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Original article

Developmental changes in frontal lobe function during a verbal fluency task: A multi-channel near-infrared spectroscopy study

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Abstract

Objective: Near-infrared spectroscopy (NIRS) is commonly used to investigate continuous changes of brain activation and has excellent time resolution. Verbal fluency task (VFT) is widely used as a neuropsychological test of frontal lobe function. The aim of this study was to investigate normal developmental change in frontal lobe function during VFT performance using multi-channel NIRS, specifically focusing on oxygenation hemoglobin (oxyHb) changes. *Methods:* The subjects were 9 adults and 37 childrens who were all healthy right-handed volunteers. Children were divided into four age groups (group A, 6–8 years; group B, 9–11 years; group C, 12–14 years; group D, 15–18 years). The [oxyHb] changes were measured with 22 channels of NIRS during VFT. We defined the frontopolar region as the region of interest for analysis, and calculated the *Z*-score to compare the data between groups. *Results:* The task performance changed with age. There were significant differences between group A and other groups. The *Z*-score of [oxyHb] also significantly increased with age, when comparing adults to groups A and B. The task performances decreased with time in all groups. In contrast, [oxyHb] only continued to increase in the adult group. *Conclusion:* The verbal retrieval functions begin to mature in early adolescence and continue to grow up to adulthood.

Keywords: Development; Frontal lobe function; Retrieval; Verbal fluency task; Near-infrared spectroscopy

1. Introduction

Near-infrared spectroscopy (NIRS) is an optical method used to investigate the oxygenation of brain tissue. NIRS employs near-infrared light that penetrates the biological tissues and is absorbed mainly by two chromophores (oxygenated hemoglobin (oxyHb) and deoxygenated hemoglobin (deoxyHb)) with different absorption spectra. From the amount of reflected near-infrared light it is possible to calculate changes in the concentration of oxyHb and deoxyHb. These NIRS data are assumed to reflect regional cerebral blood volume [1]. In contrast to other types of functional neuroimaging (e.g., fMRI and PET), NIRS is resistant to artifacts related to body movements. Patients are allowed to remain in a relaxed sitting position without head fixation and without being confined to a narrow, loud scanner environment. Moreover, NIRS has excellent time resolution and enables investigate of continuous changes in brain activation. As a result of these advantages, NIRS is suitable for psychological experiments, and is particularly well-suited for developmental studies. Indeed, recent NIRS studies have successfully measured children's cortical responses associated with

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cognitive performance [2–5]. However, almost all of these studies have focused on a particular age group (infant, pre-school) or on a single psychiatric disorder (attention-deficit/hyperactivity disorder (AD/HD), pervasive developmental disorders (PDD)). Few studies have investigated the normal development of brain function from childhood to adulthood [6]. As mentioned previously, NIRS has excellent time resolution and previous studies have found changes in [oxyHb] with time in ADHD and schizophrenia [7,8]. This pattern of [oxyHb] change during a cognitive task is thought to reflect the brain function associated with ADHD and schizophrenia. Therefore, it is necessary to evaluate brain activity over developmental time in subjects undergoing normal development for comparison with the possibly altered patterns of oxyHb change observed in abnormal development associated with neurodevelopmental disorders.

In functional neuroimaging studies, verbal fluency task (VFT) is generally used for evaluation of language lateralization, which involves Broca's area. However, VFT reflects cognitive flexibility and search strategy, which are included in executive function, and it is also a useful measurement for estimating frontal lobe function. The two most commonly used types of fluency tasks are semantic and letter fluency, and each is thought to be related to different cognitive processes and strategies. Verbal fluency can be assessed simply by asking subjects to generate as many words as possible in a limited amount of time. VFT is dependent upon executive functions [9,10], which develop from the elementary school years through adolescence [11]. Studies that have analyzed the cluster and switching formation appear to indicate that VFT strategies change with age [12,13]. Thus, VFT is a relatively simple task and it is possible for resulting data to reflect the development of frontal lobe function. We used this task to evaluate changes in frontal lobe function with age.

Functional neuroimaging studies have investigated differences in brain activation during VFT between children and adults. In their fMRI study, Gaillard et al. found that children and adults show activation in similar brain regions, predominantly in Broca's area and in the left dorsolateral prefrontal cortex, but children had increased levels of activation compared to adults [14]. However, fMRI has poor time resolution, making it impossible to examine the dramatic changes in frontal cortex activity over time using this method. Kawakubo investigated the developmental change in frontopolar cortex during VFT [6]; however, they used 2-channel NIRS, and their studies were focused on BA10. To our knowledge, no studies have investigated changes in brain activity with time course. Therefore, in this study we aimed to investigate normal development of prefrontal lobe function in a range of ages, from school-aged children to adults, using multi-channel NIRS, focusing specifically on oxyHb changes with time.

2. Methods

2.1. Participants

Nine adults (mean age, 34.8 ± 4.8 years; 4 males, 5 females) and 37 children (mean age, 16.6 ± 9.7 years; 23 males, 14 females) participated in the study. Children were divided into four age groups (group A; $n = 9$, 6–8 years, mean age, 7.6 ± 0.7 years, group B; $n = 9$, 9–11 years, 10.7 ± 0.9 years, group C; $n = 10$, 12–14 years, 13.5 ± 0.6 years, group D; $n = 9$, 15–18 years, 17.5 ± 1.2 years). All participants were healthy, native Japanese speakers and were right-handed. Children attended regular schools and had no learning disorders, neurological deficits, or developmental problems, as reported by their teachers or parents. Their academic achievements were standard in their school. Moreover, we evaluated their frontal lobe function using frontal assessment battery which was designed to evaluate frontal lobe function easily and quickly at the bedside. Subject's scores were not significantly different from healthy subject's scores. Adult participants were health care workers. The procedures for informed consent and the study design were approved by the Medical Ethical Committee of Yamanashi University, and informed consent was obtained from each participant and from the children's parents.

2.2. Task procedures

We used a block design consisting of a 30-s control task before letter VFT (pre-task control), a 60-s VFT, and a 55-s control task after VFT (post-task control). Subjects performed these tasks successively. During measurements, subjects sat in front of a personal computer in a silent room. During VFT period, the subjects were instructed to say as many words that begin with the syllable /ka/ every time the syllable was displayed on the computer screen. We displayed /ka/ every 3 s on the computer panel to prevent inattention or abandonment. In a prior Japanese study of adults, /ka/ was found to be the syllable for which it is easiest to generate words [15]. In the control task, subjects were instructed to simply repeat the Japanese syllables, /a/, /i/, /u/, /e/, and /o/ when they were displayed on the panel.

2.3. NIRS measurements

2.3.1. NIRS machine

In this study, we examined the change in [oxyHb] during VFT because previous studies showed that [oxyHb] was a more sensitive task-related indicator of rCBF