Behavioural Brain Research 215 (2010) 21–27

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Frontal cortex activation associated with speeded processing of visuospatial working memory revealed by multichannel near-infrared spectroscopy during Advanced Trail Making Test performance

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ARTICLE INFO

Article history:
Received 9 November 2009
Received in revised form 4 June 2010
Accepted 9 June 2010
Available online 19 June 2010

Keywords:
Visuospatial working memory
Multichannel near-infrared spectroscopy
Trail Making Test
Frontal cortex
Oxygenated hemoglobin
Cerebral blood volume

ABSTRACT

Although visuospatial working memory (VSWM) is commonly used during speeded and unconscious memory processing in daily life, most neuroimaging studies on VSWM use tasks that impose motor restrictions onto the examinees to avoid movement-related artifacts. Multichannel near-infrared spectroscopy (NIRS), however, can measure cortical activation during cognitive processing without interfering with task procedure. The purpose of this study is to determine whether multichannel NIRS can detect VSWM-induced frontal cortex activation similar to that seen in VSWM performance in daily-life activity. Using NIRS, we measured relative changes in the concentration of oxygenated hemoglobin as an index of frontal activation in 52 measurement points (channels) on the frontal area during the Advanced Trail Making Test (ATMT), a tool used to assess VSWM. The ATMT consists of two tasks, R and F, with the former assessing motor factors and the latter relating to both motor and cognitive factors involved in speeded and unconscious VSWM operations. Twenty-six healthy volunteers were enrolled in this study. Channel activation during Task F performance was observed bilaterally over the dorsolateral and ventrolateral prefrontal cortex. This distribution may reflect central executive function of working memory. Channel activation during Task R was circumscribed to part of the left ventrolateral prefrontal cortex partially overlapping with areas active during Task F performance, likely representing task-related motor factor activation. Our findings suggest that multichannel NIRS during ATMT performance is an appropriate means of measuring cortical activation induced by VSWM operations during daily activity.

1. Introduction

Visuospatial working memory (VSWM) is a cognitive function involved in temporal storage and effective manipulation of optical information related to object identification and spatial location [7,35,41]. It has been reported that several brain regions within the frontal lobe such as the dorsolateral prefrontal cortex (DLPFC), the ventrolateral prefrontal cortex (VLPFC), the frontal eye field (FEF) cortex, and the supplementary motor area (SMA) are involved in VSWM processing, with variation depending on task-specific features and modes of reaction [1,12,14,15,20,22,29,30,31,39,40,41]. The majority of these data stem from studies using static and conscious memory-demanding tasks, such as the delayed response task and the n-back task. Clinically convenient, these tasks use controlled stimuli and require little space and time, but they impose motor restrictions onto the examinees to avoid movement-related neuroimaging artifacts. This is an important limitation, as in daily activity, memory representation is continuously updated during fast and unconscious VSWM operations. It is therefore unclear whether aforementioned brain areas truly reflect those activated during VSWM operations in daily activity.

The Advanced Trail Making Test (ATMT) is a derivative from the Trail Making Test Part A (TMT-A), which is a simple and standardized neuropsychological test that is widely used in clinical practice [3,42]. In the TMT-A the subject is asked to connect on paper the encircled numbers 1 through 25 in ascending order by drawing a line with a pencil as rapidly as possible. In speeded memory processing, this task requires the subject to use motor factors, including visual search and visuomotor coordination as well as cognitive factors, especially VSWM processing, to memorize locations

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doi:10.1016/j.bbr.2010.06.016

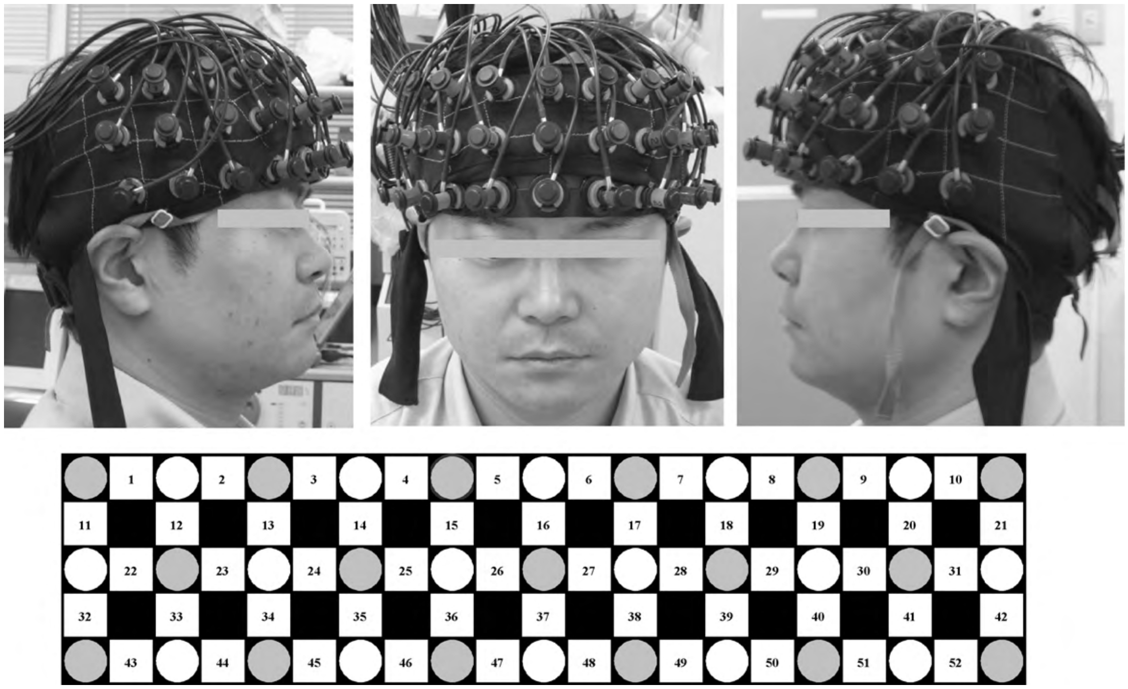

Fig. 1. Location of optical diodes and measurement points (channels). Channels 1 through 52 are depicted as white squares between laser diodes (emitters, gray circles) and photodiodes (detectors, white circles).

of sequential numbers during a visual search [2,11,33,46,49,51]. The TMT-A therefore targets speeded and unconscious VSWM operations representative of daily activity. The ATMT is highly similar to the TMT-A, but contains the following adjustments. The ATMT consists of two tasks, the Fixed Task (Task F) and Random Task (Task R). Task F and TMT-A procedures are very much alike, with the exception of Task F being administered by button pressing on a touch-sensitive panel, which allows the subjects to continue the task performance to induce enough cortical activation. A critical difference between the Task F and Task R is the latter's design to elicit activation related exclusively to motor factors to perform Task F [37,50].

Unlike other neuroimaging techniques such as MRI and PET, multichannel near-infrared spectroscopy (NIRS) is a non-invasive brain functional imaging method that does not restrict subject movement and is therefore a good choice for the ATMT. In addition, NIRS is not affected by electromagnetic noise from electric devices [34]. Near-infrared light is a powerful tool for biological analyses as it can not only penetrate deeply into tissues, but it is also differentially absorbed by hemoglobin (Hb) depending on the oxygenation state of the latter and the optical path length in the tissue (modified Beer–Lambert Law). The law is demonstrated as $A = \varepsilon CL + S$, in which A is the absorbance, ε is the molar absorption coefficient, C is the chromophore concentration, L is the optical path length between the emitter and the detector of the NIRS probe, and S is the optical attenuation related to scattering. This relationship is used in NIRS to measure relative changes in the concentration of oxygenated hemoglobin ([oxy-Hb]) and deoxygenated hemoglobin ([deoxy-Hb]) by emitting near-infrared light at several different wavelengths into brain tissue and detecting its remnant [18,24,28,47]. Areas of high neuronal activation show increased oxygen consumption and enhanced blood supply to ensure provision of oxygenated hemoglobin [19,23]. In other words, neural activation is measured by relative changes of regional cerebral blood volumes.

Several NIRS studies have reported frontal activation during TMT-A performance [33,46,52,53]. The cognitive factors measured by this task are similar to those assessed with Task F of the ATMT. The above-mentioned studies reported bilateral activation, primarily in the prefrontal cortex, although the measuring range in these experiments may have been too restricted. In the here-presented work, multichannel NIRS was used to provide wide coverage of the frontal area during the ATMT in an effort to detect VSWM-induced cortical subregions within the frontal cortex that show an activation pattern consistent with VSWM performance in daily-life activity. To confirm that Task F activation was indeed related to VSWM processing, we additionally measured activation during Task R, which is assumed to elicit exclusively motor factor-related activation. We hypothesized that the DLPFC and the VLPFC activation associated with speeded and unconscious VSWM processing in a paradigm mimicking VSWM performance in daily-life activity can be detected by using multichannel NIRS during ATMT performance.

2. Materials and methods

2.1. Subjects

Twenty-eight healthy volunteers were recruited for this study. Two were excluded due to left-handedness and excessive motion artifacts, leaving a total of 26 right-handed subjects (14 males and 12 females, age 27.2 ± 6.8 yrs; range, 19–40 years). None of the participants had a history of psychiatric or neurological disorders. This research was approved by the ethics committee of Osaka University Graduate School of Medicine and all procedures and methods were in keeping with the policies and principles contained in the Declaration of Helsinki. All subjects gave written informed consent prior to the experiments.

2.2. NIRS measurements

We measured relative changes in the concentration of oxygenated hemoglobin ([oxy-Hb]), deoxygenated hemoglobin ([deoxy-Hb]) and calculated total hemoglobin by combining the two former based on NIRS data (ETG-4000; Hitachi Medical Corporation, Tokyo, Japan) during ATMT performance. The ETG-4000 uses two kinds of near-infrared light, 695 nm and 830 nm. Seventeen laser diodes (emitter) and 16 photodiodes (detector) were mounted reciprocally at 3-cm intervals on a piece of elastic rubber headwear attached to the frontal area with adjustable straps. Approximate detection depth was 2–3 cm below the skin surface in 52 separate regions (approx. 6 cm high × 30 cm wide). The lowest center