AGE- AND EXPERIENCE-DEPENDENT MODULATION OF COHERENT VISUAL MOTION PROCESSING

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ABSTRACT

Visual motion processing dysfunction has been observed in developmental dyslexia, but the nature of the relationship between this dorsal stream function and the reading difficulties observed in dyslexia is unclear. This is due to the fact that the typical development of visual motion processing and its dorsal visual substrates has yet to be fully characterized, and as such the relationship between reading experience and dorsal stream development is ambiguous. Similarly, while visual motion processing differences observed in deaf populations have been attributed to the effects of deafness, it is unknown how experience with a visuospatial sign language may be impacting these effects. This dissertation presents two complementary studies addressing these questions. The first investigated the functional development of the neural substrates of coherent visual motion processing (e.g., area V5/MT) using both a cross-sectional and longitudinal approach, and evaluated V5/MT activation in the context of reading ability. From this, we report that the development of V5/MT is characterized by a shift in the location, rather than intensity, of peak response to coherent visual motion, and that children show greater connectivity between V5/MT and local surrounding cortex than adults. Further, our evidence does not support there being a relationship between V5/MT activity and later reading ability in typically reading children. The second study examined the effects of deafness and sign language experience on the neural substrates of coherent motion processing using a factorial analysis of four groups: hearing native users of English, hearing native users of sign language, deaf native
users of English, and deaf native users of sign language. When the effects of deafness and experience with sign language were fully disambiguated, we found there to be a main effect of sensory experience in right hemisphere auditory association cortex, and a main effect of language experience in left ventral temporal and right inferior frontal cortices. Together these studies help clarify the age- and experience-dependent effects on visual motion processing and the dorsal visual system.
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Chapter 2
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CHAPTER 1: FUNCTIONAL ANATOMY OF THE DORSAL VISUAL STREAM AND IMPLICATIONS FOR AGE- AND EXPERIENCE-DEPENDENT MODULATION OF VISUAL MOTION PROCESSING

Introduction

Early visual experience is critical for the successful development and function of the visual system (Hadad et al., 2012; Li et al., 2006, 2008; Prusky et al., 2008), whether it is having adequate input from both eyes for establishing ocular dominance columns, or in aligning binocular input for development of optokinetic nystagmus. Perturbations or alterations to visual development can have significant, long-lasting impacts on visual function as well as on behaviors that rely on visual function. Whereas in some cases the cause and effect of visual dysfunction is well-established (e.g., eye patching and imbalanced ocular dominance columns), in others this relationship is less clear.

The work in this dissertation focuses on the dorsal visual stream. The dorsal stream is a broad term used in reference to the cortical visual system projecting from V1, primary visual cortex, through extrastriate cortical areas V2 and V3a in the occipital lobe, to occipitotemporal areas V5/MT and MST, on to posterior and lateral inferior parietal cortex and frontal eye fields in the frontal lobes. It is often contrasted with the ventral stream, which, from primary visual cortex, projects ventrally to extrastriate cortical areas V2 and V4 in the occipital lobe, to inferior and ventral temporal areas including lingual and fusiform gyri, and anteriorly to the temporal pole, as described in more detail below. Input to the dorsal stream is relatively homogeneous,
originating in retinal projections to magnocellular layers of the lateral geniculate nucleus and on to layer 4B of primary visual cortex (hence it is sometimes loosely or interchangeably referred to as the magnocellular visual system, however see Skottun, 2015). The dorsal visual stream is responsible for visuospacial processing, perceiving motion, and guiding eye movements (Ungerleider & Mishkin, 1982). Dysfunction specific to this dorsal visual system has been observed in a number of developmental disorders, prompting the hypothesis that the dorsal visual system is more ‘vulnerable’ to developmental perturbation. This vulnerability, often identified through a deficit in coherent motion perception, is thought to stem from the protracted development of this system relative to other visual systems (Braddick et al., 2003; though this is a matter of debate, see Klaver, 2011), rendering this system more susceptible to disordered development. Perturbations during the development of the dorsal stream are then thought to produce downstream functional deficits that are either concomitant with or contribute to a number of developmental disorders (e.g., Williams Syndrome, autism, developmental dyslexia).

Deficits in visual processing (e.g., coherent motion detection, contrast detection, speed discrimination) have been reported in children and adults with dyslexia. The model that best captures the pattern of these visual perceptual differences is the magnocellular deficit theory (for review, see Stein, 2001). The causal nature of the relationship between magnocellular/dorsal stream function and dyslexia has been a matter of debate, however, with many arguing that it does not exist, and even if it does exist, that it is a mere correlation but no causation (Vellutino et al., 2004). One idea that has been put forward is that magnocellular visual deficits are a consequence of poor reading, and that the process of learning to read in typical readers “mobilizes” the magnocellular system (Boets et al., 2011). This debate is limited in part by the
current lack of understanding of the typical developmental time course of dorsal stream function, specifically coherent motion processing measured with functional brain imaging, and the impact of reading experience on this trajectory. Therefore, there is no current evidence in the literature to convincingly support or refute whether dorsal stream magnocellular integrity lays the groundwork for reading capacity, or whether reading experience mobilizes dorsal stream functioning. This thesis presents data from a Cross-Sectional Study (children averaged 7 years of age compared with adults) and a Longitudinal Study (children followed longitudinally from age 8 to 9 years) of the brain basis of coherent visual motion perception using functional MRI (fMRI), as a way to understand if there are age- or reading-related differences in dorsal visual stream function.

Similar questions of causality based on language experience are relevant to studies of dorsal stream function in deaf populations. While dyslexia has been associated with dorsal stream deficits, deafness has been associated with enhanced dorsal visual function. Neural reorganization and cross-modal plasticity after the loss of auditory input has been shown to produce enhanced visual perception (Bavelier et al., 2000; Bosworth & Dobkins, 1999, 2002a; see Bavelier et al., 2006, for review). Typically, enhancements in dorsal stream function and related behaviors have been reported in studies comparing deaf subjects to hearing subjects (Mohammed et al., 2005; Scott et al., 2014). However, some differences in visual system function observed in deaf populations have been attributed to the effects of their experience with sign language (Bavelier et al., 2001; Bosworth & Dobkins, 2002b). As such, both language experience (sign language) and sensory experience (deafness) need to be considered in studies of deaf populations. Most prior studies on experience-dependent plasticity in the deaf have relied on
deaf people who are users of a sign language. However, the majority of the deaf population are not native users of a sign language, because 95% of deaf people are born to hearing parents (Mitchell & Karchmer, 2004). In the USA, the majority of people born deaf use English (via speech-reading) and some learn American Sign language (ASL) later in life, but are not considered “native” users like those who are born to deaf parents and are exposed to ASL from birth. It is unknown what effect these different language experiences have on dorsal visual functions and how they interact with those effects following deafness. To address this problem, this thesis includes an investigation into the brain-basis of coherent visual motion perception and how it is altered by sensory and language experiences and their interaction in deaf and hearing native users of English or ASL.

This ‘double-edged sword’ (Stevens & Neville, 2006) of dorsal visual enhancement in deafness and decrement in dyslexia has, again, been attributed to the ‘vulnerability’ of this visual system. Yet ultimately the nature of this plasticity is not clear. As stated above, reasons for this lack of clarity are threefold: The typical developmental time course of dorsal stream function is debated. As such, it is imperative to understand what changes within this system reflect typical development before we can determine which differences reflect abnormality. Further, the nature of the experiences that can impact development and function within this system, and when, are unknown. In dyslexia, it is not clear whether dorsal stream dysfunction causes impaired reading or whether the impoverished reading experience that comes with dyslexia impacts the development of dorsal stream function. Similarly, in deaf populations, it is not clear to what extent dorsal visual stream function is impacted by deafness and the brain’s resulting neural reorganization, or whether experience with a visuospatial language such as sign language affects
function of this same system. Without an understanding or these relationships, we cannot fully understand this system nor its ‘vulnerability’.

The remaining discussion will provide further background on these topics, beginning with a description of the dorsal visual system and what we know of its development. From there, I will discuss the debate surrounding the dorsal visual system and its relationship with disordered and typical reading. Finally, I will discuss the dorsal visual stream and its relationship to the sensory and language experiences of the congenitally and early deaf.

Parallel Visual Processing Pathways

The visual system requires the function and coordination of a number of brain regions, both visually dedicated and polymodal. These visually-responsive regions are considered to be divided between two parallel visual processing streams: the ventral object processing stream and the dorsal visuospatial stream. The parallel nature of these systems begins at the level of the retina, which is comprised of a variety of ganglion cells with unique properties: midget cells (80% of all retinal ganglion cells, which project to the parvocellular layers of the visual thalamic nucleus, the lateral geniculate nucleus [LGN], have high spatial-frequency and low temporal-frequency resolution, and are responsible for color vision); parasol cells (10% of retinal ganglion cells, project to the magnocellular layers of the LGN, have low-spatial frequency and high temporal-frequency resolution and are involved in the detection of motion) (Kandel et al., 2000). These cells’ projections to their respective layers of the LGN (i.e. the parvocellular and magnocellular layers) remain discrete. At the level of primary visual cortex, parvo- and magnocellular efferents no longer receive input from only one thalamic cell-type, though their
response properties are still largely distinct (parvocellular: high spatial and low temporal frequency; magnocellular: low spatial and high temporal frequency). It is at the level of the cortex that the nomenclature for these color- and motion-responsive visual pathways shifts from parvo- and magnocellular to ventral and dorsal, respectively. Ventral and dorsal visual pathways receive mixed input derived from all retinal ganglion cell-types, but it is commonly held that their inputs are still respectively parvo- and magnocell-dominant (DeYoe & Van Essen 1988; Ungerleider & Mishkin, 1982; Van Essen & Maunsell, 1983). As such, these visual pathways are referred to as the ventral/”what” and dorsal/”where” visual streams (for review see Hubel & Livingstone, 1987; Ungerleider & Haxby, 1994). As the major focus of this dissertation is to interrogate the development and plasticity of the dorsal visual pathway, in the ensuing discussion I will focus primarily on this system.

The Dorsal Visual Pathway

Much of the original work done to delineate the cortical components and functions of the dorsal stream was done in animals, particularly nonhuman primates. Using cytochrome oxidase staining in the macaque and squirrel monkey, Hubel and Livingstone (1987) provided evidence of structural and functional distinctions between the systems, with observations that magnocellular inputs from the LGN project from layer 4B of the primary visual cortex to the cytochrome oxidase-rich blobs and stripes of V2 and on dorsally to area V3, V5/MT, and to posterior parietal cortex. This basic differentiation and layout of parallel cortical streams has been shown to be conserved across species and across anatomical and physiological methods (Hilgetag et al., 2000; Wang et al., 2011, 2012).
Within the dorsal visual pathway, area V5/MT has been of particular interest because of its unique properties as receiving primarily magnocellular input (Yabuta et al., 2001), being highly tuned to global visual motion (reviewed in Born & Bradley, 2005), and serving as a primary hub within the dorsal visual stream (Felleman & Van Essen, 1991). Discovered coincidentally in the macaque (‘V5’, Dubner & Zeki, 1971) and owl monkey (‘MT’, Allman & Kass, 1971), area V5/MT was identified based on its exhibiting almost exclusively direction-selective neuronal responses. Since then, research has determined that this region is particularly responsive to retinal position, direction of motion, speed of motion, binocular disparity, and stimulus size. Together, these neuronal properties form the foundation of V5/MT’s role in integration and segmentation of the visual field, and in facilitating eye movements involved in smooth pursuit (see Born & Bradley, 2005; Lisberger et al., 1987, for reviews), and allow this region to contribute to the computation of structure (structure-from-motion, Bradley et al., 1998; Grunewald et al., 2002). Anatomical and physiological studies in humans have identified a homologous motion-sensitive area, both anatomically in postmortem studies (DuMoulin et al., 2000; Malikovic et al., 2007; Wilms et al., 2005), as well as functionally using imaging methods such as PET, fMRI, and MEG (Huk et al., 2002; Tootell et al., 1995; Tootell & Taylor, 1995; Zeki et al., 1991).

Area V5/MT does not contribute significantly to the detection and perception of visual motion beyond computations performed in primary visual cortex. Rather, the large neuronal receptive fields and asymmetries in the spatial organization of center-surround suppression (Xiao et al., 1997) characteristic of this region make this area well-suited to detecting the speed and direction of coherent motion within the larger visual field (Britten et al., 1992; Celebrini &
Studies using single-unit recording in awake monkeys have shown that the sensitivity of single neurons within area V5/MT to a moving stimulus significantly correlate with the animals’ psychophysical motion sensitivity (Britten et al., 1992; Newsome et al., 1989; Salzman et al., 1990) and could predict the animals’ responses in a forced-choice motion detection task (Britten et al., 1996; Celebrini & Newsome, 1994). Neuroimaging studies have found V5/MT to be principally responsive to low contrast, low spatial, and high temporal frequency visual stimuli. Examples of these stimuli include low contrast moving sinusoidal gratings or random dot kinematograms, displays of low contrast dots moving randomly or coherently in the visual field. Activation within V5/MT has been shown to increase linearly with increasing stimulus coherence (see Culham et al., 2001, for review; but see Aspell et al., 2005; McKeefry et al., 1997; Nakamura et al., 2003; Paradis et al., 2000). Further, lesions of V5/MT have been shown to selectively impair coherent motion detection in monkeys (Marcar et al., 1997; Newsome and Paré, 1988) and in humans (Marcar et al., 1997; Riddoch, 1917; Zihl et al., 1983).

Though the dorsal visual stream and its constituent motion processing hub V5/MT have been studied extensively in humans regarding its anatomical and physiological characteristics, nothing is known about the brain-bases of coherent visual motion processing in typical children.

**Dorsal Stream Development**

Reports of the age at which coherent or “global” motion sensitivity reaches adult levels, and how this trajectory compares with that of ventral stream global form perception, vary depending on the method of measurement, the stimuli used, and the population tested.
Physiological findings from Distler et al. (2006), wherein levels of visually evoked uptake of C\textsuperscript{14}2-deoxyglucose during a visual motion task were compared between macaques ranging from 2 days to 4 years of age, revealed that adult levels of uptake were reached by 3 months of age, with earlier visual regions (V1, V2, V3) reaching maturity earlier than extrastriate regions (V5/MT, inferior parietal). Psychophysical testing in macaque monkeys, on the other hand, has suggested that perception of coherent motion appears earlier than perception of coherent form (Kiorpes & Movshon, 2004; Kiorpes et al., 2012), but that both approach adult levels at similar ages, continuing to develop beyond three years of age, or the equivalent of middle to late childhood in humans. The disparity in developmental estimates between these studies suggests that the brain regions supporting coherent motion perception may be metabolically mature at an early age but may continue to develop beyond infancy and early childhood.

The range of ages for purported maturity of the dorsal stream using psychophysical measures in humans is similarly broad (see Hadad et al., 2015, for review). Psychophysical and neurophysiological studies (e.g., fMRI, EEG) have shown that perception of both global form (ventral stream) and global motion (dorsal stream) are evident in 5 month old children, with global motion relatively more mature at this time point (Wattam-Bell et al., 2010; see Atkinson & Braddick, 2011; Braddick & Atkinson, 2007, for reviews). Though detection of global motion (dorsal) may initially mature earlier than detection of global form (ventral), form coherence thresholds (ventral) have been shown to reach adult levels before motion coherence thresholds (Gunn et al., 2002; Hou et al., 2009). The age of maturity for coherent motion perception has been estimated to be 7 years of age (Parrish et al., 2005), 10-11 years of age (Gunn et al., 2002; Spencer et al., 2000), to even mid-adolescence (Bogfjellmo et al., 2014; Bucher et al., 2006;
Joshi & Falkenberg, 2015). There are substantially fewer neurophysiological studies of the development of coherent motion perception in humans, but those that exist suggest that the neural substrates of motion perception (random, coherent, and form-from-motion) reach maturity between late childhood (Coch et al., 2005; Klaver et al., 2008; Mitchell & Neville, 2004) and mid- to late adolescence (Bucher et al., 2006). Stimulus parameters (speed, dot density, type of motion) likely play a role to some extent in this variability, with sensitivity to slower speeds, lower stimulus density, and more complex forms of movement (rotational vs translational) showing more protracted development. Nevertheless, it is evident that the dorsal visual stream continues to develop from early to late childhood (possibly longer).

Though frequently presented as a separate and discrete visual system, the dorsal visual stream is a network of many brain regions that requires precisely- and well-timed input from many brain regions, ventral and dorsal, in order to successfully support the perception and utilization of movement and visuospatial relationships in the visual environment. Due to frequently observed dorsal visual perceptual deficits in developmental disorders (e.g. developmental dyslexia, autism, Williams Syndrome) concomitant with intact ventral stream function, it has been proposed (see Atkinson & Braddick, 2011; Braddick et al., 2003, for reviews) that the lengthy developmental time course of the dorsal stream renders this system increasingly susceptible to developmental abnormalities. Of relevance to the current dissertation, there has been consistent evidence of children and adults with dyslexia presenting psychophysical and neurophysiological deficits in dorsal visual stream function as well as reading difficulties (Demb et al., 1998a; Eden et al., 1996; Gori et al., 2015; Hansen et al., 2001;
Dorsal Stream Vulnerability – Magnocellular Theory of Dyslexia

Developmental dyslexia is a prevalent reading disorder characterized by difficulties with word reading accuracy and fluency that are unexpected in the context of other cognitive abilities and educational opportunities (Lyon et al., 2003). While it is widely thought that phonological coding deficits represent the etiology of developmental dyslexia (Snowling, 1998; Stanovich, 1988), it is also recognized that these may not be the sole cause of reading difficulties (Peterson & Pennington, 2015). As such, there continue to be investigations into a variety of theoretical frameworks to explain the underlying causes of dyslexia (Ramus, 2004). One theory proposes that dyslexia is the consequence of a "magnocellular visual deficit" (see Stein, 2001, for review). The magnocellular theory is so-named due to evidence of performance deficits in dyslexics during tasks designed to target visual magnocellular and dorsal stream function. In an early study, Martin and Lovegrove (1984) revealed that children with specific reading disability exhibited low-level visual deficits, as measured via performance on a psychophysical task of contrast detection. Specifically, they found that disabled readers, relative to typical controls, exhibited diminished contrast sensitivity at low to medium spatial frequencies, but not at higher frequencies, and concluded a deficit in the ‘transient’ (magnocellular) visual subsystem, which preferentially responds to lower spatial frequencies. These results were soon corroborated by similar psychophysical studies focusing on magnocellular relative to parvocellular visual function under conditions that manipulated contrast, rate of flicker and spatial frequency of the
stimuli (Martin & Lovegrove, 1988). Later it was shown that children and adults with dyslexia exhibited decreased sensitivity to coherent visual motion compared to typical readers (Conlon et al., 2004; Edwards et al., 2004; Everatt et al., 1999; Gibson et al., 2006; Hansen et al., 2001; Pammer & Wheatley, 2001; Pellicano & Gibson, 2008; Raymond & Sorenson, 1998; Talcott et al., 1998; Witton et al., 1998). This corroborated the magnocellular deficit hypothesis since the cortical areas involved in the processing of visual motion receive input from the magnocellular layers of the LGN of the thalamus (Born & Bradley, 2005; Lachica et al., 1992; Livingstone & Hubel, 1988; Yabuta et al., 2001), which were observed to be abnormal in dyslexic relative to control brains (with no difference observed in parvocellular layers) in a postmortem study by Livingstone and colleagues (1991). Similarly, coherent motion detection performance has been shown to correlate with reading accuracy (Wilmer et al., 2004), letter position encoding (Cornelissen et al., 1998) and non-word reading (Talcott et al., 1998; Witton et al., 1998) and speed discrimination with reading rate (Demb et al., 1997, 1998a; Wilmer et al., 2004). Based on this behavioral work, area V5/MT was investigated using fMRI. Studies of V5/MT activity in dyslexia reported reduced V5/MT activity in dyslexics compared to controls during visual motion perception (Demb et al., 1998b; Eden et al., 1996) and contrast detection (Demb et al., 1997). As with the behavioral work, these studies have also shown positive correlations between V5/MT activity and reading rate (Demb et al., 1997), reading accuracy (Olulade et al., 2013b) and phonological awareness (Ben-Shachar et al., 2007).

Evidence for causality of the magnocellular visual deficit however, has been relatively weak, and the mechanism by which magnocellular dysfunction would lead to reading problems is controversial. Some consider magnocellular dysfunction to be causal to dyslexia (Stein, 2001).
Others regard deficient phonological processing to be the core problem in dyslexia and magnocellular deficits to be epiphenomena (Ramus, 2004) or a consequence of dyslexia (Olulade et al., 2013b). Another school of thought rules out the magnocellular deficit completely (Vellutino et al., 2004). Whereas there is strong evidence supporting benefits of phonologically-based intervention for reading (Alexander et al., 2004), evidence for interventions targeting magnocellular visual system function is sparser (Chouake et al., 2012; Gori et al., 2015; Lawton, 2007). Also, while longitudinal studies of reading have clearly identified strong phonological skills in kindergarten as an important precursor to successful reading in later years (Catts et al., 1999; Wagner & Torgesen, 1987), analogous research on the magnocellular visual deficit hypothesis is scarce (Kevan & Pammer, 2009).

In one such longitudinal study of coherent motion thresholds and reading ability, Boets and colleagues (2011) found coherent motion thresholds to be significantly higher (i.e. worse performance) in kindergarteners later diagnosed with dyslexia than those children in kindergarten who went on to become typical readers. While these results speak to a causal role for magnocellular processing in determining reading outcome, several other observations from the study are noteworthy. Firstly, this difference did not persist: coherent motion thresholds improved for all children by the time they reached 1st grade, after formal reading instruction had begun, and were no longer different between typical readers and those later diagnosed with dyslexia. Secondly, coherent motion thresholds showed a pattern of decrease with increasing age and were significantly lower in an adult group of typical readers compared to the 1st grade typical readers. This suggests better coherent motion detection with increasing age and the authors
acknowledged that magnocellular visual pathway functioning may be “mobilized” by reading experience.

A notable outcome of this work is the notion that children who are typical readers change in their ability to detect visual motion, possibly as a side product of learning to read. This offers a new interpretation for previous findings of magnocellular dysfunction in dyslexia, such that higher contrast sensitivity thresholds (Martin & Lovegrove, 1984), differences in visual motion coherence detection (Hansen et al., 2001; Wilmer et al., 2004), and lower V5/MT signal (Eden et al., 1996), may be due to dyslexics having less reading experience than typical readers rather than their dyslexia being caused by magnocellular deficits per se. In other words, children and adults with dyslexia appear to be less proficient relative to their comparison groups because these typical readers have undergone reading-induced changes, whereas the dyslexic readers have not.

**Reading and the Dorsal Stream**

However, in order to understand the role of magnocellular deficits in dyslexia it is necessary to gain an understanding of the nature of the relationship between magnocellular/dorsal stream function and typical reading. In the last decade, it has become clear that visual system function is altered by the introduction of cultural activities such as learning to read. Behavioral work, for example, has shown that the acquisition of literacy can affect performance of early visual system function. Specifically, Szwed and colleagues (2011) compared age- and socioeconomically-matched adult literates, illiterates, and ex-illiterates (who learned to read as adults) on a task of contour integration and found that the illiterate adults’ performance was worse than both literate groups. From this the authors concluded that the
extensive visual training undertaken during literacy acquisition influences not only higher-level visual processing (e.g., selectivity for the written word in the putative visual word form area [VWFA]; Dehaene et al., 2010; McCandliss et al., 2003; Puce et al., 1996), but also results in marked changes in behavior drawing on low-level visual perception. Further, studies have shown that illiterate adults differ from literate adults in visual system function (Dehaene et al., 2010), suggesting that reading can induce change in the visual system across the lifespan. Functional connectivity between dorsal visual areas and the VWFA has also been observed to increase with age and with reading ability. Vogel and colleagues (2011), from their investigation of whole-brain resting state functional connectivity with the VWFA, observed significant connectivity between the VWFA and dorsal visual/attention regions (e.g. bilateral V5/MT, FEFs and anterior inferior parietal sulci [aIPS]) in adults, whereas they did not observe significant connectivity between the VWFA and other canonical reading areas (e.g., angular gyrus, supramarginal gyrus, and inferior temporal cortex of the left hemisphere). VWFA connectivity with these dorsal stream regions was greater in adults than in children, and connectivity between VWFA and bilateral aIPS were correlated with age and standardized reading level across both groups. Together, these findings provide evidence for reading-related changes in the visual system including dorsal visual areas.

The Impact of Sensory Experience (Deafness) and Sign Language on the Dorsal Visual Stream

Converse to the decrements in dorsal visual function that have been associated with developmental disorders, behaviors associated with dorsal visual stream function in deaf
populations have been shown to be enhanced relative to hearing controls (see Bavelier et al., 2006, for review). These effects have been attributed to the neural reorganization and cross-modal plasticity that occurs following early sensory loss. The most revealing studies of how this reorganization takes place within the brain have been conducted in animals. Work using single-unit recordings in ferrets has shown that surgical unilateral deafferentation of the auditory nucleus (medial geniculate nucleus, MGN) in conjunction with ablation of the superior colliculus and visual cortical areas 17 and 18, induces retinofugal innervation of the MGN, as well as visually responsive cells in superior temporal regions, including primary auditory cortex (Roe et al., 1993; Sur et al., 1988). Further work in cats illustrated that deafferentation of the MGN alone was sufficient to induce this cross-modal wiring (Angelucci et al., 1998). In cats, cross-modal reorganization has been shown to occur in the anterior auditory field (AAF, part of core auditory cortex). In bilaterally ototoxically deafened cats, Meredith and colleagues (2011) used single-unit recordings to establish that neurons in the AAF were responsive to haptic and visual, but not to auditory, stimulation. Visually responsive cells in the AAF were identified for their preference for flashing or moving bars or dots of light. Behaviorally, congenitally deaf cats have displayed superior localization in the peripheral visual field as well as superior motion detection compared to hearing cats (Lomber et al., 2010). Lomber and colleagues (2010) demonstrated that these enhanced visual abilities were mediated by reorganized auditory cortex, in that deactivation of auditory cortical regions, through cortical cooling, led to the elimination of the peripheral localization and motion detection behavioral advantages. It is notable that the degree to which an area of sensory cortex is susceptible to cross-modal plasticity depends on its level in the processing hierarchy, with primary cortex less susceptible to reorganization (Chabot et al., 2015).
Further, the extent of change following sensory loss has been shown to rely upon onset of deafness (Chabot et al., 2015; Kok et al., 2014).

Studies in humans have reported findings consistent with the animal literature. For instance, there is evidence of cross-modal activation in the deaf, wherein visual stimuli typically subserved by dorsal visual function have been shown to elicit activation in superior temporal cortex, corresponding with auditory cortex in hearing controls (Fine et al., 2005; Finney et al., 2001; Sadato et al., 2005; Shiell et al., 2014; Vachon et al., 2013). Visually-evoked activation in auditory cortex, primarily right-lateralized activation, has proven to be robust across stimulus types (e.g., RDK, moving sinusoidal grating) and analysis (e.g., region of interest [ROI], whole-brain). Whether using a functionally defined auditory ROI in hearing controls (Fine et al., 2005; Finney et al., 2001; Shiell et al., 2014), anatomical region of interest along the superior temporal gyrus (Vachon et al., 2013), or looking across the entire brain (Sadato et al., 2005), visually-evoked activation in right superior temporal auditory cortex has been regularly reported. Shiell and colleagues (2014), in addition to observing that the right posterior superior temporal gyrus (pSTG) was responsive to visual motion in early deaf individuals, found that this pSTG region showed increased functional connectivity with a region in the calcarine fissure in early deaf individuals relative to hearing individuals. Even resting state functional connectivity of R STG has been shown to differ between deaf and hearing individuals. Ding and colleagues (2016) observed greater functional connectivity between right pSTG and bilateral anterior insula and dorsal anterior cingulate cortex in early deaf adults relative to hearing controls (and left pSTG at a more lenient statistical threshold). The bilateral pSTG regions used as seeds in their resting state connectivity analyses were identified from a previous study as regions in which deaf
participants exhibited greater activation than hearing controls during a visuospatial working memory task (Ding et al., 2015).

There is a significant difference between comparisons of deaf and hearing animals and those between deaf and hearing humans, though: language. When comparing deaf and hearing cats, the only variable that differs between these groups is hearing status. Deafness in humans, on the other hand, for whom language and communication are primarily oral/auditory, results in both altered sensory as well as altered language experience. This has not gone unnoticed, as studies have attempted to address the influence of language experience on coherent motion processing differences between deaf and hearing adults. For instance, Fine and colleagues (2005), in their study reporting visually-evoked activation in superior temporal cortex in deaf adults, compared the extent and intensity of activation within auditory cortex between hearing non-signers and deaf native-signers while they attended to or ignored a field of moving dots. Participants were instructed either to attend to the moving dot display and report when the dots dimmed in brightness, or to ignore the moving stimuli and report when a central fixation dot dimmed. Between the hearing and deaf groups, significant differences in activation were observed in right hemisphere auditory cortex. Further, the investigators observed that, though activation in the deaf in this area was significant across attentional demands, when the deaf group was instructed to ignore the moving stimuli, activation in auditory cortex was notably attenuated. As the comparison groups differed both in their hearing status (deaf vs. hearing) as well as language experience (signed vs. spoken), the investigators compared hearing non-signers’ and deaf native-signers’ activation profiles to a third comparison group: hearing native-signers (children of deaf adults, or CODAs). As the hearing native-signers did not exhibit any
significant visually-evoked activation in the auditory regions of interest, bilaterally, the authors concluded that activation in this region in the deaf group was an effect of deafness.

There have also been consistent reports of behavioral advantages in the deaf, measured as enhanced perception of visual motion in the peripheral visual field. Neville and Lawson (1987b) reported faster reaction times and larger evoked potentials in deaf relative to hearing participants when they attended to the direction of motion of a small peripheral (but not central) square. In subsequent fMRI studies wherein participants had to monitor either the periphery, center, or entire field of a moving dot display for luminance changes, Bavelier and colleagues (2000, 2001), using a region of interest approach, observed greater recruitment of area V5/MT in deaf native-signers than hearing non-signers during their task requiring attention to the periphery. Again, enhanced peripheral motion processing was attributed to sensory experience as deaf native signers exhibited greater activation while attending to the periphery than hearing native-signers. These changes in peripheral attention in the deaf were thought to be mediated by increased functional connectivity between the posterior parietal cortex and area V5/MT in deaf relative to hearing subjects (Bavelier et al., 2001).

However, effects of language experience on coherent motion processing have been observed. Bavelier and colleagues (2001), in addition to observing an effect of sensory experience on V5/MT activation while attending to the periphery, reported an effect of early exposure to sign language in the leftward lateralization of area V5/MT activity during visual motion processing in both deaf and hearing signers, and a trend toward rightward lateralization in hearing non-signers. Behavioral evidence for a right visual field (RVF) advantage for native users of sign language, both hearing and deaf, in motion direction discrimination (Bosworth &
Dobkins, 2002a,b) corroborates this leftward lateralization of V5/MT activation. Critically, Finney and colleagues (2001) found this RVF advantage to be specific for the perception of motion. When comparing performance on a task requiring contrast detection of moving gratings, a task designed to target lower level thalamocortical magnocellular function, the authors found no visual field advantage or performance differences between deaf native users of sign language, hearing native users of sign language, and hearing native users of English. From this, the authors suggested that directionally selective neurons in area V5/MT may be more vulnerable to the effects of cross-modal reorganization than lower level areas (e.g. V1, V2) subserving contrast sensitivity.

These effects of language on coherent motion processing within the deaf population cannot be assumed to be uniform, however, as language experience is not uniform within the deaf population. While deafness is often associated with sign language, deaf people whose first language is a signed language and who are considered native signers (i.e., deaf children born to deaf parents) represent a minority in the deaf population. It is estimated that 95% of deaf people are born to hearing parents (Mitchell & Karchmer, 2004), and as a result grow up as native English speakers, through lip reading and/or Cued Speech. Exposure to ASL within deaf native users of English is highly varied, with some proficient in both lip reading and ASL, some exposed to sign language later in life, and others who are sign-naïve. The effects of sensory and language experience on coherent motion processing have yet to be teased apart, as, due to the subject groups compared in analyses, there has yet to be a study designed to fully address the main effects of sensory experience, language experience, and, critically, their interaction. For instance, Mohammed and colleagues (2005) found that performance on a speech-reading task
correlated with coherent motion sensitivity in deaf adults but not in hearing adults. Performance on a task of coherent form sensitivity was not correlated with speech-reading ability in either group. The authors attributed this relationship to the effects of deafness, but both comparison groups were comprised of native signers and native English speakers with varying levels of proficiency with one or both languages. As such, there is no way to determine whether this relationship was driven in some way by an interaction between sensory and language experience.

An interaction between sensory and language experience is likely, given that both languages exhibit unique patterns of activation within the brain. A within-subject investigation of hearing native users of both English and sign language conducted by Söderfeldt and colleagues (1997), using PET imaging, observed differences in activation between signed and spoken language comprehension tasks. Spoken language significantly activated perisylvian cortex bilaterally in these subjects, whereas sign language activated bilateral visual association areas including area V5/MT. Using a similar design, Capek and colleagues (2008) studied deaf native users of both English and sign language during separate speech-reading and sign comprehension tasks. Speech-reading in these subjects generated greater activation in left midsuperior temporal cortex than British Sign Language (BSL), whereas BSL comprehension generated greater activation in bilateral temporoparieto-occipital junctions, with peaks in bilateral V5/MT. Interestingly, BSL signs that incorporated speech-like mouth actions elicited greater superior temporal activation than signs made with non-speech-like mouth actions, which elicited greater activation in posterior and inferior temporal regions, including area V5/MT. Work by MacSweeney and colleagues further corroborates the notion that sign language may exert unique demands on area V5/MT. As Capek observed greater V5/MT activation during a task of sign
comprehension than a task of speech-reading, MacSweeney and colleagues (2002b) reported that certain language features of BSL exert unique demands on area V5/MT. The authors found that comprehension of topographic BSL sentences (for which ‘real world’ spatial relationships are mapped directly in ‘sign space,’) recruited left parietal and bilateral posterior middle temporal cortices (including V5/MT) to a greater extent than non-topographic sentences. This effect was observed in both deaf and hearing native users of BSL.

While some have reported that activation in right superior temporal cortex during coherent motion processing is an effect of deafness, there is evidence to suggest that superior temporal cortical activation may be differentially recruited between users of sign language versus users of English during language comprehension. Whether these differences in superior temporal cortical activation are only relevant to tasks of language comprehension, or whether they spill-over into the neural response to perception of coherent visual motion remains to be determined, as the effects of sensory experience and language have yet to be fully disambiguated in the domain of visual motion processing, or in any domain for that matter. Similarly, while greater intensity of V5/MT activation during coherent visual motion processing has been attributed to the effects of attention on deafness, the peripheral field advantage has yet to be studied in deaf native users of English. Further, the RVF advantage and leftward laterality of V5/MT activation attributed to sign language experience has yet to be observed in deaf native users of English; again, effects of sensory and language experience on V5/MT activation are not fully resolved. Despite these differences, the majority of investigations into neural reorganization and cross-modal plasticity in the deaf have focused on deaf native users of sign language, or have studied deaf groups with mixed language backgrounds.
**Summary**

Though much has been made of a dorsal stream ‘vulnerability,’ the nature of this vulnerability remains enigmatic. Is development of this system impacted by the extensive visual training that accompanies learning to read? How plastic is this system in the brain’s response to deafness? Does the use of a visuospatial language exert unique effects on coherent motion processing? These questions must be addressed before we can understand dorsal stream development and its role in or response to the functional sequelae of unique developmental conditions.

The present dissertation aims to address these gaps in our knowledge, with the overarching goal of investigating the effects of different types of experience (i.e., reading, deafness, visuospatial language use) on the specialization of visual dorsal stream processing regions (i.e. V5/MT), which have been shown to be modulated by experience.

In Chapter 2, we provide the first brain imaging study of coherent motion development in typically developing children and adults, with which we aimed to characterize dorsal stream development using measures of functional activation and functional connectivity, and to investigate whether reading experience plays a role in this trajectory. In Chapter 3, we provide the first factorial analysis of the effects of sensory experience (deaf vs. hearing), language experience (sign language vs. English), and their interaction, on coherent visual motion processing. Using functional connectivity analyses, we also characterize the whole-brain connectivity patterns of areas identified in our factorial analysis.
CHAPTER 2: AN fMRI STUDY OF COHERENT VISUAL MOTION PROCESSING IN CHILDREN AND ADULTS

Abstract

There is a large corpus of brain imaging studies examining the dorsal visual pathway, especially area V5/MT, during visual motion perception. However, despite evidence suggesting a protracted development of the dorsal visual stream and a role of this pathway in a range of neurodevelopmental disorders, it has not been well characterized in children and in comparison of children with adults. Further, it is unknown whether intensive experiential factors such as reading acquisition, which are concomitant with development, play a modulating role in age-dependent changes of the motion-processing pathway. Here we used a coherent visual motion detection task to examine V5/MT activity and connectivity in typical participants in two studies: a cross-sectional study comparing adults (aged 18-28 years; n=15) and children (aged 7-8 years; n=13), and a longitudinal study of children (aged 7-9 years; n=12) in 2nd grade followed into 3rd grade. In the cross-sectional study, we found greater activation in bilateral V5/MT in adults compared to children using a region of interest (ROI) approach. This difference disappeared, though, when the ROI was created from an independent “pre-adolescent” sample, instead of generated from adult coordinates reported in the literature, because activity in our children was located significantly superior to that of our adults. There was, however, more functional connectivity between left and right V5/MT and nearby ipsilateral regions in both hemispheres in
the children relative to adults. The longitudinal study revealed no changes in V5/MT activation or connectivity from 2nd to 3rd grade. Further, there was no evidence to suggest a relationship between reading gains from 2nd to 3rd grade and V5/MT changes over the same period, or that V5/MT signal in 2nd grade predicted reading ability in 3rd grade. Together, our results indicate a difference in the location of area V5/MT and more functional connectivity to nearby regions in children compared to adults. These differences were, however, not measurable as change over a single elementary school year, suggesting that these changes occur over a longer time period.

Introduction

The primate visual system is functionally described in terms of two parallel processing pathways: the ventral “what” stream (form and color), and the dorsal “where” stream (motion and depth) (Livingstone & Hubel, 1988; Mishkin et al., 1983; Ungerleider & Haxby, 1994; Ungerleider & Mishkin, 1982; but see Merigan & Maunsell, 1993). Many aspects of the ventral visual system have been examined developmentally via neuroimaging studies comparing children and adults, such as during object processing (Gathers et al., 2004, Golarai et al., 2007, 2010; Scherf et al., 2007), face processing (Aylward et al., 2005; Gathers et al., 2004; Golarai et al., 2007, 2015; Joseph et al., 2011; Passarotti et al., 2003), and visual word processing (Ben-Shachar et al., 2011; Brem et al., 2009, 2010; Martin et al., 2015; Olulade et al., 2013a; Schlaggar et al., 2002; Turkeltaub et al., 2003). Yet relatively little is known about the neural bases of the typical developmental trajectory of dorsal stream function, specifically those underlying coherent motion perception. An important first step is to apply the same approach used to characterize the neural substrates of coherent motion perception in adults (Braddick et
al., 2001; Dupont et al., 1994; McKeefry et al., 1997; Paradis et al., 2000; Sunaert et al., 1999; Watson et al., 1993) to the study of children. This information will not only provide an understanding of the role that experience and development have on dorsal stream function (especially area V5/MT), but it will also provide a foundation by which to understand a number of developmental disorders that have been linked to dorsal stream vulnerability, such as autism, Williams syndrome, and developmental dyslexia (Atkinson et al., 1997, 2011; Braddick et al., 2003; Boets et al., 2011; Grinter et al., 2010; Milne et al., 2002; Pellicano et al., 2008; Stein, 2001).

Behavioral studies in children have investigated the age at which adult thresholds are reached for coherent motion perception; however, the findings of these studies vary widely, with the purported age ranging from 3 to 16 years, depending on the methods used (for review, see Hadad et al., 2015). For instance, Boets and colleagues (2011) found the amount of coherence needed to detect the direction of motion to be significantly lower in adults compared to 5-year-old children in kindergarten, and they observed a significant decrease in these children’s coherence thresholds (i.e., an improvement in performance), though still significantly higher than those of adults, one year later (in 1st grade). Hadad and colleagues (2011) found that coherent motion sensitivity continues to improve between ages 6 and 14 years, at which point sensitivity no longer differed from adults. As such, one would expect differences in performance and, accordingly, differences in brain function when comparing elementary school-aged children with adults.

Dorsal stream development has been investigated with electroencephalography (EEG). For example, in a study comparing global motion processing between infants (4-5 months old)
and adults, Wattam-Bell et al. (2010) observed a more lateral response in infants (localized to right hemisphere area V5/MT), whereas adults exhibited a more medial response (localized to V3/V3a and V6) to visual motion. Coch and colleagues (2003) found that visually evoked responses (visual event-related potentials, ERPs) to motion significantly differed between children (6-8 years old) and adults, whilst color processing did not. Mitchell & Neville (2004) investigated ERPs in 6-7-year-olds, 8-10-year-olds, and adults, and found that ventral stream ERPs in response to color stimuli differed minimally between subject groups (decreased amplitude with age), while dorsal stream ERPs in response to motion stimuli exhibited marked changes in wave shape, amplitude and latency with age. Together, these findings suggest that dorsal stream development is protracted, going beyond late childhood, and it has been proposed that this extended period of development renders the dorsal stream more vulnerable to disorders of development in comparison to the ventral stream (Atkinson & Braddick 2011; Braddick et al., 2003; Stevens & Neville, 2006).

More recent studies of motion perception have utilized functional magnetic resonance imaging (fMRI). Klaver and colleagues (2008) used whole-brain and region of interest (ROI) approaches (using regions created from a prior study in adults [Murray et al., 2003]) to compare children’s (5-6 years) and adults’ (20-29 years) responses to two different kinds of visual motion stimuli: random motion and structure-from-motion (in which contours defined by moving dots create a shape percept). For random visual motion (compared to static dots), there were no significant differences in activation between the two groups in the whole-brain analysis, but there were differences for the ROI analyses in which the left and right hemisphere ROIs were combined: adults had significantly greater activation compared to children in V3a, with a similar
effect in area V5/MT trending toward significance. When examining activation in response to the other motion stimulus, structure-from-motion (compared to random motion), in the same bilateral ROIs, the investigators found greater activation in parietal cortex in the same sample of adults compared to children. However, children showed greater activation in V5/MT compared to adults, reflecting an age-related decrease in V5/MT response to structure-from-motion perception. Further, in a study that utilized both EEG and fMRI, Bucher and colleagues (2006) compared ERPs and functional activation in adolescents (15-17 years) and adults (20-30 years) during a structure-from-motion task. While the investigators did not find a between-group difference in activation patterns, there was a delay in the adolescent group’s N1 component (attributed to area V5/MT). This suggests that the network of regions supporting visual motion processing may be established by adolescence but that fine tuning of the characteristics of the response continues to change developmentally. Taken together, these findings suggest that the dorsal stream exhibits developmental changes in activation specific to different types of visual motion stimuli (random motion and structure-from-motion) and in different regions. However, despite its common usage in publications of adult participants (Aspell et al., 2005; Braddick et al., 2000, 2001; Cornette et al., 1998; Huk et al., 2002; Nakamura et al., 2003; Paradis et al. 2000; Watson et al., 1993; Wilms et al., 2005), coherent motion perception in children has yet to be investigated.

An important aspect of developmental studies is the difficulty of disentangling brain development from experience, especially those experiences afforded by formal education. In the last decade it has become clear that visual system function is altered by the introduction of cultural activities such as learning to read. Behavioral work, for example, has shown that the
acquisition of literacy can affect performance of early visual system function. Specifically, Szwed and colleagues (2011) compared age- and socioeconomically matched adult literates, illiterates, and ex-illiterates (who learned to read as adults) on a task of contour integration and found that the illiterate adults’ performance was worse than both literate groups. From this the authors concluded that the extensive visual training undertaken during literacy acquisition not only influences higher-level visual processing in the ventral stream, as demonstrated in a separate study by the same investigators showing functional reorganization in object processing areas (Dehaene et al., 2010), but also results in marked changes in behavioral performance for low-level visual perception. The anatomical and physiological impact exerted by the formal learning of reading and writing has been shown to manifest in multiple brain regions, including visual, auditory, and motor areas (Carreiras et al., 2009; Dehaene et al., 2010). Finally, it has been suggested, based on a behavioral study of coherent motion detection in children, that learning to read in typical readers "mobilizes" the dorsal visual system (Boets et al., 2011). As such, a significant challenge is to determine whether the differences in dorsal visual stream function that are observed between children and adults are due to the discrepancy in levels of maturity or to the discrepancy in reading experiences.

Of note is that the dorsal visual motion processing pathway has been described as “vulnerable” (Braddick et al., 2003), as it plays a role in a range of developmental disorders such as autism (Spencer et al., 2001) and the reading disability dyslexia (for review, see Stein, 2001). Notably, dyslexia has been associated with difficulties in tasks reliant on the dorsal steam, such as motion perception (Cornelissen et al., 1998; Hansen et al., 2001; Wilmer et al., 2004; Witton et al., 1998), and brain activity in area V5/MT during visual motion perception has been shown
to be lower for adults (Demb et al., 1998b; Eden et al., 1996) and children (Olulade et al., 2013b) with dyslexia compared to age-matched normal readers. However, it is unclear if the association between visual motion perception and reading ability is causal or consequential, a question that would benefit from greater knowledge of brain activity in area V5/MT, and its connectivity with other regions, in typically reading children.

The present study builds on prior work using fMRI to examine differences between children and adults in brain activity underlying visual motion processing of random and structure-from-motion stimuli (Klaver et al., 2008), and extends it to coherent motion processing. The present study also includes a longitudinal component to investigate the nature of visual area V5/MT activity and functional connectivity in early elementary school readers, thereby building on the behavioral study by Boets and colleagues (2011). Our first study utilized a cross-sectional design to compare children with adults, while our second study tracked children longitudinally from 2nd to 3rd grade. In both studies, we examined activity within area V5/MT and functional connectivity between V5/MT and other brain regions using a coherent dot motion detection task contrasted with a static dot density detection task. In both studies we asked if being older was associated with greater activity in and/or connectivity with area V5/MT. In the longitudinal study, we also examined the relationship of these measures with reading proficiency by testing for predictive strengths of V5/MT activity for reading ability, and additionally, by testing for a relationship between the degree of change of both V5/MT activity and reading ability during children’s development over one year.

Our analysis approach used both whole-brain and ROI analyses to allow comparison to the published literature. While the ROI approach is well suited to our question given the
reliability of the V5/MT signal in response to motion, the absence of pediatric studies of coherent visual motion in the published literature means that the coordinates drawn from the literature will be derived from adult data. This leaves open the question of whether any differences between children and adults in an ROI analysis are driven by activity in the same brain areas but with a lesser degree of activity in children, or if they are the result of the ROI being placed in the location of optimal V5/MT activity for adults, but less optimally placed for pediatric V5/MT activity. As such, we chose to examine activity not only in an ROI based on the adult published literature, but also in another ROI derived from our own fMRI data using the same coherent visual motion paradigm in a separate group of older children (referred to as “pre-adolescents”). Together, these multiple approaches should provide comprehensive characterization of the developmental differences of the dorsal visual motion-processing stream, especially area V5/MT, during coherent motion perception.

Methods

Participants

The Cross-Sectional Study was based on 28 healthy, monolingual, right-handed, native English-speaking children (n=13, 5 female; age range 7-8 years; avg. age 7.7 years) and adults (n=15, 7 female; age range 18-28 years; avg. age 22.5 years). The Longitudinal Study involved 17 healthy, monolingual, right-handed, native English-speaking children (7 female; age range 7.9-9.3 years; avg. age 8.3 years at the first time point [T1] of the study). However, five subjects were excluded at the data analysis stage because of excessive between-scan head motion at either or both time points. Our final sample thus consisted of 12 children (5 females; age range: 7.9 to
9.3 years; mean age: 8.4 years). Demographic and behavioral information for the final groups are summarized in Tables 1 and 2.

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<th>Table 1. Cross-Sectional Demographics and In-Scanner Performance</th>
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*WRMT-R
†WJ III

Statistical significance: p<0.05

All participants underwent a behavioral battery that included the Wechsler Abbreviated Scale of Intelligence Verbal (VIQ) and Performance (PIQ) subtests (Wechsler, 1999). Reading was evaluated using the Word Identification (Word ID) and Word Attack subtests to measure single real and pseudoword reading accuracy, respectively. For the Cross-Sectional Study these subtests were measured using the Woodcock Johnson III Tests of Achievement (WJ III; Woodcock et al., 2001), and for the Longitudinal Study, the Woodcock Reading Mastery Test-Revised (WRMT-R; Woodcock, 1998) was used. Additional reading measures for the Longitudinal Study included reading fluency, using the Reading Fluency subtest of the WJ III Tests of Achievement (Woodcock et al., 2001), and phonological awareness, measured via the
Elision subtest of the Comprehensive Test of Phonological Processing (CTOPP-Elision; Wagner et al., 1999). To be included in either of the studies, all participants had to have PIQ, VIQ, Word ID, and Word Attack standard scores above 85. All subjects also had a normal birth history and no history of learning disability, ADHD, neurological, or psychiatric disorders. The adult and pediatric groups in the Cross-Sectional Study were matched on full scale IQ and Word ID standard score.

| Table 2. Longitudinal Demographics and In-Scanner Performance |
|-------------------------------|---|---|---|
|                              | T1 | T2 | p value |
| N | 12 | 12 | - |
| Sex (female/male) | 5/7 | - | - |
| Age | 8.4 ± 0.4 | 9.1 ± 0.3 | < 0.001 |
| IQ | 119 ± 12 | - | - |
| Word ID - SS* | 118 ± 10 | 114 ± 9 | 0.002 |
| Word ID - RS* | 68 ± 10 | 72 ± 9 | 0.006 |
| Word Attack - SS* | 117 ± 12 | 115 ± 14 | n.s. |
| Word Attack - RS* | 30 ± 6 | 32 ± 7 | 0.053 |
| Reading Fluency - SS | 113 ± 13 | 116 ± 13 | n.s. |
| Reading Fluency - RS | 39 ± 12 | 48 ± 12 | < 0.001 |
| CTOPP-Elision - SS | 117 ± 6 | 114 ± 10 | n.s. |
| CTOPP-Elision - RS | 17 ± 1 | 17 ± 2 | n.s. |
| Motion Accuracy | 91% ± 15% | 96% ± 5% | n.s. |
| Static Accuracy | 97% ± 4% | 97% ± 3% | n.s. |
| Motion - Static accuracy | -6% ± 12% | -1% ± 5% | n.s. |
| Motion reaction time | 1207 ± 364 ms | 1120 ± 242 ms | n.s. |
| Static reaction time | 974 ± 233 ms | 945 ± 147 ms | n.s. |
| Motion - Static reaction time | 233 ± 339 ms | 175 ± 219 ms | n.s. |

*WRMT-R
Statistical significance: p<0.05
All 17 children in the Longitudinal Study underwent behavioral testing and MRI scanning during the summers after finishing their 2nd (Time 1, T1) and 3rd (Time 2, T2) grade school years. The adults and children from the Cross-Sectional Study were drawn from other ongoing studies in the laboratory. Additionally, eight longitudinal subjects were included in the cross-sectional group of children. Five subjects contributed different data sets to the Longitudinal and Cross-Sectional Studies (longitudinal data was collected at three time points, 1st-3rd grade, from which 1st grade data were used in the Cross-Sectional Study, and 2nd and 3rd grade data were used in the Longitudinal Study), whereas three children contributed the same data set to both the Cross-Sectional and Longitudinal Studies. Some of the children’s data included in this report were also included in the control group in a study of dyslexia (Olulade et al., 2013b).

The “pre-adolescents” who were included in the group used to generate our own ROIs for analyses (see below) also met the above-described criteria for reading and IQ scores above a standard score of 85. They were also healthy, monolingual, right-handed native English-speaking children (n=14, 8 males; aged 9 to 14 years old; avg. age 10.7 years; no overlap with the children included in this study). These ROIs are referred to as the Pre-adolescent ROI.

fMRI paradigm and acquisition

We used a coherent visual motion detection task previously shown to reliably activate area V5/MT of the dorsal stream (Olulade et al., 2013b). For the active task (Motion), participants viewed low contrast, random dot kinematograms consisting of white dots moving in various directions on a black background, with 40% coherence in the horizontal direction.
Participants were asked to indicate the direction of motion via button press (e.g., left-thumb button press for leftward motion), while maintaining fixation on a central cross.

For the active control task (Static), participants performed a density judgment task during which static dots were presented on the screen with differing densities between the left and right visual fields (density differences ranged between 35% and 65%). Participants were asked to maintain fixation on a central cross and indicate via button press with the left or right thumb on which side of the screen dot density was greater.

For both the coherent motion and the static conditions, stimuli were presented for 3 s followed by a crosshair for 1.2 s, with 10 stimuli presentations per block. Alternating blocks of Static and Motion stimuli (42 s/block) were separated by blocks of Fixation (21 s). Fixation consisted of a single crosshair presented at the center of the visual field. One run consisted of two blocks each of the Static and Motion conditions. Order of alternating Static and Motion blocks was the same between runs and across subjects, with the Static task occurring first (after an initial 21 s of Fixation). Each run began and ended with an additional 9 s and 6 s of Fixation, respectively, which were not included in analysis. Two runs per participant were entered into the analysis for both the Cross-Sectional and the Longitudinal Studies.

Images were acquired on a 3T Siemens Trio Scanner located at the Center for Functional and Molecular Imaging at the Georgetown University Medical Center. For each functional run, 89 images consisting of 50 contiguous axial slices covering the whole brain were acquired with the following parameters: TR = 3 s, TE = 30ms, voxel size = 3mm x 3 mm x 2.8 mm, in-plane resolution = 64 x 64, Flip angle = 90°.
**fMRI data analysis**

All data pre-processing and statistical analyses were carried out using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). The same pre-processing procedures were applied to both the *Cross-Sectional* and the *Longitudinal Studies*. After removing the first three scans of each run to account for T1 saturation effects, each subject’s data were slice-time corrected and realigned to the mean image. A magnetization-prepared rapid gradient-echo (MP-RAGE) sequence structural scan acquired during the same scanning session was then co-registered to the mean image; structural scans were warped and segmented into gray matter, white matter, and CSF using the vbm8 toolbox; and functional and structural images were warped to standard MNI stereotaxic space and smoothed with a Gaussian kernel of full width at half maximum 8 mm.

Participant data were subsequently examined for head motion artifacts. Participants whose overall data exhibited excessive head motion (>20% of images in the run exhibiting scan-to-scan motion beyond the 1.5 mm threshold) were removed from analysis. Six rigid-body head motion parameters and global signal were used as regressors of no interest in our fMRI analyses.

Data were analyzed in a block design for each subject using the general linear model. Statistical analysis at the first level involved generating within-subject parametric activation maps for the contrast of the Motion and Static conditions relative to baseline (Motion vs. Fixation, Static vs. Fixation) and for the direct contrast between the two conditions (Motion vs. Static). Stimulus onsets were modeled using the canonical SPM hemodynamic response function, and functional datasets were high-pass filtered with a cutoff of 128 s. Second-level statistical analysis differed between the two studies, as outlined below.
Two types of statistical analyses were performed in each study. In order to characterize brain activity in the dorsal visual pathway in response to coherent visual motion in all brain regions (i.e., beyond area V5/MT), we first generated and report whole-brain within- and between-group statistical parametric maps for each of the aforementioned contrasts. In our main analysis, ROI activity was examined by applying a small-volume correction (SVC) within the ROI to the aforementioned map. For every analysis, whole-brain and ROI (small-volume corrected) results are reported (height: p<0.005 uncorrected, cluster: p<0.05 FDR corrected).

Due to our inquiry being specific to area V5/MT, our main analyses were limited to a defined ROI by using the SVC option within SPM. To best capture area V5/MT in the left and right hemispheres, we defined two 15 mm radius spheres centered on coordinates previously described by Watson et al. (1993) (MNI coordinates x, y, z: L -41, -72, -2; R 41 -69 -2). This approach is similar to that used by Klaver and colleagues (2008), who used the results from Murray et al. (2003) to generate their ROIs for random motion and structure-from-motion processing. However, due to concerns that these left and right hemisphere V5/MT ROIs would bias findings toward our adult group of participants, we performed additional ROI analyses using left and right hemisphere ROIs identified from a separate group of 14 older children using data acquired during one run of the identical visual motion experiment (same stimuli, task, and acquisition parameters). These Pre-adolescent ROIs were 15 mm radius spheres centered on coordinates identified at the group level in each hemisphere (MNI coordinates x, y, z: L -44, -78, 4; R 58, -60, 6), which were located more laterally and superiorly in both the left and right hemispheres than the Watson ROIs. (See Appendix for visual comparison.)
Cross-Sectional Study – We first sought to capture the activation profile of V5/MT in typical children and adults. Within each group separately, single-subject statistical maps for the voxel-wise contrast of Motion vs. Static from the first-level analysis were submitted to a one-sample t-test at the second level to generate a group map for each group.

Second, we addressed the question of whether V5/MT activity differed between adults and children. The single-subject statistical maps for the voxel-wise contrast of Motion vs. Static from the first-level analysis were submitted to a two-sample t-test at the second level.

Longitudinal Study – Similar to analyses for our Cross-Sectional Study, we first sought to capture the activation profile of area V5/MT in typically developing children at T1 and T2. Single-subject statistical maps generated at the first level for the voxel-wise contrast of Motion vs. Static were submitted to a one-sample t-test at the second level for both time points separately to produce a group map at each time point.

Second, to test for within-group changes in activation in area V5/MT between T1 and T2, the single-subject statistical maps generated at the first level for the voxel-wise contrast of Motion vs. Static were submitted to a paired t-test at the second level.

For the Longitudinal Study, we also examined brain–behavioral correlations as a way to capture the role of reading ability. To determine if dorsal stream function at T1 predicted reading outcome at T2, percent signal change (PSC) was extracted from spheres of 5 mm radius centered on the peak coordinates of the clusters identified from the Pre-adolescent ROI in our T1 within-time-points analysis, using the MarsBaR toolbox (Brett et al., 2002). A linear regression was performed between V5/MT activity PSC at T1 and raw reading scores (Word ID, Word Attack,
and Reading Fluency) at T2. In order to compare our results with prior behavioral studies that have shown phonological awareness to predict reading outcome (Wagner et al., 1994, 1997), we also conducted linear regression for raw scores of phonological awareness (CTOPP-Elision) at T1 and reading (Word ID, Word Attack) at T2.

Finally, we investigated the relationships between the amount of increase in V5/MT activity between the two time points and (i) the gains made in reading and (ii) the age increase experienced by the children. The time duration between testing at T1 and T2 differed amongst the children, thus providing variability in the age increases within the group. Though we did not find significant increases in V5/MT activation from T1 to T2, we used measures of non-significant changes in V5/MT activation bilaterally. PSC from T1 to T2 was measured by defining the overlap in V5/MT activation at T1 and T2 (clusters that did not survive correction at the whole-brain level), and building bilateral 5 mm spheres around the centers of mass of those areas of overlap. To determine if change in V5/MT activation from T1 to T2 was associated with gains in reading or age from T1 to T2, V5/MT activity PSC difference (T2 - T1, from the 5 mm spheres defined from V5/MT activation overlap at T1 and T2, as described above) was used to test whether change in V5/MT activity was associated with change in raw reading scores (for Word ID, Word Attack, and Reading Fluency) or change in age (months).

Functional connectivity analysis

Connectivity analysis was performed using the CONN functional connectivity toolbox (15.e, Whitfield-Gabrieli & Nieto-Castanon, 2012). The same procedures were applied to the Cross-Sectional and Longitudinal Studies. Pre-processed data were submitted to CONN for seed-
to-voxel analyses. First, data underwent several noise reduction steps, including i) regression of white matter and CSF ROI time series using aCompCor with five principal components (Behzadi et al., 2007); ii) regression of six rigid-body head motion parameters, as well as time points for which scan-to-scan motion exceeded 1.5 mm (50% of the voxel size); iii) regression of the effects of our Fixation, Motion and Static blocks; and iv) temporal high-pass filtering (f > 0.008 Hz) to reduce the effect of low-frequency drift.

For each subject, the residual time series associated with the Watson and Pre-adolescent ROIs, separately, were then submitted to a bivariate correlation to generate Fischer-Z-transformed correlation maps, in which every voxel in the brain is assigned a normalized correlation value that represents the magnitude of the correlation between that voxel and the averaged time series of all voxels within the V5/MT ROI (one for each hemisphere).

To capture the typical connectivity profile of each of our groups separately, single-subject statistical maps generated at the first level for the entire run (see Ganger et al., 2015) were submitted to a one-sample t-test. Due to the extensive significant correlations at the thresholds set for our functional analyses, we set more stringent thresholds for the connectivity analyses; height: p<0.005, FDR corrected, cluster: p<0.05, FDR corrected. To test for within- and between-group differences in whole-brain connectivity with area V5/MT, the single-subject statistical maps generated at the first level were submitted to a two-tailed (Adults vs. Children) two-sample t-test for the Cross-sectional Study, and a two-tailed (T1 vs. T2) paired t-test for the Longitudinal Study at the second level (height: p<0.005, FDR corrected, cluster: p<0.05, FDR corrected). Because the resulting connectivity profiles were similar between the analyses using
the Watson and the Pre-adolescent ROIs, only the results from the Pre-adolescent ROI-seeded analyses are reported here.

Results

Cross-Sectional Study

Behavioral

All participants performed with high accuracy on the in-scanner Motion and Static tasks. While accuracy and reaction time for both Motion and Static tasks differed between the two groups, as shown in Table 1, there was no significant difference between adults and children for reaction time when the comparison for the contrast of interest (Motion > Static) was considered. However, performance accuracy for Motion > Static differed significantly between adults and children; thus, this measure was included as a covariate of no interest in our fMRI between-group comparisons.

fMRI

Within-Group Analyses: Adults

Whole-Brain Analysis

Whole-brain analysis revealed six clusters of significant activation in the adults (Table 3, Figure 1A). In the left hemisphere, clusters were found in middle occipital gyrus (BA 19) extending to superior and middle temporal gyri (area V5/MT), in secondary visual cortex extending from the cuneus (BA 18), including area V3a, to bilateral lingual gyri, in left fusiform gyrus (BA 37), and in left cingulate gyrus (BA 24) extending to left superior parietal lobule. In the right hemisphere we observed significant activation extending from middle (V5/MT, BA 37)
to superior temporal gyrus, as well as in right cingulate cortex (BA 24) extending to right precentral gyrus.

**V5/MT Region of Interest Analyses**

*Watson ROI* – Our ROI analyses with SVC informed by the coordinates published by Watson (1993) revealed significant activity in area V5/MT, bilaterally (Table 3, Figure 1B). In the left hemisphere, expectedly similar to whole-brain results, activation extended from middle occipital gyrus (BA 19) to middle temporal gyrus. In the right hemisphere, activation extended from middle temporal gyrus (BA 37) to middle occipital gyrus.

*Pre-adolescent ROI* – ROI analyses with SVC centered on our own data-derived ROI identified similar bilateral clusters in V5/MT in our adult group (Table 3, Figure 1C), again with peak locations similar to those from the whole-brain analysis.

**Within-Group Analyses: Children**

*Whole-Brain Analysis*

In children, whole-brain analysis revealed significant activation in occipitotemporal as well as in parietal and frontal cortices (Table 3, Figure 1A). In the left hemisphere, these areas of activation included left middle temporal gyrus (BA 39) primarily dorsal to but extending minimally into area V5/MT; as well as left superior parietal lobule (BA 7) extending to inferior parietal lobule. In the right hemisphere, significant activation was observed in right middle temporal gyrus (BA 39), including area V5/MT; in right paracentral lobule (BA 5) extending to left precuneus; and in right middle frontal gyrus (BA 8) extending to superior frontal gyrus.
Table 3. Cross-Sectional Study: MNI coordinates of peak functional activation from within- and between-group comparisons in adults and children.

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<th>z</th>
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**Whole-Brain Analyses**
- Adults: Extends into left superior and middle temporal gyri,
- Children: Extends into left inferior parietal lobule.

**Watson ROI Analyses**
- Adults: Extends into left middle temporal gyri.
- Children: Extends into left inferior parietal lobule.

**Pre-Adolescent ROI Analyses**
- Adults: Extends into left middle temporal gyri.
- Children: Extends into left inferior parietal lobule.

*Note: Significance differences were not found in the comparisons.*

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Figure 1: A-C) V5/MT activity in Adults and Children A) across the whole brain, or using B) Watson ROI, or C) Pre-Adolescent ROI. D-F) Difference between Adults and Children in V5/MT activity D) across the whole brain, or using E) Watson ROI, or F) Pre-Adolescent ROI (no significant clusters). Motion > Static, voxel p < 0.005 uncorrected, cluster p < 0.05 FDR corrected. Activation up to 5 mm beneath the cortical surface is displayed.
**V5/MT Region of Interest Analyses**

*Watson ROI* – ROI analysis revealed no above-threshold clusters within the left hemisphere, but did reveal significant activation in right V5/MT (BA 19) (Table 3, Figure 1B).

*Pre-adolescent ROI* – ROI analyses identified clusters of significant activation in both hemispheres (Table 3, Figure 1C). Activation in the left hemisphere ROI extended from middle temporal gyrus (BA 39) to middle occipital gyrus, dorsal to and minimally within area V5/MT. In the right hemisphere, activation was focused within posterior superior (BA 39) and middle temporal gyri, including area V5/MT.

**Between-Group Analyses: Adults versus Children**

*Whole-Brain Analysis*

At the whole-brain level, adults showed significantly greater activation than Children in bilateral calcarine (BA 18), lingual, and inferior occipital gyri (Table 3, Figure 1D), as well as in left posterior insula (BA 13) extending to postcentral gyrus. There were no differences in area V5/MT. The opposite contrast (Children > Adults) did not identify any significant differences.

**V5/MT Region of Interest Analyses**

*Watson ROI* – ROI analyses revealed significantly greater activation in adults than Children, bilaterally (Table 3, Figure 1E). In the left hemisphere, ROI captured activation differences extending from the fusiform gyrus (BA 19) to lingual, middle and inferior occipital,
and middle temporal gyri, including area V5/MT; in the right hemisphere, ROI activation differences were found in lingual gyrus (BA 19).

*Pre-adolescent ROI* – ROI analyses revealed no significant differences in activation between adults and children within ROIs defined from our independent sample.

In sum for the *Cross-Sectional Study*, independent of whether using a whole-brain analysis, or the *Watson* or *Pre-adolescent ROI* analyses, the adult within-group maps showed bilateral activity within area V5/MT. The same was found for the within-group maps for Children, with the exception of the left hemisphere *Watson ROI*, within which activity for area V5/MT did not meet significance. An analysis comparing adults and children at the level of the whole brain did not reveal between-group differences in area V5/MT. However, between-group analyses using an ROI approach revealed greater bilateral V5/MT activity in adults compared to children in the *Watson ROI*, while a similar analysis in the *Pre-adolescent ROI* revealed no between-group differences. As such, the use of a literature-based ROI approach from a study in adults suggests an age-dependent difference in area V5/MT activity, whereas the use of the *Pre-adolescent ROI* approach and the whole-brain analysis approach did not.

To address the observed differences based on the location of the ROIs, we investigated whether there were differences between children and adults in (a) the location of the individual subjects’ foci of activity in V5/MT and (b) variability of these within the two groups. Bilateral foci were identified in each subject individually using the contrast of Motion > Static. Foci were selected in adults and children by identifying within each subject bilateral clusters closest to our *Pre-adolescent ROI* foci with peaks significant at the voxel-corrected level of at least $p < 0.001$
(most were significant at voxel-level family-wise error corrected $p < 0.05$). Within each hemisphere we used two-sample $t$-tests to compare the location of the adults’ and children’s individual peaks of activation along the x-, y- and z-planes separately. These revealed a significant difference in right hemisphere z-coordinates between the two groups, with peaks in the children located superior to those in the adults ($p = 0.008$). To determine whether the children’s right hemisphere peak locations exhibited greater variability than the adults’ peak locations in addition to being located more superiorly, we calculated the average Euclidean distance between each subject’s right hemisphere peak and the group’s average right hemisphere peak in each group separately. For example, average x-, y-, and z-coordinates for adults’ individual peaks were calculated to determine the average peak for the adult group. We then calculated the Euclidean distance between each adult subject’s peak and the average peak for the adult group. This was done for each subject in both groups. A two-sample $t$-test comparing Euclidean distances for our adult and child groups revealed a significant difference ($p = 0.041$), indicating that the children’s individual peaks were located further away from each other than the adults’ in the right hemisphere. This variability in location was distributed evenly in the x-, y-, and z-planes, as the absolute distance between each subject’s peak and the group average was not significantly different in the x-, y-, or z-directions.

**Functional Connectivity**

Seed-to-voxel analyses revealed the time courses of both left and right area V5/MT activation across the entire functional run to be significantly correlated with a large bilateral posterior portion of cortex, extending ventrally and dorsally. Figure 2A and 2B show the results
for the adults and children. Here we only describe details of only the between-group comparisons of the *Cross-Sectional Study*.

Figure 2: Bilateral V5/MT seed (Pre-Adolescent ROI)-to-voxel results in A) Adults, B) Children, C) Adults > Children (no significant differences), and D) Children > Adults. For the within-group maps, areas exhibiting positive correlations are indicated in orange/red, areas exhibiting anti-correlations are indicated in green/blue. Voxel $p < 0.005$ FDR corrected, cluster $p < 0.05$ FDR corrected. Connectivity up to 5 mm beneath the cortical surface is displayed.
Seed-to-Voxel Whole-Brain Between-Group Analyses

The contrast of adults greater than children did not produce any significant findings. However, there was greater functional connectivity in children compared to adults (Table 4, Figure 2D). For left V5/MT, Children exhibited significantly greater connectivity with ipsilateral lateral occipital cortex (LOC; BA 19) extending to left middle and inferior temporal gyri and to left fusiform gyrus, as well as greater connectivity with homotopic contralateral LOC (BA 37). For right V5/MT, children exhibited significantly greater connectivity with ipsilateral middle temporal gyrus (BA 37) extending to R LOC.

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<th>Voxel</th>
<th>Peak BA</th>
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<td>-42, -76, 6</td>
<td>L Lateral Occipital Cortex(^a)</td>
<td>1665</td>
<td>19</td>
<td>6.61</td>
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<tr>
<td></td>
<td>40, -66, 6</td>
<td>R Lateral Occipital Cortex</td>
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</tr>
<tr>
<td>R Pre-Adolescent ROI Seed</td>
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<tr>
<td>Adults &gt; Children</td>
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</tr>
<tr>
<td>Children &gt; Adults</td>
<td>54, -64, 8</td>
<td>R Middle Temporal Gyrus(^b)</td>
<td>66</td>
<td>37</td>
<td>5.40</td>
</tr>
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\(^a\)Extends into left middle and inferior temporal gyri, and left fusiform gyrus.
\(^b\)Extends into right lateral occipital cortex.

Longitudinal Study

Behavioral

All participants performed with high accuracy on the in-scanner Motion and Static tasks. As shown in Table 2, accuracy and reaction time did not differ between T1 and T2 for
performance in either the Motion or Static conditions, or when the difference between conditions for the contrast of interest (Motion > Static) was considered.

As expected, from T1 to T2 the children on average experienced gains in raw score measures of reading, significant for single real word reading (two-tailed paired $t$-test, T2>T1: Word ID-RS, $p = 0.006$), reading fluency (Reading Fluency-RS, $p = 0.003$), and trending toward significance for pseudoword reading (Word Attack-RS, $p = 0.053$).

**fMRI**

**Within-Group Analyses: Children at Time 1**

*Whole-Brain Analysis*

At T1 the children exhibited no activation above threshold for the contrast of Motion > Static at the whole-brain level.

*V5/MT Region of Interest Analyses*

*Watson ROI* – ROI analyses revealed no significant activity in either left or right area V5/MT at Time 1.

*Pre-adolescent ROI* – ROI analyses within our own data-derived ROIs revealed significant activation bilaterally (Table 5, Figure 2C). In the left hemisphere, this activation extended from middle temporal gyrus (BA 19) to middle occipital gyrus, just dorsal to canonical area V5/MT. In the right hemisphere, activation extended from superior temporal (BA 22) and middle temporal gyri, into area V5/MT and into the middle occipital gyrus.
<table>
<thead>
<tr>
<th>Whole-Brain Analyses</th>
<th>Watson ROI Analyses</th>
<th>Pre-Adolescent ROI Analyses</th>
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<tr>
<td>A. Time 1</td>
<td>B. Time 1</td>
<td>C. Time 1</td>
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<tr>
<td></td>
<td>z = θ</td>
<td>z = 10</td>
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<tr>
<td>A. Time 1 &gt; Time 2</td>
<td>B. Time 1 &gt; Time 2</td>
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**Figure 3:** A-C) V5/MT activity at T1 and T2. A) across the whole brain, or using B) Watson ROI (no significant clusters), or C) Pre-Adolescent ROI. D-F) Difference between T1 and T2 in V5/MT activity D) across the whole brain, or using E) Watson ROI (no significant clusters), or F) Pre-Adolescent ROI (no significant clusters). Motion > Stat, voxel p < 0.005 uncorrected, cluster p < 0.05 FDR corrected. Activation up to 5 mm beneath the cortical surface is displayed.
Within-Group Analyses: Children at Time 2

Whole-Brain Analysis

Whole-brain analysis revealed significant activity in two right hemisphere clusters (Table 5, Figure 3A). Children at T2 exhibited significant activation in right area V5/MT in posterior middle temporal gyrus (BA 37) extending to superior temporal gyrus, and in right middle frontal gyrus (BA 9) extending to precentral gyrus.
**V5/MT Region of Interest Activation**

*Watson ROI* – ROI analysis did not reveal activity in left or right hemisphere above threshold.

*Pre-adolescent ROI* – These ROI analyses revealed no significant activation in the left hemisphere, but showed activity in right V5/MT, in posterior middle (BA 37) and superior temporal gyri (Table 5, Figure 3C).

**Between-Time Analyses: Children at Time 1 versus Time 2**

*Whole-Brain Analysis*

For the contrast of T2 > T1, children at T2 showed significantly greater activation in bilateral cuneus (BA 19) extending to bilateral lingual gyri (Table 5, Figure 3D). There were no significant findings for the opposite contrast, T1>T2, and neither contrast revealed activation differences in area V5/MT.

*V5/MT Region of Interest*

*Watson ROI* – ROI analyses revealed no significant change in activity from T1 to T2 in left or right V5/MT.

*Pre-adolescent ROI* – ROI analyses revealed no significant changes.

In sum, for the *Longitudinal Study*, V5/MT activation at each time point varied depending on the analysis approach used. Whole-brain analyses revealed no activation in area V5/MT at T1 and significant activation at T2 only in right hemisphere V5/MT. There were no
significant changes observed in V5/MT in either hemisphere from T1 to T2. SVC within the Watson ROI (literature-based in an adult sample) did not reveal V5/MT activation at T1 or T2, whereas our Pre-adolescent ROI (defined in older children and adolescents) captured activation at both time points: bilaterally at T1 and in right area V5/MT at T2. However, for both ROI analyses there were no significant changes from T1 to T2. Together, findings from our Longitudinal Study suggest that an adult-based ROI may not be sufficient to capture V5/MT response to coherent visual motion in children, and that activation in V5/MT does not change significantly from 2nd to 3rd grade, as demonstrated in all of the analyses performed.

In order to determine whether there were shifts in V5/MT location from T1 to T2, using the same methods as described above, we investigated whether there were differences in (a) the location of the individual subjects’ foci of activity in V5/MT between time points and (b) variability of these within each time point. Paired t-tests revealed differences in right hemisphere x- (p = 0.038) and z-coordinates (p = 0.083) between the two time points, with peaks at T2 located inferior and medial to those at T1. To determine whether T1 peak locations exhibited greater variability than those at T2 in the right hemisphere, we again calculated the average Euclidean distance between each subject’s peak and the group average peak at each time point separately. A paired t-test comparing Euclidean distances at T1 and T2 revealed no significant differences.
V5/MT Activity and Reading Performance

Correlations between change in V5/MT activation and change in raw reading scores for real word and pseudoword reading accuracy as well as reading fluency on the Woodcock Johnson III (2001), from T1 to T2 yielded no significant results.

Linear regression analysis revealed that V5/MT activity at T1 did not predict reading outcome at T2 for real word reading accuracy, pseudoword reading accuracy, or reading fluency. On the other hand, phonological awareness measured via sound elision (CTOPP Elision-RS) at T1 predicted pseudoword reading accuracy outcome at T2 ($r = 0.61, p = 0.04$), and real word reading accuracy outcome at T2 at the trend level ($r = 0.56, p = 0.06$).

Functional Connectivity

Seed-to-voxel analyses revealed the time courses of both left and right area V5/MT (Watson and Pre-adolescent ROIs) activation across the entire functional run to be significantly correlated with a large bilateral posterior portion of cortex, extending ventrally and dorsally. Figure 4 shows these results for T1 and T2 of our Longitudinal Study (all data reported are based on the results from the Pre-adolescent ROI).

Pairwise connectivity analyses revealed no change in functional connectivity with left or right V5/MT from T1 to T2.
Figure 4: Bilateral V5/MT seed (Adolescent ROI)-to-voxel results at T1 and T2. Areas exhibiting positive correlations are indicated in orange/red, areas exhibiting anti-correlations are indicated in green/blue. Voxel $p < 0.005$ FDR corrected, cluster $p < 0.05$ FDR corrected. Connectivity up to 5 mm beneath the cortical surface is displayed.
Discussion

This is the first study to compare children’s and adults’ area V5/MT activation during coherent motion processing and its functional connectivity to other brain regions. Our Cross-Sectional Study of coherent visual motion processing extends the work of Klaver et al. (2008), who investigated differences in visual motion processing between children and adults for random motion stimuli and structure-from-motion stimuli, but who did not examine coherent motion stimuli. Similar to Klaver and colleagues, we used a whole-brain analysis as well as an ROI analysis approach, with the ROI based on spatial coordinates reported in a coherent motion study in adults (Watson et al., 1993). As in the study by Klaver and colleagues, between-group differences in V5/MT activation did not emerge from the whole-brain analysis, but did from the ROI analysis. To better understand whether these differences between children and adults were based on the increased statistical power that is concomitant with the ROI approach, or were due to a bias in the location of the ROI (given that it was derived from an adult study), we also applied an ROI that was based on the activation location in a group of older (“pre-adolescent”) children. This ROI was located relatively more superior relative to the ROI based on Watson et al. and resulted in no between-group differences. We followed up with an examination of the individual subjects’ maxima locations and found that the children on average had area V5/MT locations in a more superior location (significant in right hemisphere, trending in left hemisphere) compared to adults. As such, we conclude that there is a difference in location of area V5/MT (and not a difference in signal strength) between children and adults, with children’s area V5/MT located relatively superior to that of adults. Children and adults also differed in functional connectivity, with children exhibiting relatively greater local connectivity of area...
V5/MT with ipsilateral and, in the case of left V5/MT, contralateral regions. However, in our *Longitudinal Study*, we found no changes in activity or functional connectivity of area V5/MT from 2\textsuperscript{nd} into 3\textsuperscript{rd} grade, suggesting that the differences observed in the *Cross-Sectional Study* represent a maturation that occurs over a protracted period of time. We also did not find evidence to support there being a relationship between change in brain activity and change in reading ability from 2\textsuperscript{nd} into 3\textsuperscript{rd} grade, or that brain activity in 2\textsuperscript{nd} grade was predictive of reading in 3\textsuperscript{rd} grade. We did, however, find a trending difference in the location of right hemisphere area V5/MT in the inferior direction from 2\textsuperscript{nd} into 3\textsuperscript{rd} grade. In sum, we conclude that there is a gradual developmental shift in the location of area V5/MT in both hemispheres in the inferior direction with increasing age, together with a gradual decrease in functional connectivity with surrounding extrastriate visual cortex.

*Coherent Visual Motion Processing in Adults and Children*

We begin by discussing activity underlying visual motion processing at the level of the whole brain. In our *Cross-Sectional Study*, whole-brain analyses in the adult group revealed brain activity in response to coherent visual motion (compared to static dots) that is consistent with previous literature (Dupont et al., 1994; McKeefry et al., 1997; Sunaert et al., 1999; Watson et al., 1993), including significant activation in bilateral dorsal occipitotemporal cortex, including V5/MT, and significant activation also being observed in left hemisphere area V3a. Adults also displayed ventral visual cortical activation in left cuneus, extending into bilateral lingual gyri of primary and secondary visual areas, as well as in left fusiform gyrus. Coordinates of V5/MT activation reported in our whole-brain analysis in adults are similar in location to
those reported from prior similar studies (Dupont et al., 1994; McKeefry et al., 1997; Sunaert et al., 1999; Watson et al., 1993), as are those we report for left hemisphere area V3a (McKeefry et al., 1997; Sunaert et al., 1999). Additionally, differential activation for coherent motion greater than static stimuli within primary and secondary visual cortex is consistent with previous reports (Dupont et al., 1994; McKeefry et al., 1997; Sunaert et al., 1999; Watson et al., 1993). Notably, activation within these regions has been shown to be greater for coherent motion than random motion perception, as also seen in our study (Braddick et al., 2001; Paradis et al., 2000; but see McKeefry et al., 1997). Next, the children in our study exhibited functional activation in bilateral occipital and temporal areas including area V5/MT. They did not show significant activity in earlier visual areas corresponding to V1, V2, and V3. Additional clusters of activation were observed in children further along the dorsal pathway, in left superior and inferior parietal, and right middle and superior frontal cortex. When directly compared to adults, children exhibited significantly less activation in bilateral early visual cortex (V1/V2), as well as in the left postcentral gyrus. There were, however, no between-group differences in area V5/MT. In sum, like Klaver and colleagues, whose children (n=10) were 6 to 7 years of age (ours were 7 to 8 years of age), we found no differences between the children and adults except for bilateral early visual cortex and left postcentral gyrus (Adults > Children). Notably, the only difference observed by Klaver and colleagues for a whole-brain analysis was for random motion in the left precentral gyrus (Children > Adults).

Turning to the ROI analyses, our first analysis used spheres that were centered on the left and right coordinates reported in the original PET study conducted by Watson and colleagues (1993) in adults. It was motivated by a similar approach employed by Klaver and colleagues
(2008), who created spheres around the coordinates reported by Murray et al. (2003), an adult study on structure-from-motion, and applied these to their pediatric–adult comparison of structure-from-motion and incoherent motion. In adults, we found that our literature-defined Watson ROIs captured significant activation within area V5/MT bilaterally, while in children these regions only captured significant V5/MT activation in the right hemisphere. Our between-group results, similar to those reported by Klaver and colleagues for random motion stimuli, showed that adults exhibit greater activation in bilateral area V5/MT relative to children during perception of coherent motion stimuli. It should be noted that a difference in our approach is that we examined left and right area V5/MT separately (the hemispheres were collapsed in the study by Klaver and colleagues), and our focus was only on ROIs in area V5/MT, whereas Klaver and colleagues’ ROI investigation extended to additional brain areas involved in motion and form processing. Importantly, because these ROIs for left and right V5/MT were defined from an adult sample (Watson et al., 1993), there was concern over whether they adequately captured activation within our pediatric group. Indeed, when we used ROIs derived from an analysis using a “pre-adolescent” sample, we found bilateral activation of V5/MT not only in adults but also in the children. Further, the between-group comparisons using the Pre-adolescent ROIs subsequently revealed no significant differences between children and adults.

In sum, a between-group comparison using the Watson ROIs indicated significant differences in activation (Adults > Children). However, further analysis using different, more age-appropriate ROIs, suggests that this finding may be problematic, as no group difference emerged.
Coherent Visual Motion Processing in Children Measured Longitudinally at Two Time Points

The children participating in the Longitudinal Study were 8.4 years old on average and had just completed 2nd grade at the first time point. Following from the above discussion regarding the different outcomes depending on the use of a whole-brain analysis or ROI analysis, we found that, whereas there was significant bilateral V5/MT activation in our adults irrespective of the analysis employed (whole-brain and both types of ROIs), our pediatric group in the Longitudinal Study showed variable results just as the pediatric sample did in the above Cross-Sectional Study (N.B., the same data from 3 children contributed to the Cross-Sectional Study of n=13 and the Longitudinal Study of n=12). As described above, the within-group maps for children in the Cross-Sectional Study (aged 7.7 years on average) showed bilateral activation of V5/MT for all three types of analysis approaches, except the Watson ROIs, where activity for area V5/MT in the left hemisphere did not meet significance. However, at the first time point (T1) of the Longitudinal Study, activity in area V5/MT was only found using the Pre-adolescent ROIs (bilateral V5/MT activity), but not at all using the Watson ROIs or the whole-brain analysis. At the second time point (T2), activity was again not found for area V5/MT using the Watson ROIs. However, both the Pre-adolescent ROIs and whole-brain analyses revealed right but not left V5/MT activation. These results speak to the advantage of using an ROI approach centered on brain activity obtained in children, as the Pre-adolescent ROIs were most successful in showing brain activity during coherent motion processing.

The goal of the Longitudinal Study was to determine if there were short-term developmental changes in activity underlying coherent motion processing. We observed significant changes only in low-level visual cortex across this time span, as between-time-point
analyses did not reveal any significant changes in area V5/MT from 2\textsuperscript{nd} to 3\textsuperscript{rd} grade for any of our whole-brain or ROI approaches.

\textit{Location of Area V5/MT}

We considered the possibility that the location of peak response to coherent visual motion is different between children and adults, or that the variability in peak location and activation differs between these groups. Peak coordinates for our adult group fell within the range of coordinates reported in other studies (summarized in Wilms et al., 2005, Table 2), while peak coordinates from our younger groups predominantly fell outside of this range (lateral, anterior, and superior to the average). Our ROIs defined functionally in an independent “pre-adolescent” sample, however, captured functional activation fairly well in our younger groups. This suggests that the location of V5/MT shifts inferiorly across development, or that coherent visual motion tasks such as the one used here activate superior motion-sensitive visual areas in children more than they do in adults. To test this, we identified peak V5/MT activity within each of our subjects individually and compared these locations between groups. We found in the data from the Cross-Sectional Study that children’s peaks were significantly superior to adults’ peaks in the right hemisphere, with no significant difference in left hemisphere. Consistent with this, we found in the Longitudinal Study that children at T1 showed a trend toward more superior and lateral activation than at T2 in the right hemisphere, with no significant difference in the left hemisphere. This could suggest that peak activation to coherent visual motion shifts inferiorly and medially with increasing age. It is tempting to speculate what the mechanism may be for such a shift, and the most fitting explanation would be one that involves a shift of the anatomy.
following expansion of nearby cortical volume that results in moving the specific cortical area V5/MT into the inferior and medial position. Cortical thickening has been reported in children between the ages of 5 and 11 years over a two-year period in bilateral posterior perisylvian regions and suggests the possibility of a physical shift of cortex below the superior temporal gyri, including cortex housing area V5/MT (Sowell et al., 2001). Future longitudinal studies of V5/MT development should include measures of cortical thickness and/or gray matter volume to address this possibility. Greater variability of location in children may be playing a role as well.

We found that adults showed less variability in their individual peaks of activation in right hemisphere (as measured by the average Euclidean distance between individual peaks and the group average) than the children in our Cross-Sectional Study, and this variability was equivalent in the x-, y-, and z-directions (spherical distribution) for both groups. It has been reported that the position of area V5/MT on an individual level is quite variable (Fischl et al., 2008; Malikovic et al., 2007; Yeo et al., 2010, 2011), but the difference in variability we observed between groups suggests that variability in location of activation is reduced over time. According to the SPM Anatomy Toolbox (Eickhoff et al., 2005, 2007), most individual peaks were assigned to hOc4la, which is lateral occipital cortex just posterior to V5/MT. Children had more peaks assigned to PGp (a transition area between parietal and visual areas [Caspers et al., 2013]) than adults, but with majority hOc4la, whereas adults were most likely to be hOc4la and V5/MT. This pattern was similar from T1 to T2 in our Longitudinal Study, with more peaks assigned to PGp at T1, and the majority assigned to hOc4la at T2. Together, this suggests differences and variability in peak location for children and adults. While these lead to the appearance of less activation in
children, the difference between children and adults is best described not in terms of differences in activation, but rather differences in location.

There were no significant changes in activation from 2nd to 3rd grade, except in low-level visual cortex. Whether our time window of one year was too small to discern measurable differences in activation and connectivity, or whether development of this response is more contingent upon location than strength of activation, remains to be determined. Also, our longitudinal study failed to provide evidence of gains in reading being associated with changes in V5/MT activation. This was unexpected, as recent studies have suggested the idea that increased experience in reading may be yoked with increased activity in area V5/MT (Boets et al., 2011; Olulade et al., 2013b). Finally, we tested the hypothesis that V5/MT integrity may lay the groundwork for successful reading outcome by investigating the relationship between 2nd grade V5/MT activation and 3rd grade reading scores. Whereas phonological processing measured behaviorally predicts reading outcome in our sample as in previous studies (Schatzschneider et al., 2004; Wagner & Torgesen, 1987), a similar relationship between V5/MT activity and reading outcome was not supported. We cannot rule out the possibility, though, that our fMRI signal may have lacked statistical power to bear out a relationship between 2nd grade V5/MT activation and 3rd grade reading. Additionally, while previous studies of the relationship between reading and coherent motion processing have been conducted in pre-reading children, our participants had already learned to read. As a result of this, any reading-related changes in V5/MT activation may have already occurred in our participants. Further, a more compelling comparison would be to determine whether activity during a task of phonological processing in our sample at 2nd grade predicts reading at 3rd grade. Hoeft and colleagues took this approach in their 2007 study, in
which they found that neuroimaging data (fMRI during a real word rhyming task) predicted later reading in 8- to 12-year-old children with a range of reading abilities. Regardless, the current findings highlight the need to further elucidate the nuances of the relationship between dorsal stream function and reading ability.

Of note is that our results are consistent with those of Kevan and Pammer (2009), who found that a behavioral measure of pre-reading frequency doubling sensitivity, but not coherent motion sensitivity, predicted early reading measures of real and pseudoword reading. Their suggestion for why one dorsal stream measure predicted reading outcome but not the other (i.e., coherent motion perception) was that perhaps the higher-order neuroanatomical substrates of coherent motion sensitivity, as opposed to lower-level substrates of frequency doubling sensitivity, are only “assimilated” into the reading network once reading skills become more sophisticated. Whereas the authors hypothesized that perhaps their early readers (avg. age 7 years) were not yet at a level of reading advanced enough to require areas subserving coherent motion perception (e.g., V5/MT) to have been incorporated into the reading network, this explanation does not apply to our children, who were older and had more complex reading experiences.

**Differences in Functional Connectivity between Children and Adults**

Results for whole-brain connectivity patterns between V5/MT and the rest of the brain were very similar, independent of whether the Watson or Pre-adolescent ROIs were used as seeds. In our *Cross-Sectional Study*, we found differences in V5/MT connectivity such that children exhibited greater local connectivity than adults within ipsilateral regions surrounding
V5/MT and, for our left hemisphere seed, with contralateral V5/MT. While this difference is consistent with the decrease in local connectivity observed across the lifespan (Betzel et al., 2014; Fair et al., 2009; for review see Rubia, 2013), we did not observe greater long-range functional connectivity with V5/MT in our adults relative to children, which has been reported in these developmental studies of functional connectivity. As for our *Longitudinal Study*, we found no significant changes over time in connectivity in either hemisphere, again demonstrating that the differences observed between children and adults represent a protracted period of maturation.

**Conclusion**

Taken together, our two studies provide the first insight into the development of the typical neural response to coherent visual motion, particularly within area V5/MT. Foremost, our findings illustrate that the method for defining and interrogating V5/MT is critical for adequately characterizing development within this region. While we observed significant differences in V5/MT activation between children and adults, this was only present when we interrogated an ROI identified in adults. Within an ROI defined in a group of older children/pre-adolescents, V5/MT activation no longer differed between the adults and children. Further, we did not observe any significant changes in V5/MT activation from 2nd to 3rd grade, regardless of which analysis was performed. From our comparisons of subjects’ individual peaks of activation, we suggest that V5/MT development may not be characterized by changes in strength of activation, but may be driven more by peak activation becoming more focal and moving inferiorly over time. The impact of these differences appear to be localized, as our functional connectivity analyses only revealed differences only in local V5/MT connectivity, and did not reveal larger
shifts in dorsal stream connectivity between our age groups. Reading development did not appear to be driving the effects we observed. To conclude, we offer a comprehensive examination of coherent visual motion processing in children in area V5/MT, providing an important context for interpretation of the relationship between V5/MT function and other skills such as reading success.
CHAPTER 3: EFFECTS OF SENSORY AND LANGUAGE EXPERIENCE ON THE NEURAL BASES OF VISUAL MOTION PROCESSING

Abstract

Investigations into cross-modal plasticity in deaf adults have attributed greater activity during visual motion perception in parietal and superior temporal cortices to lack of audition. However, it is unknown how sign language experience contributes to these results. To address the etiology of experience-based cross-modal plasticity, we used a factorial design that included not only deaf participants with native sign language experience but also deaf native users of English, along with hearing native users of sign language and hearing native users of English. A main effect of sensory experience in right auditory cortex was due to more activity in the deaf compared to hearing groups. A main effect of language experience in left ventral temporal and right inferior frontal cortex was due to more activity in native users of English compared to native users of ASL. There was no interaction between sensory and language experience. These findings demonstrate that cross-modal activation of right superior temporal cortex is unequivocally attributed to deafness, whereas experience with a signed language does not impact canonical dorsal visual areas and is associated with less activation in ventral visual and right inferior frontal cortex. Greater functional connectivity in the deaf relative to the hearing groups between right STG and visual cortex support cross-modal mechanisms.
Introduction

Cross-modal neural plasticity has been observed in animal studies of early deafness, wherein brain areas typically dedicated to auditory processing become responsive to visual stimuli (Lomber et al., 2010; Meredith et al., 2011; Roe et al., 1992; Sur et al., 1988). In humans, it is thought that auditory cortex becomes involved in perception of visual motion in the deaf (Fine et al., 2005; Finney et al., 2001, 2003; Sadato et al., 2005; Shiell et al., 2015; Vachon et al., 2013). Visual motion perception is particularly relevant to deaf individuals, who, in the absence of auditory information, rely on visual cues to orient to new information and monitor their surroundings. Such adaptation provides important insight into the extent to which cortex is plastic versus dedicated strictly to one sensory function.

However, deafness is not the only life-long experience that differs between deaf and hearing individuals; some deaf individuals also grow up using sign language, thereby giving them a unique visual-spatial language experience in addition to and *in combination with* their altered sensory experience. For these deaf signers, visual motion perception is therefore not only important in the context of being deaf, but also critical for monitoring hand and body movements in peripheral visual space during communication. This additional reliance on peripheral visual motion processing (peripheral visual processing being magnocell-dependent) in native users of sign language has been thought to exert unique effects on the neural substrates of visual motion processing, as reflected in previous work suggesting that sign language experience affects performance on detecting direction of motion (Neville & Lawson, 1987b), brain anatomy (Olulade et al., 2014) and brain function (Bavelier et al., 2001; Cardin et al., 2013; Weisberg et al., 2012). Bavelier and colleagues (2001) reported that the neural substrates mediating visual
motion processing are altered by sign language experience separately from those changes attributed to sensory experience (i.e. deafness). They examined regions of interest for extent of and change in activation in response to visual motion perception and compared deaf users of American Sign Language (ASL) with hearing native users of ASL (children of deaf adults, CODAS) and hearing non-signers. Deaf signers compared to both hearing groups (signer and non-signers) exhibited greater percent signal change of activation in bilateral posterior parietal cortex and greater extent of activation in bilateral posterior superior temporal sulcus and bilateral V5/MT (the V5/MT finding was specific to when the task required attention to the periphery), suggesting early sensory differences as the cause. However, the same study also revealed activation differences that were attributed to language experience: greater leftward lateralization of area V5/MT activation was found in deaf and hearing native signers relative to hearing non-signers and was attributed to a modification of the language-dominant hemisphere following the use of visual motion to perceive movement of the hands, body and face during sign language. These results suggest that brain activity underlying motion perception is influenced not only by sensory but also by language experience.

While Bavelier and colleagues did not investigate auditory cortex with their region of interest (ROI) approach, several studies over the last 15 years have reported that auditory cortex in right posterior superior temporal gyrus (STG) is more responsive to visual motion in deaf compared to hearing adults (Fine et al., 2005; Finney et al., 2001; Sadato et al., 2005; Shiell et al. 2014; Vachon et al., 2013). Interestingly, the effect has been shown when combining a variety of visual stimuli (Vachon et al., 2013), has been localized to primary auditory cortex (Shiell et al., 2014) and has been found to be more robust in right than left hemisphere (Fine et al., 2005;
Finney et al., 2001; Sadato et al., 2005; Shiell et al., 2014; Vachon et al., 2013). However, the ability to interpret these findings is limited because heightened activity in the deaf participants in auditory cortex could represent cross-modal plasticity following deafness or following life-long experience with a signed language, or an interaction between the two. The comparison of deaf signers with hearing non-signers (Vachon et al., 2013), makes it difficult to attribute between-group differences solely to the participants’ life-long auditory experience, since the groups differ in both auditory and language experiences. The inclusion of hearing participants with native sign language experience helps to address this confound, but two of the studies mixed the participants in their groups instead of examining them separately: Sadato and colleagues (2005) compared a group of deaf signers with a mixed group of hearing subjects (signers and non-signers); another study (Shiell et al., 2014) compared hearing non-signers with a mixed group of deaf participants (signers and non-signers). Fine et al. (2005) separated the groups of deaf signers, hearing signers (CODAs) and hearing non-signers, much like the Bavelier study (2001), but had only six subjects per group (Finney et al., 2001 only reported on the deaf signers and hearing non-signers, but not the hearing signers). Further, while the study of these three groups helps address the respective roles of sensory and language experience, the three groups are short of a fourth group required for factorial design which investigates not only the main effects of these experiences but also their interaction.

In another line of research investigating the intersection of sensory and language experience, in this case in sign language processing, Cardin and colleagues (2013) studied not only deaf native signers but, critically, deaf native English speech-readers who did not grow up using sign language. Both of these deaf groups were compared with a group of hearing native
English speakers, allowing the authors to better delineate the effects of sign language experience versus deafness. In a recent investigation into gray and white matter anatomical differences in deaf people, Olulade et al. (2014) employed a factorial design on data acquired in hearing native users of English, hearing native signers (CODAs), deaf native users of English, and deaf native signers. This approach allowed testing for a main effect of sensory experience (by combining the two types of language experiences, i.e. native use of ASL or English and comparing deaf versus hearing), main effect of language experience (combining subjects who were hearing or deaf and comparing ASL versus English) and their interactions. The study found an interaction effect, suggesting that not only does language experience play a role, but the nature of the role is modulated by deafness. Specifically, Olulade and colleagues found less white matter volume in left superior temporal and inferior frontal gyri and in a right fusiform region in the deaf native users of ASL compared with the hearing native users of ASL, while white matter was equal in the deaf native users of English and hearing native users of English. These results speak to experience-dependent differences in brain anatomy due to deafness, but constrained to deaf native signers.

Here we take the same approach to address the fact that prior studies examining the role of auditory experience on visual motion perception have not disambiguated the effects of deafness from the life-long use of a visuospatial language when considering the neural basis of visual motion perception. Our deaf native users of English did not grow up with sign language and instead had access primarily to English (through speech-reading, sometimes in combination with Cued Speech, and later via reading English text). These participants are actually more representative of the deaf population, 95% of whom are born to hearing parents (Mitchell &
Karchmer, 2004) and therefore do not experience early sign language exposure as do deaf children born to deaf parents. The exclusion of deaf participants who are not native users of sign language in prior studies is surprising, given how this group can aid in addressing the role of language experience in the deaf, and given that they represent the largest constituency of the deaf population than those growing up using sign language from birth.

In sum, we studied (i) hearing native users of English (born to two hearing parents); (ii) hearing native users of ASL (born to deaf parents), sometimes referred to here as “hearing signers”; (iii) deaf native users of English (born to two hearing parents); and (iv) deaf native users of ASL (born to deaf parents), sometimes referred to as “deaf signers.” We used a factorial design to allow examination of the effect of sensory experience (Hearing vs. Deaf), language experience (English vs. ASL) and their interactions. We used a whole-brain analysis approach for identifying differences in brain activity so as not to restrict ourselves to primary auditory cortex, and also followed up these findings with an investigation into the functional connectivity of those areas demonstrating differences in brain activity. We found evidence for a main effect of Sensory Experience in right superior temporal (Deaf > Hearing) cortex, a main effect of Language Experience in left ventral temporal and right inferior frontal cortices (English > ASL), but no interaction between the two factors. Subsequent analyses revealed greater functional connectivity between right superior temporal and bilateral occipital cortex in the Deaf groups relative to the Hearing groups, in support of cross-modal plasticity between visual and auditory cortices, and greater functional connectivity between left ventral temporal and bilateral superior frontal cortex in the users of English relative to the users of ASL. Together, our studies provide evidence that sensory experience, not sign language experience, is the driving factor of the
functional reorganization of right auditory cortex underlying the perception of visual motion in the deaf, and that language experience impacts visual motion processing but not within the dorsal visual stream (e.g., area V5/MT).

Methods

Participants

Data from 59 participants (31 female) were used to compare the effects of sensory experience (deaf vs. hearing) and language experience (English vs. ASL) on the neural bases of visual motion processing. Participants were divided into four groups, consisting of deaf native users of ASL (i.e., deaf individuals born to deaf parents, n = 14), hearing native users of ASL (i.e., hearing individuals born to deaf parents, n = 15), deaf native users of English (i.e., deaf individuals born to two hearing parents, n = 14), and hearing native users of English (i.e., hearing individuals born to two hearing parents, n = 16). Deaf participants were either congenitally deaf or became deaf before two years of age, and had severe hearing loss of at least 75 dB in the better ear. Demographic information is provided in Table 1 and was previously described in Olulade et al., 2014.
To be included in the study, participants’ scores on the Wechsler Abbreviated Scale of Intelligence Performance (PIQ) subtest had to be greater than 85. Participants were right-handed and had no history of neurological or psychiatric disorders. Groups are equated on PIQ, age, and in-scanner accuracy and reaction time for the contrast of interest, Motion > Static (single-factor...
ANOVA, n = 59; main effect of group was nonsignificant; p > 0.1 for all measures). For consistency with the two-way ANOVA used for the functional data (see “fMRI data analysis”), these behavioral data were also submitted to an ANOVA examining main effects of sensory experience (deaf vs. hearing), language experience (ASL vs. English), and their interaction. This analysis revealed a significant main effect of accuracy (two-way ANOVA, n = 59; p < 0.05) and an interaction for reaction time (n = 59; p < 0.05). These effects were such that the hearing participants performed the Motion task with greater accuracy than the deaf participants, and deaf native users of English and hearing native users of ASL exhibited a larger discrepancy between reaction times to the Motion and Static stimuli. To control for these effects, accuracy and reaction time for the contrast of Motion > Static were included as covariates of no interest in our functional factorial analyses.

The Georgetown University and the Gallaudet University Institutional Review Boards granted approval of the study, and participants provided informed written consent for their participation.

fMRI paradigm and acquisition

We used a coherent visual motion detection task previously shown to reliably activate area V5/MT of the dorsal stream (Olulade et al., 2013b). For the active task (Motion), participants viewed low-contrast, random dot kinematograms consisting of white dots moving in various directions on a black background with 40% coherence in the horizontal direction. Participants were asked to indicate the direction of motion via button press (e.g., left-thumb button press for leftward motion), while maintaining fixation on a central cross.
For the active control task (Static), participants performed a density judgment task during which static dots were presented on the screen with differing densities between the left and right visual fields (35-65% density contrast). Participants were asked to maintain fixation on a central cross and indicate via button press on which side of the screen dot density was greater.

For both the coherent motion and the static conditions, stimuli were presented for 3 s followed by a crosshair for 1.2 s, with 10 stimuli presentations per block. Alternating blocks of Static and Motion stimuli (42 s/block) were separated by blocks of Fixation (21 s). Fixation consisted of a single crosshair presented at the center of the visual field. One run consisted of two blocks each of the Static and Motion conditions. Order of alternating Static and Motion blocks was the same between runs and across subjects, with the Static task occurring first (after an initial 21 s of Fixation). Each run began and ended with an additional 9 s and 6 s of Fixation, respectively, which were not included in analysis. Two runs per participant were entered into the analysis for both studies.

Images were acquired on a 3T Siemens Trio Scanner located at the Center for Functional and Molecular Imaging at the Georgetown University Medical Center. For each functional run, 89 images consisting of 50 contiguous axial slices covering the whole brain were acquired with the following parameters: TR = 3 s, TE = 30 ms, voxel size = 3 mm x 3 mm x 2.8 mm, in-plane resolution = 64 x 64, Flip angle = 90°.

**fMRI data analysis**

All fMRI and connectivity data preprocessing and analyses were carried out using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). After removing the first three
scans of each run to prevent T1 saturation effects, we ran several preprocessing steps: each subject’s functional data were slice-time corrected and realigned to the mean image; a magnetization-prepared rapid gradient-echo (MP-RAGE) sequence structural scan acquired during the same scanning session was then co-registered to the mean image; structural scans were warped and segmented into gray matter, white matter, and CSF regions-of-interest using the vbm8 toolbox; and functional and structural images were warped to standard MNI stereotaxic space and smoothed with a Gaussian kernel of full width at half maximum 8 mm. Participant data were examined for head motion artifacts. Participants whose overall data exhibited excessive head motion (>20% of images in the run exhibiting scan-to-scan motion beyond the 1 mm threshold) were removed from analysis. Global signal and time-points for which scan-to-scan motion exceeded 1 mm were used as regressors of no interest.

Data were analyzed in a block design for each subject using the general linear model. Statistical analysis at the first level involved generating within-subject parametric activation maps for the contrast of the Motion and Static conditions relative to baseline (Motion vs. Fixation, Static vs. Fixation) and for the direct contrast between the two conditions (Motion vs. Static). Stimulus onsets were modeled using the canonical SPM hemodynamic response function, and functional datasets were high-pass filtered with a cut-off of 128 s.

To distinguish the effects of sensory experience from the effects of language experience on coherent visual motion processing, the single-subject statistical maps generated at the first level for the voxel-wise contrast of Motion vs. Static were submitted to a two-way ANOVA at the second level (height: p<0.005 uncorrected, cluster: p<0.05 FDR corrected). We extracted percent signal change from significant clusters using MarsBar (Brett et al., 2002) to determine
the direction of effects revealed in the ANOVA. All coordinates are reported using MNI convention. Using the SPM Anatomy Toolbox (Eickhoff et al., 2005, 2007), the locations of the peaks of the activations were examined to estimate the most likely cytoarchitectonic area using the maximum probability map.

**Connectivity data analysis**

Preprocessed data were submitted to the CONN functional connectivity toolbox (15.e, Whitfield-Gabrieli & Nieto-Castanon, 2012) for seed-to-voxel analyses. First, data underwent several noise reduction steps that included regression of white matter and CSF ROI time series using aCompCor with five principal components (Behzadi et al., 2007); regression of six rigid-body head motion parameters as well as time-points for which scan-to-scan motion exceeded 1 mm; regression of the effects of our Fixation, Motion and Static blocks; and temporal high-pass filtering (f > 0.008 Hz) to reduce the effect of low-frequency drift.

At the first level, the residual time series associated with clusters surviving the ANOVA, described above, were individually submitted to a bivariate correlation for each subject. As the ANOVA revealed both a main effect of sensory experience and a main effect of language experience, we tested for where the deaf participants exhibited greater whole-brain connectivity with the significant cluster exhibiting a main effect of sensory experience, as well as where native users of English exhibited greater whole-brain connectivity with clusters exhibiting a main effect of language experience. For these analyses we submitted the single-subject statistical maps generated at the first level for the entire run (see Ganger et al., 2015) to two-sample, one-tailed t-
tests, Deaf > Hearing and English > ASL (height: $p<0.005$, uncorrected; cluster: $p<0.05$, FDR corrected).

**Results**

*fmri*

**Within-group Analyses**

Maxima coordinates and cluster information, including full description of cluster extent, for our within-group findings can be found in Table 2, with renderings of the whole-brain activations found in Figure 1.

*Hearing Native Users of English*

Whole-brain within-group analysis of activation for the contrast of interest (Motion > Static) in our hearing native users of English revealed significant activation in one large cluster in primary and association visual cortex with peak activation in left lingual gyrus (Brodmann Area [BA] 18), extending to bilateral V5/MT (Table 2, Figure 1A).

*Hearing Native Users of Sign Language*

We observed left hemisphere activation in two extrastriate cortical clusters, one in left middle occipital gyrus with peak in left cuneus (BA 18) extending to V5/MT, and one in left lingual gyrus (BA 18). Right hemisphere activation was observed in right middle occipital gyrus with peak in right cuneus (BA 19) extending to V5/MT, as well as in right middle frontal gyrus (BA 6) (Table 2, Figure 1B).
Figure 1: Whole-brain within-group functional activation for A) Hearing Native Users of English, B) Hearing Native Users of Sign Language, C) Deaf Native Users of English, and D) Deaf Native Users of Sign Language, voxel $p < 0.005$ uncorrected, cluster $p < 0.05$ FDR corrected. Activation up to 5 mm beneath the cortical surface is displayed.
Deaf Native Users of English

In the left hemisphere, activation was found in left superior occipital gyrus with peak in left cuneus (BA 18), in left middle occipital gyrus with peak in left middle temporal gyrus (BA 39; within and posterior to V5/MT), and in left inferior frontal gyrus with peak in precentral gyrus (BA 6). In the right hemisphere, deaf native users of English exhibited activation in right
superior occipital gyrus with peak in right cuneus (BA 19), right lingual gyrus (BA 18), right superior temporal gyrus with peak in right middle temporal gyrus (BA 39; within and posterior to V5/MT), and right inferior frontal gyrus with peak in right middle frontal gyrus (BA 8) (Table 2, Figure 1C).

*Deaf Native Users of Sign Language*

Our deaf signing group exhibited activation in left superior occipital gyrus with peak in middle occipital gyrus (BA 19) and extending to left V5/MT and left superior temporal gyrus (auditory association cortex). Additional activation was observed in right superior occipital gyrus with peak in middle occipital gyrus (BA 19), as well as in right lingual gyrus (BA 18). Further, activation in right superior temporal gyrus with peak in middle occipital gyrus (BA 19) extended to right V5/MT and to right auditory association cortex. Significant activation in frontal cortex was found in right middle (BA 6) and inferior frontal gyri (BA 45) (Table 2, Figure 1D).

In sum, our four groups exhibited bilateral activity in response to coherent visual motion (Motion > Static) in occipitotemporal cortices, including area V5/MT.

**Factorial Results**

Maxima coordinates and cluster information, including full description of cluster extent, for our factorial findings can be found in Table 3, with renderings of the whole-brain activations found in Figure 2.

Whole-brain factorial analysis of activation for the contrast of interest (Motion > Static) revealed a significant main effect of Sensory Experience in the right temporal lobe in the STG
Here deaf participants (native users of English and ASL combined) exhibited greater activation than hearing participants (native users of English and ASL combined). We also observed a significant main effect of Language Experience in left ventral temporal cortex, extending to the fusiform, lingual and inferior temporal gyri with peak in left parahippocampal gyrus (BA 19), as well as in right inferior frontal gyrus (BA 9) extending to right precentral gyrus (Table 3, Figure 2). Within these clusters, native users of English (deaf and hearing combined) exhibited greater activation than native users of ASL (deaf and hearing combined). We did not observe a significant interaction between Language Experience and Sensory Experience.

Table 3. MNI Coordinates of maxima of functional differences for whole-brain ANOVA.

<table>
<thead>
<tr>
<th>MNI Coordinates</th>
<th>Peak Anatomical Region</th>
<th>Voxel Count</th>
<th>Peak BA</th>
<th>Peak F</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main effect of sensory experience</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaf &gt; Hearing</td>
<td>x=68, y=-12, z=6</td>
<td>R superior temporal gyrus</td>
<td>1028</td>
<td>42</td>
</tr>
<tr>
<td><strong>Main effect of language experience</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>English &gt; ASL</td>
<td>x=-22, y=-57, z=-9</td>
<td>L parahippocampal gyrus&lt;sup&gt;a&lt;/sup&gt;</td>
<td>611</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>x=51, y=0, z=27</td>
<td>R inferior frontal gyrus&lt;sup&gt;b&lt;/sup&gt;</td>
<td>458</td>
<td>9</td>
</tr>
<tr>
<td><strong>Interaction: sensory experience x language experience</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No significant clusters</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<sup>a</sup>Cluster extends into the left lingual, fusiform, and inferior temporal gyri

<sup>b</sup>Cluster extends into the right pre- and postcentral gyri
Figure 2: A) Significant clusters exhibiting a main effect of sensory experience, Motion > Static, voxel p < 0.005 uncorrected, cluster p < 0.05 FDR corrected. Activation up to 5 mm beneath the cortical surface is displayed. B) Average percent signal change for our deaf participants (orange) and our hearing participants within these clusters, separately. Error bars indicate standard error. C) Significant clusters exhibiting a main effect of language experience, Motion > Static, voxel p < 0.005 uncorrected, cluster p < 0.05 FDR corrected. D) Average percent signal change for native users of ASL (red) and our native users of English (yellow) within these clusters, separately. Error bars indicate standard error.
**Functional Connectivity**

Maxima coordinates and cluster information, including full description of cluster extent, for our connectivity findings can be found in Table 4, with renderings of the whole-brain activations found in Figures 3 and 4.

Our factorial analysis showed a main effect of Sensory Experience in the right superior temporal gyrus (Deaf > Hearing) and a main effect of Language Experience in left parahippocampal and right inferior frontal gyri (English > ASL). Our primary goal for connectivity analysis was to further characterize the nature of these activation differences. In particular, we were interested in characterizing the functional connectivity of these areas in the Deaf relative to the Hearing groups as a way to test if there was a relationship across sensory modalities. As such, we conducted whole-brain connectivity analyses for the contrast of Deaf greater than Hearing seeded by the right STG cluster which exhibited a main effect of sensory experience, described above. For this right temporal lobe cluster we found stronger connectivity with numerous areas in the Deaf compared to Hearing groups: left and right anterior insula extending into inferior frontal gyri, with peaks in left and right putamen, respectively; left middle frontal gyrus with peak in precentral gyrus (BA 6); bilateral anterior cingulate and paracingulate gyri with peak in right cingulate gyrus (BA 32); bilateral supramarginal gyri with peaks in left postcentral gyrus (BA 40) and right inferior parietal lobule (BA 40); right lateral occipital cortex with peaks in superior occipital gyrus (BA 19) and superior parietal lobule (BA 7); bilateral calcarine cortex with peaks in left precuneus (BA 7) and right cuneus (BA 17); and left cerebellar lobules VIII and VIIb, with peak in left uvula. These are depicted in Table 4 and Figure 3.
Table 4. MNI Coordinates of maxima of connectivity differences for seed-to-voxel between-group comparisons of deaf and hearing participants.

<table>
<thead>
<tr>
<th>MNI Coordinates</th>
<th>Peak Anatomical Region</th>
<th>Voxels</th>
<th>Peak BA</th>
<th>Peak T</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Deaf &gt; Hearing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Seed: R temporal lobe cluster</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-22  10  -6</td>
<td>L lentiform nucleus(^a)</td>
<td>2300</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>-46  0   32</td>
<td>L precentral gyrus(^b)</td>
<td>264</td>
<td>6</td>
<td>3.9</td>
</tr>
<tr>
<td>-56  -38 56</td>
<td>L postcentral gyrus(^c)</td>
<td>316</td>
<td>40</td>
<td>4.2</td>
</tr>
<tr>
<td>-22  -54 42</td>
<td>L precuneus(^d)</td>
<td>349</td>
<td>7</td>
<td>4.7</td>
</tr>
<tr>
<td>-16  -74 44</td>
<td>L uvula(^e)</td>
<td>449</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>24   14  -6</td>
<td>R lentiform nucleus(^f)</td>
<td>7999</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>8    16  34</td>
<td>R cingulate gyrus(^g)</td>
<td>1367</td>
<td>32</td>
<td>4.2</td>
</tr>
<tr>
<td>60   -34 38</td>
<td>R inferior parietal lobule(^h)</td>
<td>506</td>
<td>40</td>
<td>5.1</td>
</tr>
<tr>
<td>32   -76 26</td>
<td>R superior occipital gyrus(^i)</td>
<td>411</td>
<td>19</td>
<td>4.7</td>
</tr>
<tr>
<td>28   -62 48</td>
<td>R superior parietal lobule(^j)</td>
<td>404</td>
<td>7</td>
<td>3.9</td>
</tr>
<tr>
<td>14   -86 4</td>
<td>R cuneus(^k)</td>
<td>4146</td>
<td>17</td>
<td>4.9</td>
</tr>
<tr>
<td><strong>English &gt; ASL</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Seed: L ventral temporal cluster</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2    36  52</td>
<td>R superior frontal gyrus(^l)</td>
<td>597</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td><strong>Seed: R inferior frontal cluster</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>*No significant clusters*</td>
<td></td>
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</tr>
</tbody>
</table>

\(^a\)Cluster extends into left insular cortex (502 voxels), frontal operculum (252 voxels), orbitofrontal cortex (166 voxels), and pallidum (102 voxels).

\(^b\)Cluster extends into left middle frontal gyrus (113 voxels).

\(^c\)Cluster extends into left supramarginal gyrus (237 voxels).

\(^d\)Cluster extends into left superior parietal lobule (205 voxels) and lateral occipital cortex (89 voxels).

\(^e\)Cluster extends into left cerebellar lobules VIII (253 voxels) and VIIb (134 voxels).

\(^f\)Cluster extends into bilateral thalami (850 voxels), brainstem (445 voxels), right striatum (656 voxels), insula (535), planum polare (144 voxels), precentral gyrus (370 voxels), middle (235 voxels) and inferior frontal gyri (529 voxels), orbitofrontal cortex (392 voxels), temporal pole (183 voxels), inferior temporal gyrus (115 voxels), left fusiform (312 voxels) and lingual gyrus (69 voxels), cerebellar lobule VI (335 voxels) and Crus I (157 voxels).

\(^g\)Cluster extends into bilateral anterior cingulate (615 voxels) and paracingulate cortices (343 voxels).

\(^h\)Cluster extends into right supramarginal gyrus (422 voxels).

\(^i\)Cluster extends into right supramarginal gyrus (362 voxels).

\(^j\)Cluster extends into right lateral occipital cortex (205 voxels) and superior parietal lobule (108 voxels).

\(^k\)Cluster extends into bilateral occipital pole (825 voxels) and intracalcarine cortex (477 voxels), left lingual gyrus (193 voxels), lateral occipital cortex (415 voxels), right fusiform (427 voxels) and lingual gyrus (193 voxels), and cerebellar lobule VI (125 voxels).

\(^l\)Cluster extends into the left superior frontal gyrus (65 voxels).
**Figure 3:** Whole brain connectivity with R temporal lobe cluster, two-sample, one-tailed t-test, Deaf > Hearing, voxel $p < 0.005$ uncorrected, cluster $p < 0.05$ FDR corrected. Connectivity values up to 5 mm beneath the cortical surface is displayed.

**Figure 4:** Whole brain connectivity with L ventral temporal cluster, two-sample, one-tailed t-test, English > ASL, voxel $p < 0.005$ uncorrected, cluster $p < 0.05$ FDR corrected. Connectivity values up to 5 mm beneath the cortical surface is displayed.
Whole-brain connectivity analyses for the contrast of English greater than ASL were conducted with the left ventral temporal and right inferior frontal clusters as seed regions. The left ventral temporal cluster exhibited greater connectivity with bilateral superior frontal gyri (Table 4, Figure 4). We did not observe any significant differences in functional connectivity with the right inferior frontal cluster.

Discussion

The goal of this investigation was to identify experience-dependent plasticity in deaf and hearing adults in brain regions involved in visual motion processing, specifically with respect to sensory experience (hearing versus deaf), language experience (native use of English versus native use of ASL), and any interactions thereof. We report two principal findings: First, a two-by-two ANOVA revealed a main effect of sensory experience such that deaf adults, irrespective of whether they were native users of ASL, exhibited greater activity in the right STG (secondary auditory cortex) during a visual motion processing task. Further, there was greater functional connectivity in the deaf relative to the hearing groups between this cluster and early visual cortex. These results demonstrate clear cross-modal plasticity following a life-long history of deafness. The second principal finding was a main effect of Language Experience such that native users of English exhibited greater activation in left ventral temporal and right inferior frontal cortices relative to native signers during a visual motion processing task. As such, language experience has an impact on brain regions that process coherent visual motion, but this effect is not within canonical dorsal visual regions and, further, is not specific to deaf signers (i.e. we did not observe an interaction between sensory and language experience). We also observed
greater functional connectivity in deaf compared to hearing adults between the right superior temporal cortex and bilateral cerebellar, occipital, inferior parietal, and insular/inferior frontal cortices. From this it is clear that the re-organization following deafness involves cortico–cortical connections between auditory and visual areas, as described by Shiell et al. (2014), but also between auditory and association cortices. Differences in connectivity related to language experience were less pronounced than those related to sensory experience.

**Cross Modal-Plasticity Following Deafness in STG**

Studies of the impact of deafness on the animal brain have shown reliable cross-modal plasticity of functional response as well as enhanced performance in non-deprived sensory perception. Work in ferrets has shown that surgical unilateral deafferentation of the auditory nucleus (medial geniculate nucleus, MGN) in conjunction with ablation of the superior colliculus and visual cortical areas 17 and 18 induces retinofugal innervation of the MGN, as well as visually responsive cells in superior temporal regions, including primary auditory cortex, as measured by single-unit recordings (Roe et al., 1992; Sur et al., 1988). Cross-modal reorganization in post-natally ototoxicity deafened cats has been shown to occur in the anterior auditory field (part of core auditory cortex). Meredith and colleagues (2011) used single-unit recordings to establish that neurons in the anterior auditory field were responsive to somatosensory and visual, but not to auditory, stimulation. These visually responsive cells displayed preferences for motion direction and velocity. Further, congenitally deaf cats have displayed superior localization in the peripheral visual field as well as superior motion detection compared to hearing cats (Lomber et al., 2010). Lomber and colleagues (2010) demonstrated that
these enhanced visual abilities were mediated by reorganized auditory cortex, as deactivation of the posterior auditory field and dorsal zone of auditory cortex, through cortical cooling, led to the elimination of the peripheral localization and motion detection behavioral advantages, respectively. Based on these it has been hypothesized that human studies using brain imaging technology would reveal reallocation of auditory cortex to visual motion perception in the congenitally deaf. Indeed, several studies have supported this expectation (Fine et al., 2005; Finney et al., 2001; Sadato et al., 2005; Shiell et al., 2014; Vachon et al., 2013), with some showing activity during visual motion in the deaf directly in primary auditory cortex (Fine et al., 2005; Finney et al., 2001). Finney, Fine, and colleagues used an auditory task in their hearing participants to define an ROI representing auditory cortex by which to examine activity in their deaf participants. Based on cross-checking Talairach coordinates with probabilistic atlases, the authors determined that visually evoked activation within this ROI in their deaf participants corresponded with secondary and association auditory areas (BA 42 and 22, respectively). In addition, they noted that ‘several voxels’ (23% of the cluster) fell within primary auditory cortex (BA 41). In the present study, we did not take this auditory ROI approach. However, to better understand the proximity of the right STG activity we observed to A1, we used the SPM Anatomy Toolbox (Eickhoff et al., 2005, 2007) to determine the cytoarchitectonic make-up of the superior temporal cluster identified as exhibiting a main effect of sensory experience. For this atlas, TE1 is considered to be BA 41 and TE3 is BA 22. We found this cluster to have only 0.1% of its voxels assigned to primary auditory cortex (1 voxel covering 0.1% of TE 1.0). Fifty percent of voxels in this cluster were assigned to auditory association cortex (511 voxels covering 6.1% of area TE3).
**Prior Studies Examining Visual Motion Perception in the Deaf**

In the introduction we described some of the variability in the methods used to test for cross-modal experience-dependent plasticity in deaf adults during visual motion perception. Here we focus on some of the discrepancies in the results of these studies. First, we note that the in-scanner performance differences between our deaf and hearing groups are not consistent with behavioral outcomes reported in other studies. Prior studies comparing visual motion processing between deaf and hearing participants have either reported no differences in accuracy or reaction time for in-scanner tasks (Fine et al., 2005; Sadato et al., 2005; Shiell et al., 2014), or behavioral advantages in deaf participants over hearing participants (Bavelier et al., 2001; Neville et al., 1987a). In these instances, deaf participants were significantly faster and more accurate performances in detecting direction of motion in the visual periphery. Our task was designed to be simple enough that performance would be at ceiling across groups; it was therefore unexpected that our hearing participants exhibited significantly more accurate performance on the motion detection task than our deaf participants. As participants were instructed to maintain fixation on a central cross during all tasks, the behavioral differences we observed may reflect the advantages in motion detection observed in hearing relative to deaf participants when attention is oriented to the center of the visual field (Bavelier et al., 2001; Neville et al., 1987a). However, we did not indicate to our participants whether they should attend to the center or the periphery of the visual field during the motion task, though, so we cannot say whether the difference in performance that we observed is due to to this attentional effect.
Regarding findings from our ANOVA, the increased activation we observed in the right STG was specific to the perception of visual motion (Motion > Static). Notably, that Vachon et al. (2013) reported activation in this region (auditory association cortex, BA 21/22) to be present across visual tasks (coherent motion, form-from-motion, and static dots), but not for the contrasts of coherent motion or form-from-motion versus static. The authors suggested that this reflected an unspecified role of auditory cortex in visual processing, as opposed to a motion-specific role. Further, the observed rightward lateralization of this effect is consistent with previous findings in the deaf (Fine et al., 2005; Finney et al., 2001; Sadato et al., 2005; Shiell et al., 2014) and related studies in hearing participants which have found predominantly right-hemisphere temporal/parietal activation in response to sound motion (Baumgart et al., 1999; Griffiths et al., 1998; Zatorre et al., 2002). This asymmetry may reflect a right hemisphere preference for extracting information from longer integration windows (i.e. time windows sufficient for coherent motion perception), as put forth in Poeppel’s ‘asymmetric sampling in time’ hypothesis (2003). Interestingly, while our deaf group demonstrated a significant increase from the baseline condition (Static) in right STG, the hearing participants showed a decrease in activation in this region during visual motion perception relative to both Static and Fixation. In the hearing participants, this observation suggests a functional interplay between sensory modalities, wherein attention paid to one sensory modality leads to reduced activation in other sensory cortices (Haxby et al., 1994; Johnson & Zatorre, 2005; Laurienti et al., 2002; but see Shulman et al., 1997). Importantly, this is overridden in the deaf participants, who instead show heightened activity in right STG during perception of visual motion. This suggests that, in the deaf, auditory
cortex adopts the functional characteristics of visual cortex in response to visual coherent motion perception.

**Impact of Sensory and Language Experience on the Functional Organization of Visual Motion Perception**

While prior studies have reported STG activity in deaf participants during visual motion perception, these studies could not clearly attribute this difference to deafness or language experience due to the nature of the groups compared. The use of two hearing and two deaf groups with native ASL or native English experience addresses this question directly, and our findings determine that cross-modal activation of right STG in deaf participants during perception of visual motion is an effect of sensory experience. As mentioned in the introduction, Olulade and colleagues (2014) used this approach in a voxel-based morphometry (VBM) factorial analysis performed in the same group of participants as the current study. This revealed main effects of sensory experience on gray matter in similar areas to those reported here from our factorial functional activation analysis. In the VBM study, deaf participants exhibited greater gray matter volume (GMV) in right middle temporal gyrus, anterior to the right superior temporal functional cluster we observed in the present study. As a VBM study, however, these results did not speak directly to the mechanism underlying the brain matter differences observed. We cannot attribute these differences to a particular task, but our current findings suggest that these GMV differences between hearing and deaf participants may be related to the sensory-dependent functional differences in visual motion processing.
Though we have determined that cross-modal activation in right STG is due to sensory experience, we did observe an effect of language experience such that native users of English exhibited greater activation in left ventral temporal and right inferior frontal cortex for the contrast of Motion > Static than native users of ASL. The ventral temporal cluster is similar in location to the fusiform face area (Grill-Spector et al., 2004; Kanwisher et al., 1997), and studies of deaf and hearing native users of English have reported significant activation in left lingual and parahippocampal cortex during speech-reading (MacSweeney et al., 2001, 2002a). As the common experience with spoken language between our deaf and hearing native users of English is speech-reading, we suggest that the effect of language we observed in left ventral temporal cortex reflects associations formed between face and visual motion processing due to extensive experience with monitoring lip movement for language comprehension.

Regarding the effect of language observed in right inferior frontal cortex, studies using EEG (Neville et al., 1987a) and fMRI (Bavelier et al., 2001) have reported differences in hemispheric asymmetry of activation between deaf and hearing native users of ASL and hearing native users of English. Though Bavelier and colleagues only reported a rightward asymmetry of functional activation in hearing native users of English that was specific to area V5/MT, theirs was an ROI analysis that did not cover inferior frontal cortex. Our right inferior frontal finding may therefore reflect the rightward asymmetry of visual motion processing in native users of English.

It was unexpected that we did not observe an effect of language within area V5/MT in our functional analysis. Effects of language on motion-processing areas have been indicated in reports of sign language eliciting greater activation than spoken language in bilateral posterior
middle temporal gyri (MacSweeney et al., 2002c; Söderfeldt et al. 1997). These effects were found, however, in hearing native signers and deaf native signers who were proficient lip-readers during tasks of signed and spoken language perception. Thus, the involvement of area V5/MT may have been task-specific or an effect of bilingualism. Additionally, though Bavelier et al. (2001) reported an effect of language experience in area V5/MT during visual motion processing, we did not replicate this effect, even after conducting an ROI analysis centered upon V5/MT coordinates reported in that study. Bavelier and colleagues observed this effect in deaf and hearing signers relative to hearing non-signers, and it may not have borne out had deaf native users of Cued Speech been included. Alternatively, as the authors later suggested, this could have been an effect of language on the neural substrates of attention as opposed to visual motion perception (Brozinsky & Bavelier, 2004). However, the VBM analyses of gray and white matter from Olulade and colleagues (2014), mentioned above, revealed significant main effects of language experience (more GMV in right hemisphere motor planning regions in native signers, including right middle and inferior frontal gyri) and an interaction between sensory and language experience (less white matter volume in left hemisphere language regions in deaf signers). While those results reflect the impact of language experience on the brain, particularly that of a signed language, the present study suggests that functional the effects of language on regions underlying visual motion processing are distinct from structural effects. Whereas we observed greater activation in left ventral temporal and right inferior frontal cortices in native users of English relative to native users of ASL, Olulade et al. did not observe any areas of greater gray or white matter volume in users of English relative to users of ASL. Further, native users of ASL exhibited greater GMV than native users of English in right middle frontal gyrus,
and greater gray and white matter in right inferior frontal gyrus, anterior, lateral, and inferior to the right inferior frontal functional cluster we observed showing the opposite effect in the present study. Taken together, these studies indicate that there is not a direct relationship between structure and function in the context of neural reorganization following deafness and sign language experience.

*Functional Connectivity in Deaf Adults and in Deaf and Hearing Native Users of English*

Functional connectivity analyses did not reveal extensive differences related to language experience. There were no significant differences in whole-brain functional connectivity with our right inferior frontal cluster, and the only areas showing significant differences in connectivity with our left ventral temporal cluster were bilateral superior frontal gyri. Most notably, the differences in activation and connectivity attributed to experience with a signed language were outside of regions previously suggested to be affected by language experience (e.g., V5/MT). Again, these discrepancies emphasize the importance of a factorial approach in teasing apart the effects of sensory and language experience on visual motion processing.

As for the effect of sensory experience that we observed, the right superior temporal gyrus has been shown to be recruited during auditory motion processing in hearing adults (Baumgart et al., 1999; Lewis et al., 2000; bilateral STG in Thivard et al., 2000; Warren et al., 2002), suggesting that perhaps this region has been incorporated into and serves as an additional hub in the visual motion processing stream in deaf adults. Our analyses of functional connectivity allowed us to better understand the unique network activity potentially contributing to these functional differences in our deaf participants. Seed-to-voxel analyses with the right
STG cluster seed revealed that our deaf participants exhibited increased connectivity between this region and areas in the dorsal visual stream, including primary visual cortex and bilateral parietal cortices. In addition to these regions, right STG showed connectivity with bilateral anterior insula and the anterior cingulate cortex. Ding et al. (2016) observed a similar resting-state connectivity profile with right STG in deaf greater than in hearing adults. Because we removed task effects from our connectivity analyses, these findings indicate that the right STG has greater connectivity with the visual system in deaf adults in general, and that this relationship may be influenced by top-down attention/salience regions. The influence of these higher-order regions has been observed previously, as studies have reported a behavioral advantage (Bavelier et al., 2001; Neville et al., 1987b) as well as functional differences (Fine et al., 2005) in various visual perceptual tasks that involve allocation of attention. Studies of functional connectivity in the early blind have indicated reduced connectivity between occipital cortex and other sensory cortices (Burton et al., 2004; Liu et al., 2007; Yu et al., 2008), whereas in the deaf it has been shown to be greater than in hearing (Shiell et al., 2014), as we confirm here. Though studies of cross-modal reorganization in the blind have reported occipital functional activation during haptic or auditory tasks (Burton et al., 2002, 2004; Cohen et al., 1997; reviewed in Bock & Fine, 2014), it is suggested that this may be driven by higher-level frontal regions involved in attention rather than by lower-level primary sensory or auditory cortices. The connectivity with both primary visual cortex and higher-order cortices in the present study suggest that feed-forward as well as top-down mechanisms play a role.

Taken together, our findings suggest that sensory experience-dependent cross-modal plasticity plays a role in visual motion processing in deaf adults, and that this cortical
reorganization is manifest in right hemisphere STG. While it was previously unknown to what degree sign language experience influences this reorganization, by fully accounting for the effects of language and sensory experience, our findings clearly indicate that the observations in right temporal cortex can be attributed to deafness, and that the effects of language on the neural substrates underlying visual motion perception do not impact area V5/MT and canonical dorsal visual regions.
CHAPTER 4: CONCLUSIONS, LIMITATIONS, AND FUTURE DIRECTIONS

Overview

This thesis focuses on two empirical studies examining the effect of experience on the neural bases of coherent visual motion perception: the first tests the hypothesis that there are age-related differences in V5/MT activation in typically developing children and adults; the second tests the hypothesis that sensory deprivation in the auditory modality alters the neural correlates of coherent motion processing and examines the modulating role of language experience in this process. Specifically, the work presented in Chapter 2 examines the impact of age, and with that the impact of reading experience (which is greater in adults compared to children) on functional activation of and connectivity with area V5/MT during coherent motion processing. Chapter 2 was comprised of two studies: (1) a cross-sectional investigation of differences in brain activity and connectivity between children and adults, and (2) a longitudinal investigation of changes in brain activity and connectivity in children from 2nd through 3rd grade; this study also examined of the relationship between changes in reading ability and brain activity over this time period. The results of these studies provide the first insight into the development of brain activation during coherent motion processing, specifically within area V5/MT, and are followed by a discussion of factors affecting V5/MT development and methodological considerations necessary for future investigations. Further characterization of the effect of experience on the dorsal visual stream is
provided by the work in Chapter 3, which utilized a factorial design to test for the main effects of deafness and sign language use and their interaction on brain activation during coherent motion processing. Results presented from these analyses are the first to fully disambiguate the effects of ASL use from deafness on the functional anatomy of coherent motion processing in visual and auditory cortices. The study also involves characterization of the functional connectivity of these regions as a way to better understand the mechanisms of this cross-modal and experience-dependent plasticity.

The Cross-Sectional Study described in Chapter 2 demonstrated that the focus of activation in response to coherent visual motion within or near area V5/MT is likely to become less variable between subjects and be located more inferiorly and medially with increasing age, particularly in the right hemisphere. Further, we determined that the location of regions of interest used is critical, as we found that activation differences between children and adults within area V5/MT were contingent upon how we defined our V5/MT regions of interest. When we used foci of V5/MT activation reported from a study in adults (Watson et al., 1993) to define our bilateral regions of interest, we found that activation was less in children relative to adults, bilaterally. While this was consistent with findings from a similar study examining random motion processing in children and adults, when we investigated regions defined from foci of V5/MT activation in pre-adolescent children we no longer found differences between children and adults.

These findings dovetailed with results from the Longitudinal Study presented in this chapter: we did not observe any change in V5/MT activation from 2nd to 3rd grade independent of the analysis used (at the whole-brain level or using ROIs defined in adults or pre-adolescents),
but we did observe an inferior shift in right hemisphere V5/MT activation at the trend level between time points. V5/MT activation at our first longitudinal time point did not predict reading ability at the second time point, failing to provide evidence that dorsal stream function (as indexed by V5/MT activity) is a contributing factor to successful reading acquisition, as would be expected based on with the magnocellular deficit hypothesis of dyslexia. Nor did we observe any change in V5/MT activation between time points, failing to support a relationship between V5/MT activation and age/reading ability.

Returning to the Cross-Sectional Study, we found less activation in primary and secondary visual cortex as well as left posterior insula in children relative to adults in the whole-brain analysis. This study provides insight into differences in the brain’s response to coherent visual motion perception in the context of age and reading development.

The fMRI study presented in Chapter 3 used the same coherent motion processing task as the studies presented in Chapter 2 to investigate the effects of the altered sensory and language experiences associated with deafness on the brain’s response to coherent visual motion. Specifically, data were acquired from four groups of subjects while they performed the coherent motion and dot density detection tasks: hearing native users of English (hearing individuals born to two hearing parents), hearing native users of sign language (hearing individuals born to deaf parents, also referred to as children of deaf adults [CODAs]), deaf native users of English (deaf individuals born to two hearing parents, whose first and primary language is English), and deaf native users of sign language (deaf individual born to deaf parents). Factorial analysis of brain activation during the coherent motion task (greater than the static dot density task) revealed a significant main effect of sensory experience (Deaf vs. Hearing) as well as a main effect of
language experience (English vs. ASL). There was no Sensory x Language interaction. We found there to be a main effect of sensory experience in right hemisphere superior temporal cortex corresponding mostly to auditory association cortex in BA 42 (Deaf > Hearing), and a main effect of language experience in left ventral temporal and right inferior frontal cortex (English > ASL). This suggests that the cross-modal activation of right auditory cortex during coherent visual motion processing that has been consistently observed in the literature is a result of deafness, whereas experience with a signed language leads to differences in regions outside of canonical dorsal visual cortices during coherent motion processing.

To further characterize the effects on these regions, we examined where whole-brain functional connectivity was greater with the right superior temporal region for the deaf participants relative to hearing participants (users of English and ASL combined), as well as with the left ventral temporal and right inferior frontal regions for the native users of English relative to native users of ASL. Deaf participants (compared to the hearing participants) exhibited significantly greater connectivity between the right superior temporal lobe cluster and bilateral anterior insulae and inferior frontal gyri, bilateral cingulate cortex, left superior parietal lobule, right supramarginal gyrus, and ventral temporal cortex extending into the cerebellum. For the left ventral temporal cluster, native users of English (relative to native users of ASL) exhibited greater connectivity with bilateral superior frontal gyri. Together, findings from Chapter 3 indicate that language experience does impact the neural substrates of visual motion processing, while deafness specifically induces increased activity in right auditory cortex during coherent visual motion processing, and increases functional connectivity between auditory, visual, and higher order frontal regions.
Conclusions and Limitations

In the introduction to this dissertation (Chapter 1), we aimed to address unresolved questions concerning the development and plasticity of the dorsal visual pathway underlying perception of coherent visual motion. These questions were largely spurred by the ‘dorsal stream vulnerability’ hypothesis which posits that, due to its protracted development, the dorsal visual stream is more vulnerable to the impact of developmental perturbations and atypical experience. Bolstered by evidence of atypical dorsal stream function in developmental disorders (e.g., developmental dyslexia) and in the altered sensory and language experiences inherent in deafness, the nature of this ‘vulnerability’ was tenuous as a number of central questions had yet to be fully considered. Outstanding questions addressed in this dissertation include: How does the neural response to coherent visual motion processing, particularly within area V5/MT, differ in typical children? Is development of this system impacted by the extensive visual training that accompanies learning to read? How does deafness affect coherent visual motion processing? Does the use of a visuospatial language exert unique effects on coherent motion processing?

The final part of this dissertation will discuss the findings and limitations of studies presented in Chapters 2 and 3 as they pertain to the questions listed in the Introduction. These sections will be followed by future directions for the investigation of the development of the dorsal visual pathway and the neural response to coherent visual motion processing.
Development of area V5/MT is reflected in shift in location, not intensity, of activation over time.

The studies described in Chapter 2 identified an age-dependent difference in location of peak activation to coherent visual motion rather than differences in intensity of activation. As described above and more extensively in Chapter 2, our conclusions regarding developmental differences in area V5/MT were contingent upon how we defined our regions of interest. Klaver and colleagues (2008) justified their use of adult-derived regions of interest by providing similar patterns of activation between an ‘exemplary’ subset of adults and children (n = 2/group). Further, studies have shown that comparisons between adults and children using MRI and fMRI are valid, as structural differences observed between children and adults after spatial normalization to an adult template were not large enough to affect functional comparisons at standard image resolutions (Burgund et al., 2002; Kang et al., 2003). When integrated with findings reported in Chapter 2, although adult-derived regions of interest may be interrogating similar brain regions in adults and children, the issue could be that coherent motion elicits activation in children within a region that is different from that in adults, either because the same cortex is physically moved due to nearby anatomical changes that create a physical shift of the same tissue with age or because the neurons in a particular area change with age in terms of their functional dedication to motion perception. These options will be discussed below. A limitation of these studies is that, without longitudinal measures of cortical thickness or sulcal pattern matching (for further discussion, see below), we cannot directly track these areas of peak activation in order to characterize what is contributing to this inferior shift. As such, our interpretation relies on previously reported findings in the literature.
While speculative, one could envision how a structural shift in temporoparietal cortex could follow from the kind of anatomical changes reported in longitudinal studies of brain development using magnetic resonance imaging. Sowell et al. (2004) reported cortical thickening of bilateral posterior perisylvian regions in 5- to 11-year-old children, the expansion of which might cause shifts in the relative location of neighboring cortical areas, e.g. middle temporal cortex including V5/MT. Further corroboration of this explanation comes from the same group (Sowell et al., 2002), with a report that the posterior extent of the Sylvian fissure in the right hemisphere of adults is significantly more superior to that in children (with no differences in the left hemisphere). Sylvian fissure asymmetry increased with age, between children (7-11 years old), adolescents (12-16 years old) and adults (23-30 years old) and corresponded with concomitant age-related increases in temporoparietal gray matter density. Together, these findings suggest that the inferior shift in putative V5/MT with age corresponds with increased gray matter density within posterior temporoparietal cortex which contributes to the superior shift of the Sylvian fissure in adults, as reported by Sowell and colleagues (2002).

Another possibility regarding this shift is that it is the result of functional reorganization. Brain regions within or near the MT complex may respond differentially to coherent motion over time, such that coherent motion processing may preferentially activate a region in children that is superior to adults. As discussed in Chapter 2, according to the SPM Anatomy Toolbox (Eickhoff et al., 2005, 2007), coordinates of peak activation were on average assigned to different cytoarchitectonic regions between children and adults. Granted, the cytoarchitectonic probability maps developed by Eickhoff and colleagues were defined in adult brains, so this could reflect a mislabeling of child peaks based on developmental differences in the absolute location of
cortical regions. However, there is evidence from developmental studies of the ventral visual pathway, specifically face processing, to support there being developmental shifts in regional functional activation. Gathers and colleagues (2004) reported differences in the neural correlates of face processing between younger children (5-8 years old), older children (9-11 years old) and adults. While all groups showed preferential activation for faces within ventral visual cortex, the authors observed an anterior shift in face processing with age, such that younger children showed face-preferential loci in posteroventral occipital cortex, while older children and adults showed this activation near the classical temporal fusiform face area. The authors suggested that this difference was due to functional shifts in the neural architecture of the ventral stream to accommodate maturation of nearby neural pathways and connections. Similar findings were reported by Golarai and colleagues (2007, 2010) wherein the authors observed age-related increases in the extent of face-preferential activation in fusiform regions, with the extent of expansion into surrounding cortex correlating with face recognition memory.

In the context of the empirical work presented in Chapter 2 of this dissertation, shifts in coherent visual motion-related activation over time continue past 8 years old (the average age of our children in the Cross-Sectional Study). Using adult-based regions of interest should be approached with caution in future studies comparing children and adults. Differences in activation between adults and children may be due to structural or functional maturation of nearby structures, but we did not find a significant correlation between age and peak location, nor between change in age and change in peak location in the studies presented in Chapter 2. This shift may also be experience-dependent (akin to correlations between the extent of face-related activation and face recognition memory [Golarai et al., 2007, 2010]). As development of
the dorsal visual pathway has been found to be ‘vulnerable’ to experience-dependent plasticity, subsequent questions addressed in this dissertation pertained to the extent to which different experiences impact dorsal visual pathway function.

**Does age or reading experience shape V5/MT response to coherent visual motion?**

Behavioral correlations presented in Chapter 2 did not reveal evidence of correlations between V5/MT activation in children in 2nd grade and their reading ability in 3rd grade. This was unexpected, as much has been made of previously observed relationships between reading ability and V5/MT activation in people with dyslexia, leading to the expectation that V5/MT activity would predict later reading. For instance, neuroimaging studies have reported reduced activation in area V5/MT in dyslexics compared to their typically reading peers while performing psychophysical tasks designed to target the dorsal visual stream, including coherent motion perception (Eden et al., 1996, Demb et al., 1997, 1998b). These activation differences were reported to represent the magnocellular impairments thought to be responsible for behavioral differences between dyslexic and age-matched typical readers during performance of similar tasks (Cornelissen et al., 1995; Edwards et al., 2004; Everatt et al., 1999; Gibson et al., 2006; Hansen et al., 2001; Lovegrove, 1980; Pammer & Wheatley, 2001; Pellicano & Gibson, 2008; Raymond & Sorenson, 1998; Wilmer et al., 2004; Witton et al., 1998; though see Skottun, 2016).

The studies presented in Chapter 2 were aimed in part to address the question of whether these differences come about as a result of differences in reading experience between typical readers and those with dyslexia, as opposed to representing the etiology of dyslexia itself. Support for the former comes from Olulade et al. (2013b), in which they demonstrated that V5/MT activity
in response to visual motion perception differed between age-matched dyslexic and non-dyslexic children, but critically was the same when the dyslexic sample was compared to reading level-matched controls. Further, Olulade and colleagues went on to demonstrate significant increases in V5/MT activity in dyslexic children after undergoing an 8-week reading intervention (but saw no significant differences after an 8-week math intervention). Together these studies suggest that dorsal stream deficits in dyslexia result from impoverished reading experience as opposed to causing it. However, in a longitudinal sample of typically developing children, we found no evidence to suggest that changes in reading ability are concomitant with changes in coherent motion-related V5/MT activity. Additionally, we did not find that V5/MT activation predicted future reading ability, as the magnocellular theory of dyslexia would suggest. This could suggest that there is only a relationship between reading ability and dorsal stream function in people with dyslexia, possibly stemming from genetic or developmental factors that are unique to that population. Our null results could also indicate limitations in our study design. As Kevan & Pammer (2009) suggested that coherent motion is only assimilated into the reading network once reading skills become more sophisticated, it could be that our reading measures (reading fluency, single- and pseudoword reading accuracy) were not adequate to capture ‘sophistication’ of the children’s reading ability. Additionally, while differences in measures of in-scanner task accuracy between children and adults in our cross-sectional study would suggest that the children were not yet performing at adult levels, without a measure of coherent motion sensitivity in our subjects, we cannot determine how differences in activation (or the lack thereof) were related to relative levels of coherent motion sensitivity between our groups.
**Deafness and language experience induce functional reorganization of response to coherent visual motion**

In the functional response to coherent visual motion, the right posterior superior temporal cortex (in auditory association areas, greater activation in deaf relative to hearing subjects) demonstrated a main effect of sensory experience. Additionally, consistent with previous reports, connectivity between right superior temporal and visual cortices was enhanced in the deaf relative to hearing subjects (Shiell et al., 2014), as well as between right superior temporal cortex and anterior insula and anterior cingulate cortices (Ding et al., 2016). Left ventral occipital and right inferior frontal cortex (greater activation in native users of English than native users of ASL) demonstrated a main effect of language experience. Functional connectivity between left ventral temporal and bilateral superior frontal regions was enhanced in native users of English relative to native users of ASL.

We did not, however, find any effects of sensory or language experience on V5/MT response to coherent visual motion. Previous studies from Bavelier et al. (2000, 2001) reported enhanced activation in area V5/MT in deaf subjects relative to hearing. Though measured in response to coherent visual motion, these differences in activation were attributed to differential effects of attention between groups. Enhanced activation of area V5/MT in deaf relative to hearing subjects was observed when subjects were instructed to attend to the periphery of the coherently moving stimulus while maintaining central fixation (Bavelier et al., 2000, 2001). This effect was reversed (Hearing > Deaf; Bavelier et al., 2001) or eliminated (Hearing = Deaf; Bavelier et al., 2000) when subjects were instructed to attend to motion at the center of the stimulus. As a result of our task requiring central fixation with no instruction as to where in the
visual field participants should direct their attention, this discrepancy between our findings and those previously reported is likely due to different effects of attention between tasks and represents a limitation of our analysis in being able to address all reported effects of deafness on coherent motion processing.

Leftward laterality of V5/MT activation attributed to experience with a visuospatial signed language has been reported, based on findings of greater left V5/MT activation than in right V5/MT in deaf and hearing signers, as opposed to a rightward laterality in hearing non-signers (Bavelier et al., 2001). In the analyses presented in Chapter 3, we did not observe greater activation in left V5/MT as a main effect of language experience. While we used the approach of whole-brain analysis, Bavelier and colleagues utilized regions of interest, which may have provided the increased statistical power necessary to observe this effect (though we did not find statistically significant activation within ROIs centered on V5/MT coordinates reported in their study).

The most important difference between the analyses presented in Chapter 3 and previous investigations into the effect of deafness and language experience on the neural substrates of coherent motion processing is that, with our four participant groups, we were able to fully disambiguate the effects of both factors. This, in addition to our longitudinal and cross-sectional studies of dorsal visual development presented in Chapter 2, represent significant contributions to the discussion of dorsal stream development and plasticity by 1) providing the first study on the neural substrates underlying coherent motion processing (particularly that of area V5/MT) in children (compared with adults), 2) examining V5/MT activity in the context of changes in reading in typically developing children, 3) determining that language experience (with ASL)
does not exert an effect on area V5/MT, as has been previously reported, and 4) demonstrating that activation of auditory cortex during visual motion processing is an effect of sensory experience (i.e. deafness) and is driven by greater connectivity with visual and higher level frontal regions.

**Future Directions**

Future studies should seek to address the limitations discussed above. This final section of the dissertation provides suggestions for how to do so. For instance, more longitudinal neuroimaging studies of dorsal stream development and its response to coherent visual motion are needed. In addition to functional brain imaging, such studies would benefit from the incorporation of quantitative structural measures. This combined approach would allow investigators to co-localize individual peaks of activation to the underlying neuroanatomy provided by structural images of higher spatial resolution. Thus, longitudinal quantification of changes in volume, thickness, sulcal pattern, and/or relative location can be tracked in addition to changes in activation over time. Together, these approaches would address the ambiguity regarding the underlying cause of peak activation differences between children and adults observed in Chapter 2. Additionally, future longitudinal studies that incorporate a larger number of time points across a larger age span can further clarify the time frame within which developmental shifts in V5/MT occur, and when V5/MT activation and location reach adult levels. Behavioral measures of more advanced reading ability would provide additional opportunity to characterize the relationship between dorsal stream development and reading ability.
Though not mentioned above, studies of structural brain development have reported different developmental trajectories between males and females. Whereas males have typically larger brains (reflected in greater volumes of gray and white matter, globally and locally), females typically reach peak brain volumes earlier than males (see Lenroot & Giedd, 2006 for review). The studies presented in Chapter 2 did not have the statistical power necessary to include analyses of sex differences in V5/MT development and relationship with reading. Future studies should address potential sex differences in development of coherent motion processing and V5/MT so as to determine whether these are contributing to the varied ages at which coherent motion processing has been reported to reach maturity.

The rightward asymmetry of the findings presented in this dissertation is striking (e.g., significant activation of right, and not left, V5/MT in children at the whole-brain level, inferior shift in right V5/MT developmentally, effect of deafness in right auditory cortex), and would be interesting to address in future studies. Whether this is due to the right hemisphere being more tuned to global processing could be addressed by the utilization of visual motion tasks that emphasize global versus local attention within the visual field. Or whether this is due to unique patterns of connectivity within the right hemisphere during visual motion processing can be investigated through further analyses of functional connectivity, comparing the left and right hemispheres.

Finally, regarding the functional connectivity observed in deaf subjects relative to hearing subjects: while connectivity analyses presented in Chapter 3 identified unique patterns of covariance between regions, future investigations into the differences in effective connectivity between these regions can provide insight into whether these distinct ‘connections’ are being
driven by bottom-up or top-down processes. This approach would further clarify the nature of the functional reorganization that occurs following deafness, which may also inform the nature of vulnerability within this system.

Summary

The studies presented herein demonstrate the utility of functional neuroimaging and thoughtful study design in providing insight into the development and plasticity of the dorsal visual stream. This dissertation described two complementary studies: the first investigated the functional development of the neural substrates of coherent visual motion processing (e.g., V5/MT) using both a cross-sectional and longitudinal approach, and evaluated V5/MT activation in the context of reading ability, given that a relationship between the two has been the focus of some studies of developmental dyslexia; the second examined the effects of deafness and visuospatial language experience on coherent visual motion processing using a factorial analysis of hearing native users of English, hearing native users of sign language, deaf native users of English, and deaf native users of sign language. The former study reports that development of V5/MT in response to coherent motion is characterized by a shift in the location of peak response rather than change in intensity of response within this region, and that children show greater connectivity between V5/MT and local surrounding cortex than adults. This study further suggests that there is no relationship between V5/MT activity and later reading in typically reading children.

The second study examined the effects of neural reorganization following deafness and visuospatial sign language experience on the neural substrates of coherent motion processing. A
main effect of sensory experience was identified in right auditory association cortex, as well as an effect of language experience in left ventral temporal and right inferior frontal cortices, yet no sensory x language interaction, nor any effects on activation within area V5/MT. The region affected by sensory experience exhibited enhanced functional connectivity with an extensive network of regions including visual cortex, bilateral anterior insulae extending into inferior frontal gyri, anterior cingulate cortices, and parietal cortices.

Together, these findings help inform hypotheses of dorsal stream development and vulnerability by illustrating that regions within the dorsal visual pathway exhibit differences over time and with deafness, but that areas within this pathway (e.g. V5/MT) are not particularly influenced by written language (reading) or sign language experience.
APPENDIX

Comparisons between regions of interest and individually-defined group averages.

**Figure A:** Visualization of locations of Watson (green; MNI coordinates x, y, z: L -41, -72, -2; R 41 -69 -2) and Adolescent (red; MNI coordinates x, y, z: L -44, -78, 4; R 58, -60, 6) ROIs. ROI up to 5 mm beneath the cortical surface is displayed.

**Figure B:** Visualization of locations of Watson (green; MNI coordinates x, y, z: L -41, -72, -2; R 41 -69 -2) and Adolescent (red; MNI coordinates x, y, z: L -44, -78, 4; R 58, -60, 6) ROIs, Adult (blue; MNI coordinates x, y, z: L -46, -73, 6; R 49, -70, 4) and Children (gold; MNI coordinates x, y, z: L -45, -71, 10; R 50, -70, 9). Up to 5 mm beneath the cortical surface is displayed.
**Figure C:** Visualization of locations of Watson (green; MNI coordinates x, y, z: L: -41, -72, -2; R: 41, -69, -2) and Adolescent (red; MNI coordinates x, y, z: L: -44, -78, 4; R: 58, -60, 6) ROIs; T2 (blue; MNI coordinates x, y, z: L: -48, -72, 11; R: 53, -69, 12) and T1 (gold; MNI coordinates x, y, z: L: -49, -74, 7; R: 49, -70, 6). Up to 5 mm beneath the cortical surface is displayed.

**Figure D:** Visualization of locations of T2 (green; MNI coordinates x, y, z: L: -48, -72, 11; R: 53, -69, 12) and T1 (red; MNI coordinates x, y, z: L: -49, -74, 7; R: 49, -70, 6) ROIs; Adult (blue; MNI coordinates x, y, z: L: -46, -73, 6; R: 49, -70, 4) and Children (gold; MNI coordinates x, y, z: L: -45, -71, 10; R: 50, -70, 9). Up to 5 mm beneath the cortical surface is displayed.
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