

available at www.sciencedirect.comwww.elsevier.com/locate/brainres**BRAIN
RESEARCH****Research Report****Hemodynamic responses to visual stimuli in cortex of adults and 3- to 4-year-old children**Gerard B. Remijn^{a,e,*}, Mitsuru Kikuchi^a, Yuko Yoshimura^a, Kiyomi Shitamichi^a, Sanae Ueno^a, Kikuko Nagao^{b,c}, Toshio Munesue^b, Haruyuki Kojima^d, Yoshio Minabe^a^aDepartment of Psychiatry and Neurobiology, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan^bResearch Center for Child Mental Development, Kanazawa University, Kanazawa, Japan^cHigher Brain Functions and Autism Research, Department of Child Development, United Graduate School of Child Development, Osaka University, Kanazawa University and Hamamatsu University School of Medicine, Osaka University, Osaka, Japan^dKanazawa University, Department of Psychology, Kanazawa, Japan^eKyushu University, International Education Center, Fukuoka, Japan

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ABSTRACT

In this study we used near-infrared spectroscopy (NIRS) to measure relative changes in cortical hemodynamics from 19 adult and 19 preschool children (aged 3–4 years old), while they watched epochs of static and motion pictures extracted from TV programs. The spatio-temporal characteristics of oxygenated and deoxygenated hemoglobin volumes (oxy- and deoxy-Hb) of both subject groups were described and compared where appropriate for five regions of interest (ROIs). These were striate, left and right middle temporal, and left and right temporo-parietal areas. Over these areas, deoxy-Hb volumes did not differ between both groups. Preschool data showed significant increases in oxy-Hb over striate, middle temporal and temporo-parietal areas in response to visual motion stimuli. Static stimuli caused a significant oxy-Hb increase over striate and left middle temporal areas. Surprisingly, changes in adult oxy-Hb were not profound and did not show a significant oxy-Hb increase in striate and middle temporal areas in response to the motion stimuli, warranting further research. In spite of oxy-Hb volume differences, oxy-Hb recovery to baseline followed a similar pattern in both groups in response to both static and motion stimuli. Together, the results suggest that near-infrared spectroscopy is a viable method to investigate cortical development of preschool children by monitoring their hemodynamic response patterns.

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1. Introduction

Neuro-imaging studies on the developing brains of preschool children have seldom been performed without medical necessity and/or sedation (Dowker, 2006; Redcay et al., 2007). Yet

exactly in this particular age group a wealth of developmental processes occur in the brain. To name but a few, behavioral studies with 3- to 5-year-olds have shown development in cognitive and sensory functioning pertaining to the understanding of symbolic concepts, i.e., the formation and use of

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representations (DeLoache, 1989), temporal causality (Povinelli et al., 1999), the use of verbal and nonverbal memory (Simcock and Hayne, 2003), perspective-taking in communication (Nilsen and Graham, 2009), reading (Lonigan et al., 2000), grammar comprehension (Bannard et al., 2009), word category formation (Skipp et al., 2002) and a range of multimodal integration skills (e.g., Liégeois and Schonen, 2002). From a clinical perspective, atypical cortical development can also come to light in this age group. Examples of this are attention deficits and/or hyperactivity (Calis et al., 1990), and autism spectrum disorder (Wiggins et al., 2006). Monitoring cortical functioning in preschool children would greatly enhance our understanding of (a-)typical development processes.

Studies that have monitored cognitive functioning in the brain of healthy 3- to 5-year-olds often had to deal with motion artifacts. Attempts to shorten the experimental task and allowing rest periods during the task have been fruitful in a study that measured visual evoked potentials (Johansson and Jakobsson, 2006). Another way to deal with motion artifacts has been monitoring preschoolers while they were asleep. Functional magnetic resonance imaging (fMRI) studies with sleeping preschoolers have obtained insightful results, especially with regard to the auditory modality. Schumann et al. (2010), for example, showed that typically developing 2- to 4-year-old brains revealed functional connectivity between (sub)cortical areas, as well as changes in the blood oxygenated level dependent (BOLD) signal in response to speech and non-speech. In the visual modality, however, the magnitude of the BOLD responses in occipital cortex is thought to be influenced when sleep-inducing anesthetics are used. Even without anesthetics, the fact that the participants have their eyes closed during experiments is thought to cause unnatural BOLD responses as compared to those from participants in normal viewing conditions (Marcar et al., 2004; Redcay et al., 2007). Another limitation of research on the visual modality with sleeping preschoolers is that stimuli are often restricted to flashes or checkerboard patterns with a high luminance contrast.

Recently, a study by Moriguchi and Hiraki (2009) has shown that monitoring the visual cortex of healthy, awake preschool children has become increasingly feasible with a relatively new neuro-imaging technique called near-infrared spectroscopy (NIRS; e.g., Jöbsis, 1977; Hoshi, 2007). In a nutshell, NIRS is a non-invasive technique that comprises the use of arrays of infrared light-emitting and -receiving optodes. Arranged in a checkerboard-like pattern, the optodes are placed on a part of the brain. The light-emitting optodes send infrared light through the scalp and skull onto the brain and the light-receiving optodes pick up the amount of reflected light returning from the brain. The difference between emitted and received light allows estimation of the amount of oxygenated and deoxygenated hemoglobin (oxy-Hb and deoxy-Hb) over that area. These hemodynamic measures can provide an indication of local cortical activity (Devor et al., 2005). As reviewed by Aslin and Mehler (2005), several advantages of NIRS over other existing brain imaging techniques are its safety and tolerance to bodily movements, including head movements. This makes NIRS a suitable alternative for monitoring the brains of preschool children during awake, non-sedated behavior without any restrictions to the sensory stimuli.

Until now, however, little is known about the hemodynamic response patterns of preschoolers monitored with NIRS. Apart from the Moriguchi and Hiraki study (2009), most NIRS studies have involved healthy and at-risk babies generally younger than 1 year old (Meek et al., 1998; Sakatani et al., 1999; Taga et al., 2003; Bortfeld et al., 2007; Otsuka et al., 2007; Wilcox et al., 2009). These studies revealed two characteristics of hemodynamic activity particular to neonates as compared to adults. In adults, oxy-Hb in a targeted cortical area typically increases 3–6 s after the onset of sensory stimulation and then gradually recovers to baseline (Hoshi, 2007). In neonates, this oxy-Hb recovery to baseline is relatively slow in that peak values are maintained for a longer duration than in adults (Bortfeld et al., 2007). A second characteristic of neonate hemodynamics is increased deoxy-Hb, rather than flat or decreased deoxy-Hb levels as often measured over adult cortex (Meek et al., 1998; Wilcox et al., 2005). Immature neurovascular coupling is often mentioned as underlying both characteristics of hemodynamic activation patterns in neonate brain. Late oxy-Hb recovery to baseline is assumed to be a ‘plumbing’ issue: a relatively less smooth redirection of oxy-Hb between cortical areas, for example, in response to multimodal stimuli (Bortfeld et al., 2007). Wilcox and colleagues (2005), in explaining the relative increase of deoxy-Hb in temporal cortex of infants aged 6.5 months, mentioned that the ratio of oxygen consumption change to blood flow change could vary between cortical areas, indeed involving developmental differences in neurovascular coupling. It is still unknown, however, until what age cortical hemodynamic activity patterns show these two trends that are typical to neonate hemodynamics. The NIRS study with preschool children found adult-like trends in prefrontal hemodynamic activity of 5-year-olds (Moriguchi and Hiraki, 2009). However, oxy-Hb recovery over time and deoxy-Hb levels relative to those of adults were not described in detail.

In the present study, we further wish to investigate the feasibility of NIRS in monitoring characteristics of hemodynamic responses in healthy preschool cortex. We monitored hemodynamic activity over posterior cortical areas of 19 adults and 19 3- to 4-year-olds in response to visual stimuli consisting of fragments of TV programs made for a preschool audience (Fig. 1). The stimuli comprised of static and dynamic motion pictures with, respectively, a low and high number of cut-scenes (or “jump scenes”). Both the static and motion stimuli were accompanied by sound, but only in the motion stimuli was this synchronized with visible actions of the TV program’s characters. The aim was to describe the hemodynamic characteristics of 3- to 4-year-olds in response to these stimuli. The preschool data set was compared, where appropriate, with adult hemodynamic responses to the same stimuli in spatio-temporal characteristics including deoxy-Hb volume and oxy-Hb recovery.

Five cortical regions of interest (ROIs) were defined (Fig. 1C; see details in section 4.4). The first was a striate cortical area (V1 or primary visual cortex). This area is known to mediate early stages of visual processing and responsive to even low-contrast visual stimuli when fMRI is used (e.g., Mendola et al., 2006). The second and third ROI were, respectively, left and right middle temporal and medial superior temporal areas known to mediate motion processing. These areas have been

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