffuse brain pathologies for its complex recruitment of cognitive processes, since PASAT imposes high demands on the subject's working memory capacity, requiring controlled information processing (attention), good auditory functioning and calculating abilities (Sherman et al., 1997).

Visual version of the task (Paced Visual Serial-Addition Task, PVSAT), in which digits are displayed on a screen, was also described (Diamond et al., 1997).

fMRI has been used for studying brain networks engaged during both auditory (Audoin et al., 2003; Mainero et al., 2004; Au Duong et al., 2005; Forn et al., 2006) and visual (Staffen et al., 2002; Lazeron et al., 2003; Rachbauer et al., 2006; Bonzano et al., 2009) adapted versions of PASAT/PVSAT. The results show good agreement on the expected distributed brain networks related to the engaged processes, namely fronto-parietal working memory and attention networks. Nevertheless, differences in the task and acquisition

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Abbreviations: ACC, anterior cingulate cortex; BOLD, blood oxygen level-dependent; DMN, default mode network; FEF, frontal eye field; fMRI, functional magnetic resonance imaging; IFJ, inferior frontal junction; IPS, intraparietal sulcus; LOC, lateral occipital complex; MFG, middle frontal gyrus; MRI, magnetic resonance imaging; PASAT, Paced Auditory Serial-Addition Task; PET, positron emission tomography; PVSAT, Paced Visual Serial-Addition Task; SMA, supplementary motor area.

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parameters do not permit exact assessment of the commonalities and differences in the brain networks activated by PASAT and PVSAT. So far no direct comparison of the two versions investigated within a single study has been published, even though visual and auditory versions of a related *n*-back task demonstrated significant differences according to sensory modality, mainly in the prefrontal and posterior temporal and occipital regions (Crottaz-Herbette et al., 2004; Rodriguez-Jimenez et al., 2009).

Finding differences in the volume of multimodal association cortical areas might also explain the described small difference in behavioral PASAT and PVSAT performance (Diamond et al., 1997). Furthermore, almost all previously published studies utilizing PASAT or PVSAT in healthy subjects or patients focused on describing and comparing regions of brain activations (task-related increases in blood oxygen level-dependent (BOLD) signal). Regions of brain deactivations are usually omitted from those studies, even though deactivation and default mode network (DMN) suppression disturbances are drawing increasing attention and differences in deactivations between multiple sclerosis patients and healthy controls were recently published (Morgen et al., 2007; Forn et al., 2013). Omitting deactivations from the considerations might lead to misinterpretations of the neuroimaging results since a contrast between two datasets could be caused by activation in one dataset or by deactivation in the second one (Crottaz-Herbette et al., 2004; Daselaar et al., 2004). To our knowledge, only one map of PASAT-induced deactivations was published in a study of patients suffering from sleep apnea (Archbold et al., 2009).

The aim of our work was to directly compare the auditory and visual versions of the paced serial addition test (PASAT/PVSAT) in a group of healthy volunteers and describe the commonalities and differences in both activated and deactivated brain regions. We hypothesized that both tasks will share active brain networks underlying attention, working memory and calculation, both tasks will deactivate the default mode system, whereas the differences may be related to higher-level sensory processing, phonological encoding of visual stimuli (Crottaz-Herbette et al., 2004; Suchan et al., 2006) or differences in task performance (Diamond et al., 1997).

EXPERIMENTAL PROCEDURES

Participants

Twenty volunteers (ten women, ten men), with a mean age of 23.0 (SD 2.7) years, participated in this study. All participants were university students or recent graduates, all were right-handed according to Edinburgh inventory (Oldfield, 1971). The research protocol was approved by the institutional ethics committee, subjects participated after providing written informed consent. Before the scan, the PASAT and PVSAT tasks were explained and practiced.

Data acquisition

Magnetic resonance imaging (MRI) data were acquired on a 1.5-Tesla scanner (Siemens Avanto, Erlangen, Germany) with a standard head coil. The subject's head was immobilized with cushions to assure maximum comfort and minimize head motion. The MR imaging protocol included functional T_2^*-weighted BOLD images during task performance and control state. BOLD images were acquired with gradient-echo echo-planar imaging (30 axial slices parallel to the AC-PC line, 5-mm thick, repetition time/echo time = 2500/41 ms, flip angle 80°, field of view = 220 mm, matrix 64 × 64) to provide 3.4-mm × 3.4-mm × 5.0-mm resolution. In total, 144 images were acquired per each 6-min functional run. Anatomical spin echo T_1-weighted images (30 axial 5-mm in-plane slices, repetition time/echo time = 500/15 ms, flip angle 90°, field of view = 230 × 173 mm, matrix 192 × 144) and a high-resolution 3-dimensional scan (magnetization-prepared rapid acquisition gradient echo, MPRAGE) were acquired to provide an immediate overlay with functional data and better anatomical reference.

In-plane fluid-attenuated inversion recovery (FLAIR) images were used to screen for unsuspected brain lesions.

fMRI tasks

Participants completed two 6-min runs of the PASAT and two similar runs of the PVSAT modified for MRI setting as described previously (Staffen et al., 2002; Mainero et al., 2004; Archbold et al., 2009).

During six blocks of 30 s each, the subjects were required to add up the presented semi-randomized single digits (ranging from one to nine), adding each digit to the one immediately preceding it. A new stimulus was presented every 3 s. Subjects were instructed to add up the numbers silently and to raise their right thumb whenever the sum equaled 10. There were 14 or 15 such instances during each run. A single observer recorded response accuracy during image acquisition. Six PASAT/PVSAT-blocks were alternated with six control periods of 30 s each in which digits were presented in the same timing and subjects were instructed to raise their right thumb whenever the number ''10'' was presented (Mainero et al., 2004; Archbold et al., 2009).

In PASAT, auditory stimuli were presented through fMRI compatible headphones. The duration of auditory stimuli was 305–634 ms (mean 475 ms). Sound volume was adjusted so that each participant could hear the stimuli properly. Participants had their eyes closed during the PASAT runs.

In PVSAT, visual stimuli were presented via a rear projection screen and a mirror on top of the head coil. Single digits were located in the center of the screen (font Arial, vertical view angle 4.4°), every digit was displayed for 500 ms followed by 2500 ms of blank screen.

The order of the PASAT and the PVSAT runs was counterbalanced across the subjects.

Statistical analysis

Numbers of correct responses to target sums in PASAT and PVSAT runs were compared using a paired two-sample *t*-test.