CHAPTER 1
Attention in the Brain and Early Infancy

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HYPOTHESIS: INFANT ATTENTION DEVELOPMENT IS CONTROLLED BY INFANT BRAIN DEVELOPMENT

Attention shows dramatic changes over the period of infancy. At birth, there is little intrinsic control of behavior and attention is affected mainly by salient physical characteristics of the infant's environment. By the age of 2 years, the infants' executive control systems are functioning and infants voluntarily direct information processing flow by allocating attention on the basis of well-defined goals and tasks. These changes in attention affect a wide range of cognitive, social-emotional, and physiological processes.

The attention changes in young infants occur simultaneously with substantial changes in the brain. At birth, the structure, myelination, connectivity, and functional specialization of the brain are relatively primitive. Much of the brain's structural development occurs between birth and 2 years. Many brain areas showing these changes are closely linked in adult participants to cognitive processes such as attention. A natural inclination is to hypothesize that the changes in attention development are caused by the changes in these brain areas.

One example of the brain changes is the axonal myelination of neurons. Myelin is a fatty substance that in adult brains covers the axons of many neurons. Figure 1.1 shows a "typical" neuron with an unmyelinated portion (cell body, dendrites) and whose axon is completely covered by the myelin sheath. Myelin appears as "white" when viewed in the brain (fatty tissue reflects light). Thus, in autopsied brains, there are large areas called "white matter" that consist of long myelinated axons. Myelination is seen in magnetic resonance imaging (MRI) T1-weighted scans as long channels of white matter surrounded on the edges by gray matter. Figure 1.1 shows MRIs from a newborn, 6-month-old infant, 15-month-old infant, 10-year-old child, and an adult. The changes in the myelination appear to be rapid from birth to the 15-month MRI scan, then slower afterwards. Myelination of the axon results in less noisy and quicker transmission, making the communication between neurons more efficient. It often is used an explanatory mechanism for how changes in the brain affect cognitive development (e.g., Klingberg, 2008; Yakolev & Lecours, 19672008). The changes in myelin have been documented in several publications, most notably in the work of Yakolev and Lecours (1967), Kinney and colleagues (Kinney, Brody, Kloman, & Gilles, 1988; Kinney, Karthigasan, Borenshteyn, Flax, & Kirschner, 1994), and Conel (1939 to 1967). (also see Johnson, 1997; Klingberg, 2008; Sampaio & Truwit, 2001).

The relationship between brain development and attention development has been hypothesized by several models. I recently reviewed my own view of the relationship between brain centers controlling eye movement, brain development in these areas, and developmental changes

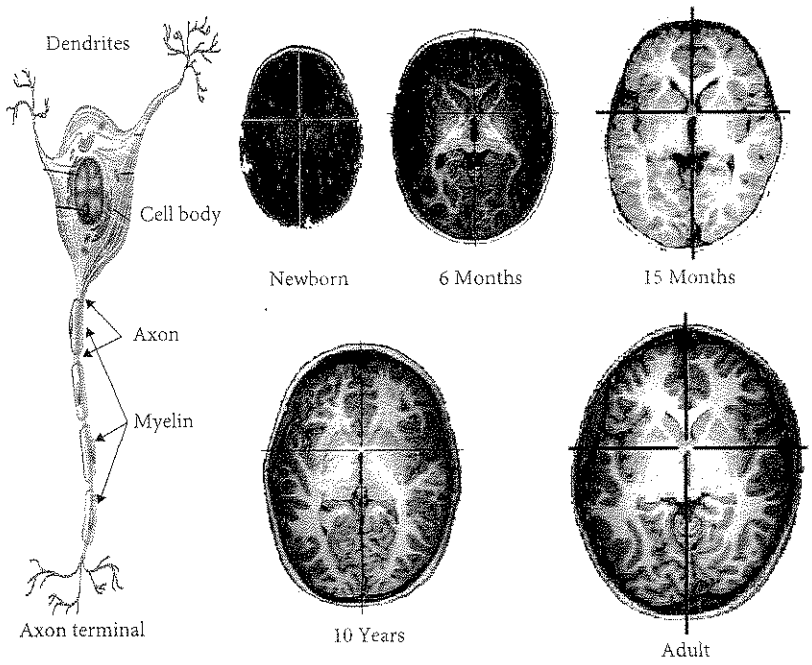
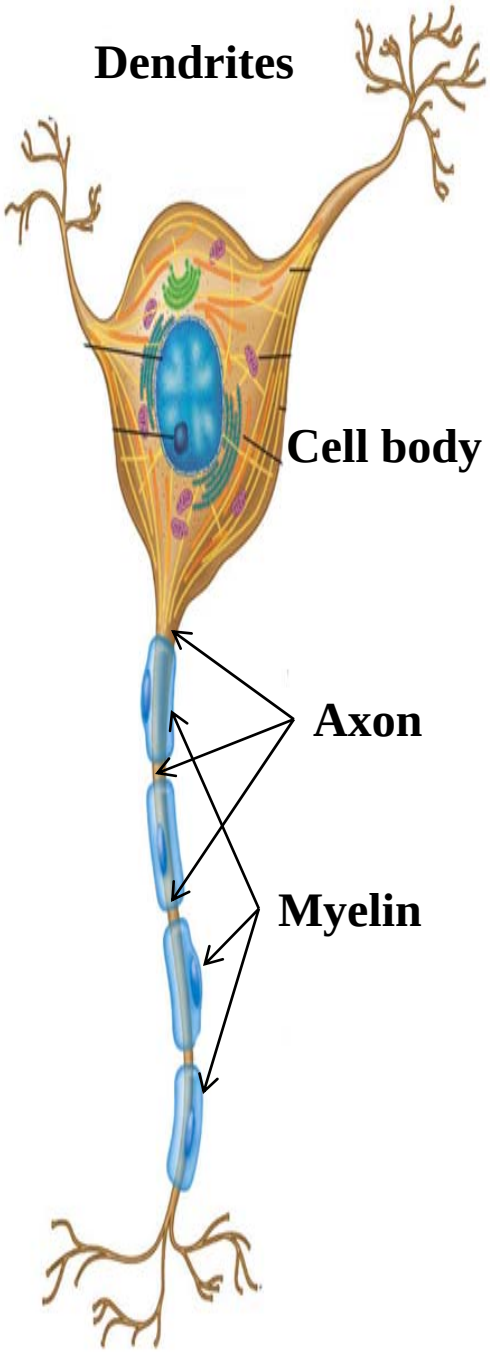


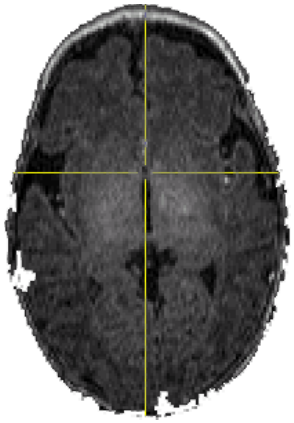
Figure 1.1 The left figure is a cartoon drawing of a "typical" neuron with unmyelinated dendrites, cell body, and axon terminal, and the myelin sheath covering the axon. The MRIs are T1-weighted slices taken at the same anatomical level (anterior commisure) from participants from birth to adult. The myelination of the long axons in the brain is seen as "white" matter in the adults and there are large changes from the newborn to the adult period.

in attention (Richards, 2008). I will briefly summarize my observations here.

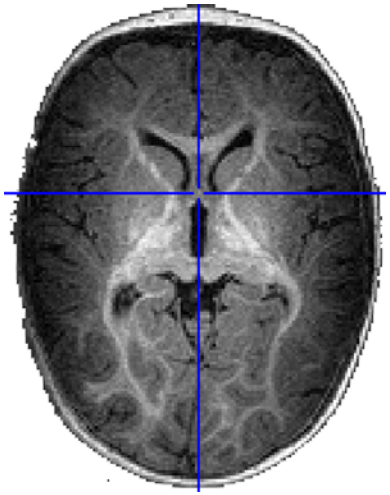
There are three types of eye movements used to track visual stimuli and each eye movement type is controlled by areas of the brain that show different developmental trajectories. "Reflexive saccadic" eye movements occur in response to the sudden onset of a peripheral stimulus, are controlled largely by subcortical brain areas, and are largely intact by 3 months of age. "Voluntary saccadic" eye movements are under voluntary or planned control, involve several parts of the cortex (occipital, fusiform gyrus, parietal cortex, frontal eye fields), and show rapid development from 3 to 9 months of age. "Smooth pursuit" eye movements occur either voluntarily or involuntarily toward smoothly moving objects, involve several cortical areas of the brain involved in voluntary saccadic eye movements and some areas not involved in voluntary saccadic eye movements (medial temporal, parietal), and show changes beginning at 3 months and lasting throughout the period of infancy.

There have been several models theorizing how the areas of the brain controlling the eye movement develop, and how these changes affect attention-controlled eye movements, including models by Bronson (1974, 1997), Maurer and Lewis (1979, 1991, 1998), Johnson and colleagues (Johnson, 1990, 1995; Johnson et al., 1991, 1998, 2003, 2007), Hood (Hood, 1995; Hood, Atkinson, & Braddick, 1998), and Richards (Richards, 2002, 2008; Richards & Casey, 1992; Richards & Hunter, 1998). Iliescu and Dannemiller (2008) review several pertinent "neurodevelopmental" models. These models hypothesize that change in the brain areas controlling the eye movements result in the overt changes in the eye movements. With respect to attention-directed eye movements, particularly in the first few months, the

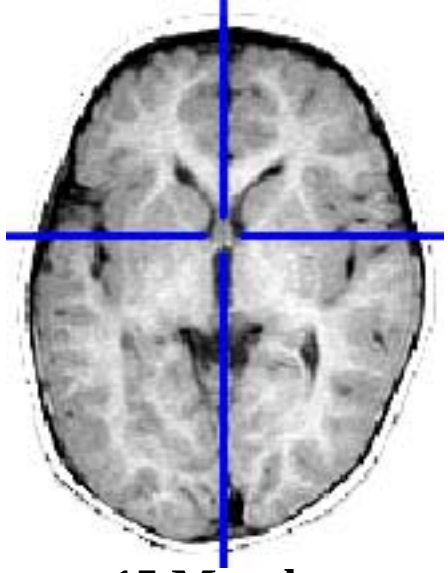




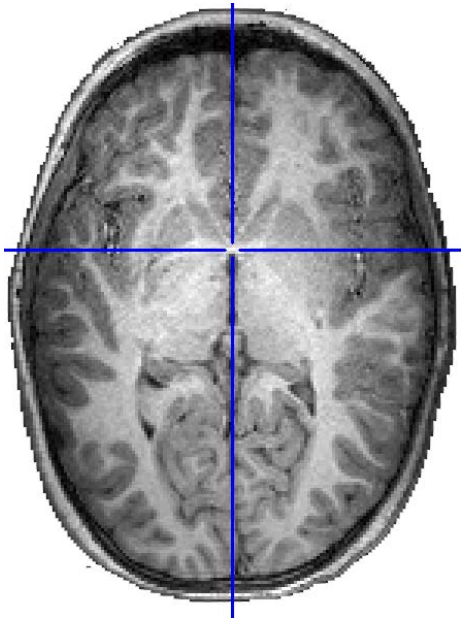
Newborn



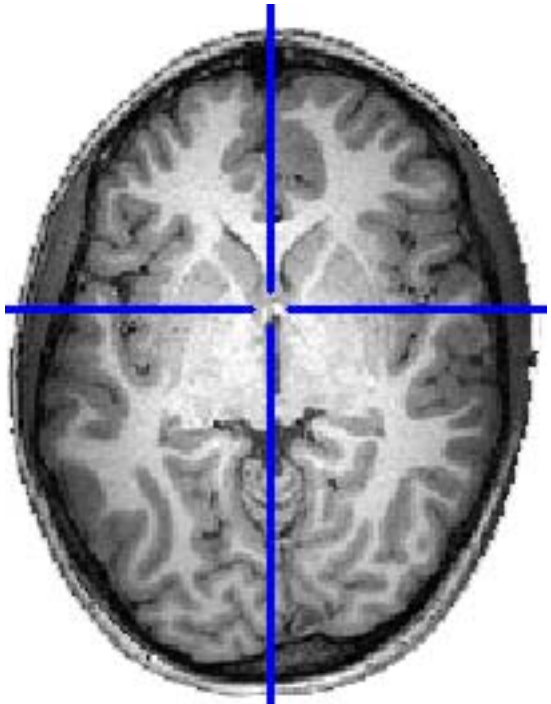
6 Months



15 Months



10 Years



Adult

voluntary saccadic system is most relevant. It has been hypothesized that connections within primarily visual areas of the cortex (e.g., primary and secondary visual cortex) and myelination/connectivity to other areas of the cortex (e.g., parietal area PG) show growth spurts in about 3 to 6 months. These brain changes are accompanied by changes in the voluntary tracking of objects in the visual field (Richards & Holley, 1999), changes in the attention-directed eye movements toward peripheral visual targets (Hunter & Richards, 2003, submitted; Richards & Hunter, 1997), and changes in the ability to shift attention "covertly" without making an eye movement (Richards, 2000a, 2000b, 2001, 2005, 2007b; also see Richards, 2004b, and the section "Brain and Attention: Spatial Orienting").

What's inside a baby's head?

The previous section presented the hypothesis that brain changes in young infants are responsible for the changes seen in psychological processes, with an emphasis on attention-directed eye movements. There are many aspects of infant cognitive development that have been explained as a function of brain development; the field of "developmental cognitive neuroscience" uses this as a basic explanatory mechanism (Johnson, 1997; Nelson & Luciana, 2008). However, these models are severely limited in their description of what the actual brain is like for infants at a specific age or a specific infant at a specific age. They also are limited in their measurement of brain function (see the section "How to Measure Brain Activity in Infants"). I will review two ways in which brain development has been modeled in past research. Then, I will assert that structural MRI techniques should be used for this purpose.

The primary information about brain development in infants comes from nonhuman animal models of brain development, primarily primates. For example, our knowledge of the patterns of myelination, synaptogenesis, and neurochemical development comes primarily from study of normally developing nonhuman animals. Nonhuman animals may be studied by sacrificing the animal at a specific age and performing a brain dissection, or with invasive neuroscientific techniques such as direct neural recording or lesions. These techniques may be applied to individuals who also participate in tasks measuring behavioral performance and psychological processes. An example of this approach is work on infant memory by Bachevalier (2008). She has shown that changes in memory in young monkeys are closely related to the development of the brain areas that are the basis for this type of memory in adults. Lesioning these areas in the infant monkey disrupts the onset or occurrence of this type of memory. Bachevalier makes the parallel between the age-related monkey performance and human infant performance on analog versions of the visual preference procedure and visual discrimination tasks. She concludes that her experiment suggests that the basic neural systems underlying these memory tasks in monkeys and humans are parallel, and that studies of infant monkeys inform us about comparable memory development in infant humans.

There are several assumptions necessary for the study of the study of infant nonhuman animal to be relevant to human infants. First, this study requires that a correlation can be made between ages of the nonhuman animals and human infants. For example, in a study of changes in synaptogenesis in visual areas, Bourgeois (1997) showed changes in rat, cat, macaque monkeys, and humans. Figure 1.2 shows comparable changes in the primary visual cortices of four different species. These changes show some similarity in the overall pattern of change. However, the pattern of changes often is not isomorphic across species (e.g., compare the prolonged decay in synaptic density in humans in Figure 1.2), and a comparison of development between species in one brain area might not be the same for other brain areas. Second, one can relate the changes in the brain in the nonhuman animals, the importance of these brain areas for a specific psychological process, and the changes in these psychological processes in human infants. This analysis presumes that there is an unequivocal relationship between the psychological process and the brain area in development, which is a questionable assumption.

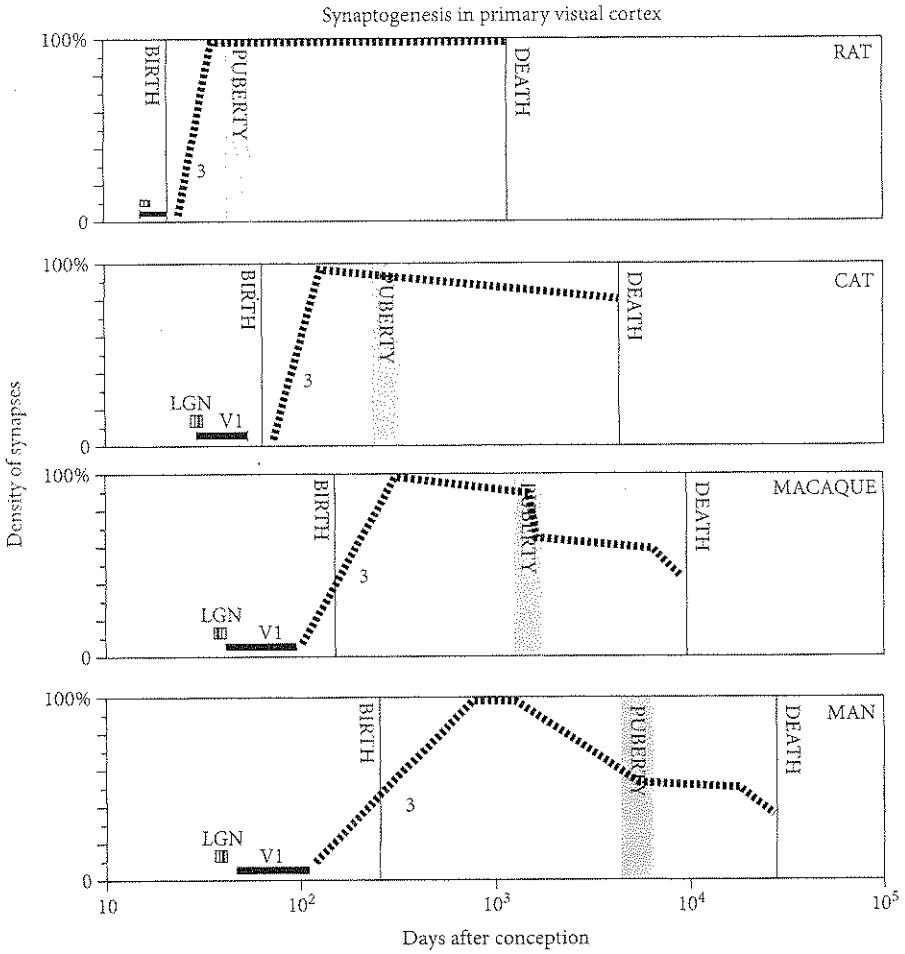


Figure 1.2 Changes in the relative density of synapses in the primary visual cortex for four species. The increase in synaptic density indicates synaptogenesis occurring, and the decline represents synaptic pruning. Note the differences in the pattern of development relative to specific developmental events (birth, puberty, death) in the four species. From Bourgeois (1997).

This type of analysis does not take into account different developmental patterns for other brain areas and the influence of these brain areas on human infant psychological activity. Third, this type of study assumes that brain–behavior relations in nonhuman animals are comparable to those in humans. This assumption is doubtful due to the complexity of human behavior relative to animals, the extremely large changes in brain size between nonhuman animals and humans, and the relative size of brain areas in humans and nonhuman animals (e.g., prefrontal cortex; occipital cortex). Finally, these types of studies use analogical reasoning as a basis for nonhuman animal models being relevant for human infants. They cannot apply the invasive methods directly to human participants and cannot inform us about the developmental status of the brain of individual infants.

A second way in which information about human brain development has been obtained is from postmortem studies of young infants. Infants who die of neural-related causes and/or other causes have been studied for a wide range of neuroanatomical, neurochemical, and cytoarchitectural processes (synaptogenesis

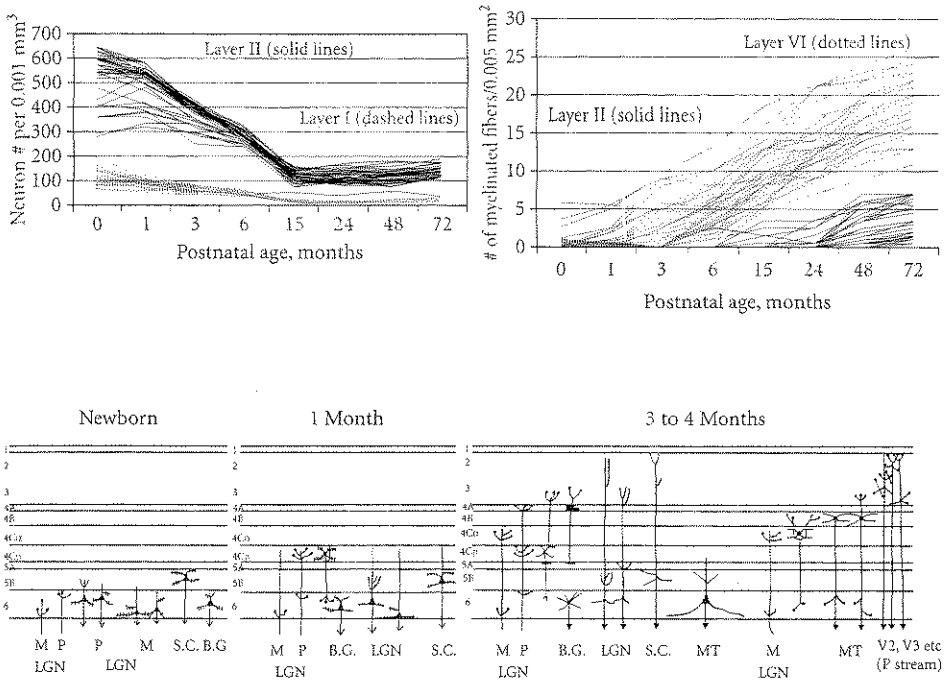


Figure 1.3 Work from Conel's postmortem neuroanatomical studies (Conel, 1939 to 1967). The top graphs show neural density in layers I and II (left figure) and the myelinated fiber density in layers II and VI (right figure), both shown as a function of postnatal age (from Shankle et al., 1998). The bottom figures show innervations of the layers in the primary visual cortex by different cell types at birth, 1 month, and 3 to 4 months of age.

in Huttenlocher, 1990, 1994; myelination in Kinney et al., 1988, 1994). The most well-known version of this kind of study is a series of studies by Conel (1939–1967). Conel studied the neuroanatomical and cytoarchitecture of the layers of the human cerebral cortex in autopsied individuals. He measured six anatomical features, including cortical layer thickness, cell density, numbers of cell types, and myelinated fiber density (Shankle, Romney, Landing, & Hara, 1998). Figure 1.3 shows two types of results from these studies. The top figures display neuron density and number of myelinated fibers in two cortical layers as a function of age. Notice that the myelination of the layer 6, which receives input from noncortical areas and is involved in simple cortical functioning, shows myelination changes very early. Alternatively, layer 2, which has communications within layers and with other cortical areas and is involved in more complex cortical functioning, shows an extended time course for myelination. The bottom figures show the types of neurons that innervate the cortical layers at different ages.

Conel's work has been popular in developmental cognitive neuroscience because of the specificity of the information about the neurophysiological processes being studied and its large age range. For example, Johnson (1990, 1995; Johnson et al., 1991, 1998) posits that development in the layers of the the primary visual cortex (e.g., Figure 1.3, bottom figures) acts as a limiting factor for visual behavior and visual attention controlled by brain systems. Such developmental changes in the layers of the primary cortex from birth to about 6 months act as a gateway for the onset of these eye movements in young infants.

There are limitations of these postmortem studies for developmental cognitive

neuroscience. An implicit assumption is that the individuals measured at different ages are representative of that age and provide knowledge about the brain status of specific individuals of that age. It is likely true that the changes across age are large enough that groups of infants at one age will have neuroanatomic and cytoarchectural similarities differentially from groups at different ages. However the developmental status of the brain of an individual are likely to show idiosyncratic individual differences in brain development between individuals at the same age. Second, these studies typically are limited to small samples (single individual at each age) and restricted to infants who died. If the reasons for the death are related to the characteristics being studied, the results will not be applicable to a wide range of participants. Without some independent verification of the generality of the findings, these surely cannot be applied to determine the status of individual participants. These studies typically have used extremely limited samples for young infants and children.

One technique that may be used to examine the brains of individual infants is MRI. MRI has been described in several publications (e.g., Huettel, Song, & McCarthy, 2004; Thomas & Tseng, 2008) and I will provide a brief overview emphasizing its use for studying the brain. MRI applies a very large magnetic field to the head. The head's media (skull, cerebrospinal fluid [CSF], brain) have magnetic properties such that the magnetic field aligns spinning protons in the same direction as the field. Radiofrequency (RF) energy pulses cause disruption of the magnetic fields and disrupt the alignment of the protons. MRI measures the disruption in alignment due to the RF pulse and return of the alignment to the strong magnetic field. Different body tissue types have differing times to return to alignment, and these differing times (or different resonance frequencies and/or differing on/off durations of the RF pulses) may be used to identify where different types of media are located in the head. This allows the identification and visualization of skull, skin, CSF, white and gray matter, myelin, vascularization, and other components in the head. MRI measurement has been used to measure developmental changes in myelination (Sampaio & Truwit, 2001), distribution of white and gray matter in the cortex (O'Hare & Sowell, 2008), and biochemical characteristics of the developing brain (Sajja & Narayana, 2008). An interesting use of the MRI is the application of "diffusion tensor imaging," which details the connectivity of axons between different areas in the brain (Wozniak, Mueller, & Lim, 2008).

The use of structural MRI for determining brain developmental status is relatively new but well underway. The most comprehensive study of brain structural development with MRI is currently ongoing. The "NIH MRI Study of Normal Brain Development" (Almli, Rivkin, & McKinstry, 2007; Evans, 2006; NIH, 1998) is a multicenter research project sponsored by the National Institutes of Health to perform anatomical scans of about 800 children ranging in age from birth to 18 years. This study uses 1.5T scanners to get T1- and T2-weighted images, proton density excitation, DTI, and other scans. An interesting aspect of this study is the collection of a large battery of neuropsychological and developmental tests. This will allow the correlation of psychological processes, neuropsychological status, and developmental level with the brain status of individual participants. The study will provide individual MRIs to researchers interested in these aspects, and likely will provide standardized or stereotaxic scans in the "MNI" framework (Montreal Neurological Institute brain atlas, Mazziotta, Toga, Evans, Fox, & Lancaster, 1995; Evans, Collins, & Milner, 1992; Evans et al., 1993) or Talairach space (Talairach &Tournoux, 1988; also see Talairach Atlas Database Daemon, Fox & Uecker, 2005; Lancaster, Summerlin, Rainey, Freitas, & Fox, 1997; Lancaster et al., 2000). Currently (late 2007) MRIs are available for children ranging in ages from 4 to 18 years. Most of the MRIs for the infant participants have been collected but are undergoing quality control.

A second approach I am using in my current work is to acquire structural MRIs on infant participants who also participate in studies of attention, and relate the information found about specific individual's brain developmental

status to performance in attention tasks. Parents of infants are contacted in the normal course of our contact system for psychological experiments. The parents who agree to participate in the MRI have several visits. First, the parent(s) and infant come to the MRI center located at a local community/teaching hospital. The parent is shown the equipment and the process is described. Second, the parents return to the MRI center for the scan. The procedures for the MRI recording use infants during sleep (Almli, Rivkin, & McKinstry, 2007; Evans, 2006; NIH, 1998). The infant and parent come to the MRI center in the evening at the infant's normal bedtime. The infant and parent go into the darkened room with the MRI and the infant is put to sleep. Then the infant is placed on the MRI table, earplugs and headphones put on, and then the recording is done. Figure 1.4 shows an infant lying on the MRI bed—the headphones and cloths surrounding the infant can be seen. When the infant is in the MRI tube, a research assistant reaches in and has a hand on the infant to see if the baby moves or wakens. Getting the baby to sleep usually takes about 45 to 60 min, and the MRI recording itself has scan sequences lasting in total about 20 min. Previous studies from several laboratories have described procedures for performing MRI recording of nonsedated infants with success rates that range from 66% to 90% (Almli et al., 2007; Dehaene-Lambertz, Dehaene, & Hertz-Pannier, 2002; Evans, 2006; Gilmore et al., 2004; Paterson, Badridze, Flax, Liu, & Benasich, 2004; Sury, Harker, Begent, & Chong, 2005). We have had 100% success *after* the infant is sleeping; several infants have not been able to get to sleep. The parent is in the scanner room during the scan, along with a pediatric nurse. Finally, the infant and parent then come to a psychophysiological laboratory for studies of attention (see the section "Brain and Infant Attention: Spatial Orienting").

Figure 1.4 An infant lying on the MRI bed going into the MRI tunnel. The infant is covered with a sheet and has a restraining strap lightly placed across its body. The headphones and cloths surrounding the infant can be seen in this picture. A research assistant (left side of picture) and the parent (right side of picture) are close to the baby during the scan.

Several procedures are followed to insure the infant's safety, obtain a good recording, and minimize the amount of time in the scanner. Potential risks of MRI recording include scanner noise, the magnetic fields, and magnetic gradients. We use earplugs and earphones to minimize scanner noise. The scans in our 3T magnet are optimized for the lowest sound levels and fastest recording. The infants are placed on the bed on "memory foam," covered snugly with sheets, and have rolled washcloths around the head for restricting head movement comfortably. The U.S. FDA considers MRI recording in infants to be a "nonsignificant" risk when used within FDA-specified parameters (USFDA, 2003, 2006). This assessment is based on over 20 years of MRI recording in neonate and infants (e.g., Barkovich, Kjos, Jackson, & Norman, 1988; Rivkin, 1998) with no reports of deleterious long-term effects. Outcome studies of such effects show that the magnetic field or the magnetic gradients do not threaten the concurrent physiological stability of the infant during scanning (Battin, Maalouf, Counsell, Herlihy, & Hall, 1998; Taber, Hayman, Northrup, & Maturi, 1998; Stokowski, 2005) and there are several studies showing no short-term or long-term effects from this type of recording (Baker, Johnson, Harvey, Gowland, & Mansfield, 1994; Clements, Duncan, Fielding, Gowland, Johnson, & Baker, 2000; Kangarlu, Burgess, & Zu, 1999; Kok, de Vries, Heerschap, & van den Berg, 2004; Myers, Duncan, Gowland, Johnson, & Baker, 1998; Schenck, 2000). These risks are discussed in detail in several sources (Barkovich,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2005; Dehaene-Lambertz, 2001; Evans, 2006; Stokowski, 2005).

Three scans are done on each infant. First, we do a localizer sequence (45 s) to orient the subsequent high-resolution slices. This orients the longitudinal fissure parallel with the saggital plane, perpendicular to the coronal and axial planes, and the line between the anterior commisure (AC) and posterior commisure (PC) is on the center MRI slice. This will orient the scan so that the MRI may be oriented relative to the origin for the stereotaxic space defined by Talairach (Talairach & Tournoux, 1988). Second, the localizer scan is followed by a 3D MPRAGE T1-weighted scan. The T1-weighted (T1W) scan results in an MRI volume that shows maximal distinction between gray matter and white matter. The MPRAGE employs a TI of 960 ms, a delay of 3000 ms between shots and an 8° flip angle, with a very short TE (4.9 ms). Using this sequence, we can collect a 1 mm isotropic (150 × 256 × 256 mm FOV) in about 9 min. The gray matter, white matter, and CSF can be segmented from the T1W scan, but a subsequent T2-weighted (T2W) scan helps to discriminate white matter and CSF with automatic segmenting routines. The T2W scan emphasizes liquid in the brain, so CSF is very bright (high voxel values) relative to other brain matter. This is acquired as a dual contrast proton density and T2-weighted sequence with a dual echo fast spin echo sequence. The dual echo acquisition takes 4 min to acquire (256 × 256 matrix with rectangular FOV, 1 × 1mm pixel size, 2 mm slice thickness, no slice gap, 50 saggital slices in two interleaved packages, echo train length of 10, first TE=13 ms, second TE=101 ms, TR=4640 ms, parallel imaging factor = 2). Any of the sequences may be repeated if degraded by motion artifacts; however, all infants we have tested have been sleeping and still during the entire scanning protocol. If only the T1W scan is available, some automatic classification/segmentation routines are substituted with manual segmentation routines of the T1W scan.

What are the MRI scans used for? Briefly, the purpose of the attention studies is to identify areas of the brain involved in sustained attention and how they affect specific cortical/cognitive processes. Neural activity produces electrical currents that pass through the media of the head and can be recorded on the surface of the scalp. This electrical activity is the electroencephalogram (EEG). We use the EEG for cortical source analysis. One aspect of this analysis is the necessity to have a realistic head model for the quantification. We obtain this from the MRI. Figure 1.5 shows the MRI recorded from the infant pictured in Figure 1.4. The middle section shows the media identified inside this baby's head (i.e., gray matter, white matter, CSF, skull). The right section shows a tetrahedral wireframe model of the identified sections. This wireframe model is used in computer program such as BESA, EMSE, and my own computer program (Richards, 2006, submitted) to identify the current sources of the EEG on the head. I will describe the details of the EEG analysis in the next section (section on "How to Measure Brain Function") and some results from the study in a following section (section on "Brain and Infant Attention: Spatial Orienting"). Whereas our use of these MRIs is primarily as an adjunct to current source analysis of EEG signals, specific aspects of the MRI can be used such as amount of myelination in brain areas, structure of brain areas, and perhaps connectivity between brain areas.

Why is this approach important? The first and perhaps obvious answer is that "cognitive neuroscience" requires measurement of both the cognitive and the neural aspects of cognitive neuroscience. A developmental cognitive neuroscience study without measures of brain development will be extremely limited. Second, the structural MRI of individual infants is necessary to relate the findings for particular participants to the functional data of particular infants. This is especially important given the wide range of topographical changes over this age, and the possibility that large individual differences might occur in infant brains. An example of this problem is shown in Figure 1.6. This shows MRIs at a common stereotaxic position (axial level of anterior commisure) across a wide range of ages. The wide range of head sizes across this age, and some variability within

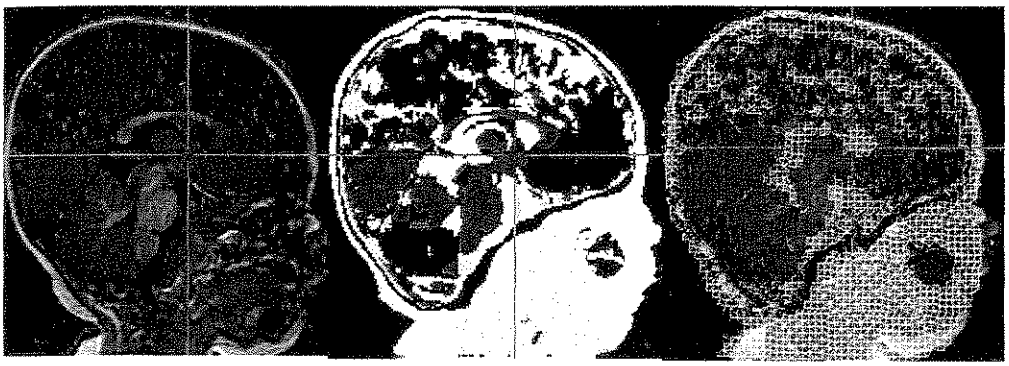


Figure 1.5 The MRI from the infant shown in Figure 1.4. The left scan is a saggital view of the T1-weighted scan, with the cross-hairs indicating the position of the anterior commisure. The middle figure is the brain segmented into skin and muscle (white), gray matter (red), white matter (green), CSF (cerebralspinal fluid, yellow), dura (pink), skull (blue), and nasal cavity (purple). The right figure is a representation of the tetrahedral wireframe used in EEG source analysis programs.

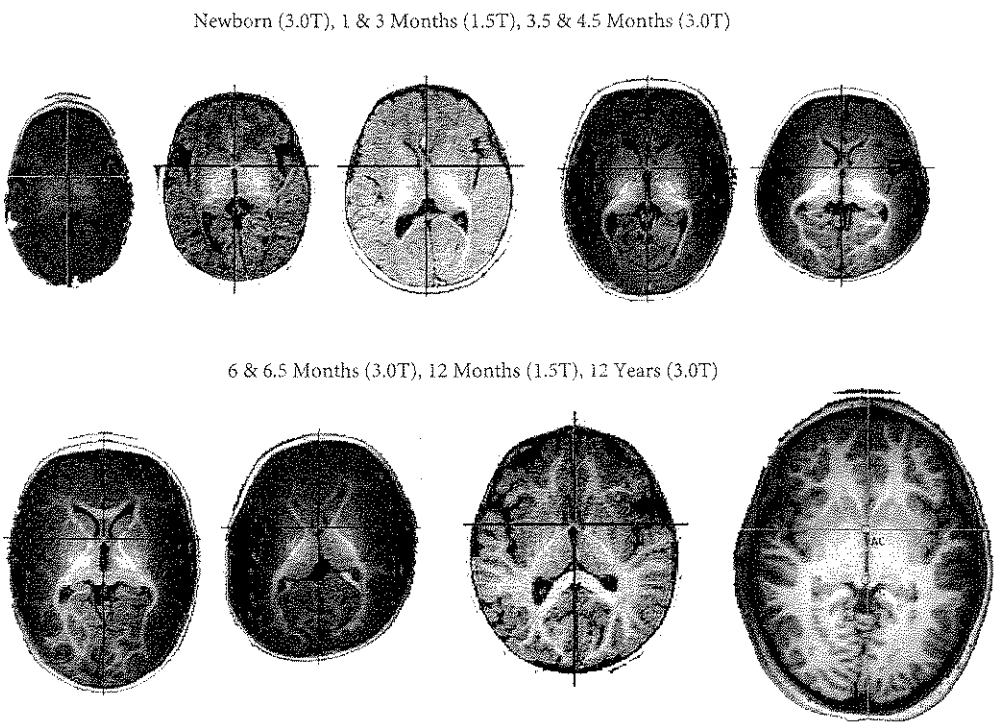
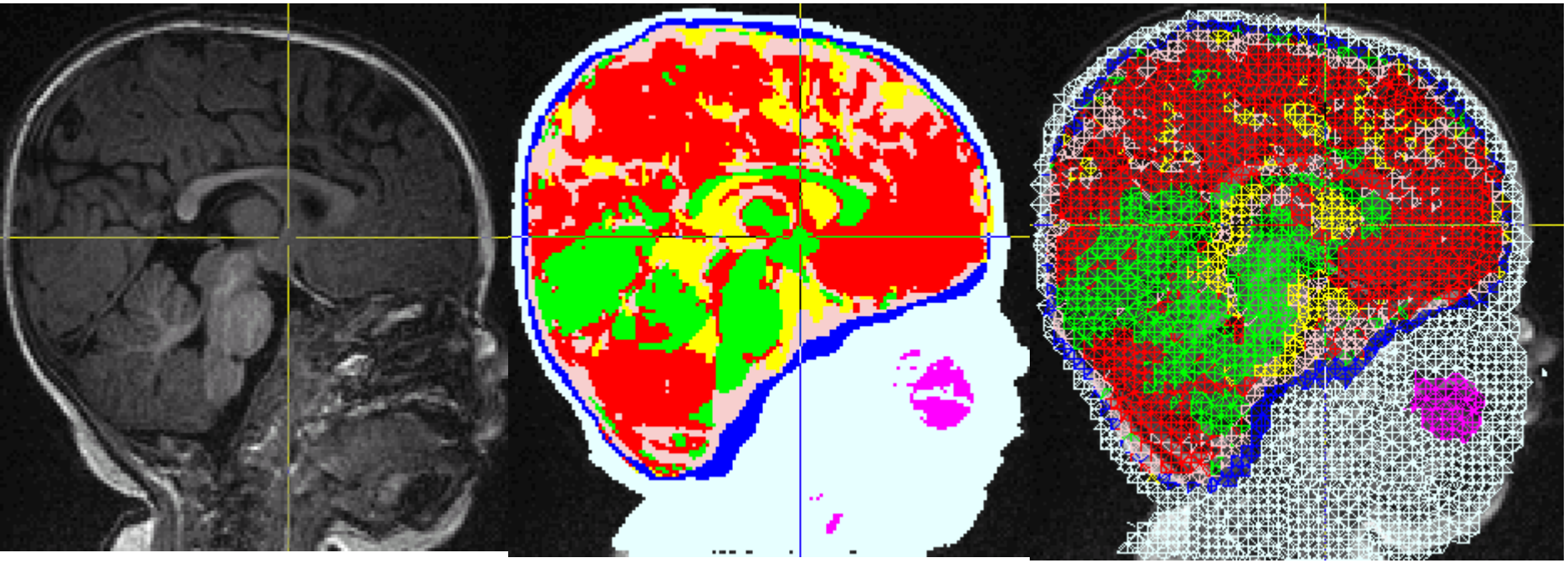


Figure 1.6 Axial T1-weighted MRI scans for participants ranging from birth to 12 years. Each scan is presented at the axial level of the anterior commisure (blue cross-hairs). Note the large change in shape and size, differences in the type of brain underlying similar skull locations, and the changes in myelination across these ages.



ages, is clear in these examples. Additionally, the exact type of brain media under the same skull location differs across the infants. It is important for the study of brain development to have structural information on particular infants.

A third reason why this approach is important is that this allows specific comparisons across age in related structures. Figure 1.7 shows brains of infants at 3 and 6 months, and a 10-year-old child. The MNI brain is also shown (Montreal Neurological Institute brain atlas, Mazziotta et al., 1995; Evans et al., 1992, 1993). The MNI brain consists of the average of 152 college-age participants. Several brain areas have been identified for the MNI brain. For example, Figure 1.7 (bottom right panel) shows various anatomical structures that have been identified on the MNI brain. The MNI brain and associated brain areas may be used as a stereotaxic atlas to identify structures in children at younger ages. The bottom part of the figure shows the structure identified on the MNI brain (bottom right panel), which is then transformed to the head size and shape of the participants at the other ages (three bottom panels on left). This may allow the direct comparison of the development of specific brain areas across a wide range of participants.

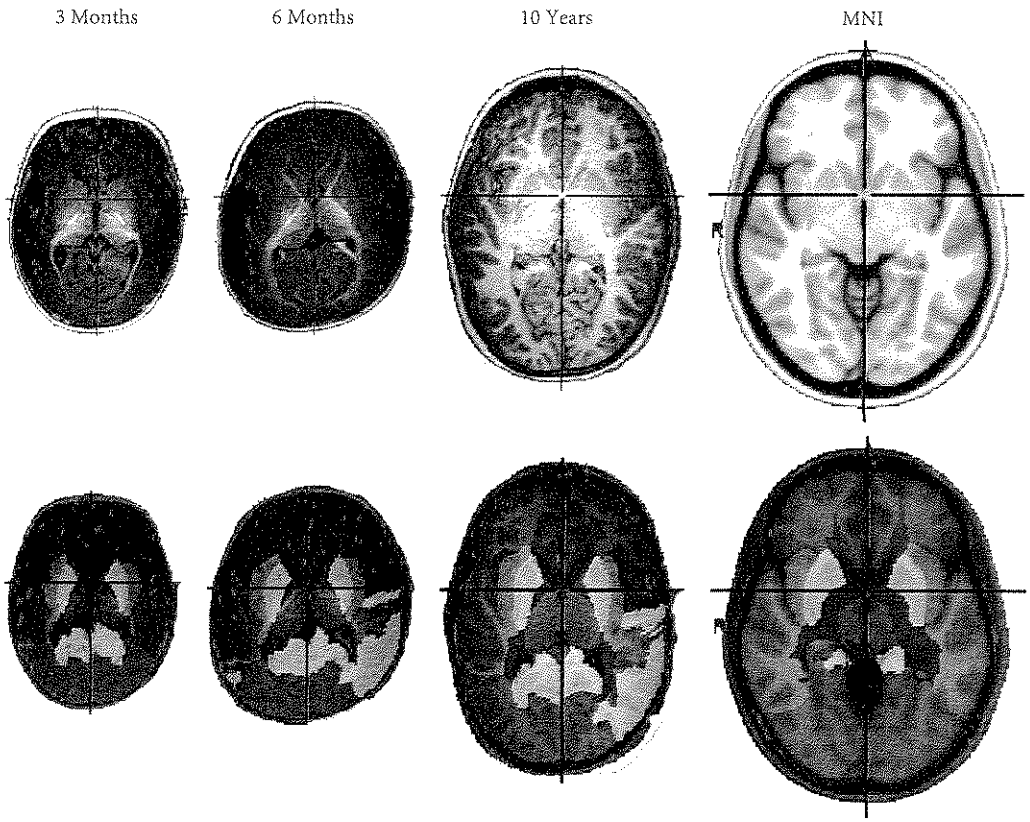
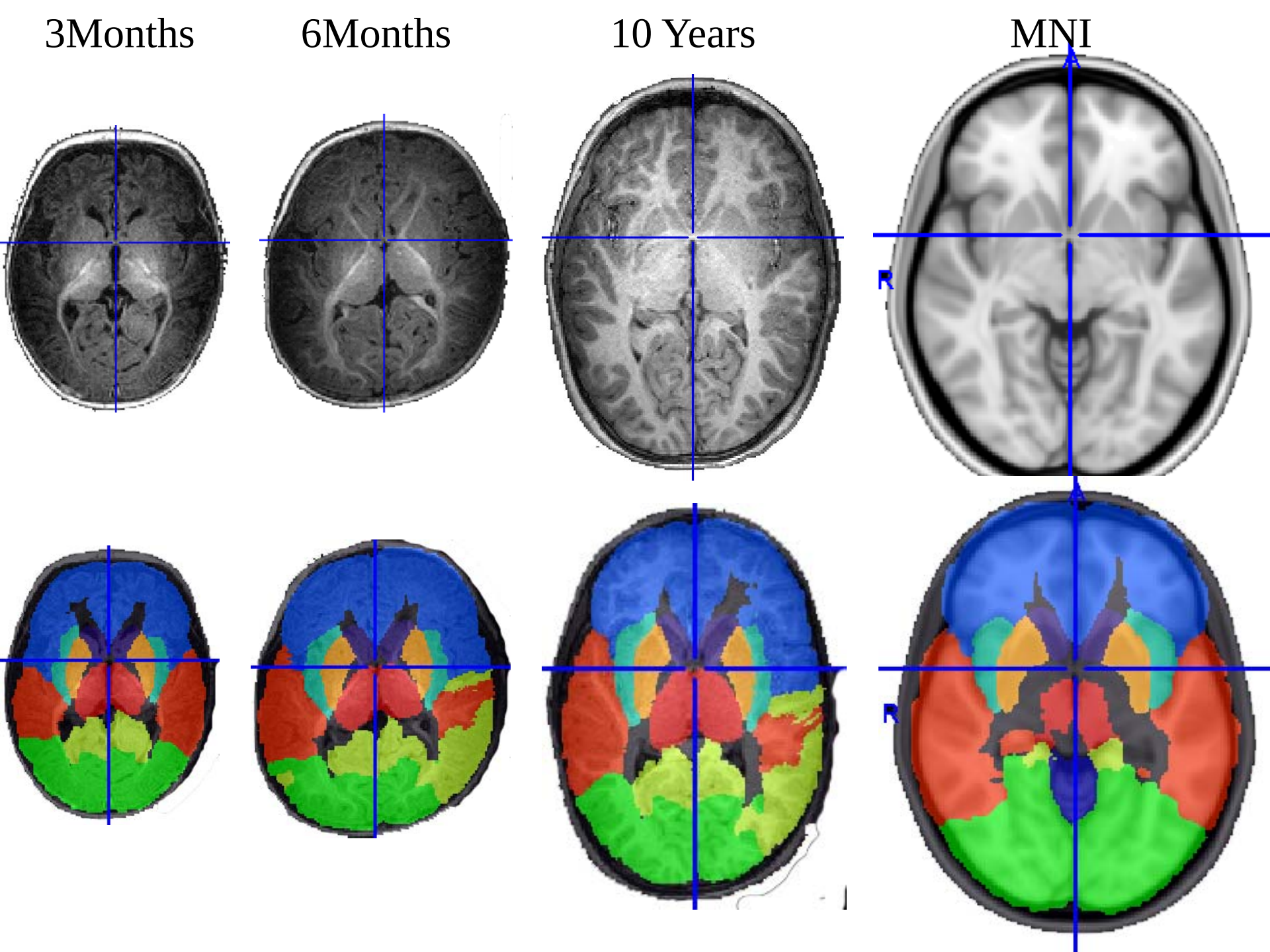


Figure 1.7 Axial T1-weighted MRI scans for participants at 3 and 6 months, 10 years, and the "MNI" brain, located on the axial level of the anterior commisure (cross-hairs). The bottom right MRI has the anatomical locations overlaid in color derived from the MNI brain, and structures such as the prefrontal cortex (blue), temporal (red) and occipital (green) cortex, and several subcortical structures may be seen. The three figures on the bottom left are the single participant brains with the stereotaxic anatomical areas translated from the MNI brain to the individual participant.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How to measure brain activity in infants

There are multiple aspects of brain development that might be important in the development of cognitive processes. The previous section gave some illustrative examples of the development of brain anatomy (brain structure). The field of cognitive neuroscience is interested in the functioning the relationship between the brain, and cognitive and psychological processes. The development of brain functioning is as important for developmental cognitive neuroscience as is the development of brain structure.

The measurement of brain activity during psychological tasks in infant participants has been as difficult as the measure of brain structure. Most of the neurodevelopmental models of infant attention mentioned in section 1 were based on the brain function of nonhuman animals, so-called "marker tasks," or speculative relations between overt behavioral measures and putative brain markers. I will briefly review the older measurement techniques and then comment on three new techniques.

Most neurodevelopmental models have relied either on measurement of brain function in animal models, or the measurement of overt behavior putatively linked to brain activity. Johnson (1997) calls the latter measures "marker tasks." Marker tasks are behavioral activities that can be measured overtly but which are thought to be controlled by specific brain areas. Johnson proposes that such tasks may be used in infants with the understanding that development in these tasks implies brain development in the associated areas. I have discussed this proposal previously (Richards, 2002, 2008; Richards & Hunter, 2002). Similarly, there are a wide range of studies using physiological indices in the infant in psychological tasks (Richards, 2004c; Reynolds and Richards, 2007). These psychophysiological measures (e.g., heart rate, EEG) have known physiological processes that cause their activity and thus may show changes in these processes linked to experimental manipulations or cognitive processing. Like the marker tasks, psychophysiological measures are indirect measures of brain function and do not tell us about the developmental status of the brain for an individual participant. With proper caution, marker tasks and psychophysiological measures allow inferences to be made about brain development and help to inform a developmental cognitive neuroscience approach to attention.

I have been using the EEG and scalp-recorded event-related potentials (ERP) as measures of brain activity. The EEG is electrical activity located on the scalp that is generated by neural activity occurring in cell bodies or extracellular neural tissue. ERP are EEG activity that is time-locked either to experimental events or to cognitive events. Recently I have been advocating the use of these measures with "cortical source analysis" (Reynolds & Richards, 2007, 2009; Richards, 2003b, 2005, 2006, 2007a, 2007b, submitted). Cortical source analysis uses high-density EEG recording (Johnson et al., 2001; Reynolds & Richards, 2009; Tucker, 1993; Tucker, Liotti, Potts, Russell, & Posner, 1994) to hypothesize cortical sources of the electrical activity and identifies the location of the brain areas generating the EEG or ERP (Huizenga & Molenaar, 1994; Michel et al., 2004; Nunez, 1990; Scherg, 1990, 1992; Scherg & Picton, 1991; Swick, Kutas, & Neville, 1994). The activity of these cortical sources may be directly linked to ongoing behavioral manipulations or psychological processes. This results in a description of the functional significance of the brain activity, i.e., functional cognitive neuroscience. Greg Reynolds and I have been using this technique to study infant recognition memory in the paired-comparison visual-preference procedure (Reynolds, Courage, & Richards, 2006; Reynolds & Richards, 2005) and have recently reviewed our use of this technique (Reynolds & Richards, 2009). I will present a brief introduction to this work but we have reviewed it elsewhere (Reynolds & Richards, 2007, 2009).

The basic outlines of this technique are as follows. Recording of electrical activity on the head (EEG, ERP) is made. The cortical source analysis hypothesizes electrical dipoles generating current inside the head as the sources of the EEG (ERP) changes measured on the scalp. The source analysis estimates the location and

amplitude of the dipole. Figure 1.8 (top left MRI slices) shows the dipoles for an ERP component known as the "Nc" that occurs in young infants in response to brief familiar and novel stimuli (from Reynolds & Richards, 2005; also see Reynolds et al., 2006, and Richards, 2003a). The spatial resolution of EEG for localizing brain activity is typically believed to be about 5 cm (Huettel et al., 2004), whereas source analysis with realistic models has spatial resolutions closer to 1 cm (Richards, 2006).

The activity of the dipoles can be estimated over time and in relation to psychological events. Figure 1.8 (bottom figures) shows the activity of these dipoles for stimuli that were novel or familiar, and which elicited attention or did not. The activity of the dipoles distinguishes the type of stimuli (experimental manipulation), the attention state of the infant (psychological process), and the temporal unfolding of the brain activity. Since neural activity is generating the EEG, the temporal resolution of this procedure is on the same time course of neural activity (1 ms). Our conclusion from this analysis is that we have identified the brain areas that generate the scalp-recorded

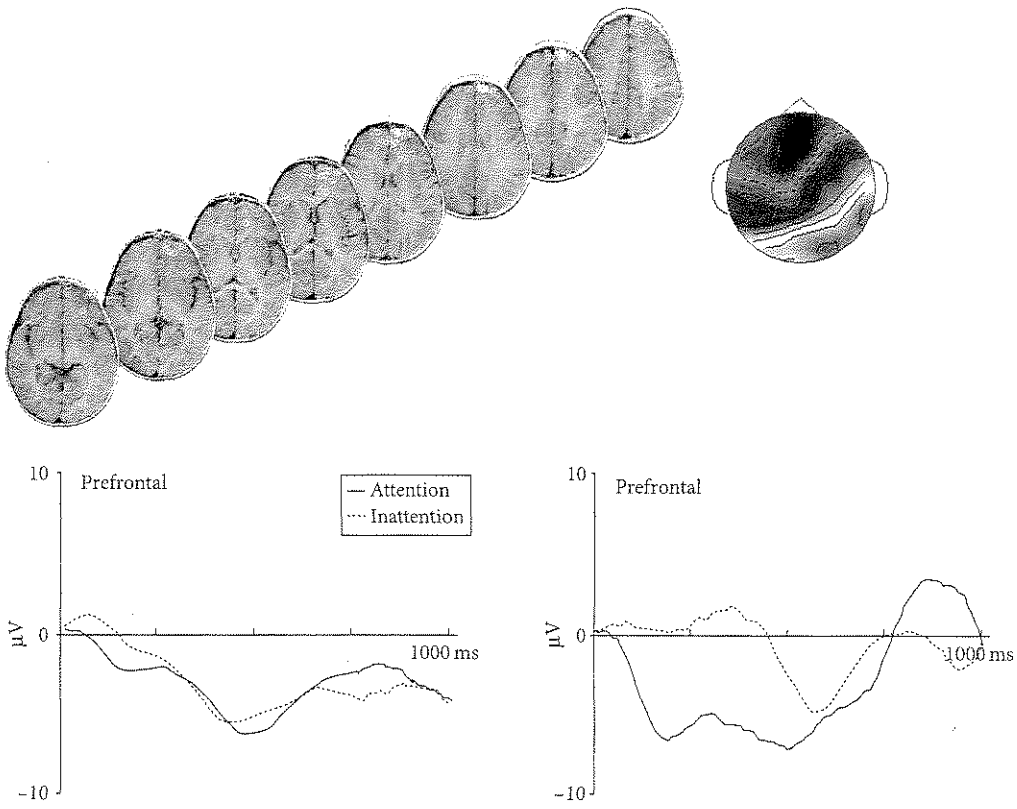
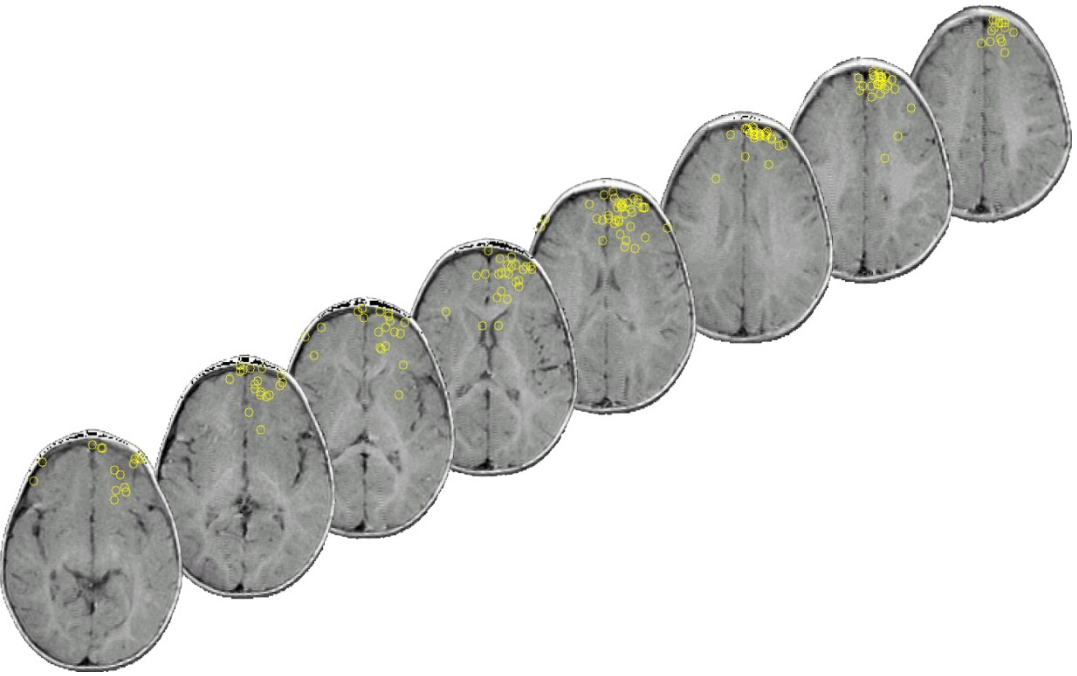
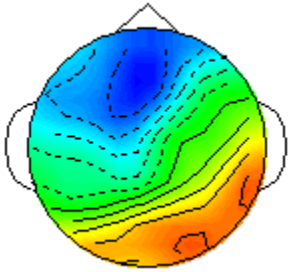
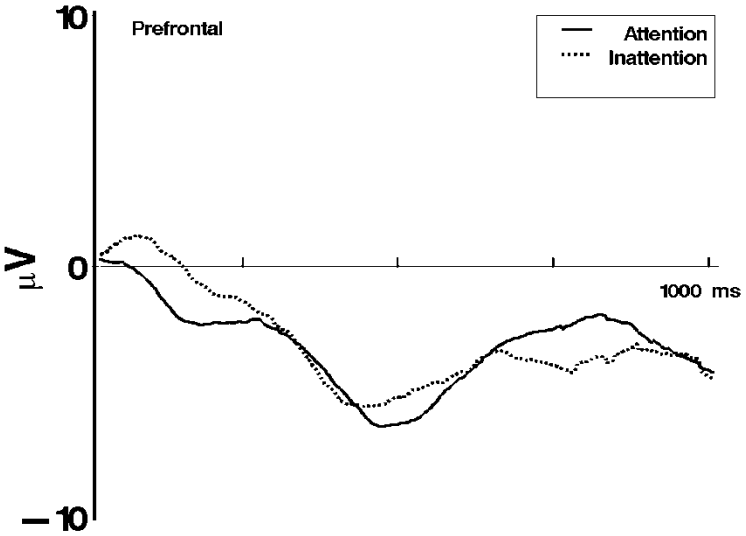


Figure 1.8 The sequence of MRI slides shows the dipole locations (yellow circles) for an ERP component known as the Nc (topographical scalp potential maps on upper right figures). The activity of the dipoles is shown in the bottom figures as a function of experiment condition (familiar stimuli on left, novel on right), psychological process (attentive dark line, inattentive solid line), and temporal pattern (0 to 1000 ms following stimulus onset).



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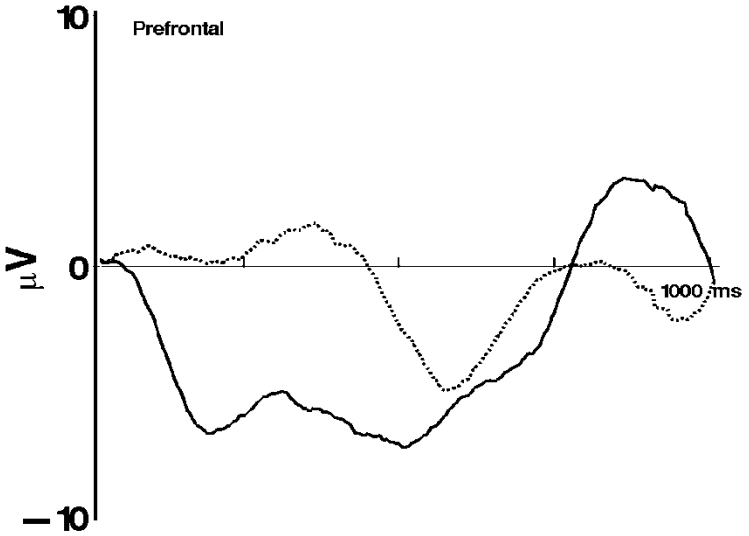
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Nc ERP component. The effects of attention on this brain activity are to enhance the amplitude of the brain activity and make it occur more quickly to novel stimuli. This technique offers a noninvasive tool for the measurement of brain activity, with spatial resolution sufficient to locate anatomical areas in the brain and temporal resolution occurring on the same time frame as activity in neurons (Reynolds & Richards, 2009; Richards, 2006).

I will mention two other techniques that might be useful to measure brain activity in young infants. Both measure the change in blood flow that occurs following neural activity. Neural activity occurring in a localized area of the brain results in changes in brain tissue resulting from the neural activity (e.g., neurotransmitter release, ionic exchange between neuron and surrounding media). These local changes affect arterial capillaries and arteries to effect the transport of oxygen and nutrients to the area. Some of these changes occur over wide areas of the brain whereas some are limited to the area in which the neural activity occurred.

Two techniques have been used in adult participants in cognitive neuroscience to measure these blood flow changes. The most familiar is "functional MRI" (fMRI; Huettel et al., 2004; Thomas & Tseng, 2008). Oxygenated and deoxygenated blood have differing magnetic properties that may be distinguished in MRI recording. When the blood flow (and resulting oxygenation) change occurs immediately after neural activity, the MRI may be used to localize these areas and show their time course. This signal may then be related to the experimental manipulations or cognitive processes, i.e., functional neuroimaging. This procedure has been used extensively in young children and adolescents (Thomas & Tseng, 2008), but has been applied only rarely in infant participants. The less-familiar technique for measuring activity-dependent blood flow is near-infrared optical spectroscopy (NIRS) or optical topography (OT). An infrared emitter placed on the skull can send an infrared signal that penetrates several millimeters (2 to 3 cm) into the skull. Infrared light of differing wavelengths is differentially absorbed/reflected by oxygenated and deoxygenated hemoglobin. The reflected light can be measured with a detector placed near the emitter, and the time course of the oxygenated and deoxygenated blood flow can be measured. This procedure is being applied to infant participants routinely (Mehler, Gervain, Endress, & Shukla, 2008).

Both techniques have been applied to infant participants. The recording of fMRI was done in young infants of 2–3 months of age to study speech perception (Dehaene-Lambertz et al., 2002). Infants were presented with speech and backward speech in 20 s blocks, alternating with 20 s periods of silence. MRI sequences were recorded about every 2 s (usually done in 3 mm slices). The fMRI technique examines the blood flow in the brain during the presentation of the sounds, subtracting the blood flow measurements during the periods of silence. Figure 1.9 shows where in the brain these changes occurred. The MRI slices on the top left are from three different levels. Brain activity during speech was larger than during the silent periods in the colored areas on the MRI slices. This occurred over a wide range of areas in the left temporal cortex. The time course of this activity is shown in Figure 1.9 (top left figure). There was a gradual increase in blood flow to these areas that peaked about 6 to 7 s after sound onset, continued during the presentation of the sound, and lasted for nearly 10 s into the silent period.

The NIRS procedure has been used to study functional brain activity in newborns and young infants (Mehler et al., 2008). For example, one study investigated language perception in newborns (Peña et al., 2003). Figure 1.9 (bottom left figure) shows the location on the scalp on which the emitters and detectors were placed. The numbers indicate the area on the scalp under which the blood flow is reflected. The middle figure shows the same locations overlaid on the brain. This study presented newborn infants with forward and backward speech, with 15 s stimulus periods and 25 to 35 s silent periods. The bottom left figure shows the changes in the total blood flow as a function of time for the 12 recording locations. The blood flow changes for

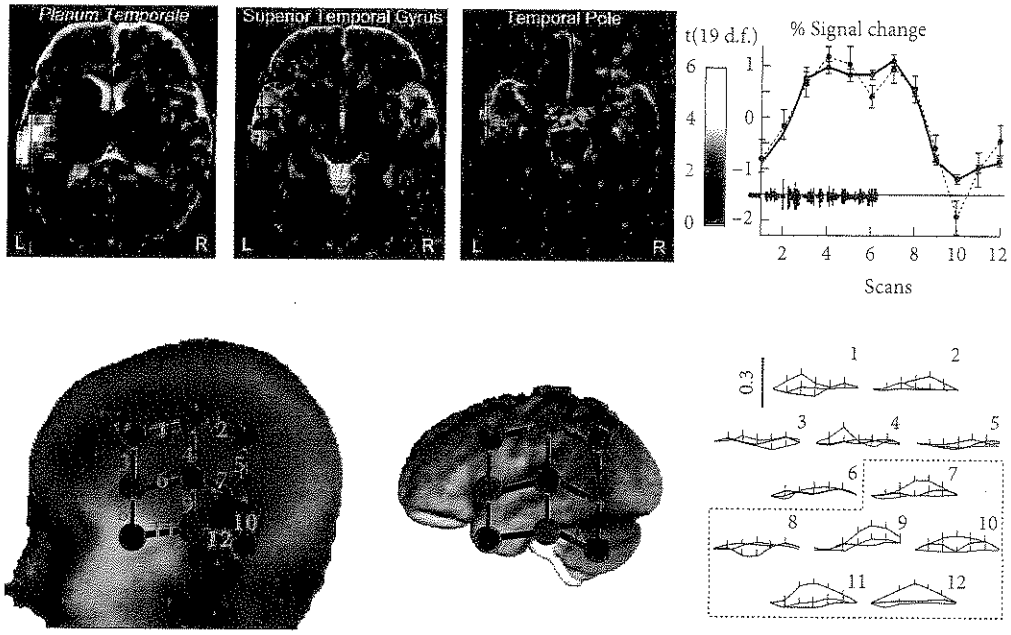
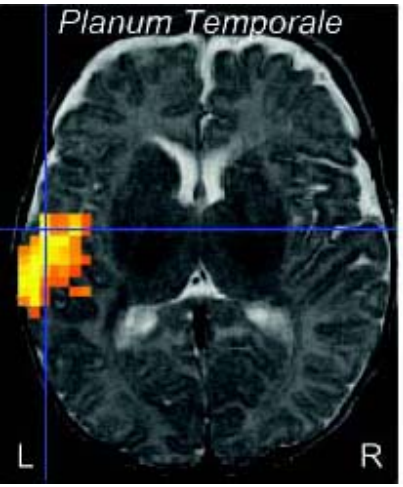


Figure 1.9 Blood-flow-based neuroimaging techniques in infant participants. The upper figures show the fMRI activations for activity at three levels of the temporal cortex, and the time course of this activity is seen in the upper right figure (about 6 scans per 10 s). The bottom left figure shows the positioning of the NIRS detector (blue) and emitter (red) probes, and the lines and numbers between the probes are the location of the scalp under which blood flow is measured. The middle figure shows the putative brain locations being measured, and the right figure shows the time course of total hemoglobin activity for forward speech (red), backward speech (green) and silent periods (blue).

the forward speech (red lines) were different in the recordings over the left temporal cortex than those for backward speech (green) or silent periods (blue). Comparable regions on the right temporal cortex (not shown) were not different for forward, backward, and silent periods. The onset of the maximal peak was 10 to 15 s following stimulus onset and the blood flow changes lasted 10–15 s after sound offset. These results show that infants are sensitive to the properties of speech at birth. Areas of the brain similar to those in older infants (i.e., Figure 1.9. top MRI figures) respond differentially to forward and backward speech.

I will comment briefly on the relative advantages of these three techniques (EEG source localization, fMRI, NIRS) for the measurement of brain function in infant participants. First, the fMRI technique provides the most direct measure of brain structure and function since the procedure is directly measuring blood flow in the location of the cortical activity. The EEG source analysis procedure uses quantitative inferential techniques to estimate such locations. The NIRS is limited to the analysis of the scalp-recorded optical changes. This restricts its value for localizing brain activity. The exact type of brain material under the same skull location differs across infants at the same age and across ages (Figure 1.6). Second, the NIRS and fMRI have a slower temporal resolution than EEG/source analysis. The underlying measurement phenomenon in the former are changes in blood flow, which occur over seconds (6–7 s for fMRI, 10–15 s for NIRS, Figure 1.9) and continues to respond for several seconds after stimulation. Alternatively, the EEG changes are caused by neural electrical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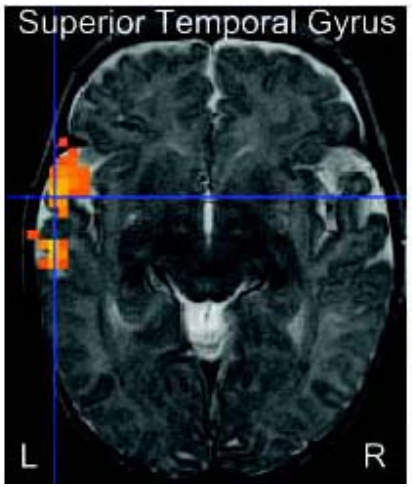
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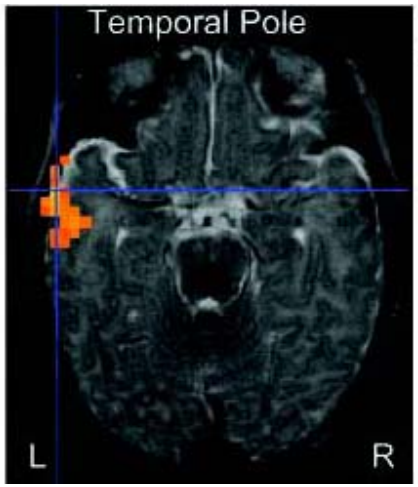
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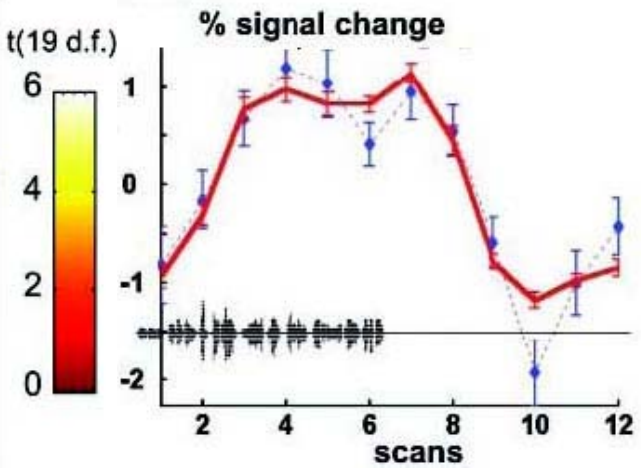
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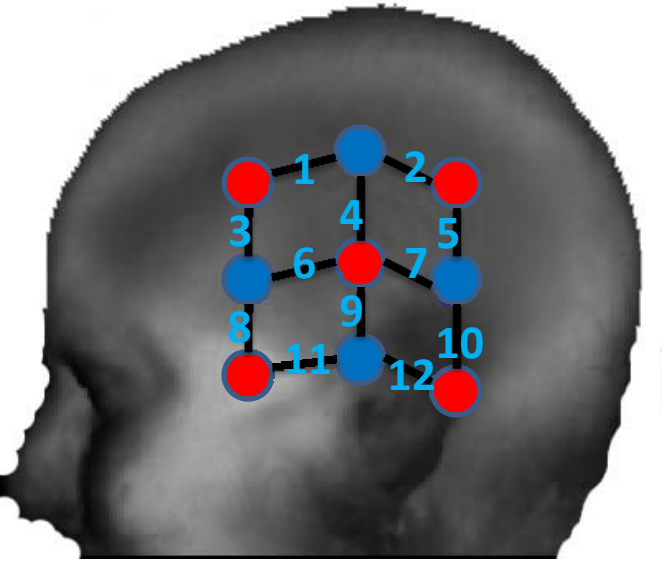
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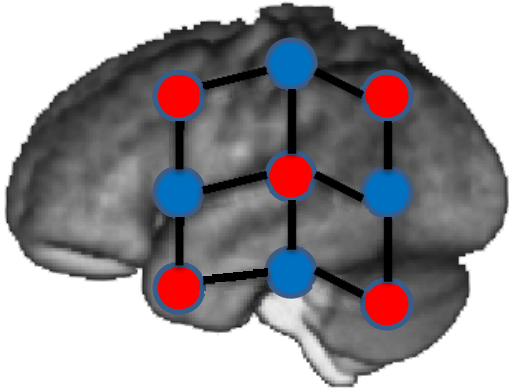

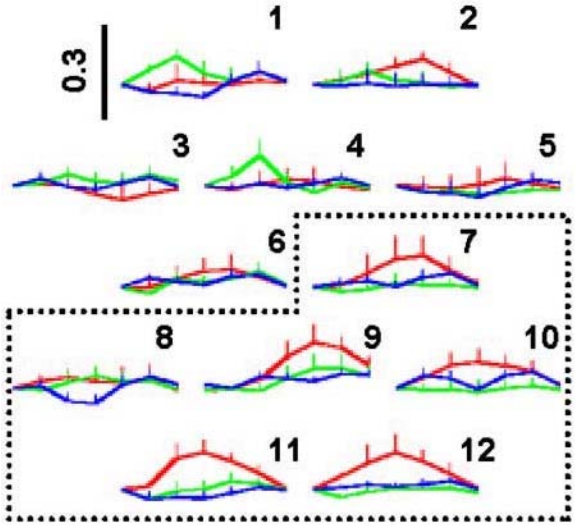
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activity occurring around the time of the synaptic potential changes of the neuron and are responsive to short-latency changes in this neural activity (e.g., 100–200 ms in Figure 1.8). Third, the spatial resolutions of the three techniques vary. MRI recording has <1 mm resolution for structural scans, and fMRI uses 3 mm slices and needs to perform averaging over a wide area. Motion artifacts may also degrade the spatial resolution of fMRI, especially for infant participants. The EEG techniques typically have resolution in the 5 cm range, though EEG source analysis with realistic head models probably lowers this to about 1 cm (10 mm). The NIRS technique has the poorest spatial resolution, since its measurement technique demands that emitter/detector distance be about 2–3 cm. It also may have its resolution blurred by larger arterial vascular changes occurring on the surface of the cortex carrying blood to intracortical capillaries. Fourth, the three techniques vary in "ease of use." The NIRS and EEG recordings are noninvasive and can be done easily on infant participants behaving in relatively unrestrained situations. The fMRI recording is extremely sensitive to motion artifacts and is best done in sleeping infants. This restricts its use for the study of a wide range of psychological processes in infant participants. The NIRS has the fewest quantitative requirements; EEG source analysis and fMRI requires extensive and sophisticated modeling with computer programs. The most used measure of the three for infant cognitive neuroscience is EEG, and NIRS is beginning to be used. The fMRI technique has rarely been used. Whereas I prefer the EEG source analysis technique as a temporally relevant and spatially appropriate method for infant cognitive neuroscience, the three techniques offer complementary information about infants' developmental cognitive neuroscience. They provide measurement of brain activity (and structure) in individual participants, rather than relying on brain measurement in other participants (i.e., nonhuman animals, postmortem or autopsy studies) or on techniques, which at best only indirectly measure brain activity (marker tasks, indirect psychophysiological recording).

Brain and Infant Attention: Spatial Orienting

The previous sections have outlined the proposal that brain development and attention development were closely related (section "Hypothesis: Infant Attention Development is Controlled by Infant Brain Development), and elaborated on methods used to measure brain structure (section "What's Inside a Baby's Head?") and function ("How to Measure Brain Function in Infants"). The current section details a type of attention, "covert attention" or "covert orienting" that has been studied behaviorally, psychophysiologically, and with the functional brain measurement described in the previous two sections.

Studies with adult participants have shown that attention may be moved around our environment flexibly. This is shown by the voluntary movement of the eyes from one location to another, which requires disengaging fixation (and attention) at one location, moving fixation (attention) to another location, and engaging attention in the new location. The flexibility of spatial attention is shown most dramatically in "covert attention" or "covert orienting." Michael Posner first studied this type of flexibility with the spatial cueing procedure (Posner, 1980; Posner & Cohen, 1984). In this procedure, a participant is directed to pay attention to a location in space where a target will occur. The target identifies some action needed to be done by the participant. The target occurs in the periphery and target identification is done without moving the eyes to the location, either during the target or in the time preceding target onset. The participant's response to the target is affected by several factors, which show that attention may be moved about in space covertly. The cueing procedure can use a cue in the same location as the target, in which case the psychological process is called "covert orienting." Alternatively, when a cue in a different location than the target, or cues are based on simple directions to "pay attention to the right side," the resulting psychological processes are called "covert attention."

Behavioral studies of this type of spatial orienting have been done in infant participants.

The spatial cueing procedure developed by Posner was first adapted by Hood (1995) to study covert orienting in infant participants. Hood presented 3- to 6-month-old infants with an interesting (color and movement) pattern on the center of a video monitor. When the infant began to fixate on this pattern, a stimulus was presented on the right or left side of the center; the center pattern remained on. Infants at this age will not shift fixation from a center pattern that is engaging fixation to the peripheral pattern. Thus, any differential response to the side on which the cue was presented, or the cue on the side, would indicate that the infant was able to covertly orient toward the peripheral pattern in the absence of overt eye movements. Note that this procedure differs from the typical Posner-type spatial cueing procedure in which verbal instructions are given to the participant to keep fixation oriented toward the center of the display.

There are a number of behavioral findings for infants in this spatial cueing procedure. A common variant is to present the peripheral pattern when the central stimulus is present, then turn both stimuli off, then present a pattern, functioning as a target, to which an eye movement will be made. The target can be presented on the same side as the cue ("valid trials"), on the opposite side ("invalid trials"), not presented ("no-target control"), or can be presented on a trial without the cue being presented ("neutral"). A number of studies show that in 2- and 3-month-old infants, the time to move the eyes from the center location to the target is faster when the cue and target are on the same side (valid trials) than when no cue was presented or the cue and target were on opposite sides (Hood, 1993, 1995; Hood & Atkinson, 1992; Johnson & Tucker, 1996; Richards, 2000a, 2000b, 2001, 2004a, 2004b, 2006, 2007). Figure 1.10 shows this finding for 14-, 20-, and 26-week-old infants (Richards, 2000a). The left-hand figures show the time to move the eyes from the center location to the target when the stimulus-onset asynchrony (SOA) was 350 ms. This time was

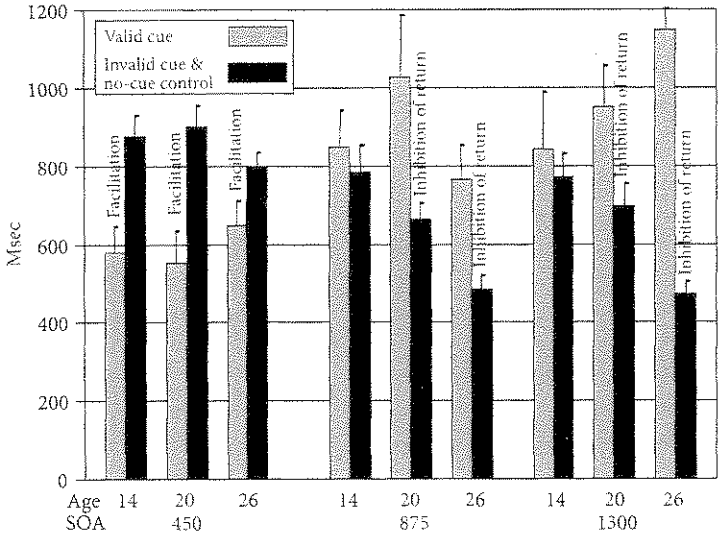


Figure 1.10 Reaction time in the spatial cueing procedure for infants at 14, 20, and 26 weeks of age, as a function of stimulus onset asynchrony (SOA) and cueing type. The short SOA shows faster response times for the valid cued trials than the invalid and neutral trials for the three testing ages, whereas the medium and long SOA show inhibition of return only for the 20 and 26 week old infants. From Richards (2000a).

shorter on the valid trials for the three testing ages. This facilitation shows that the presence of the cue registered in the infant's cognitive system even though fixation continued on the central stimulus; i.e., covert orienting.

An additional finding comes from the 20- and 26-week-old (4.5 and 6 months) infants. On trials when the time between the cue and target was relatively brief (e.g., 350 ms in Richards, 2000a), infants showed the facilitation of the response to valid targets. Alternatively, if the SOA was large enough (e.g., 700 to 1000 ms), the opposite occurred. The movement of the eye from the center position to the target was longer on the valid trials than on either the invalid trials or neutral trials with no cue stimulus. This longer response time may be seen in Figure 1.10 for the middle and right sets of bars. The 20- and 26-week-old infants showed lengthened reaction times for the valid trials at the 750 and 1300 ms SOA in this figure. Posner labeled this slowing of the response at intermediate SOA levels "inhibition of return." Interestingly, the inhibition of return occurs at late ages only for "covert orienting." If the cue is shown and fixation is moved to the cue, and then back to the center pattern, "overt orienting," young infants and newborns take longer and are less likely to move fixation back to the cued location (Butcher, Kalverboer, & Gueze, 1999; Clohessy, Posner, Rothbart, & Vecera, 1991; Simion, Valenza, Umilta, & Barba, 1995; Valenza, Simion, & Umilta, 1994).

The effects showing covert shifts of attention (covert orienting, covert attention) in adult participants have been studied with methods to determine the brain bases of these responses. Study methods have included fMRI, ERP, study of pathological populations, and invasive studies in animal preparations. The response facilitation that occurs at short SOAs is hypothesized to be due to the enhancement of sensory processing of information occurring in the attended portion of visual space (Hillyard, Luck, & Mangun, 1994; Hillyard, Mangun, Woldroff, & Luck, 1995). This has been shown with ERP studies that find enhanced amplitude of the early components of the ERP elicited by the target (Hillyard et al., 1994, 1995), and by studies linking these ERP changes with fMRI recording (Martinez et al., 1999). For example, in response to a target occurring in one part of the visual space, there is an enhanced ERP component labeled "N1" that occurs on the posterior scalp on the contralateral side, i.e., where the occipital brain areas for the opposite visual field are. This enhanced N1 seems to be caused by areas in the extrastriate occipital cortex and the fusiform gyrus (Martinez et al., 1999). The inhibition of return effect is thought to be mediated by the superior colliculus (Posner, Rafal, Choate, & Vaughan, 1985; Rafal, 1998; Rafal, Calabresi, Brennan, & Sciolto, 1989). It is thought that the activation of pathways in the superior colliculus responsible for fixation shifts, and the inhibition of those pathways during the spatial cueing procedure, results in inhibition of return.

Researchers studying infants in the spatial cueing procedure have adopted this neurophysiological perspective (Hood, 1993, 1995; Johnson & Tucker, 1996; Richards, 2000a, 2000b, 2001, 2004b, 2005, 2007b; Richards & Hunter, 2002). The spatial cueing effects have three putative developmental phases for infants. First, the superior colliculus is relatively mature at birth and should support inhibition of return. One can find in newborns, using the procedure in which there are overt shifts of fixations, examples of inhibition of return (Simion et al., 1995; Valenza et al., 1994). Second, the facilitation of response times at short SOAs must occur in cortical areas supporting visual processing. Only by 3 or 4.5 months is this area mature enough to support such response facilitation; thus the emergence of shortened response times to valid targets occurs by about 3 months of age (Richards, 2000a, 2000b, 2001, 2005, 2007b). Finally, the emergence of inhibition of return following covert attention shifts by 4.5 or 6 months of age must be due to the increasing influence of cortical systems on fixation in this task. Perhaps these cortical systems inhibit fixation to the peripheral stimulus during the presentation of the cue, leading to an inhibition of return of the attention system to the cued area. The changes in covert attention shifts found between 3 and 6 months of age must therefore be due to cortical changes in areas such as the parietal cortex and

frontal eye fields involving saccadic planning and attention shifting. This interpretation is consistent with the general view that that there is an increase in the first 6 months of life of cortical control over eye movements that occur during attention and increasing cortical control over general processes involved in attention shifting (e.g., Hood, 1995; Richards, 2008; Richards & Hunter, 1998, 2002).

I have studied the areas of the brain involved in covert orienting effects in infants using ERPs and cortical source analysis. I briefly presented the use of scalp-recorded EEG for the measure of brain activity (section "How to Measure Brain Activity in Infants"). An EEG recording is made of the electrical activity occurring on the scalp. The EEG is generated by neural activity occurring in neural tissue inside the head. The infant is placed in the experimental situation with the spatial cueing procedure and changes in EEG are measured that are linked in time to the experimental presentations, i.e., ERP. The ERP thus is a measure of brain activity, recorded on the scalp, which is synchronized with the experimental manipulations or the psychological processes occurring in the spatial cueing procedure. The link between the scalp-recorded activity and the experimental manipulations is therefore a functional neuroscience method.

The studies I have done have tested infants at 14, 20, and 26 weeks of age (e.g., Richards, 2000a, 2000b, 2001, 2005, 2007b). The spatial cueing procedure adapted for infants was used and the ERP was measured at the beginning of target onset or immediately before saccade onset. Figure 1.11 shows the ERP changes occurring at target onset for the occipital electrode that was contralateral to the target (Richards, 2000a). This contralateral occipital electrode is interesting because visual information from the eye first reaches the cortex in the contralateral occipital cortex, which is just underneath the scalp near this electrode. A large positive deflection in the ERP occurred about 135 ms following target onset. This potential was the same size for the 14-week-old infants for the valid and other conditions, slightly larger for the valid condition for the 20-week-old infants, and largest for the valid condition for the 26-week-old infants. This ERP component occurred about the same time and has similar morphology to the "P1" ERP component often found in adults. This enhanced P1 is often found in response to a valid target in adult participants, and has been labeled the "P1 validity effect" (Hillyard et al., 1994, 1995). The study suggests that areas of the brain that control this response are developing over this age range. Presumably this brain development is related to the behavioral changes occurring in response facilitation or inhibition of return.

The cortical locations that generate the P1 validity effect was further examined with

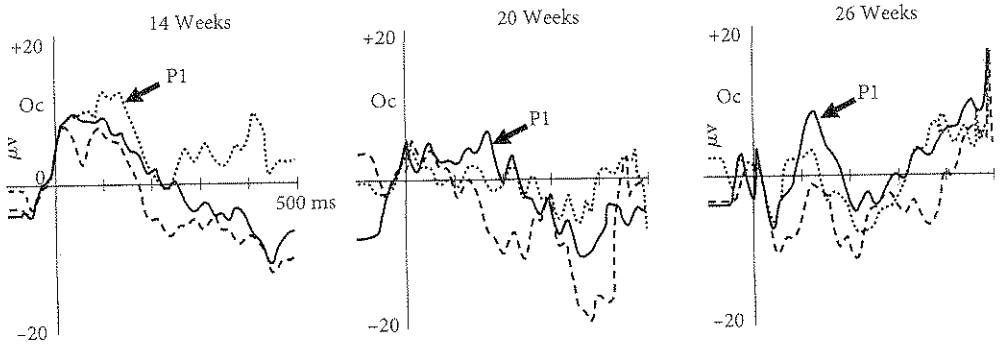


Figure 1.11 The ERP changes occurring at target onset in the occipital electrode contralateral to the target side. The valid (solid), invalid (dotted), and neutral (dashed) targets produced the same ERP response in the 14-week-old infants. The P1 ERP component was larger for the valid trials in the 20- and 26-week-old infants. From Richards (2000a).

cortical source analysis (Richards, 2005, 2007b). The section "How to Measure Brain Activity in Infants" introduced cortical source analysis. In this analysis, electrical dipoles that can generate the current resulting in the ERP component may be identified. The dipoles represent the location of the source of the cortical activity that is related to the experimental manipulations or psychological processes, i.e., functionally localized brain sources. Activity in these dipoles changes over time so that cortical activity that generates the temporal characteristics of the ERP can be shown.

I first will discuss the change over time occurring in several locations. Cortical sources for ERP recording were found in several areas of the cortex, including the posterior occipital cortex, extrastriate occipital cortex (including fusiform gyrus), and temporal cortex. Figure 1.12 shows the activity of these areas over time. A significant difference between the valid and the invalid/neutral trials is highlighted with the hatched bars. The posterior occipital cortex and the temporal cortex showed a large negative activity (brain activity resulting in negative scalp recordings), whereas the extrastriate occipital cortical areas

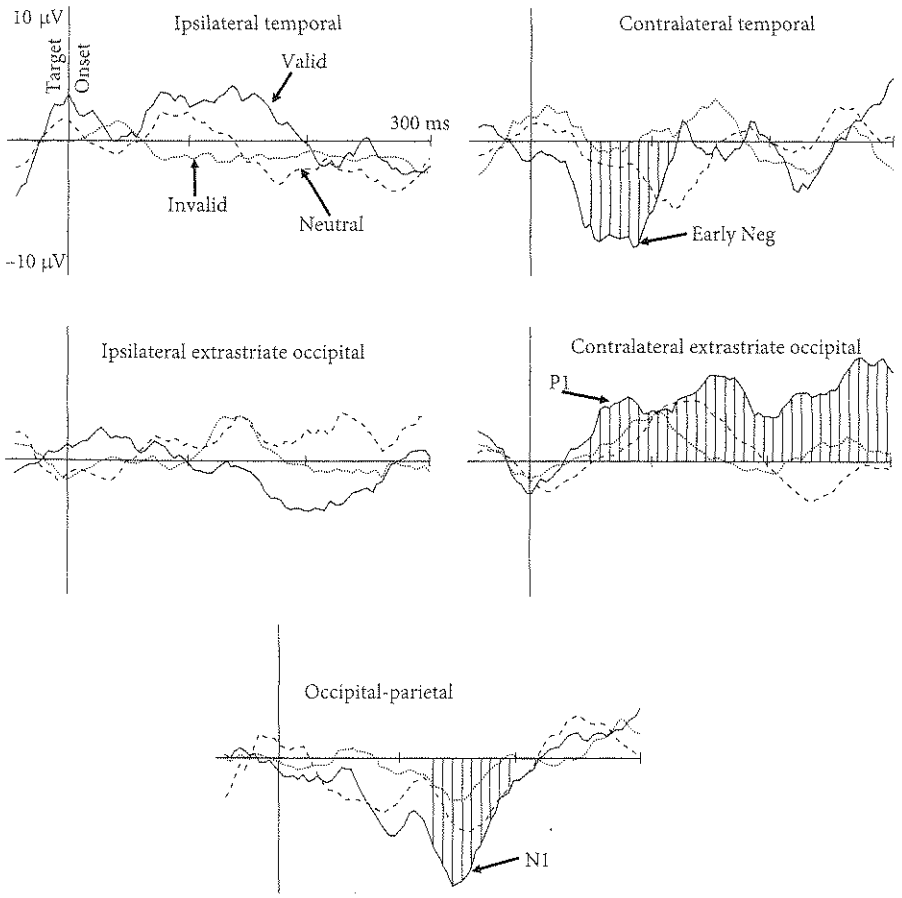


Figure 1.12 The time course of activity for the dipoles located with cortical source analysis. The valid trials (solid line) produced a significantly larger response in the posterior occipital cortex, extrastriate occipital (including lateral occipital, lateral-medial occipital, fusiform gyrus), and temporal regions (hatched areas). The cortical source analysis identifies only "activity" of the sources, and the direction of the source is determined from the direction of the ERP occurring in these locations.

showed the positive activity. This latter activity was similar in time course and electrical current direction to the P1 ERP component.

The activity for the contralateral extrastriate occipital areas will be examined further. Figure 1.13 (top left figures) shows a topographical scalp potential map for the ERP activity occurring in this area. The cortical sources for this brain area may be seen in the figure on the top right. These sources occurred in middle and superior occipital areas (Brodmann areas 18, 19) and in the fusiform gyrus. These areas are pathways that lead from the primary visual area to the object identification areas in the temporal cortex ("ventral processing stream"). Figure 1.13 also shows these activations in a bar graph separately for 14- and 20-week-old infants, and separately for the valid, invalid, and neutral conditions. The largest response was for the 20-week-old infants. This parallels the earlier finding of the gradual increase in the P1 validity effect over this age (Figure 1.11; Richards, 2000a). This implies that changes occurring in this area of the cortex underlie the P1 validity effect changes and perhaps some of the behavioral changes occurring in this task.

An interesting comparison can be made between the findings that areas of the contralateral extrastriate occipital cortex are the brain sources for the P1 validity effect in infants and a combined ERP/fMRI study in adults (Martinez et al., 1999). The Martinez study used a spatial cueing procedure in which participants were instructed to direct fixation to either the right or left side, and then targets were presented in either the attended or the unattended side. This procedure was done separately in a psychophysiological session using ERP and in a functional MRI session. They found the typical P1 validity effects in the ERP and localized the cortical sources to extrastriate occipital areas. These areas showed enhanced blood oxygen level–dependent (BOLD) activity in the fMRI experiment when attention was directed to the contralateral visual field. Alternatively, areas of the primary visual cortex did not show the ERP validity effect.

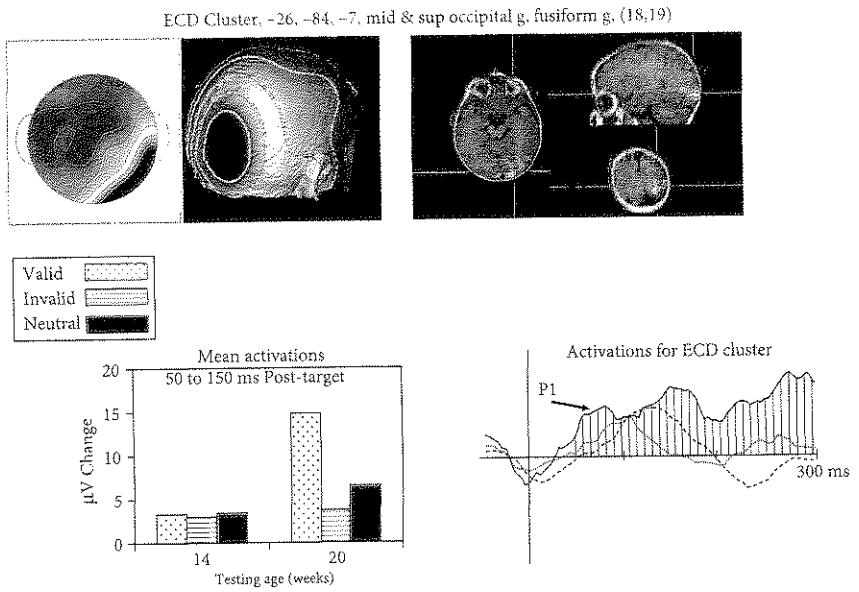
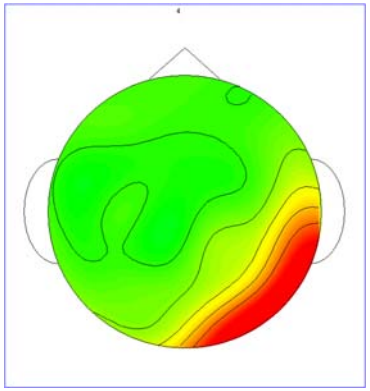
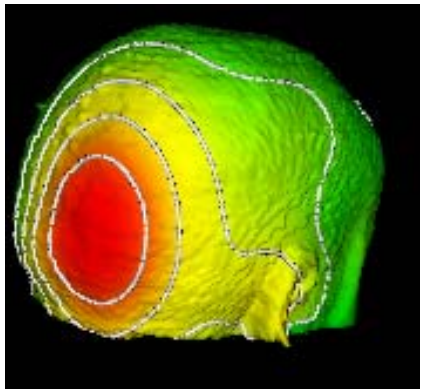
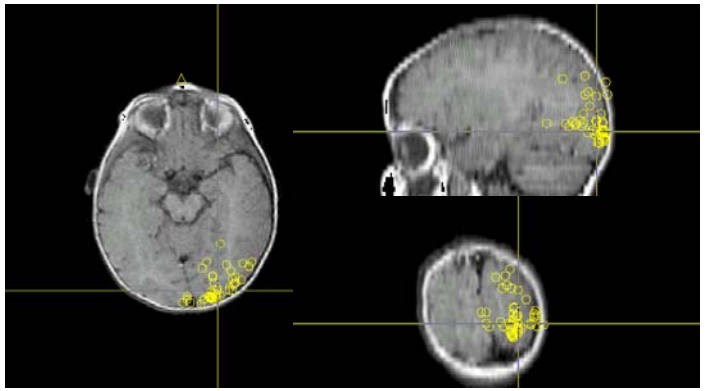


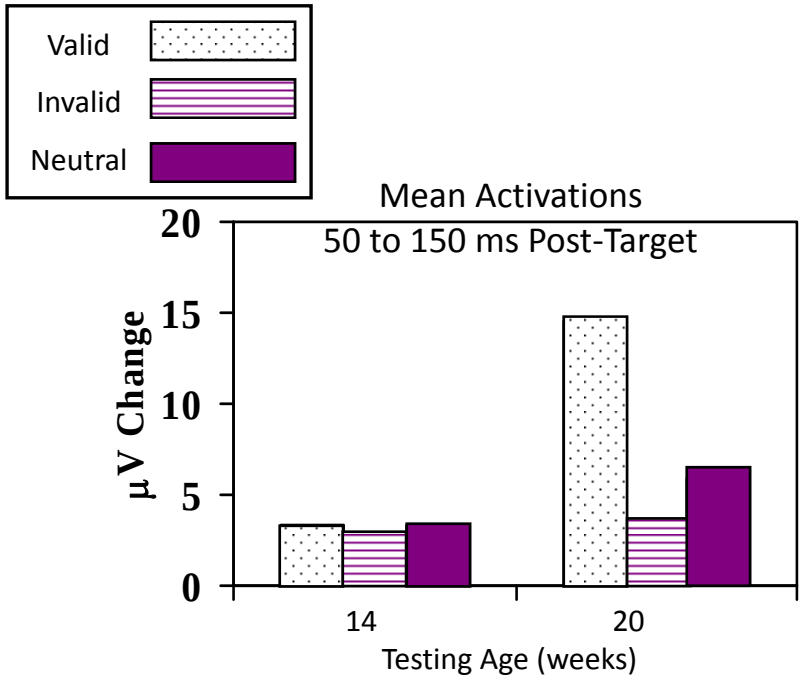
Figure 1.13 Topographical scalp potential maps for the contralateral extrastriate occipital areas (top left) and the cortical sources located in the brain (top right). The activity in this area was largest for the 20-week-olds in the valid cueing condition (bottom left figure).

ECD Cluster, -26, -84, -7, mid & sup occipital g, fusiform g, (18,19)









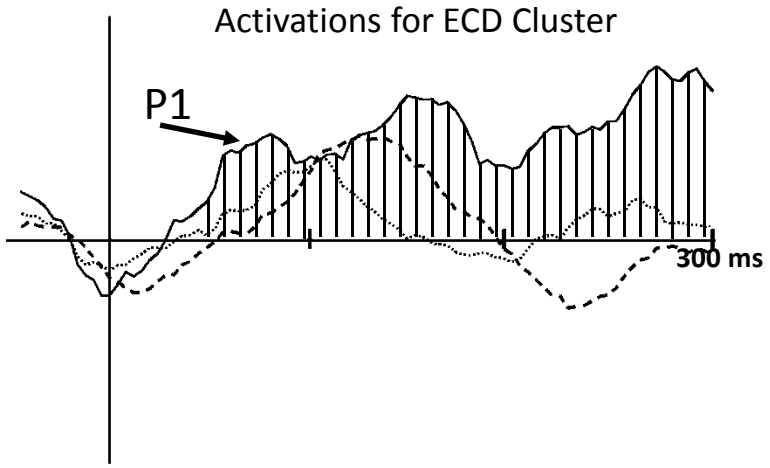


Figure 1.14 compares the findings from the Martinez et al. (1999) study to the Richards (2005) results. Figure 1.14 shows the fMRI areas in the Martinez et al. study (upper left corner) and the cortical sources plotted on MRI slices from the Richards (2005) study. The green and red arrows point from the fMRI areas where an attention effect was observed to the comparable areas in the cortical sources of Richards, representing the contralateral extrastriate occipital areas that was the basis for the infant P1 validity effect. These areas are very similar in both studies. The yellow arrows point to the areas in the primary visual cortex in the studies of Martinez et al. (1999) and Richards (2005) where no validity effects occurred.

The Martinez et al. (1999) and the Richards (2005) results are compared further in Figure 1.15. The average MRI from several infants in the range from 3 to 6 months is shown as the MRI in Figure 1.15. Superimposed upon the MRI in the cross-hatched area are the middle and superior occipital cortex (top figures) or lateral-occipital cortex/occipital-fusiform gyrus (bottom figures). These areas were identified from the relevant anatomical areas derived from the MNI brain (Figure 1.7). The small yellow circles represent individual source dipoles from the cortical sources found in Richards (2005), both areas which show a P1 validity effect in their activation. The larger filled circles are the average Talairach locations for the superior occipital

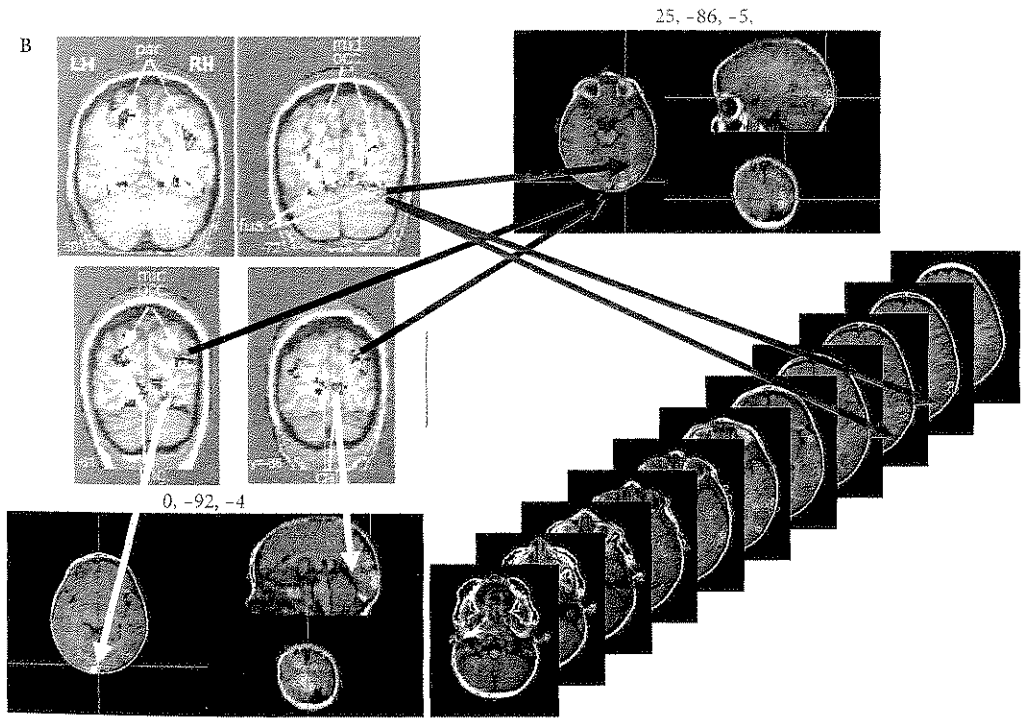
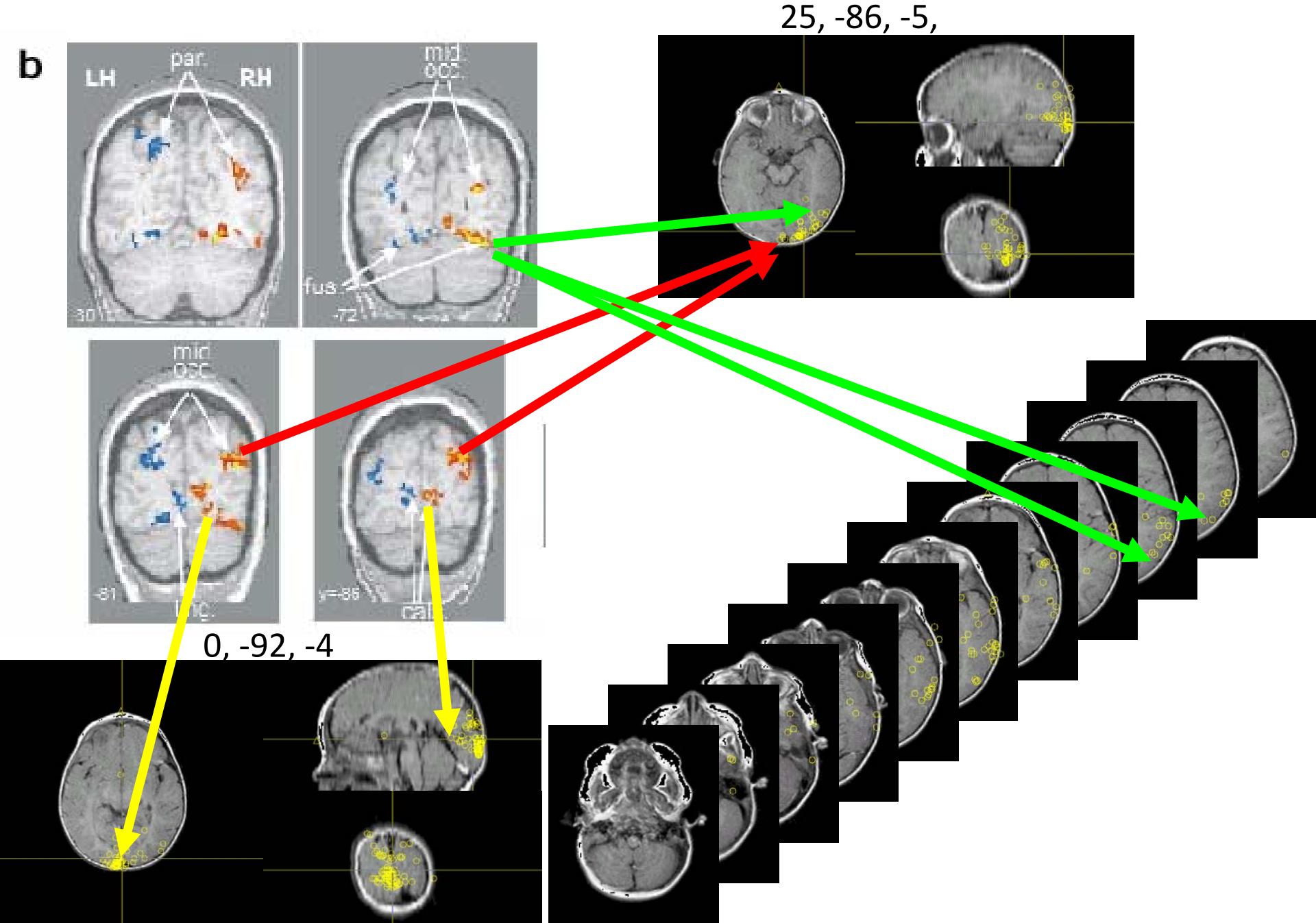


Figure 1.14 Comparison of results from a study of adults with fMRI (Martinez et al., 1999) and infants with source analysis of ERP (Richards, 2005). The upper left panels show the sources that were active in the fMRI study. The green lines are areas in the lateral occipital cortex and fusiform gyrus that were more active when attention was shifted to the contralateral side (fMRI) and the lateral occipital and fusiform gyrus locations that showed a P1 validity effect (infant ERP). The red arrows point to middle and superior occipital areas showing attention effects in both studies. The yellow areas are occipital cortex areas representing the primary visual cortex, showing attention effects in the adult fMRI but not in the infant ERP.


b
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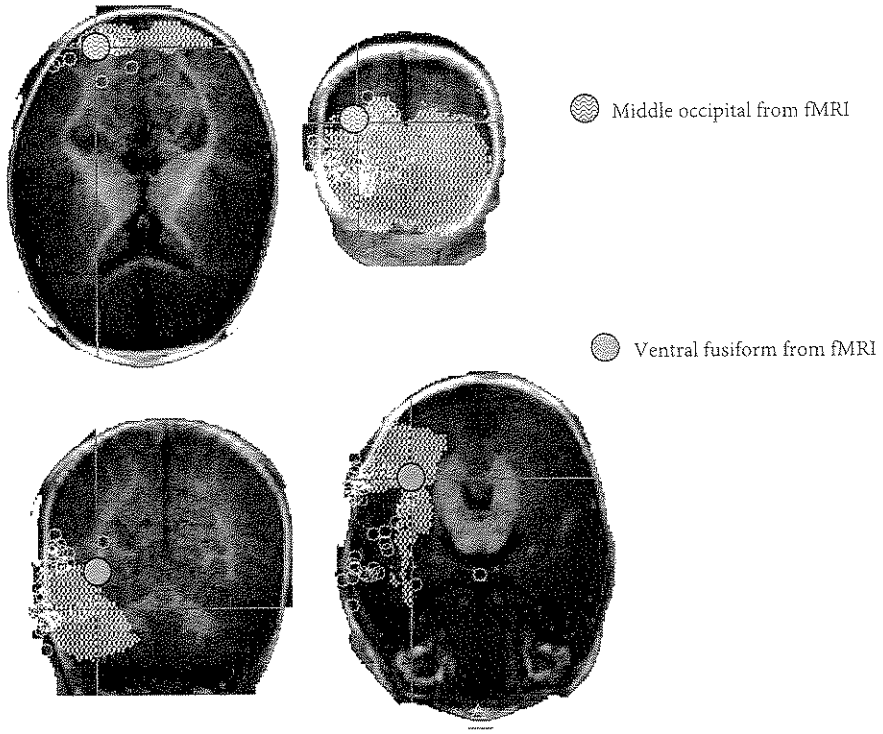
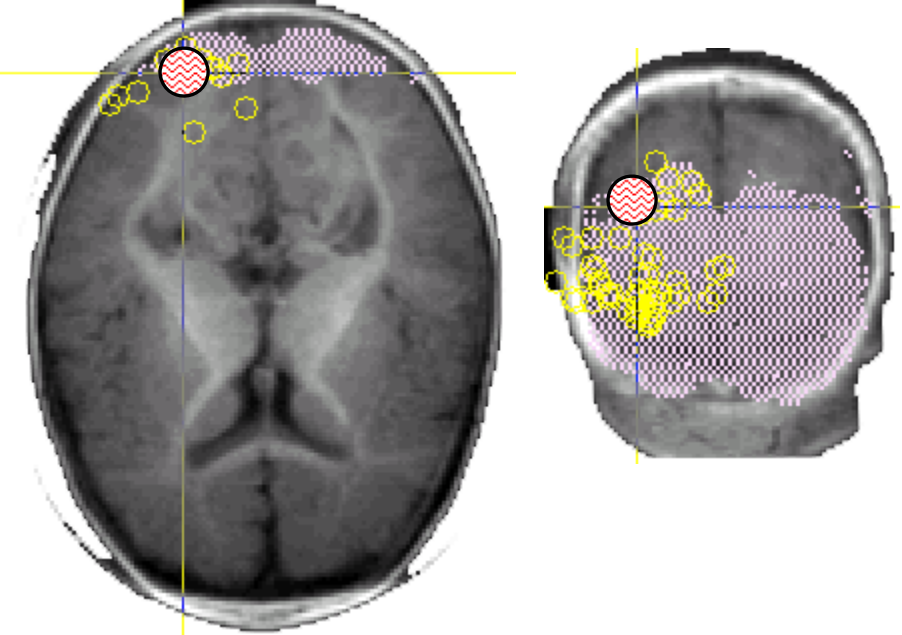


Figure 1.15 The distribution of cortical sources in Richards (2005) which were the cortical sources for the P1 validity effect in the ERP (yellow circles), compared with the cortical source locations found with adult ERP for this effect (large circles). The light purple hatched areas represent the anatomical locations of these areas translated from the MNI stereotaxic atlas (Figure 1.7) to an average of infant MRIs from 3 to 6 months of age.

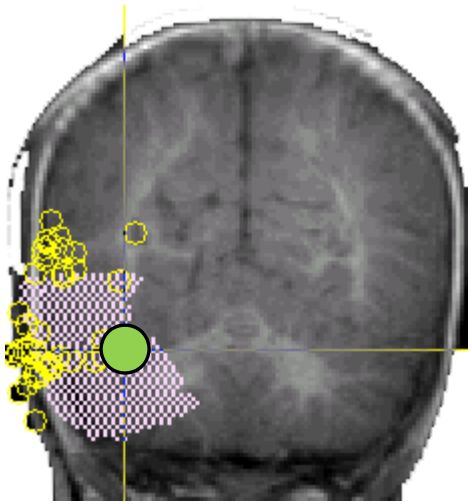
and fusiform gyrus locations identified in the Martinez et al. study as showing the P1 validity effect in the ERP. Figure 1.15 shows how similar are the locations of the cortical source analysis found in these two studies.

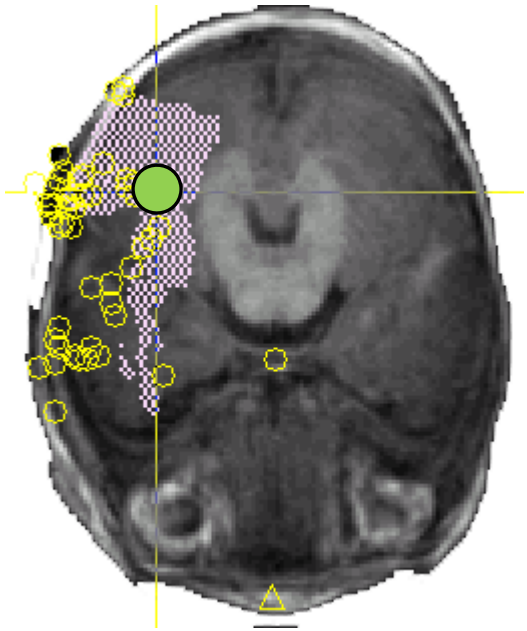
There are two implications of the work showing the ERP components accompanying covert orienting in young infants and their cortical bases. The first implication is that the brain areas involved in the control of sensory processing and the effects of attention on these brain areas may form the basis for the changes in attention to peripheral stimuli in young infants. These techniques may be useful in showing how brain changes in these areas parallel developmental changes in the behavioral components of these tasks. The use of scalp-recorded ERP and the source analysis allow a "functional cognitive neuroscience" for infant participants. Second, the brain changes found in the P1 validity effect (Figures 1.11 and 1.13) parallel those findings of the inhibition of return rather than those of the response facilitation (Figure 1.10). This suggests that the development of the inhibition of return may be linked to the enhanced processing of stimuli occurring initially in the sensory systems. I have argued that cortical areas involved with saccade planning (presaccadic ERP; frontal eye fields; see Richards, 2000a, 2001, 2005, 2007b) may be more closely related to the inhibition of return effect. This may occur as attention-based saccade planning and fixation control comes to inhibit the movement of the eyes from the center to the cued location. These areas are likely in prefrontal cortex rather than posterior regions.



Middle Occipital from fMRI

Ventral Fusiform from fMRI





Brain and Infant Attention: Future Directions

This chapter reviewed the hypothesis that changes in brain areas controlling attention strongly influence the development of attention in infant participants. A considerable portion of the chapter examined the methodological advances in imaging showing what is inside the infant's head and how to measure brain activity in infant participants. I have focused on my work using cortical source analysis of ERP in the spatial cueing procedure as an example of how this might be done. The goal of research in this area is to link measures of infant brain development and measures of attention development.

There are aspects of this work that require further advances. Greg Reynolds and I (Reynolds & Richards, 2009) describe in more detail the application of cortical source analysis to infant participants. One limitation we note is that the cortical source analysis has been based on parameters for use with adult participants. The forward solution used impedance values for the matter inside the head (gray matter, white matter, CSF, skull) that are derived from adult participants. We know these are incorrect—adult skin has higher impedance than infant skin because of the accumulation of dead skin cells in adults, and infant skulls are less dense and thinner than adult skulls so that adult skulls have higher impedance than infants. This is being addressed by taking individual participant MRIs (section "What's Inside a Baby's Head?") from infants and using source analysis based on that infants head topography and infant-based values of the impedance of head materials (Reynolds & Richards, 2009; Richards, 2006, 2007a, submitted).

A second aspect of this work that requires advancement is the association of specific cortical changes with specific behavior changes in individual infant participants. The work discussed in the previous section (section "Brain and Infant Attention: Spatial Orienting") relied on average change in the group on the measures of behavior (Figure 1.10), ERP validity effect (Figure 1.11), and source activation and brain change (Figures 1.12 to 1.15). An individual approach would be to first identify aspects of brain development in individual participants and relate those aspects to that infant's behavioral performance. For example, perhaps extent of myelination (Figure 1.1) of the occipital areas (Figures 1.13 to 1.15) in an infant would be related to the existence of response facilitation but not inhibition of return for that infant, and the inhibition of return would be closely related to the size of the P1 validity effect. Alternatively, myelination in frontal areas occurring in this age range may be closely related to ERP changes indicating attention-directed saccade planning and the presence of inhibition of return. Such analyses would show directly the relation between brain development and attention development. An example of this kind of work is that of Klingberg (2008) showing in children and adolescents a close relation between myelination characteristics and cognitive and linguistic status.

Finally, I am working on several improvements to the spatial cueing procedure to make it more amenable to EEG and ERP analysis. One advance I have made is to create a testing protocol that results in a large number of presentations. In prior studies (Richards, 2000a, 2000b, 2001, 2005), the infants were presented with a single presentation of center stimulus, cue, target, and reaction time, interspersed with intertrial intervals with no stimulus present. This took from 5 to 15 s and resulted in 20 to 40 trials per participant. This allowed us to obtain numbers of trials sufficient for ERP analysis, but not optimal for relating individual performance with brain areas active in the task. Currently, I am using a procedure that presents a variegated background with continuous presentation of a stimulus that is foveated, cue, target, response, and then continued presentations. Between 75 and 200 trials can be obtained with this procedure and the infants are very cooperative. This allows for more manipulations in a single participant, larger numbers of trials for ERP averages, and examination of the relation between ERP characteristics, brain source activation, and different behavior patterns on a trial-by-trial basis. I have presented some results from this procedure (Richards, 2007b) and am continuing with

other studies using this procedure. We also are using this procedure to test individual participants who have had anatomical MRIs. This allows the correlation between the structural characteristics of the individual infant's brain and its performance in the task.

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