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# Frontal Lobe Activation during Object Permanence: Data from Near-Infrared Spectroscopy

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**The ability to create and hold a mental schema of an object is one of the milestones in cognitive development. Developmental scientists have named the behavioral manifestation of this competence object permanence. Convergent evidence indicates that frontal lobe maturation plays a critical role in the display of object permanence, but methodological and ethical constrains have made it difficult to collect neurophysiological evidence from awake, behaving infants. Near-infrared spectroscopy provides a noninvasive assessment of changes in oxy- and deoxyhemoglobin and total hemoglobin concentration within a prescribed region. The evidence described in this report reveals that the emergence of object permanence is related to an increase in hemoglobin concentration in frontal cortex.** © 2002 Elsevier Science (USA)

## INTRODUCTION

The second half of the human infant's first year is marked by the emergence of several cognitive and emotional competences (Kagan, 1984; Bell and Fox, 1994) including the initial appearance of object permanence (stage IV of Piaget's sensory motor period) (Piaget, 1954). The first sign of this attainment, observed typically at 7–9 months, is the directed search for an object observed being hidden by an adult. The infant's search for the object is interpreted as indicating that she believes that the object exists despite the fact that it cannot be seen. Object permanence paradigms are made more difficult by increasing the length of time during which the infant must wait—and, therefore, maintain a schema for the object—before being allowed to search. Convergent data from nonhuman primates (Diamond and Goldman-Rakic, 1989) and human infants (Bell and Fox, 1992) implicate maturation of the frontal lobe as critical for the ability to tolerate increasing delays. Human and monkey infants, and adult monkeys with lesions of the dorsolateral prefrontal cortex, are unable to perform correctly on the simplest tests (those with the shortest delays) of object permanence (Diamond *et al.*, 1989). Bell and Fox (1992), who examined electroencephalograph (EEG) recordings from frontal scalp regions in human infants between the ages of 7 and 12 months, found that increased EEG power in the frontal areas was associated with better performance on difficult permanence tasks. Post-mortem studies have revealed that there is a surge in synaptic proliferation that occurs as the infant's first year ends. Maximum synaptic density has been reported to occur at approximately 12 months (Huttenlocher, 1979); further, positron emission tomography (PET) has demonstrated a maturational rise in prefrontal glucose metabolism between 8 and 12 months of age (Chugani and Phelps, 1986).

Study of frontal lobe maturation in healthy human infants with traditional neuroimaging methods has been limited by methodological obstacles. For example, fMRI and PET have not been approved for use with infants in nonclinical settings. Further, if collection of data from infants using either of these techniques were permissible, it would require that the infant be sedated to acquire data free of motion artifacts. This requirement makes both of these techniques unsuitable for the study of neurophysiology in awake, behaving infants. More recently, a relatively new technique, near-infrared spectroscopy (NIRS), has been used to measure changes in cerebral oxygenation in human subjects.

The use of NIRS rests on the idea that the recording of activity-dependent changes in cerebral blood volume, cerebral blood flow (CBF), or oxygen saturation is generally dependent on detecting changes in the amount, dynamic properties, or concentration of hemoglobin in its different chemical binding forms. In addition to possessing unique magnetic properties, which make it traceable by MRI, hemoglobin is a chromophore with useful optical properties. In particular, the absorption spectra of oxyhemoglobin (HbO) and deoxyhemoglobin (Hb) differ significantly for near-infrared light between 750 and 1000 nm (Villringer and Chance, 1997). At the same time, biological tissue is



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weakly absorbent of this portion of the light spectrum. The optical properties of hemoglobin and the weakly absorbent nature of the light spectrum between 750 and 1000 nm make possible, and indeed highly effective, the noninvasive spectroscopic determination of HbO and Hb concentrations *in vivo.* In sum, NIRS is able to accurately measure absolute changes in the local concentrations of intravascular oxyhemoglobin, deoxyhemoglobin, and, from their summated change, total hemoglobin (THb) (Villringer *et al.,* 1993; Soul and duPlessis, 1999).

There are two crucial principles governing interpretation of NIRS data. The first is that changes in the amount of absorption of near-infrared light by hemoglobin molecules is related to changes in the state of oxygenation. The second is based on the idea that changes in HbO and Hb detected by NIRS reflect changes in neurophysiological activity and, as a result, may be used as an index of brain activity. Increased activity of neurons is associated with increases in glucose and oxygen consumption. In addition to these intracellular events, local brain activity induces a local arteriolar vasodilation and, consequently, an increase in local cerebral blood volume and blood flow (see Villringer and Chance (1997) for a review). It has been assumed, therefore, that there is a tight coupling between regional cerebral metabolism and regional CBF in the normal brain (Raichle *et al.,* 1976).

Despite the fact that NIRS is a relatively new technique, there have been a number of reports that have demonstrated changes in the NIRS signal during behavioral tasks in both human adults and human infants. Following the tradition of functional magnetic resonance imaging and positron emission tomography, initial studies using NIRS examined stimulation of primary sensory areas. These areas have been chosen for exploration because of their reliable anatomical localization and the case with which they can be stimulated physiologically. These initial studies found a consistent and reliable increase in HbO in response to neural activation. In some of the studies there was also an increase in Hb, but this finding was not as consistent. In summary, the most typical NIRS finding is an increase in local HbO and often a smaller increase in Hb that sum to produce consistent increases in THb in response to localized brain activity (see Zaramella *et al.* (2001) for a review of these findings).

NIRS has also been used to examine changes in cortical blood volume in infant subjects. Meek *et al.* (1998) examined 20 infants between the age of 3 days and 14 weeks. Oxygenation changes in the occipital cortex during a visual stimulation task were examined. All infants viewed a checkerboard with a 5-Hz pattern reversal. Nine of the 10 infants showed an increase in both Hb and HbO in the occipital cortex during visual stimulation. This response was not observed in a frontoparietal control region (Meek *et al.,* 1998). Sakatani and colleagues (1999) have reported bilateral frontal lobe activation in a group of 28 newborn infants (mean age 3.1 days). The investigators examined changes in Hb and HbO prior to and during auditory (popular piano music) stimulation. Data from prefrontal cortex revealed significant increases in HbO during auditory stimulation compared with a baseline resting state (Sakatani *et al.,* 1999). Zaramella and colleagues (2001) have also used NIRS to examine neural response to auditory stimulation in infants. Nineteen newborn infants (mean age 15 days) were exposed to a tone that increased in frequency from 2 to 4 kHz. NIRS data were collected from left and right temporal cortex. Increases in HbO and THb were found for 13/19 infants (Zaramella *et al.,* 2001). Finally, increases in left orbitofrontal HbO were also reported in 23 infants (mean age 48 h) in response to olfactory stimulation (Bartocci *et al.,* 2000). Taken together, these findings are consistent with the behavior of adult cortex under similar stimulus conditions and therefore add considerable validity to the use of NIRS in studies of infant brain function.

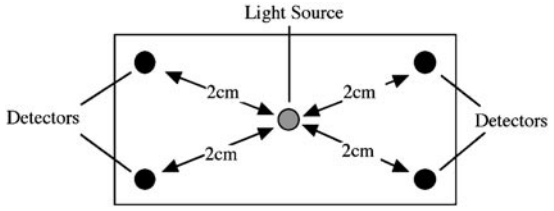


**FIG. 1.** Schematic diagram of the NIRS probe. A single 1-mm bifurcated light source is located centrally, surrounded in a rectangular formation by four 1-mm detectors.

The present study sought to use NIRS to monitor the activity of the frontal cortex as indexed by the hemodynamic response prior to, and following, the emergence of object permanence.

## METHODS

*Subjects.* Twelve healthy full-term infants (6 females) were observed initially at 5 months of age and followed longitudinally at 4-week intervals until 12 months of age. Institutional review board approval and written parental consent were obtained before the study began.

*Imaging protocol.* The NIRS system used in the current study (MGH-NIRS system; Boas, 2000) was similar to those used in other investigations of infants (Meek *et al.,* 1998; Taga *et al.,* 2000; Bartocci *et al.,* 2000; Zaramella *et al.,* 2001). A single emitting source fiber was positioned at Fz using the EEG 10–20 system. Four 1-mm detector fibers were positioned equidistantly in a rectangular pattern around the source (see Fig. 1). All detectors were placed 2 cm from the source (interoptode distance 2 cm). This placement al-

**FIG. 2.** Subjects were seated on their parent's lap for the duration of the study. The NIRS probe, (described in Fig. 1) was secured on the infants head using a soft terrycloth headband with a Velcro closure. The fiber optic cables were bundled together and hung behind the infant.

lowed us to collect signal from an area of approximately 6 $cm^2$ on the infant's forehead. In every individual, this placement covered the F3 and F4 positions in the EEG 10–20 system (see Fig. 2). A personal computer converted absorption changes at each wavelength, recorded every 50 s, into relative concentration changes in cerebral chromophores HbO and Hb. The sum of changes in HbO and Hb enabled the calculation of the changes in THb.

The sources in this system were two low-power laser diodes that emit light at discrete wavelengths, 785 nm (Sanyo; DL7140-201) and 830 nm (Hitachi; HL8325G). These two wavelengths were combined in a 1-mm bifurcated source fiber. The two different wavelengths were used because of the differential characteristic absorption patterns of oxyhemoglobin and deoxyhemoglobin (Villringer and Chance, 1997). The system had four separate detector modules (Hamamatsu; C5460-01), which were optically and electrically isolated from each other. The incoming signal at a given detector was composed of both source colors, which were separated by synchronous (lock-in) detection using the two source signals as a reference. These two components are low-pass filtered at 20 Hz and digitized by a computer.

*Behavioral methods.* All 12 infants were administered several object permanence tests while they sat on their parents' laps. NIRS data were collected continuously from left and right frontal areas (see Fig. 2). The object permanence tests were carried out on a table that was placed between the mother/infant and the experimenter. Each infant was administered four object permanence trials. Each trial began with the infant manipulating a small toy. The toy was then removed from the infant and placed under a cloth in front of the infant. The infant was allowed to search for the hidden object after a 3-s delay. Subjects were considered to have achieved object permanence if they searched for the object on all four trials.

*Data analysis.* Data were analyzed separately for each detector using the modified Beer–Lambert law. Changes in Hb, $HbO_2$, and THb were examined (see Villringer and Chance, 1997). Data that were more than two standard deviations above or below the mean for the entire time series were considered motion artifacts and not included in the analysis. Due to the fact that the data from the four detectors were highly similar in all subjects, the four detectors were averaged together to increase overall signal strength. To summarize the results, each subject's data were averaged over the four object permanence trials. The onset of each trial corresponded to the disappearance of the object under the cloth because that moment marked the time when the infant had to maintain a schema of the object. For each subject, the data collected during the visit in which they demonstrated object permanence (permanent condition) were compared to the data of the previous visit, in which they did not search for the object on any of the four trials (pre-permanent condition). Sessions that consisted of some successful and some unsuccessful trials were not included in the data analysis. In these cases ($n = 4$) data from 2 months prior to permanence was used for the pre-permanent condition.

## RESULTS

NIRS data collected from frontal cortex were compared pre- and postemergence of object permanence. THb increased significantly in the permanent condition compared with the pre-permanent condition ($F(1,11) = 7.54$, $P = 0.02$, repeated-measures ANOVA) (see Fig. 3a). This effect was much greater with regard to changes in HbO ($F(1,11) = 17.98$, $P < 0.01$, repeated-measures ANOVA) (see Fig. 3b.) compared with the nonsignificant changes observed in Hb (see Fig. 3c). This is consistent with previous reports that have suggested that increases in HbO are consistently associated with increases in neural activity, while changes in Hb are not as reliable, sometimes increasing, sometimes decreasing, and sometimes showing no change (Hoshi *et al.*, 2000, 1998). Interestingly, Fig. 3a also illustrates a decrease in frontal lobe THb concentration in the prepermanent condition. It is possible that this task-related decrease in Thb concentration prior to the emergence of object permanence reflects the functional immaturity of the frontal lobe. More precisely, it is

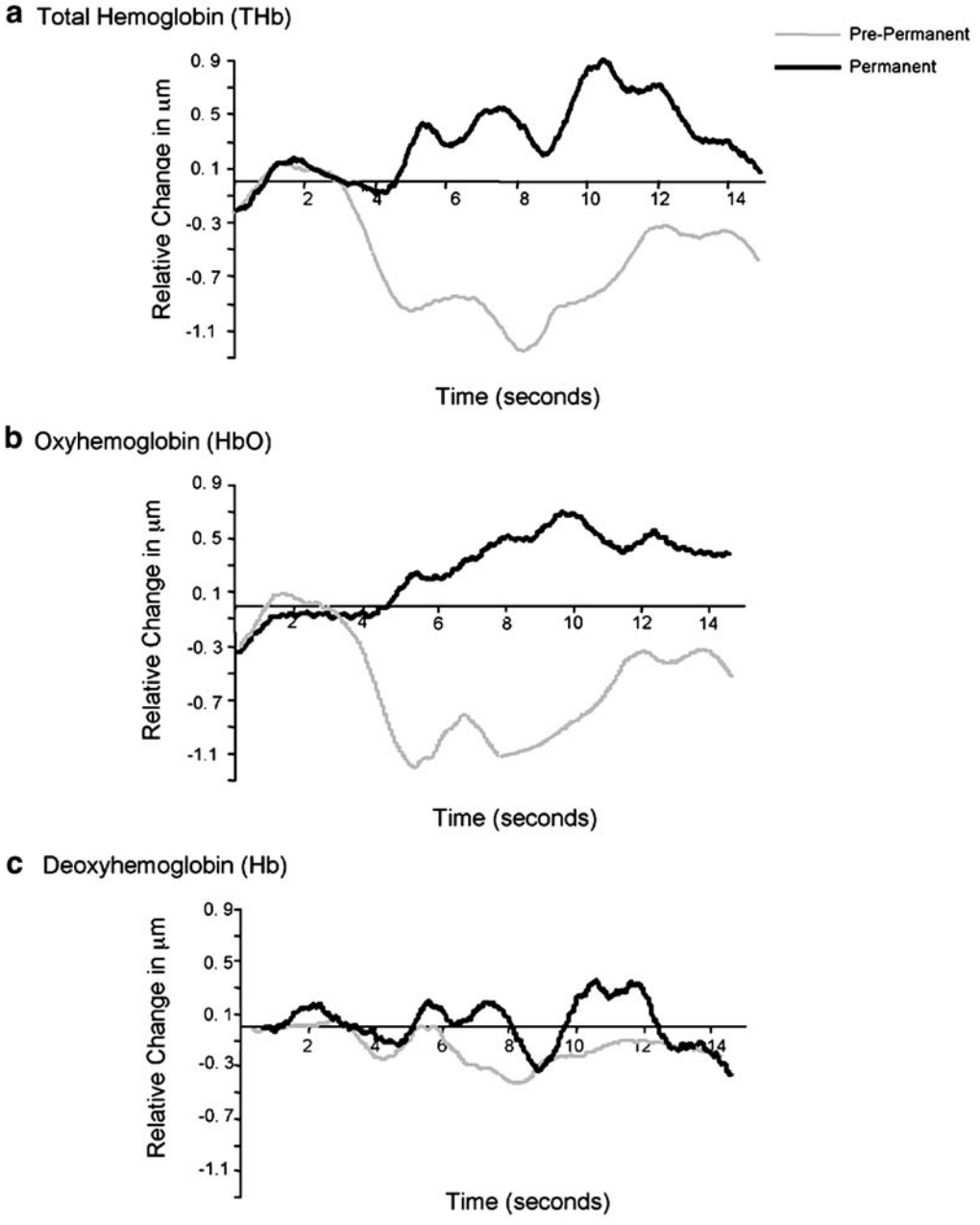


**FIG. 3.** Changes in frontal lobe blood volume pre/post object permanence. (a) Average changes in total hemoglobin concentration (THb) for 12 infants prior to (in gray) and following (in black) object permanence. Time zero corresponds to the moment that the object was placed under a cloth. Total hemoglobin concentration was calculated by summing changes in oxyhemoglobin (HbO) (b) and deoxyhemoglobin (Hb) (c).

conceivable that, due to the region's immaturity, blood is shunted to more functionally mature regions, for example, visual and motor cortex.

In terms of individual differences, all 12 subjects demonstrated increases in total hemoglobin concentration in the permanent condition, compared with the pre-permanent condition; however, this increase was greater for some subjects than for others (see Fig. 4). Importantly, these data were the result not of chronological age but of behavioral competence. Although subjects reached permanence as they grew older (mean = 7.1 months; range 6.0–8.3 months), the variability associated with the age at which a child attained object permanence prevented any straightforward evaluation of the relation between frontal lobe THb concentration and age ($r = 0.26$, $P = 0.23$). There was, on average, a delay of 4 s before THb concentration began to increase in infants once they had attained

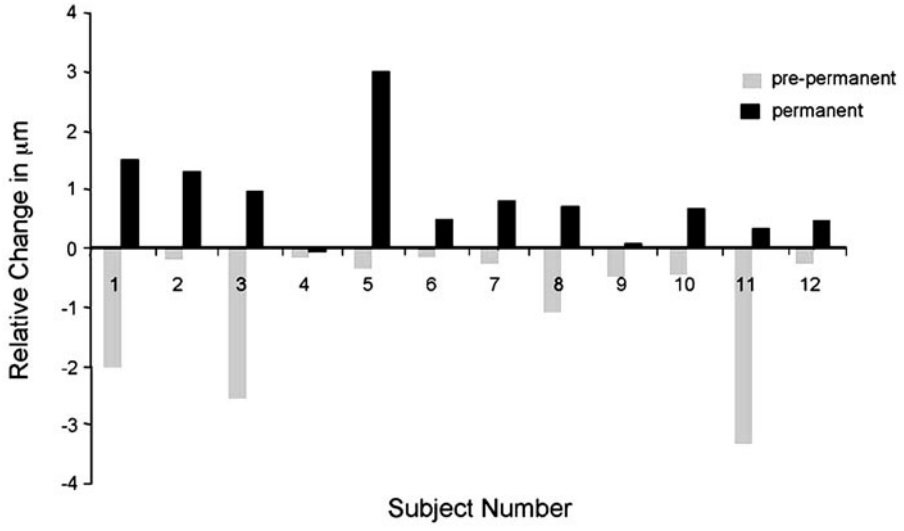


**FIG. 4.** Data for individual subjects are depicted. Changes in frontal lobe total hemoglobin concentration prior to object permanence appears in gray: changes in total hemoglobin concentration following the emergence of object permanence appears in black. All 12 subjects demonstrated an increase in total hemoglobin concentration in the permanent condition relative to the prepermanent condition.

object permanence. This delay is consistent with other reports of hemodynamic response in this region of the brain (Fallgatter and Strik, 1997; Chance *et al.*, 1993)

To more closely examine the specificity of the frontal lobe changes observed in the present study, changes in THb were examined during manual manipulation of objects pre- and post-object permanence (the infant was playing with toys). Data were also examined from time periods during which the infant was seated quietly on the parent's lap and not engaged in a specific task. There were no significant changes in frontal THb in either the pre-permanent condition or the permanent condition during the manual manipulation of objects or when seated on the parent's lap and not engaged in a specific task. Further, data for subjects who reached for the cloth covering the object (but did not pursue the object) prior to the emergence of object permanence were examined. There were no significant differences in frontal THb, HbO, or Hb concentrations in infants who did ($n$ = 5) and did not ($n$ = 7) reach prior to object permanence (see Fig. 5).

## DISCUSSION

These preliminary data suggest that NIRS has the sensitivity to detect activation in the prefrontal cortex of human infants who are able to successfully complete an object permanence task. Further, the present results suggest that the observed relation between the emergence of object permanence and an increase in

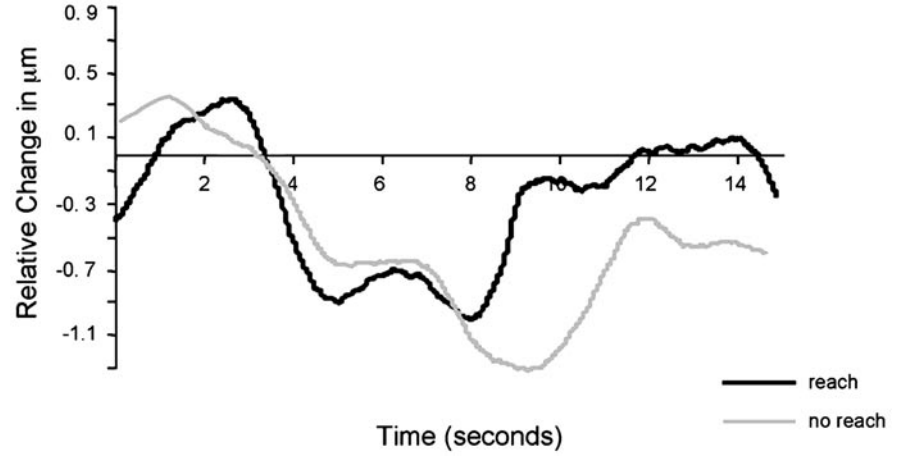


**FIG. 5.** Changes in frontal lobe total hemoglobin concentration in the pre-permanent condition. Infants who reached for the cloth covering the object in the object permanence task but did not pursue the object itself ($n$ = 5) appear in black. Infants who did not reach during the pre-permanent condition ($n$ = 7) appear in gray. Time zero refers to the time when the object disappeared under a cloth.

frontal lobe THb concentration reflects, in part, the functional maturation of areas within the frontal cortex. These results are in agreement with those of reports that have detailed the significant role of the frontal cortex in object permanence tasks (Diamond and Goldman-Rakic, 1989; Bell and Fox, 1992). The present findings, however, add significantly to this growing body of literature in that the present behavioral and neurophysiological data were collected simultaneously. The findings from this study are particularly significant as they demonstrate the examination of cortical physiology in awake and behaving infants. Additionally, there was not a significant difference in frontal activation in the infants who reached and those who did not reach for the object prior to the emergence of object permanence. This finding adds considerable validity to the idea that the observed post-permanence increases in frontal lobe THb concentration were associated with the emergence of the ability to maintain an internal schema of an object and were not simply an artifact of generalized brain maturation or motor activity.

There are several limitations to the present study. First, only one cortical region was examined; future studies should include cortical regions not hypothesized to be preferentially activated during object permanence tasks. It is also possible that the findings reflect the maturational integration of multiple cortical areas (Johnson, 2000). Unfortunately, the current data cannot address this theory. Second, because of individual neuroanatomical differences, there is no way of being absolutely certain of the cortical regions underlying the location of the detectors. While we feel confident that we consistently sampled from anterior frontal regions, ideally future technological advances will allow structural neuroimaging data to be acquired from very young subjects, thereby ensuring the placement of source/detector pairs. Third, due to the intervals at which subjects were tested it is difficult to make inferences about the causal relationship between neurophysiological maturation and behavioral competence. While our data clearly support a strong correlational relationship between neurophysiological activation and behavioral competence, infants would ideally be sampled on a more frequent basis to more adequately address any causal relations.

Although interpretation of these results must remain preliminary, they demonstrate the feasibility of using NIRS to measure aspects of neurophysiological development in infants and affirm the popular hypothesis that successful performance on object permanence tasks requires, at least in part, the contribution of the frontal lobes.

Finally, these data clearly demonstrate the feasibility of optical neuroimaging. Using NIRS, scientists are able to collect data from children while they are performing a task; this is not possible with fMRI or PET because of motion artifacts. Additionally, NIRS is not subject to the ethical constraints that limit the use of other neuroimaging procedures. NIRS is a harmless, noninvasive technique that uses no ionizing radiation or contrast agents, does not require the subject to be lying quietly in a scanner, and makes no noise. Therefore, NIRS is particularly well suited to repeated use in neuroimaging studies of infants and children.

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