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Contribution of Magnocellular and Parvocellular Pathways to Visual Attention

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CONTRIBUTION OF MAGNOCELLULAR AND PARVOCELLULAR PATHWAYS TO VISUAL ATTENTION

by

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CONTRIBUTION OF MAGNOCELLULAR AND PARVOCELLULAR PATHWAYS TO VISUAL ATTENTION

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PSYCHOLOGY

ABSTRACT

Troxler Fading (TF) is a visual phenomenon in which a peripheral stimulus fades from awareness. TF occurs over tens of seconds and is asymmetric across the peripheral retina in which performance is better on the horizontal than vertical meridian. The mechanisms of TF are uncertain, but there appears to be both cortical and subcortical components. The purpose of this dissertation was to examine the contribution of both magnocellular and parvocellular pathways to visual attention via healthy and impaired performance after simulated focal lesions created by repetitive Transcranial Magnetic Stimulation (rTMS). Nine healthy, right-handed subjects (*M* age=23.5) completed 3 primary tasks – TF, Texture Detection (TD) a PC task, and Motion Detection MD) an MC task – as well as a visual reaction time task. Both magnocellular and parvocellular processing was asymmetric across the peripheral retina similar to TF. The most comprehensive model for predicting TF included both magnocellular and parvocellular processing and visual reaction time. The rTMS study indicated lateralized effects for the visual tasks and contributed to the development of a complex visual model of TF.

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TABLE OF CONTENTS

Page

LIST OF TABLES

Table *Page*

LIST OF FIGURES

Figures *Page*

INTRODUCTION

COMPLEXITIES OF TROXLER FADING: EVIDENCE FOR CONTRIBUTIONS OF MAGNOCELLULAR, PARVOCELLULAR AND ATTENTIONAL PROCESSING

USING 1 HZ rTMS TO DISRUPT TROXLER FADING, PARVO AND MAGNOCELLULAR PROCESSING IN NORMAL SUBJECTS REVEALS LATERALIZED EFFECTS

INTRODUCTION

A German physiologist, I.P.V. Troxler, first observed in 1804 that a target located in peripheral vision fades from awareness when a central target is fixated for a sufficient length of time (typically from 5-20 seconds during nonstabilized fixation; Mennemeier, Chatterjee, Watson, Wertman, Carter, & Heilman, 1994). This phenomenon is now known as Troxler Fading (TF). Central targets will not fade from awareness during ordinary fixation unless the images are stabilized on the retina (Gerrits, 1978; Millodot, 1965). This finding helped establish that stimulus movement prevents image fading. Drifts and micro-saccades are sufficient to prevent image fading at the fovea, where receptive field sizes are relatively small, but not in the peripheral retina where receptive field sizes are larger. Hence, TF time is inversely proportional to retinal eccentricity such that fade time decreases as eccentricity increases (Olson, Tulunay-Keesey, & Saleh, 1993; Clarke, 1961). However, this relationship is not uniform throughout the peripheral retina.

One study indirectly indicated that TF was faster on the vertical than horizontal meridian since fading occurred shortly after motion adaptation, which was found to be 50% faster on the vertical meridian (Hunzelmann & Spillmann, 1984). Studies using naïve healthy subjects have found and replicated these TF asymmetries. Further, they used asymmetries as markers to test hypotheses about the nature of TF (Barrett, Mennemeier, Chatterjee, Fuhr, & Novack, 2002; Taylor-Cooke & Mennemeier, 2005). For example, while it may be posited that TF asymmetries are due to binocular summation or binocular

viewing, it was found that similar asymmetries exist in monocular as well as binocular viewing conditions (Taylor-Cooke & Mennemeier, 2005). TF asymmetries were also compared with asymmetries observed in studies of visual attention. For example, the visual search field has been referred to as the "field of attention" (Chaikin, Corbin, & Volkmann, 1962) and it is suggested that this field depends on an extrapersonal, attentional mechanism involving the ventral (parvocellular) visual pathway (Previc & Blume, 1993). When TF times are plotted across the retina, they have a shape similar, oval shape, to that of the visual search field (see Figure 1; Taylor-Cooke & Mennemeier, 2004; Chaikin et al., 1962; Previc & Blume, 1993). Overlap in the shape of these two fields could indicate that TF and visual search share a common processing pathway. However, current explanations concerning the locus of TF are conflicting.

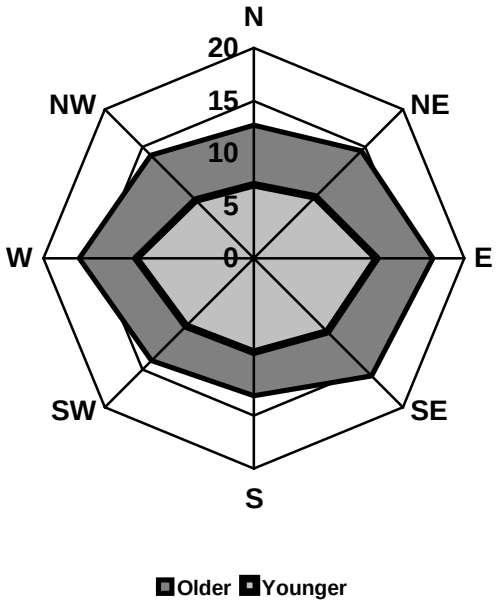

Figure 1. Mean TF fade times in seconds across the eight peripheral locations by group.

Some investigators posit that retinal ganglion cells are the locus of TF (Kotulak & Schor, 1986), whereas others implicate the lateral geniculate nucleus (Clarke & Belcher, 1962). In contrast to these studies, patient studies reveal a cortical contribution to TF. One study reported accelerated fading in the right hemispace of a patient with a left parietal-occipital tumor (Holliday, Kennard, & Ruddock, 1985). A larger case-series study (Mennemeier et al. 1994) found that fading was absent in patients with frontal lobe lesions and markedly accelerated in contralateral space in patients with parietal lobe lesions. In fact, some patients with parietal lesions reported fading of moving as well as stationary stimuli in peripheral vision. TF was also doubly dissociated in one patient with both a left parietal and right frontal lesion. She exhibited accelerated fading in her right visual field and absent fading in her left visual field.

Research has indicated that advanced age is associated with longer TF times, but not different TF asymmetries. In fact, TF times were consistently longer across all eight peripheral locations in an older group compared to a younger group (see Figure 1). The fact that TF increases with age may suggest that normal cortical changes across the lifetime contributes to this change thus suggestive of a cortical contribution to TF. It could be argued that age related visual changes would explain this finding; however, neither visual acuity nor contrast sensitivity contributed to the model during analyses (Taylor-Cooke & Mennemeier, 2005). Therefore, it can be presumed that the increased time cannot solely be answered by visual changes in older subjects.

Psychophysical studies have investigated the roles of magnocellular (MC) and parvocellular (PC) processing in vision. Livingstone & Hubel (1987) have argued that fading occurs too rapidly within the MC system because of its physiological properties of

high contrast sensitivity, fast temporal and low spatial resolution promoting rapid habituation. In contrast, they suggest the nearly opposite physiologic properties of the PC system resist image fading. This conceptualization of the roles of the MC and PC systems were criticized based on the use of equiluminant stimuli, which may compromise MC systems as well as PC systems (Schiller, Logothetis, & Charles, 1990a, 1990b). However, it is well established that the magnocellular pathway extends visual processing along temporal domains and habituates faster to stationary stimuli than the parvocellular system (Schiller et al., 1990b). If this is true then it is expected that the parvocellular system would have a stronger relationship to TF based on the length of time it takes for stimuli to fade.

A comprehensive psychophysical model of image fading, based on the fading of stabilized foveal images and viewed as a process of adaptation (Olson, Tulunay-Keesey, & Saleh, 1994) suggests that adaptation (or habituation) occurs in three stages. The first stage is an instantaneous scaling response to image luminance that is inversely proportional to background luminance. The second is a much slower process that involves the building of a negative afterimage which is presumably subtracted from the output of stage one. Stage three is a process similar to contrast adaptation. It allows for changes in contour threshold detection depending on luminance and contrast values. Whereas, the first stage of this model is thought to occur in the retina, the second is believed to involve the parvocellular pathway, and the third is believed to be cortical in origin. The model suggested by Olson et al. (1993) suggests an interaction between early and middle visual pathways and higher cortical functions.

Taken together, studies of TF implicate a neural system with both subcortical and cortical components (a processing pathway). Such studies also reveal convergence between TF and PC and MC processing, suggesting that these pathways may represent a common mechanism.

MC and PC Pathways

Both the MC and PC pathways originate from the retina as ganglion cells and project along parallel paths to specific areas of the lateral geniculate nucleus and then continue to the primary/striate cortex of the occipital lobe or area V1 (Brodmann's area 17). Up to this point, each pathway maintains distinct retinotopic maps. They then diverge from area V1 into separate extrastriate cortical regions; however, distinct anatomic segregation is lost in a complex system of interconnections and feedback projections (Bogousslavsky & Caplan, 2001).

Principle projections of the PC pathway course from area V1 through areas V2 and V4 towards the temporo-occipital region (Bogousslavsky & Caplan, 2001). This projection system is considered to be more specialized for object identification (Ungerleider, & Mishkin, 1982). Its physiological properties are specialized for high spatial resolution, low temporal resolution, and color (Livingstone & Hubel, 1987; Schiller, Logothetis, & Charles, 1990). As previously mentioned, owing to low temporal resolution and high spatial resolution (which actually work to resist image fading) only the PC system could account for image fading (habituation) over the course of 10s of seconds. If this is correct, then lesions that disrupt the PC functions should lead to accelerated TF because images cannot be sustained.

Specific regions of the human cortex have been mapped in fMRI studies that correspond to form/shape identification and are considered to be part of the PC pathway. Although several areas are activated within the posterior cortex, there are two main areas which appear to become strongly activated in processing form or shape. According to brain mapping research, one of the largest areas activated is the posterior inferior temporal gyrus (post-ITG). A second, smaller region is the middle fusiform gyrus (mid-FG; Denys, Vanduffel, Fize, Nelissen, Peuskens, Van Essen, & Orban, 2004). These two regions correspond to Brodmann's areas 37 and 19 respectively.

While MC projections may not fully account for TF, there are at least two ways in which the MC pathway might influence fading. Projections of the MC pathway course from area V1 through areas V2, V3, and V5 towards the posterior parietal and superior temporal cortex. The MC system is considered to be more specialized for processing motion perception (Ungerleider, & Mishkin, 1982; Bogousslavsky & Caplan, 2001). Its physiological properties are specialized for low spatial resolution and high temporal resolution (Livingstone & Hubel, 1987) and fast, low contrast motion (Schiller et al., 1990). Since the speed of information conduction is much faster and transient in the MC than PC system, image fading occurring over the course of many seconds is not expected to occur within the MC pathway (Livingstone & Hubel, 1987). However, feedback projections of the MC pathway to V1 (Bullier, 2001) might interrupt image fading in the PC pathway if stimulus movement is detected (in fact, this may be the principle reason why images do not fade under normal viewing conditions). If so, then lesions in posterior parietal and superior temporal cortex should lead to accelerated TF because these areas could no longer interrupt fading within the PC system through updating and refreshing images.

Secondly, the MC system might influence TF via its connectivity with the frontal lobe. Brodmann's area 46, the dorsalateral prefrontal cortex, has been found to have connections with the MC system (Buchel & Friston, 1997). Brodmann area 8 also receives input from the MC pathway (Barbas and Pandya, 1991). Therefore, in response to detecting motion, the MC system may inhibit regions of the frontal lobe that normally serve to habituate attention, over time, to non-novel stimuli. If so, then lesions of the frontal lobe should actually prolong or preclude fading because damage to these mechanisms may prevent attentional habituation.

Regions identified for motion detection in fMRI studies indicate that area MT (V5) projects into the inferior parietal lobule corresponding to the upper portion of Brodmann's area 39 and the posterior inferior portions of 7. When examining activated areas while viewing moving random dots, most activation was found in two regions: at the junction between the intraparietal sulcus and parieto-occipital sulcus and the posterior end of the dorsal lips of the intraparietal sulcus. Along with these regions in the posterior portion of the brain, the frontal eye fields were also activated (Orban, Fize, Peuskens, Denys, Nelissen, Sunaert, Todd, & Vanduffel, 2003), which supports the connectivity between the parietal lobe and frontal lobe.

Attention

The cortical regions mentioned temporo-occipital, posterior-parietal, superior-temporal, and dorsalateral prefrontal cortex are all components of the attentional systems that modify sensory experience (Behrmann, Geng, & Shomstein, 2004; Mesulam, 2000; Shipp, 2004). These systems can both "draw" attention to sensory stimulation and habitu-

ate attention. The parietal lobe is thought to identify relevant spatial stimuli and enhance attention towards that location; whereas distinct areas of the frontal lobe can both initiate and inhibit attention and action (Mesulam, 2000). Lesions in the parietal lobe are predicted to accelerate TF because they can impair one's ability to sustain attention, whereas lesions in areas of the frontal lobe that modulate MC and PC processing are expected to retard or prevent fading because they impair habituation and release those systems from inhibition.

Attentional modulation of vision is also posited to occur in the lateral geniculate nucleus (LGN). Directed attention facilitates visual processing in the LGN, which enhances responses to an attended stimulus in comparison to an ignored stimulus (Kastner & Pinsk, 2004). Once again the role of the parietal lobe in enhancing attention toward a location is supported. This indicates that higher visual processing must occur to direct the attention so that it may be enhanced at a lower level. If this were incorrect and the LGN was responsible for this enhanced attention, then it would occur regardless of whether the stimuli were attended or ignored. Furthermore, the LGN receives approximately 30% of its modulatory influence from the primary visual cortex, which in turn receives feedback projections from the parietal cortex, and another 30% of modulatory inputs from the thalamic reticular nucleus, which has been implicated in selective attention.

Two modes of modulatory influence are suggested. The first is a tonic influence, which relays constant information for processing in the visual system, and a burst mode, which consists of transient information with considerable distortion (Kastner & Pinsk, 2004). Should brain damage occur in a region that would disrupt the tonic modulatory influence in the LGN, we might expect faster fade times in TF since incoming informa-

tion is disrupted or distorted. Alternatively, damage to the parietal region may disrupt efferent and afferent information of the reticular formation. Since this system is posited to control the burst mode of the LGN, we might expect fading for moving stimuli since the transient information created by motion is no longer delivered to the system that would provide enhanced attention. This is posited since fMRI studies have indicated that during an attentional task both the ascending reticular activating system (a portion of the reticular formation) and the parietal region discussed above are activated (Kinomura, Larrson, Gulyas, & Roland, 1996).

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) involves the relatively painless delivery (at low frequency) of electromagnetic pulses to an area of cortex through the scalp. Repetitive TMS (rTMS) delivers trains of pulses to a specific area of the cortex and is inhibitory at 1 Hz when the duration is approximately 15 minutes (Wassermann, 1998), which is the proposed frequency and duration for this project. The electromagnetic pulse creates a spatially distributed voltage difference in an area under the coil. Whereas high frequency rTMS (> 1 Hz) results in excitation or depolarization of the neurons, low frequency rTMS (≤ 1 Hz) results in inhibition or hyperpolarization of the neurons (Liebetanz, Fauser, Michaelis, Czeh, Watanabe, Paulus, Frahm, & Fuchs, 2003). The use of a figure-of-eight coil results in a more focal stimulation directly under the area where the figure-of-eight meets.

Although seizures can be induced with rTMS, the risk appears to be greatly decreased or eliminated for low-frequency rTMS (1 Hz), even at durations greater than 15

minutes when following safety procedures developed by the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation (Wassermann, 1998). Furthermore, researchers have determined that rTMS is a safe procedure when following safety guidelines of intensity and frequency in regards to epilepsy (Ebert & Ziemann, 1999), cerebral hemodynamics (Pecuh, Evers, Folkerts, Michael, & Arolt, 2000), and cognition (Wassermann, 1998). A review of rTMS suggested the low-frequency rTMS used in this project is safe with no known adverse effects when established stimulation parameters are used (Tassinari, Cincotta, Zaccara, & Michelucci, 2003).

TMS and rTMS have been investigated in visual perception. Many studies have used single-pulse TMS, which creates phosphenes and disrupts visual processing only within a short time (measured in milliseconds) after stimulation (Kammer, Puls, Strasburger, Hill, & Wichmann, 2004). TMS also has been used to investigate motion detection, which provided evidence that the MC pathway can be disrupted when the parietal cortex is stimulated, causing motion perception deficits in the contralateral hemispace (Walsh, Ellison, Ashbridge, & Cowey, 1999). Furthermore, studies on rTMS have shown that stimulation to the right parietal cortex can simulate left neglect – unawareness of visual stimuli (Fierro et al., 2000; Hilgetag, Theoret, & Pascual-Leone, 2001). Another study found that subjects could not identify a target in the left hemispace, following rTMS of the right parietal lobe, when targets were presented to both hemispaces (Pascual-Leone et al., 1994). This effect is similar to double simultaneous extinction commonly seen in people with neglect. These findings suggest that rTMS can be used to simulate lesions capable of transiently disrupting visual attention and MC processing.

Specific Aims

The following manuscripts focused on investigating the questions brought up in previous studies. The following are the specific aims and hypotheses for the current studies.

Specific Aim 1: Determine whether spatial asymmetries, similar to those found in TF, also occur on tasks sensitive to PC and MC functions.

Hypothesis 1: TF, and PC and MC processing, are predicted to converge such that TF will take longer, and PC and MC processing will be more efficient (faster discrimination and detection) on the horizontal compared to the vertical meridian.

Hypothesis 2: PC task performance will be more predictive of TF time than MC task performance, because TF occurs within the PC pathway.

Specific Aim 2: Determine effects of localized cortical dysfunction on TF, PC, and MC tasks.

Hypothesis 1: Lesions that impair PC processing (temporo-occipital) will cause accelerated TF in contralateral space because the PC system will be less able to resist image fading and sustain attention to stimuli. Additionally, lesions that impair MC processing (superior temporal and posterior parietal) will also cause accelerated TF because the MC system will fail to interrupt fading and inhibit the process of habituation.

Hypothesis 2: Lesions in areas that habituate PC processing, those regions of the frontal lobes (Brodmann area 46) that receive projections from superior temporal and posterior parietal cortex, will lead to both an absence of TF and more efficient PC processing.

Manuscripts

It is the complex interconnectivity between TF, and MC and PC pathways, which we explored in the following studies. The first manuscript extends research investigating Troxler Fading (TF) asymmetries across the horizontal and vertical meridians. We posit TF to be a measure of visual attention. Although TF is well known to be asymmetric, we are unaware of any current research reporting similar asymmetries on MC and PC tasks. Tasks were created to specifically assess these processing pathways (Texture Discrimination and Motion Detection; Schiller et al., 1990) in the same visuospatial locations in which Troxler Fading has been investigated. In addition, the first manuscript also extends research attempting to elucidate the unknown neural mechanisms of image fading. Investigating this aspect of image fading was conducted by assessing prediction of TF by MC and PC processing and followed up by adding a reaction time task, a visual attention measure, to the model. The results of the first manuscript contributed to the proposal of an initial cortical description for visual attention processing.

The second manuscript is a progression both from the previous manuscript and existing research investigating the effects of lesion location on visual attention. Current literature on TF indicates a cortical contribution. Our study extended this research by using repetitive Transcranial Magnetic Stimulation (rTMS) to simulate lesions in a controlled fashion. Low-frequency rTMS is inhibitory and thus interrupts processing in a two cm diameter around the focal location. The study not only enhanced scientific knowledge about complex visual attention, but added to the initial model proposed in the first manuscript.

COMPLEXITIES OF TROXLER FADING: EVIDENCE FOR CONTRIBUTIONS OF MAGNOCELLULAR, PARVOCELLULAR AND ATTENTIONAL PROCESSING

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Complexities of Troxler Fading: Evidence for Contributions of Magnocellular, Parvocellular and Attentional Processing.

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Abstract

Troxler Fading (TF) refers to the fading of images in peripheral vision during prolonged central fixation. It is asymmetric across the peripheral retina. The mechanisms contributing to this phenomenon are uncertain. The current study examined how magnocellular (MC) and parvocellular (PC) processing contribute to TF. Nine, right-handed, healthy subjects (*M* age=23.5) completed 3 tasks – TF, Texture Discrimination (TD) a PC task, and Motion Detection MD) an MC task. MC and PC processing was asymmetric across the peripheral retina similar to TF. Performance on the PC task was most predictive of that on TF; however, MC processing also accounted for variance in TF. Simple reaction time during a vigilance test also added to the predictive model for TF indicating that attentional systems also mediate TF. A description of cortical visual processing is developed based on current data.

Complexities of Troxler Fading: Evidence for Contributions of Magnocellular, Parvocellular and Attentional Processing

A German physiologist, I.P.V. Troxler, first observed in 1804 that a target located in peripheral vision fades from awareness when a central target is fixated for a sufficient length of time (typically from 5-20 seconds during nonstabilized fixation: Mennemeier, Chatterjee, Watson, Wertman, Carter, & Heilman, 1994). This phenomenon is called Troxler Fading (TF). Central dioptic targets do not fade from awareness during ordinary fixation unless the images are stabilized on the retina (Gerrits, 1978; Millodot, 1965). This finding helped establish that stimulus movement prevents image fading. Drifts and micro-saccades are sufficient to prevent image fading at the fovea, where receptive field sizes are relatively small, but not in the peripheral retina where receptive field sizes are larger. Hence, TF time is inversely proportional to retinal eccentricity, such that fade time decreases as eccentricity increases (Olson, Tulunay-Keesey, & Saleh, 1993; Clarke, 1961). However, this relationship is not uniform throughout the peripheral retina.

Fading is asymmetric across the retina. Fade times are faster on the vertical than horizontal meridian. This finding modifies the tenant that fade time decreases with retinal eccentricity. A research study concerning motion adaptation to a spinning periodic disk found that the disk faded after coming to an apparent standstill and fading on the vertical meridian was 50% faster than on the horizontal meridian (Hunzelmann & Spillmann, 1984). This serendipitous finding was confirmed in a formal study of TF (Barrett, Mennemeier, Chatterjee, Fuhr, & Novack, 2002). These asymmetries are robust in young and

old subjects and they are not due to binocular summation (Taylor-Cooke & Mennemeier, 2005).

Several findings link TF with the parvocellular processing (PC). First, based on the physiological properties of the PC system, Livingstone & Hubel (1987) suggested that image fading must occur within the PC system because the MC system processes information too quickly to account for fading that occurs over 10s of seconds. Next, the shape of the visual search field is similar to that for TF (Chaikin, Corbin, & Volkmann, 1962; Previc & Blume, 1993; and Taylor-Cooke & Mennemeier, 2005). Visual search is posited to depend on an extrapersonal, attentional mechanism that involves processing within the ventral, visual pathway where the extrastriate PC processing is thought to course (Previc & Blume, 1993). Whereas the shape of the visual search field is described in terms of how far out stimuli can be detected and TF is measured in terms of how long it takes for images to fade; both results are consistent with PC processing. Visual search involves shape detection and TF is a measure of resistance to image fading which presumably occurs in the PC pathway. Thus, these two different tasks could share a common pathway that might explain greater efficiency along the horizontal than vertical meridian. However, identifying a common mechanism has not been straightforward as studies also show horizontal and vertical asymmetries for a variety of other tasks (i.e., contrast sensitivity and visual acuity; Carrasco, Evert, Chang, & Katz, 1995; Carrasco, Talgar, & Cameron, 2001; Rijsdijk, Kroon, & van der Wildt, 1980).

The locus of TF is unknown. Some investigators posit that retinal ganglion cells are the locus of TF (Kotulak & Schor, 1986), whereas others implicate the lateral geniculate nucleus (Clarke & Belcher, 1962). The most comprehensive theory posits a process

by which images are registered in the retina, matching cortical representations or "after-images" are formed, and the balance between sensory input and afterimages lead to habituation (Olson et al., 1994). This theory obviously puts image fading in the cortex. In fact, Mennemeier et al. (1994) demonstrated accelerated image fading in patients with parietal lesions and prolonged or absent fading in patients with lesions in frontal cortex. The implication of this study is the parietal cortex plays an important role in sustaining awareness for visual images; whereas the frontal cortex plays a role in habituating attention to redundant or non-novel sensory information. Together, these theories and research observations suggest TF is sustained by a neural system with cortical and subcortical components.

The current research study examined how asymmetries in TF correlate with asymmetries in PC and MC processing. Simple reaction time during a vigilance task was measured to learn how attentional processes contribute to TF. The physiological properties of the PC system include high spatial and low temporal resolution which may serve to resist image fading (Livingstone, & Hubel, 1987). The physiological properties of the MC system include high contrast sensitivity, fast temporal and low spatial resolution that promote very rapid processing which could not account for TF (Livingstone, & Hubel, 1987). If this is true, then we would expect to see a correlation between TF and performance on tasks sensitive to processing within the PC but not the MC pathway. Alternatively, it is possible that TF occurs in the PC pathway with input from the MC pathway (i.e., information about image movement detection that may prolong or prevent TF). In such a case, we would expect performance on both the MC and PC tasks to correlate with

TF and, like TF, we would expect to observe asymmetries with more efficient processing on the horizontal than vertical meridian.

Although MC and PC processing are commonly assessed using steady-pedestal and pulsed-pedestal tasks, these tasks are not conducive to examining asymmetries across the peripheral locations. Some research has shown asymmetries in MC and PC processing when comparing the upper vertical meridian to the lower vertical meridian (Carrasco et al., 2001; Carrasco, Giordano, & McElree, 2004; Liu, Heeger, & Carrasco, 2006; Skrandies, 1987; Talgar & Carrasco, 2002); however, we do not know of any previous study that examined either PC or MC processing in the peripheral retina. Livingstone and Hubel (1987) used equiluminant tasks to isolate functions of the PC pathway; however, both PC and MC processing are compromised during equiluminant conditions (Schiller, Logothetis, & Charles, 1991). We created tasks based on the types of functions that have been shown to be specific to PC and MC pathways in studies of rhesus monkeys (Schiller, Logothetis, & Charles, 1990; see Methods for descriptions of tasks). Schiller's study demonstrated texture discrimination to be specific for the parvocellular pathway such that monkeys with lesions restricted to the PC pathway were unable to perform the task. The same was true for motion detection when monkeys with lesions restricted to the MC pathway attempted the tasks. Therefore, we developed texture and motion detection tasks based on Schiller's description and results. It is important to note that TF is a task of visual habituation; whereas both the MC and PC tests involve visual detection (like visual search tasks). So, longer TF times are expected to correlate with quicker image detection as measures of processing efficiency for the habituation and detection tasks, respectively. Additionally, we expect performance on the PC task to predict performance on the TF

task if image fading occurs within the PC pathway. Finally, if attentional systems are involved in TF then reaction time is expected to also correlate with TF.

Method

Participants

Nine right-handed, healthy subjects (two women, six men, age range=22 to 27, *M* age =23.5), recruited at the University of Arkansas for Medical Sciences, completed the study. Two additional subject's (two men, *M* =34) data were discarded due to a change in parameters of the TF program (lighter background). All subjects were healthy, right-handed with no history of neurological illness, psychiatric disorders, or eyeglasses that were bifocal, trifocal, multifocal or monovision. Table 1 displays subject demographics. Power analyses were conducted on a pilot study, which indicated that ten subjects would be sufficient to provide power of 0.89 for our hypotheses. The Institutional Review Board of the University of Arkansas for Medical Sciences approved the study and IRB approval from the University of Alabama at Birmingham was obtained for the data use agreement and analyses. All subjects underwent an informed consent process and gave written consent.

Apparatus and Materials

All programs were created using the Visual Stimulus Generator (VSG2/4F; Cambridge Research Systems) and the stimuli were delivered on a Sony Trinitron (Multiscan 17seII) color monitor. Stimulus presentation was controlled by a GP7-500 Gateway computer. All responses were made on a response box connected directly to the computer. A Black and White Mini Camera (BD-108W-X), which can be used to view in darkness down to 0.003 Lux, was used to monitor fixation. Visual diagnostics were conducted with

the Pelli-Robson Contrast Sensitivity Chart from HS Clement Clarke International (1988) and a visual acuity card to assess acuity for the distance of the monitor from the subjects' eyes. The Wechsler Test of Adult Reading (WTAR), shown to be a valid estimate of IQ, was used to estimate IQ.

Tasks

Troxler Fading: The visual stimuli are dots subtending 0.23 degrees of visual angle. Dots were presented in peripheral vision at 19.61 degrees of visual angle. Dots are gray (luminance=14.6 cd/m^2), the central fixation point was yellow (luminance=96.71 cd/m^2), and the background screen was dark gray (luminance=0.57 cd/m^2). Dots appeared in random order across the eight visual locations and remained until the subject responded or the time-out limit (30 seconds).

Texture Discrimination: The visual stimulus was a field of dark gray, diagonal dashed lines (luminance=0.81 cd/m^2) presented on a light gray background (luminance=71.62 cd/m^2) with a red crosshair for fixation (luminance=21.28 cd/m^2). One of the eight locations had dashed lines perpedicular to dashed lines on the rest of the screen, which subtended 3.75 degrees of visual angle and was presented at 14.85 degrees of visual angle. Stimuli faded in at a constant rate from a blank screen. Subjects were asked to press the response button once they were able to disciminate the location of the target and then name the location.

Motion Detection: The visual stimulus was a screen of black random dots (luminance=0.1 cd/m^2), subtending 0.23 degrees of visual angle, on a gray background (luminance=4.30 cd/m^2) with a yellow fixation crosshair (luminance=96.71 cd/m^2). During trials, dots were presented at 14.85 degrees of visual angle. Random dots appeared all at

once over the entire screen. In one of the eight locations a group of dots began to move slowly and increased in distance of movement (pixels per second) at a constant rate until the location was identified.

Reaction Time (RT): The visual stimulus was a light gray dot (luminance=71.62 cd/m^2) subtending 1.15 degrees of visual angle, on a black background (luminance=0.1 cd/m^2). The stimulus was briefly presented at randomized variable rates (one to five second intervals) in the center of the screen.

Procedures

Tasks were counterbalanced across subjects and administered in a darkened room with a black shield surrounding the monitor to prevent glare and distraction from the examiner's monitor and movements. Subjects heads were secured in a head and chin rest 30.48 cm from the computer screen, which was parallel to their eyes and level with the pupils. All trials were randomly presented in blocks of eight over the eight peripheral locations (e.g., North, North East, East etc). Subjects responded by pressing a button on a response box. The number of trials used was determined based on pilot study results. Subjects completed eight practice trials and a specified number of test trials on each task as follows: 1) TF - 40 test trials, 2) Texture Discrimination - 48 test trials, 3) Motion Detection - 40 test trials. Trials were recycled when clear breaks in fixation occurred or an incorrect response was given.

Data Analysis

An Asymmetry Index (AI) was created to assess asymmetries across the vertical and horizontal meridians [AI=(N+S)-(E+W)]. The AI provided a difference between the two meridians such that a positive score means that it takes longer to respond to stimuli

on the vertical meridian and a negative score means that it takes longer to respond to stimuli on the horizontal meridian. Planned comparisons were conducted to assess differences between TF and TD and TF and MD performance. Since the main interest was assessing vertical versus horizontal differences, the oblique locations were not analyzed. Likewise, our previous studies did not indicate any differences across the horizontal meridian, so these were not analyzed either. In addition, our previous studies with TF have suggested the oblique locations resulted in performance between that of the vertical and horizontal meridian and did not differ from upper to lower locations. Therefore, the current study focused on the cardinal meridians where the greatest differences are located and can be more easily compared across tasks. Given prior research indicating differences between the upper and lower vertical meridian, comparisons were made across the vertical meridian for each task.

A regression analysis was conducted across all eight locations to investigate whether texture discrimination (posited to be a parvocellular processing task) could predict TF performance. Performance on motion detection (posited to be a magnocellular task) was added to the regression model to see assess whether it contributed significantly to the model. Finally, a post-hoc analysis was conducted after obtaining some anecdotal evidence regarding the contribution of attention to TF. Thus, reaction time was added to assess incremental variance.

Results

All subjects were similar in age, IQ, visual acuity and health, and education. See Table 1 for subject demographics and visual diagnostics.

Asymmetries were demonstrated on all three tasks. Motion detection task performance resulted in faster detection on the horizontal than vertical meridian [$t(8)=18.79$, $p<.0001$] as did performance on texture discrimination $t(8)=9.56$, $p<.0001$. In contrast, TF performance resulted in longer fade times on the horizontal compared to vertical meridian, $t(8)=9.02$, $p<.0001$(see Figure 1). The asymmetry index for both motion detection and texture discrimination were significantly different from the TF asymmetry index [$t(8)=29.04$, $p<.0001$ and $t(1)=28.00$, $p<.0001$ respectively]. No differences were found when comparing the upper vertical to the lower vertical meridian on TF [$t(8)=-1.12$, $p>.10$], texture discrimination [$t(8)=1.28$, $p>.10$], or motion detection ([$t(8)=1.65$, $p>.10$). Power analyses indicated a sample size of twelve would have provided sufficient power to detect a difference between the upper and lower vertical meridian on the motion detection task. However, texture discrimination would have required a sample size of 42 and TF would have required a sample size of 68. For our tasks these results indicate that the vertical asymmetries are more robust for motion detection.

Regression analyses indicated that texture discrimination significantly predicted TF performance, $F(1, 70)=12.03$, $p=.001$. However, texture discrimination performance alone only accounted for 15% of the variance. When motion detection was added the model improved prediction of TF and accounted for an additional 6% of variance [incremental $F(1, 69)=5.24$, $p<.05$]. Post-hoc analyses indicated adding reaction time as a measure of attention to the regression model improved prediction of TF by accounting for an additional 8% of variance [incremental $F(1, 68)=8.20$, $p<.01$].

Discussion

The purpose of this experiment was to assess whether MC and PC processing is asymmetric across the peripheral retina in a manner similar TF and whether texture discrimination performance predicts TF performance. This is the first study to our knowledge to assess performance on tasks designed to be sensitive to MC and PC processing in the far peripheral retina. Interestingly, performance on all tasks were similarly asymmetric. Image detection for both the PC and MC tasks was quicker along the horizontal than vertical meridian and image fading took longer on the horizontal than vertical meridian (see Figure 1). One way of interpreting these findings is that performance is more efficient along the horizontal than vertical meridian. Since TF is actually measuring resistance to image fading, the longer fade time for the horizontal than vertical meridian indicates the image is persisting longer, such that it resists habituation longer on the horizontal than vertical meridian. There is no readily apparent structural explanation of these asymmetries to our knowledge. For instance, the distribution of cone density varies across the retina, but does not specifically follow the pattern of task asymmetries described here (Curcio, Sloan, Kalina, & Hendrickson, 1990). Likewise, cortical magnification cannot explain the asymmetries since the magnification factor is approximately the same at a given retinal eccentricity (Howard & Rogers, 1995). It seems likely, therefore, that these asymmetries reflect the outcome of visual processing rather than structural differences across the retina.

As noted previously, some researchers have reported a difference on the vertical meridian in which stimuli are processed more efficiently on the lower vertical meridian (Carrasco et al., 2004; Liu et al., 2006; Skrandies, 1987). Our study did not produce this

result. In fact, the only task that came close to producing even a trend for more efficient processing on the lower vertical meridian was motion detection (p=.136). When the data are viewed in a plotted graph (see Figure 1), the visual difference across the vertical meridian is obvious even though it has not yet reached significance. Therefore, it is likely that a larger sample size would lead to a significant differences across the vertical meridian. Even so, the vertical meridian asymmetry is not as robust as the difference between the horizontal and vertical meridian.

Performance on texture discrimination, a PC task, predicted TF; however, performance on motion detection and reaction time significantly raised the total amount of variance accounted for to 29%. The most likely interpretation of this result is that TF may occur within the PC pathway but the MC pathway mediates fading. Since image movement across the retina retards and prevents TF, it seems likely that the MC system contributes by updating images based on motion detection. This observation fits well with anatomic information showing many interconnections between the PC and MC systems beyond the striate cortex. Even so, the model only accounts for 21% of the variance in TF. Adding reaction time to the model, an attentional measure, increased the amount of variance accounted for to 29%. Reaction time during a vigilance task is a classic measure of the influence of attention on intrinsic alertness. Alertness falls as vigilance continues. Attention is required to boost alertness (Posner, 1975; Posner, Nissen, & Ogden, 1978; Parasuraman, 1984; Sturm et.al., 2004). Anecdotal information gathered after the study similarly supported the role of attentional mechanism in TF. Most of our subjects were in medical school where they are required to spend many hours studying. Individuals with faster TF times also seemed more able to filter out redundant or non-relevant environ-

mental stimuli. For example, many reported they could study and focus regardless of noise level or background commotion. In contrast, individuals with slower TF times often reported the need to study in quiet environments.

The model to predict TF still only explains 29% of the variance. One possible way to increase the amount of variance explained would be to obtain reaction time in the same locations where TF was investigated. During this study, we presented the RT stimuli in the center of the computer screen. Presenting the stimuli in peripheral vision may enhance prediction of the model since it is not only possible, but likely, for there to be a difference in RT between center and peripheral vision.

In summary we found that, like TF, PC and MC processing are asymmetric across the peripheral retina and that TF performance was best accounted for by a model that included PC, MC and attentional processing. As such the extrastriate brain mechanisms involved in TF are likely to include both the dorsal (MC) and ventral (PC) visual processing streams and structures involved in sustained attention and attentional habituation such as the dorsolateral prefrontal cortex, anterior cingulate gyrus, the midline thalamic nuclei and possibly nucleus reticularis of the thalamus (Behrmann, Geng, & Shomstein, 2004; Mesulam, 2000; Shipp, 2004). We suspect that when a visual stimulus is perceived, a cortical representation of the image is developed in the PC pathway. The MC pathway contributes to maintenance of this image whenever stimulus movement is detected across the retina via feedback mechanisms that refresh cortical representation. This process is consistent with subject reports that stimuli tend to fade, blink and dim prior to disappearing and that they may be nearly faded but return if the eye moves. Habituation occurs via attentional mechanisms that normally inhibit redundant sensory information; much the

same way one habituates to noises and smells after a short period of time. Future work directed at dissociating the influences of the PC, MC and attentional systems on TF, such as using transcranial magnetic stimulation to temporarily inhibit these systems, may confirm these speculations.

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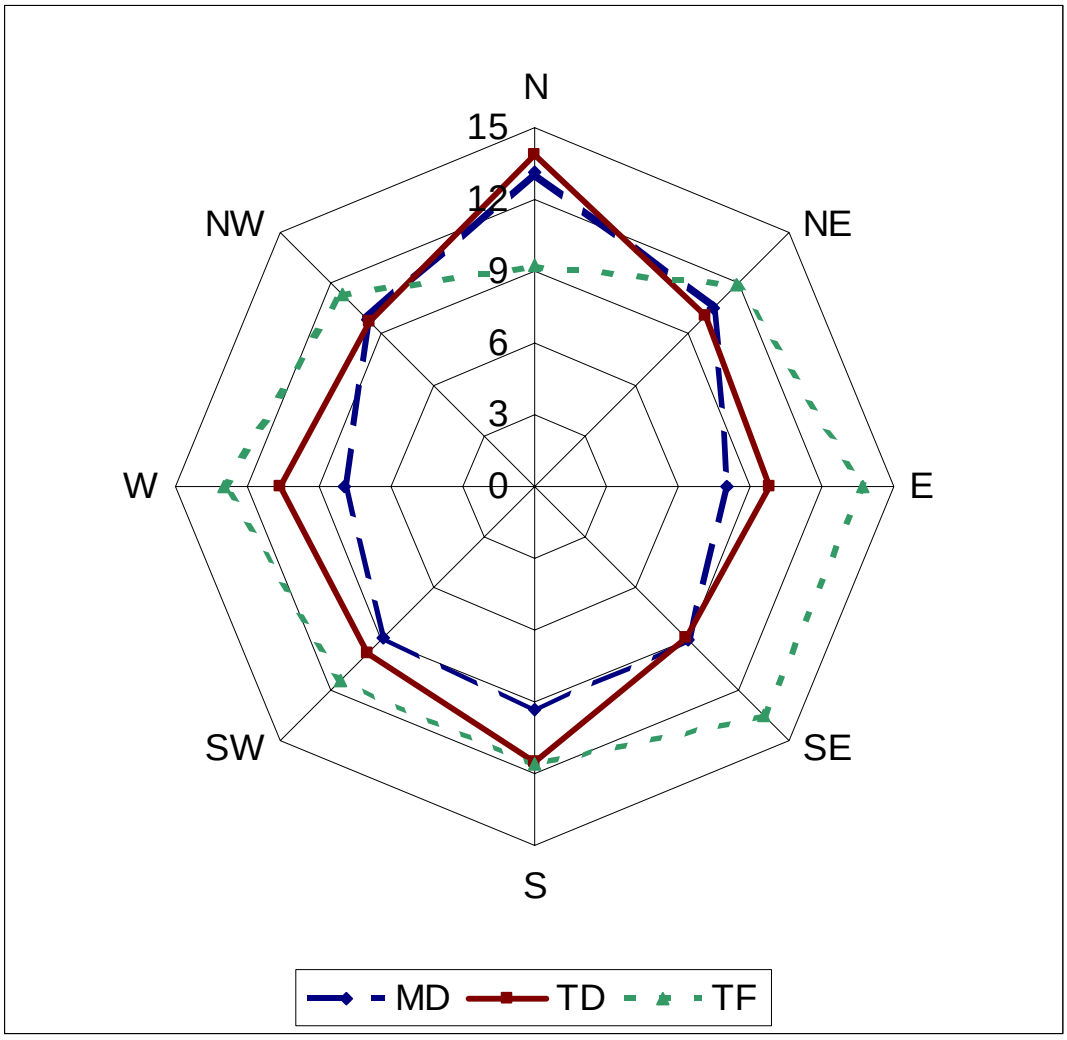
Table 1

Subject Demographics, Visual Diagnostics, and IQ.

Subjects	Male		Female	
N	7		2	
Age	24	(2)	23	(1)
Education	18	(1)	17	(1)
Visual Acuity	20/20	(0)	20/20	(0)
Contrast Sensitivity	1.9	(0.2)	1.9	(0.1)
Estimated FSIQ	112	(5)	116	(6)

Figure Caption

Figure 1. Mean performance plotted in speed of detection across visual locations for Texture Detection and Motion Detection and speed of habituation for Troxler Fading.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USING 1 HZ rTMS TO DISRUPT TROXLER FADING, PARVO AND MAGNOCELLULAR PROCESSING IN NORMAL SUBJECTS REVEALS LATERALIZED EFFECTS

by

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Running Head: rTMS REVEALS LATERALIZATION IN VISUAL FUNCTIONING

Using 1 Hz rTMS to Disrupt Troxler Fading, Parvo and Magnocellular Processing in Normal Subjects Reveals Lateralized Effects

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Abstract

Troxler Fading is a complex visual phenomenon for which the neural mechanisms are not certain. The current study used simulated lesions via repetitive Transcranial Magnetic Stimulation (rTMS) to investigate the contribution of parvocellular and magnocellular pathways and attentional mechanisms to image fading. Nine, right handed healthy subject completed 3 tasks– TF, Texture Detection (TD) a PC task, and Motion Detection MD) an MC task – after undergoing 15 minutes of low-frequency rTMS. Results revealed lateralized effects on the visual tasks subsequent to rTMS. The left hemisphere may provide a larger contribution to resistance of image fading, whereas the right hemisphere may be more dominant for processes serving to retard image fading (i.e., stimulus movement). Focal inhibition via rTMS contributes to the understanding of a complex visual model.

Using 1 Hz rTMS to Disrupt Troxler Fading, Parvo and Magnocellular Processing in Normal Subjects Reveals Lateralized Effects

A variety of models have been proposed to describe the complexity of visual pathways; their interconnections and feedback mechanisms (Posner, Nissen, & Ogden, 1978; Ungerleider, & Mishkin, 1982; Van Essen, & Maunsell, 1983; Livingstone, & Hubel, 1987; Schiller, Logothetis, & Charles, 1990; Mangun, 1995). Some of these models are derived from primate research. In general they posit that visual information originates from the ganglion cells of the retina and project along two main parallel paths [magnocellular (MC) and parvocellular (PC)] to specific layers of the lateral geniculate nucleus (LGN) of the thalamus and then continue to the primary/striate cortex of the occipital lobe (area V1; Brodmann's area 17). Each pathway maintains distinct retinotopic maps up to this point. They then diverge from the primary visual cortex into separate extrastriate cortical regions, but anatomic segregation is lost in a complex system of interconnections and feedback projections (Bogousslavsky & Caplan, 2001; Bullier, 2001).

Beyond striate cortex it is difficult to trace the specific trajectory of the MC and PC pathways, but a general projection zone is thought to exist for each pathway. Principle projections of the PC pathway purportedly course from area V1 through areas V2 and V4 towards the temporo-occipital region (Bogousslavsky & Caplan, 2001). This projection system is considered to be more specialized for object identification (Ungerleider, & Mishkin, 1982). Its physiological properties are specialized for high spatial resolution, low temporal resolution, and color (Livingstone & Hubel, 1987; Schiller, Logothetis, & Charles, 1990, 1991). In contrast, principle projections of the MC pathway course from area V1 through areas V2, V3, and V5 towards the posterior parietal cortex. The MC sys-

tem is considered to be more specialized for processing motion perception (Ungerleider, & Mishkin, 1982; Bogousslavsky & Caplan, 2001). Its physiological properties are characterized by low spatial resolution and high temporal resolution (Livingstone & Hubel, 1987) and fast, low contrast motion (Schiller, et al., 1990). Importantly, both pathways have the capability to process information in both spatial and temporal domains, but each pathway extends visual processing along one specific domain (i.e., PC extends the spatial domain and MC extends the temporal domain; Schiller et al., 1990). Historically, the two pathways were thought to process relatively distinct types of visual information, but more recent research indicates they have extensive interconnections and feedback projections and both systems receive input from dorsalateral prefrontal cortex (DLPF; Buchel & Friston, 1997; Bullier, 2001).

Transcranial magnetic stimulation (TMS) has been used to investigate a variety of different types of visual processing. TMS induces electrical stimulation of cortical neurons by creating a brief, focused magnetic field over the surface of the brain. When magnetic pulses are delivered repetitively and rhythmically, the process is called repetitive TMS (rTMS). The magnetic field induced by TMS is brief (microseconds), relatively weak (except directly under the coil, where 1–3 cm of tissue is stimulated depending on coil configuration; Cohen et al., 1990), and declines rapidly with distance away from the coil (Bohning, 2000; Roth, Momen, & Turner, 1994). Thus, current TMS coils are only able to directly stimulate the superficial cortex, but deeper brain structures and distant regions of cortex may be affected by TMS via cortical–subcortical and cortical-cortical connections.

The effects of TMS can be excitatory or inhibitory and can be evaluated at different points in time following stimulation (George et al., 2002). Immediate effects are thought to result from direct excitation of inhibitory or excitatory neurons, such as a muscle twitch immediately following stimulation. Intermediate effects of TMS (occurring minutes after stimulation) may depend on changes in local pharmacology, which can have inhibitory or excitatory effects on the cortex depending on the frequency of rTMS. For example, low-frequency repeated stimulation of a single neuron produces long-lasting inhibition of cell–cell communications (long-term depression; Bear, 1999; Stanton, & Sejnowski, 1989) whereas high-frequency stimulation can improve cell–cell communication (long-term potentiation; Malenka, & Nicoll, 1999). Even though TMS stimulates hundreds to thousands of neurons, studies of the motor cortex have shown that low-frequency stimulation (≤1 Hz) produces an inhibitory intermediate effect (Chen et al., 1997) whereas high-frequency stimulation (>5 Hz) can produce excitatory intermediate effects (Pascual-Leone, Tormos, Keenan, Tarazona, Canete, & Catala, 1998; Wu, Sommer, Tergau, Paulus, 2000). Studies combining rTMS and functional neuroimaging suggest that low-frequency rTMS reduces cortical excitability, both locally and in functionally linked cortical regions through synaptic transmission (Richter et al., 2006; Smith et al. 2007; Fox et al., 1997; Kimbrell et al., 2002).

Transcranial magnetic stimulation has been used extensively to study visual perception. Low frequency rTMS has been used to create “virtual lesions” in normal subjects that disrupt processing temporarily. For example, motion detection can be disrupted by inhibiting parietal cortex with low frequency TMS – causing deficits contralateral to stimulation (Walsh, Ellison, Ashbridge, & Cowey, 1999). Low frequency rTMS over

right parietal cortex can simulate both left neglect, inattention to visual stimuli (Fierro et al., 2000; Hilgetag, Theoret, & Pascual-Leone, 2001), and extinction, disrupting target identification contralateral to stimulation when targets are presented to both spatial hemifields (Pascual-Leone, Gomez-Tortosa, Grafman, Always, Nichelli, & Hallett, 1994). Finally, low frequency rTMS over right frontal and right parietal cortex lead to deficits consistent with motor-intentional and sensory-attentional neglect, respectively (Ghacibeh, Shenker, Winter, Triggs, & Heilman, 2007). Research also suggests neurons in the superior temporal sulcus are involved in motion processing (Grossman, Battelli, and Pascual-Leone, 2005) and neurons in parietal cortex are involved in visual search (Rosenthal, Walsh, Mannan, Anderson, Hawken, & Kennard, 2006). These findings appear to contradict views that motion processing occurs within the MC pathway and target identification within the PC pathway. However, it is uncertain from rTMS studies whether these areas actually process a particular type of information or whether rTMS merely affects processing by disrupting interconnections between these areas.

The current study sought to use low frequency rTMS to selectively disrupt MC and PC processing. We used tasks developed on the basis of Schiller et al. (1990) work in the monkey to examine MC and PC processing. Texture discrimination was used to measure PC processing as Schiller's work showed that texture detection is mediated exclusively within the PC system. Motion detection was used to measure MC processing because of its reliance on the MC pathways. We reviewed fMRI studies to help guide the placement of the TMS coil so as to disrupt PC and MC systems selectively. These studies have attempted to "map" regions of cortex involved in form/shape identification which are considered to be mediated primarily by the PC pathway. Several areas within poste-

rior cortex become activated by form and shape but two areas were strongly activated. The largest is the posterior inferior temporal gyrus (post-ITG). A second, smaller region is in the middle fusiform gyrus (mid-FG; Denys et al., 2004), corresponding to Brodmann areas 37 and 19, respectively. The middle fusiform gyrus is too deep in the brain to be reached by conventional TMS. We targeted the posterior aspects of the middle and inferior temporal gyri as these areas are accessible to TMS and they are in close proximity to the sites activated in the above fMRI studies.

Functional MRI studies have also attempted to "map" cortex involved in motion detection. Motion detection is mediated primarily within the MC pathway which projects to the inferior parietal lobule (Brodmann's area 39) and the posterior inferior portions of superior parietal cortex (Brodmann's area 7). Functional MRI studies that examined brain activity while viewing dots that move at random found activation at the junction of the intraparietal sulcus and the parieto-occipital sulcus and at a the posterior intraparietal sulcus. Because the junction of the intraparietal and parieto-occipital sulcus is known to be a convergence zone(Orban, Fize, Peuskens, Denys, Nelissen, Sunaert, Todd, & Vanduffel, 2003), where input from MC and PC pathways combine, we targeted the posterior aspect of the intraparietal sulcus for rTMS to more selectively interrupt MC processing.

This study also examined performance on a task known as Troxler Fading (TF) - the fading of an image in peripheral vision during steady fixation. TF occurs over 10s of seconds and is disrupted by image movement. The primary reason for examining TF was a hypothesis proposed by Livingston and Hubel (1987) decades ago that image fading must occur within the PC pathway because processing in the MC pathway occurs too fast to account for fading over 10s of seconds. If this hypothesis were true then performance

on TF should be similar to that for texture but not motion detection. An alternative hypothesis is that TF depends on both PC and MC processing. Whereas fading may occur over time within the PC system; the MC system may "cancel" TF by detecting movement and updating the visual image. If this hypothesis is true then performance on motion detection tasks should share variance with that on TF. We conducted a behavioral study examining texture and motion detection and TF, which indicated that while performance on texture detection was the best predictor of TF, a model that included performance on motion detection improved prediction (Taylor-Cooke, Chacko, Chelette, & Mennemeier, 2008). This study will go further by examining disruptions in TF following low-frequency rTMS in the target sites described above to disrupt PC and MC processing. The previous study also examined processing asymmetries across the peripheral retina. Earlier work had shown that TF is faster on the vertical than horizontal visual meridian (Hunzelmann & Spillmann, 1984, Barrett, Mennemeier, Chatterjee, Fuhr, & Novack, 2002; Taylor-Cooke & Mennemeier, 2005). Our behavioral study uniquely showed that processing on PC and MC tasks is similarly asymmetric across the peripheral retina but opposite that of TF. Texture and motion detection are faster rather than slower on the horizontal than vertical meridian. The difference is simply due to the different nature of the tasks. Whereas TF involves habituation, which is relatively preserved along the horizontal meridian, the PC and MC tasks involve detection which is faster along the horizontal meridian (Taylor-Cooke, et al., 2008). The asymmetries may be viewed as processing efficiencies.

Since all of these visual tasks involve attentional processing mediated by the frontal lobes, we chose to examine processing performance on PC, MC and TF tasks after

low-frequency stimulation of dorsolateral prefrontal cortex (DLPF) in addition to the parietal and temporal cortex. The DLPF is an important component of the attentional systems that modifies sensory experience (Behrmann, Geng, & Shomstein, 2004; Mesulam, 2000; Shipp, 2004). As mentioned above, both the PC and MC pathways receive input form DLPF cortex. Studies of TF involving patients with brain injury showed that lesions to DLPF cortex inhibit and even prevent TF; whereas, lesions in parietal cortex accelerate image fading (Mennemeier, Chatterjee, Watson, Wertman, Carter, & Heilman, 1994). These results revealed an important influence of attention on image fading. Parietal cortex appears to work to preserve attention for visual percepts; whereas attentional processes mediated by the frontal lobes work to habituate processing for redundant sensory information (such as the peripheral image during TF). Reaction time during a vigilance task is a classic measure of the influence of attention on sustained performance (Posner, 1975; Posner et al., 1978; Parasuraman, 1984; Sturm et.al., 2004). In the behavioral study mentioned above that examined texture and motion detection and TF, texture detection predicted TF performance and motion detection added to the model; however, adding reaction time during a vigilance task to the model significantly improved the amount of variance accounted for in TF. The results suggest that TF could occur within the PC pathway but is influenced by the efficiency of MC and attentional processes.

The current study addressed several hypotheses. First, if TF occurs exclusively within the PC system, then virtual lesions that impair PC processing (posterior temporal; Brodmann's area 37) will cause accelerated TF contralateral to stimulation because the PC system is impaired and its resistance to image fading is compromised. If TF depends on both PC and MC processing, then virtual lesions that impair MC processing (posterior

parietal; Brodmann's area 7) will cause accelerated TF contralateral to stimulation because the MC system will fail to interrupt fading via motion detection. (Here we are referring to the ability to detect image movement across the retina due to micro and corrective saccades during fixation which normally resist TF). Third, virtual lesions in the DLPF (Brodmann's area 46) will either retard or prevent TF because they impair habituation. Additionally, such lesions will render PC and MC processing more efficient (improved performance) because they will release these systems from frontal lobe inhibition.

Method

Participants

Nine right-handed, healthy subjects (two women, six men, age range=22 to 27, *M* age =23.5) were recruited at the University of Arkansas for Medical Sciences. See Table 1 for subject demographics. All subjects were healthy with normal MRI scans that were reviewed by the study physician (JC), a neuro-ophthalmologist. Exclusion criteria included a history of neurological illness, uncontrolled medical conditions, epilepsy, severe psychiatric disorders, metal implants in the head or neck, current medications known to lower seizure threshold, prior head injuries, migraines, drug dependency or abuse, and eyeglasses that were bifocal, trifocal, multifocal or monovision. Since no prior similar studies had been conducted, the number of subjects recruited was determined by a power analysis based on data from patients with lesions. Power analyses indicated that six subjects were required to provide power of 0.99 for our hypotheses. The Institutional Review Board of the University of Arkansas for Medical Sciences approved the study. All subjects underwent an informed consent process and gave written consent.

Apparatus and Materials

All programs were created using the Visual Stimulus Generator (VSG2/4F; Cambridge Research Systems) and the stimuli were delivered on a Sony Trinitron (Multiscan 17seII) color monitor. Stimulus presentation was controlled by a GP7-500 Gateway computer. All responses were made on a response box connected directly to the computer. A Black and White Mini Camera (BD-108W-X), which can be used to view in darkness down to 0.003 Lux, was used to monitor fixation. Visual diagnostics was conducted with the Pelli-Robson Contrast Sensitivity Chart from HS Clement Clarke International (1988) and a visual acuity card to assess acuity for the distance of the monitor from the subjects' eyes. The Wechsler Adult Reading Test (WTAR), shown to be a valid estimate of IQ, was used to estimate IQ.

Tasks

Troxler Fading: The visual stimuli are dots subtending 0.23 degrees of visual angle. Dots were presented in peripheral vision at 19.61 degrees of visual angle. Dots are gray (luminance=14.6 cd/m^2), the central fixation point was yellow (luminance=96.71 cd/m^2), and the background screen was dark gray (luminance=0.57 cd/m^2). Dots appeared in random order across the eight visual locations and remained until the subject responded or the time-out limit (30 seconds) was reached.

Texture Discrimination: The visual stimulus was a field of dark gray, diagonal dashed lines (luminance=0.81 cd/m^2) presented on a light gray background (luminance=71.62 cd/m^2) with a red crosshair for fixation (luminance=21.28 cd/m^2). One of the eight locations had dashed lines that were perpendicular to the lines filling the screen,

which subtended 3.75 degrees of visual angle and was presented at 14.85 degrees of visual angle. Stimuli faded in at a constant rate from a blank screen. Subjects were asked to press the response button once they detected the location of the target and then named the location.

Motion Detection: The visual stimulus was a screen of black random dots (luminance=0.1 cd/m^2), subtending 0.23 degrees of visual angle, on a gray background (luminance=4.30 cd/m^2) with a yellow fixation crosshair (luminance=96.71 cd/m^2). During trials dots were presented at 14.85 degrees of visual angle. Random dots appeared all at once. In one of the eight locations a group of dots began to move slowly and increased in distance of movement (pixels per second) at a constant rate until the location was detected.

Reaction Time: The visual stimulus was a light gray dot (luminance=71.62 cd/m^2) subtending 1.15 degrees of visual angle, on a black background (luminance=0.1 cd/m^2). The stimulus was briefly presented at randomized variable rates (one to five second intervals) in the center of the screen.

Procedure

Subjects completed eight testing sessions (Baseline, six rTMS sessions, and a follow-up session). All sessions were separated by at least 48 hours. Tasks and rTMS locations were counterbalanced across subjects. During the baseline session were involved in the informed consent process, completed basic visual diagnostics (contrast sensitivity, visual acuity), completed practice trials of each task just before completing the same full task, and they were scheduled for their next session.

Tasks were administered in a darkened room with a black shield surrounding the monitor to prevent glare and distraction from the examiner's monitor and movement. Subjects heads were secured in a head and chin rest 30.48 cm from the computer screen, which was parallel to their eyes and the central fixation was level with the pupils. Visual fixation was monitored by the mini black and white camera affixed to the black shield just below the monitor screen. The camera was connected to a small television set placed where the examiner could monitor fixation. The set-up provided a full view of the subjects eyes. All trials were randomly presented in blocks of eight trials and participants responded by pressing a button on a response box. The number of trials used during the baseline session was determined based on pilot study results. All tasks were randomly presented in blocks of eight trials for the eight peripheral locations (e.g., North, North East, East etc). Baseline testing was conducted to familiarize subjects with tasks by completing eight practice trials and a specified number of test trials on each task as follows: 1) TF - 40 test trials, 2) Texture Discrimination - Stimuli fade in at a constant rate from a blank screen. Subjects were asked to press the response button once they have detected the location of the target and then name the location. A total of 48 test trials were administered, 3) Motion Detection - Random dots will appear all at once filling the entire screen. In one of the eight locations a group of dots began to move slowly and increased in distance of movement (pixels per second) at a constant rate until the location is detected. Forty test trials were administered. The follow-up session was the same as baseline, but visual diagnostics were not repeated. Trials were recycled when clear breaks in fixation occurred.

On the days subjects underwent rTMS, subjects completed four practice trials of each task to refamiliarize them with the tasks just prior to determining motor threshold. Immediately following the 15 minutes of rTMS each subject completed 16 test trials of each task followed by 30 RT trials. A timer was set at the completion of rTMS to allow tracking of the amount of time it took to complete the visual tasks and ensure the tasks were completed within the inhibition period of rTMS. Occasionally, a couple of trials would fall outside of the ten minute period. When this occurred those trials were excluded from analyses. It is important to note that when trials were excluded, enough trials remained to continue analyses. At no point did all trials or more than one block of 8 trials out of the two blocks occur outside of the allowed time.

rTMS. T1 weighted MRI scans were obtained using GE scanners at UAMS. A neuronavigational system (Brainsight Frameless Stereotaxy, Rouge Research) was used to guide the application of rTMS to the selected neuroanatomical regions. The Brainsight system allows real-time visualization of the coil in relation to a cortical area targeted for treatment on the MRI scan, which was downloaded as a DICOM file into the Brainsight system. A MagStim 200 series TMS machine with an air-cooled 70-mm figure-of-eight coil was used to deliver stimulation (MagStim Co., UK). The motor threshold (MT) was determined by placing the TMS coil over the cortical motor area and delivering single pulses of increasing intensity until the optimal area of stimulation was found. Threshold was defined as the percentage of the maximum stimulator output necessary to elicit a motor evoked potential (MEP) of 50 μvolts recorded from the thenar muscle of the contralateral hand in 3 of 6 stimulus trials. MEPs were recorded with AgCl surface electrodes fixed on the skin with a belly-tendon montage. The EMG signal was filtered (10 Hz–1

kHz bandpass) and displayed on a computer screen. As a precautionary measure to prevent any possible adverse effects to the subject's hearing from the loud popping of the rTMS coil, subjects wore foam moldable ear plugs during rTMS.

Cortical stimulation sites were identified by neuroanatomical markers to ensure correct localization for each subject and avoid stimulating different sites due to individual variability in neuroanatomy. The location identified to interrupt MC processing was the dorsal lips of the posterior end of the intraparietal sulcus, which was located by finding the intraparietal sulcus, following it to the posterior end, and setting the target location on the dorsal lips. The location identified for PC processing was the posterior temporal lobe, which was located by finding the temporal lobe in each individual, setting the stimulation target approximately 1.5 cm anterior to the occipital lobe and 1.5 cm inferior to the superior most aspect of the temporal lobe at this location. The location identified for interrupting attentional mechanisms was Brodmann's area 46, which was located by finding the middle third of the mid-frontal gyrus and centering the stimulation target in this region. The Brainsight system was used to position the coil directly over the identified cortical location. Each subject received 15 minutes of 1 Hz rTMS (low frequency; 900 stimuli per session) at 110% of the subject's motor threshold. Subjects then completed behavioral tasks for 10 minutes following stimulation. Convention holds that 15 minutes of stimulation at this intensity and frequency should produce inhibition that lasts 8 to 10 minutes. A neuro-ophthalmologist trained in the safety precautions for TMS was on site for safety monitoring.

Data Analysis. All analyses were conducted after visual task scores were transformed into z scores (M=0, SD=1) to avoid contamination of the results by between-

subjects variability. Since there appeared to be a learning effect across sessions on the task performance, the z scores were regressed on session number to obtain a predicted score. The predicted score was then subtracted from original z scores to obtain residuals. The residualized performance scores were then used in the analyses, which serve to remove linear changes across sessions. Specific contrasts were selected to address each of the hypotheses and limit the number of analyses conducted to prevent the need to adjust for multiple comparisons. To compare the changes occurring in contralateral hemispace across tasks a change score from baseline was used for each task. The main interest was contralateral hemispace, which consists of three peripheral locations. Therefore, scores were collapsed across the three locations to obtain one average score to use for contralateral hemispace performance. Change scores were then compared using the specific contrasts to assess differences, particularly in opposite directions, as this was the expected directions for each hypothesis. For instance, for left stimulation a contrast was used to assess a collapsed score on northeast, east, and southeast locations across the two tasks.

Results

To address the hypotheses change scores from baseline to performance after left and right stimulation of each cortical location were compared. Results indicated a difference in contralateral hemispace for TF and texture discrimination performance after left temporal stimulation [$F(1, 16)=4.93$, $p<.05$], but not after right temporal stimulation ($p>.05$). Left temporal stimulation led to impaired texture discrimination (PC processing; $M= -0.66$, $SE=.68$) and faster TF performance ($M=1.47$, $SE=.68$). Negative scores indicate slower performance after stimulation, whereas positive scores indicate faster performance. No differences were found when comparing contralateral performance be-

tween texture discrimination and TF after rTMS to the right temporal region [F(1, 16)=0.61, *p*>.10]. Further, no differences were found when examining contralateral performance for motion detection and TF for left parietal rTMS [F(1,16)=0.77, *p*>.10] or right parietal rTMS [F(1, 16)=0.01, *p*>.10]. Likewise, no differences were found between TD and TF for left frontal [F(1, 16)=0.00, *p*>.10] or right frontal rTMS [F(1, 16)=0.01, *p*>.10]. Additional analyses investigating differences in contralateral between motion detection and TF were not significant after left frontal [F(1, 16)=0.02, *p*>.10] or right frontal rTMS [F(1, 16)=0.56, *p*>.10.

Post-hoc analyses compared overall performance (an average of all eight peripheral locations) for right versus left rTMS across tasks and cortical locations. Overall TF times were slower following left parietal rTMS and faster following right parietal rTMS, t(8)=3.78, *p*=.05 (See Figure 1). No differences were found for TF between left and right after frontal [t(8)=0.03,*p*>.10] or temporal stimulation [t(8)=2.31,*p*>.10]. It should be noted though that temporal stimulation did approach a trend between left and right for TF (*p*=.13) in which fade times were faster after left temporal stimulation (*M*=-0.93, *SE*=.71) than right temporal stimulation (*M*=0.58, *SE*=.70). No differences were found on motion detection when comparing right to left stimulation at the frontal [t(8)=1.10, *p*>.10], parietal [t(8)=0.61, *p*>.10], or temporal stimulation sites [t(8)=0.61, *p*>.10]. Likewise, no differences were found for texture discrimination for right versus left frontal [t(8)=2.11, *p*>.10], parietal [t(8)=1.20, *p*>.10, or temporal stimulation [t(8=0.20, *p*>.10]. Notably, comparisons between right and left texture discrimination after temporal rTMS approached significance (*p*=.15). Motion detection was faster contralateral to rTMS than ipsilateral for right frontal stimulation, t(1)=4.10, *p*<.05 (see Figure 2). No other compari-

sons for ipsilateral versus contralateral performance after stimulation were significant (p>.05) compared to baseline.

Discussion

We examined how low-frequency rTMS delivered to selected sites in parietal, temporal, and frontal cortex disrupt processing on tasks designed to be sensitive to PC and MC processing and how such stimulation influenced TF. Low-frequency rTMS can both have an inhibitory effect beneath the stimulation coil and a disinhibition effect (a release) in projection sites that are distant to the stimulated brain region (Kimbrell et al., 2002). The first hypothesis was that impairing PC processing by stimulation of the posterior-temporal lobe would cause accelerated TF contralateral to stimulation. This hypothesis was supported following stimulation of the left hemisphere but not the right hemisphere. Texture discrimination was also slower contralateral to left temporal stimulation and TF was faster, providing validity for the hypothesis that impaired PC processing impairs TF – providing less resistance to image fading. This result is also consistent with the hypothesis that TF is mediated within the PC pathway as proposed by Livingston and Hubel (1987); however, it is not obvious why right hemisphere stimulation failed to have the same effect.

The alternative prediction that stimulation of the parietal cortex would impair MC processing and accelerate TF was not supported. Whereas direct stimulation of parietal cortex did alter TF, left hemisphere stimulation led to slower TF and right hemisphere stimulation to faster TF; it did not impair performance on the motion detection task. Therefore, we cannot conclude that TF was affected by impaired MC processing. Either TF is not influenced by inhibition of the MC pathway, we failed to stimulate the MC

pathway, or the motion detection task is not sensitive to MC processing. It is also possible that the numerous projections of the MC pathway from the visual cortex compensate for the region we inhibited with rTMS. These data simply do not allow one to conclude which alternative is correct. It is interesting though that a hemispheric difference is present for TF. Inhibiting neurons in left parietal cortex via low frequency rTMS can cause disinhibition of neurons in a homologous region of the right hemisphere via callosal projections (Kimbrell et al., 2002). Left hemisphere stimulation may slow TF (i.e., make images more resistant to fading) not only because the left cortex is inhibited but also because neurons in the right hemisphere are released from left hemisphere inhibition. This result could suggest a right hemisphere dominance model for processes related to TF such as updating either the cortical representation of the stimulus image or its location in space. This dominance of the right hemisphere for processing TF is further supported by the fact that right hemisphere inhibition resulted in faster image fading, which was a much stronger result than left stimulation demonstrated. Therefore, the right parietal lobe may be the main region for pathways updating the stimulus to prevent fading. When inhibited, the feedback mechanisms serving to promote updating of the stimulus are reduced and fading accelerates.

The hypothesis that frontal lobe stimulation would retard or prevent TF and improve PC and MC processing was only partially supported for the MC processing task (motion detection). Again a hemispheric effect was present showing an effect for the right but not left hemisphere. Whereas, DLPF stimulation did not affect TF or texture discrimination (PC processing); stimulation of the right frontal lobe did alter motion detection in a systematic fashion. Motion detection was faster (i.e., improved performance)

contralateral to stimulation than ipsilateral to stimulation. It is important to note that ipsilateral hemispatial performance was slower but not different from healthy/pre-rTMS performance. Damage to frontal cortex is known to releases parietal cortex from inhibition via intrahemispheric projections. Low-frequency rTMS to the right frontal cortex may have released parietal cortex in the same hemisphere from inhibition. This could simultaneously lead to faster performance on the motion detection task contralateral to stimulation via release of the right parietal area from frontal inhibition. As mentioned above, direct stimulation of parietal cortex may have failed to disrupt motion detection because we stimulated the wrong parietal region or the numerous projections of the MC system compensated for the region inhibited by rTMS. The DLPF is a convergence zone with reciprocal connections to other convergence zones like the junction between temporo-parieto-occiptal (TPO) region that is strongly linked to motion processing. We avoided this area to get greater specificity on MC processing and due to the overlap with the PC pathway in the TPO region (Orban et al., 2003). If the junction had been chosen for direct stimulation it may well have disrupted performance on the motion detection task. For instance, one patient with a unilateral right hemisphere lesion (upper portion of Brodmann's area 37, lower portion area 39, and anterior portion of 19 or the TPO region), due to an arterial venous malformation, completed the same tasks. Interestingly, compared to a healthy population the patient demonstrated impaired performance (longer detection time) on the motion detection task with greater impairment in the contralateral hemispace. The patient also demonstrated improved performance on TF (greater resistance to image fading), but only on the horizontal meridian (Taylor-Cooke, Mark, & Mennemeier, 2006). This performance is opposite that found with rTMS such that right

stimulation led to faster fading or impaired performance. However, since the lesion was caused by an arterial venous malformation it is possible that the organization of function in this patient is different compared to a healthy individual. Alternatively, the patient data may indicate a greater interruption of MC pathways when the TPO region is involved.

Results indicating that inhibition of the left posterior temporal region lead to impaired PC processing are also consistent with Schiller et al. (1990) work indicating texture detection is specific to at least the early processing stage of the PC pathway. Our results indicate as well that the PC pathway demonstrates specificity for texture discrimination beyond striate cortex. When the left posterior temporal region is inhibited the parvocellular pathway performs poorly taking longer to discriminate texture. Inhibition of the same area led to a faster TF. These data are consistent with the notion that fading occurs within the PC pathway because impaired processing within this pathway causes images to be more susceptible to habituation. We cannot conclude; however, that the PC pathway is solely responsible for image fading. Clearly, direct stimulation of the parietal lobe altered TF and our behavioral study showed that motion detection and attentional processing also predict TF.

In a previous study, we posited that a visual stimulus or image may be represented and maintained within the PC pathway. As such, PC processing works to resist image fading. The MC pathway may mediate the length of time it takes for images to fade via feedback mechanisms based on motion detection that refresh the visual image or its location when motion occurs. In TF experiments, most subjects report that images blink, dull or flicker prior to fading. This could well be due to input from MC system because steady fixation is hard to achieve and so the visual image moves slightly across the retina. At-

tentional mechanisms, particularly those in frontal cortex, tune out or habituate to redundant sensory information. Fading may occur as these systems actively work to constrain attention to novel environmental features. Attention may be squelched either for representations of images maintained in the PC pathway, the location coordinates of images in parietal cortex or both (Taylor-Cooke et al., 2008). The current study supports earlier theories that TF involved a complex visual processing system.

The results following rTMS to the right posterior parietal cortex are consistent with previous research demonstrating accelerated fading in patients with parietal lesions (Mennemeier et al., 1994). One difference is the rTMS study showed opposite effects for left and right parietal stimulation, whereas the lesion study showed accelerated fading following right and left parietal damage. A second difference is that the rTMS study failed to reveal an effect of frontal lobe stimulation on TF; whereas, lesions to the frontal lobe retarded or prevented image fading. These differences almost certainly relate to the potency of rTMS for disrupting behavior versus that for structural brain injury. The effect size of low-frequency rTMS on behavior is obviously much smaller than that for stroke. The value of following a stroke study with an rTMS study lies in replicating effects due to stroke in subjects who do not have all the complications associated with stroke and in suggesting new possibilities like the lateralized differences observed in this study. For example, the left hemisphere appeared to play a greater role than the right in PC processing whereas the right hemisphere appeared to have a greater role in MC processing. These findings are consistent with theories that posit processing specialties between the left and right hemisphere such as local-global, part-whole, and serial and parallel process-

ing. It is possible these distinctions will have some basis in PC and MC processing, respectively.

In summary, the results of the current study allow us to propose a more comprehensive model of the visual attention system. We propose that a stimulus is perceived and maintained within the PC pathway located in the posterior temporal cortex, which resists image fading when working efficiently. The left hemisphere may play a greater role in this process than the right. If this region is damaged then the PC pathway is less efficient (impaired) at resisting image fading and the stimulus disappears at a quicker rate. The parietal cortex contributes to the length of time it takes for images to fade via feedback mechanisms that serve to refresh or update the visual image, which creates the perception that the stimulus is blinking or fading in and out prior to disappearing. The right hemisphere may be dominant for aspects of stimulus processing that retard TF, such as being more sensitive to movement. When this system is damaged, the feedback mechanisms are no longer refreshing or updating the image and image fading accelerates. Attentional mechanisms in the DLPF habituate to redundant stimuli in the environment and serve as a filter to inhibit the resistance of the PC pathway thus leading to image fading. The parietal cortex enhances and directs attentions toward a stimulus. When the frontal lobe is inhibited, the parietal cortex may be released from inhibition and better able to detect movement. The results of this study uniquely demonstrate the interplay between PC processing and TF and laterality effects on both TF and tasks designed to be sensitive to PC and MC processing. They suggest that the complexities of TF might be understood in terms of the ventral and dorsal visual processing streams and attentional systems that gate percepts in and out of consciousness.

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Table 1

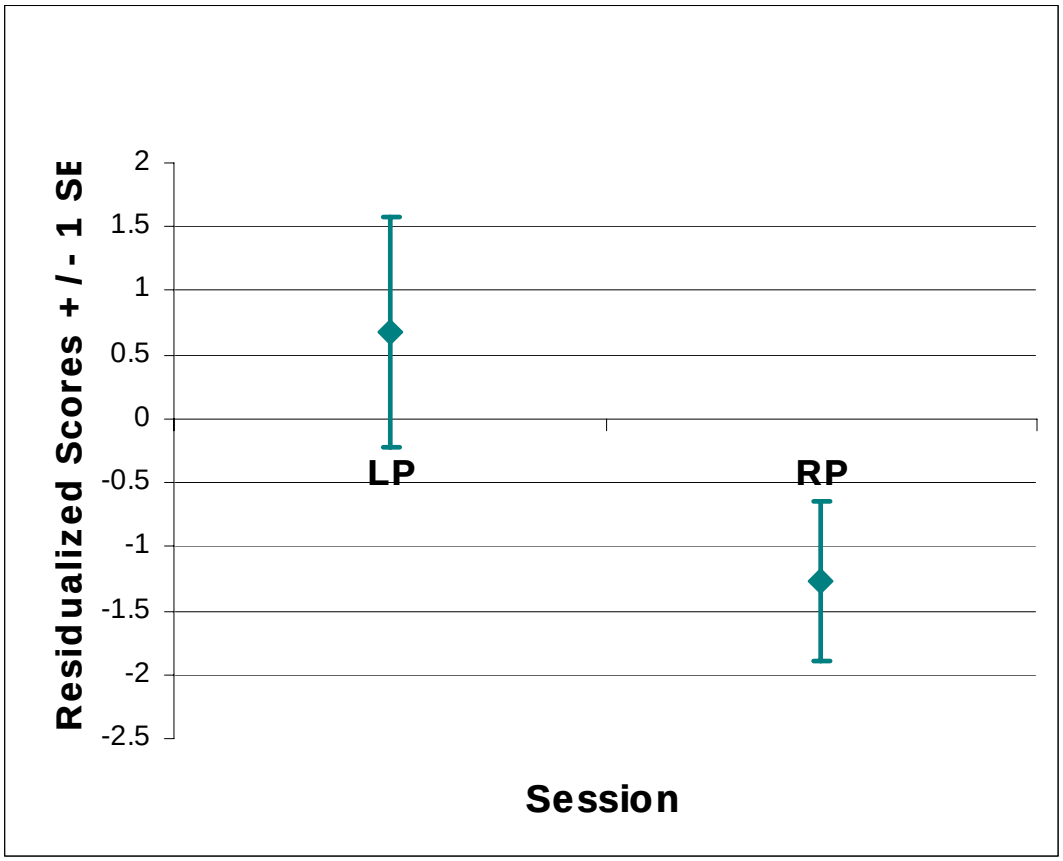
Subject Demographics, Visual Diagnostics, and IQ.

Subjects	Male		Female	
N	7		2	
Age	24	(2)	23	(1)
Education	18	(1)	17	(1)
Visual Acuity	20/20	(0)	20/20	(0)
Contrast Sensitivity	1.9	(0.2)	1.9	(0.1)
Estimated FSIQ	112	(5)	116	(6)

Figure Caption

Figure 1. TF residualized performance scores averaged across all eight peripheral locations after right and left rTMS.

Figure 2. Motion detection residualized performance scores collapsed across the three contralateral peripheral locations and the three ipsilateral peripheral locations after right frontal rTMS.


Residualized Scores + / - 1 SE
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1
0.5
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-0.5
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-1.5
-2
-2.5
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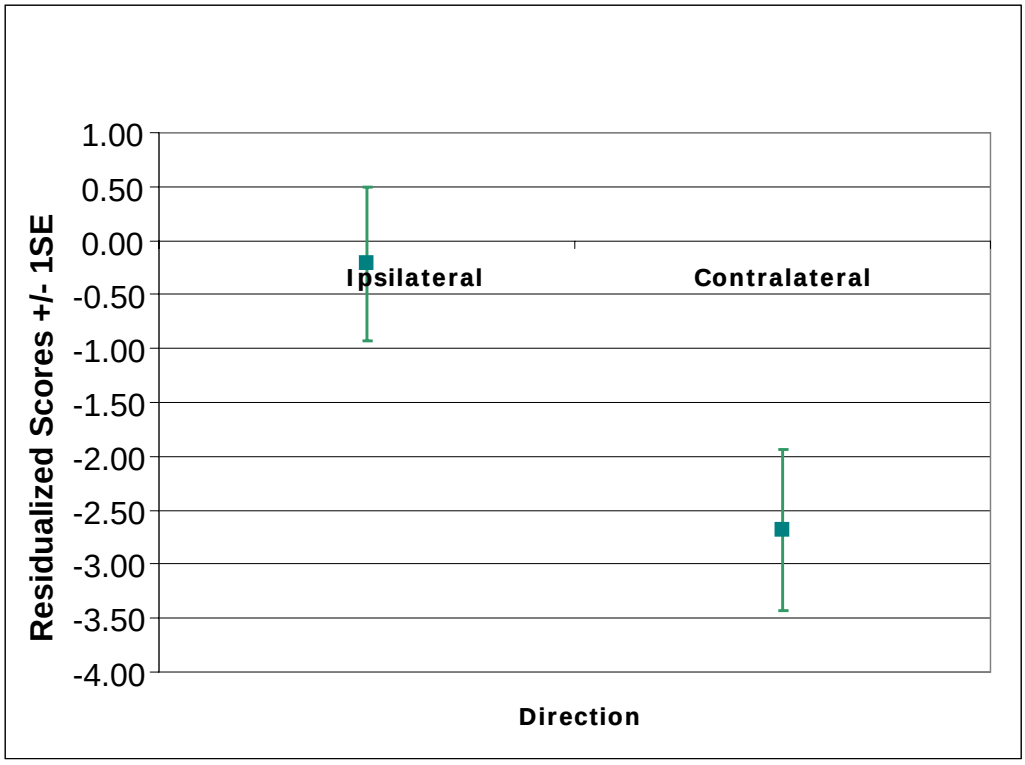
Session


1.00
0.50
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Residualized Scores +/- 1SE
Ipsilateral
Contralateral
Direction

SUMMARY

The studies completed in this dissertation extend previous research and enhance knowledge of TF and visual attention. Asymmetries in TF were replicated indicating a robust effect across a variety of conditions. Both PC and MC processing also result in similar asymmetries across the peripheral retina, which to our knowledge has not been reported in the scientific literature at this point in time. We are unaware of any structural mechanism that would lead to asymmetries on the tasks, since no report could be found suggesting any visual relating structures that could account for the asymmetries. Therefore, the cause of asymmetries on visual tasks remains unclear.

TF performance was thought to occur in the ventral (PC) visual processing stream. However, based on the results from our studies TF is best accounted for by a model that included PC, MC, and attentional processing. As such the extrastriate brain mechanisms involved in TF are likely to include both the dorsal (MC) and ventral (PC) visual processing streams and structures involved in sustained attention and attentional habituation such as the dorsolateral prefrontal cortex, anterior cingulate gyrus, the midline thalamic nuclei and possibly nucleus reticularis of the thalamus (Behrmann, Geng, & Shomstein, 2004; Mesulam, 2000; Shipp, 2004).

The first manuscript led to the development of a possible visual processing model. We suspect that when a visual stimulus is perceived, a cortical representation of the image is developed in the PC pathway. The MC pathway contributes to maintenance of this image whenever stimulus movement is detected across the retina via feedback mecha-

nisms that refresh cortical representation. This process is consistent with subject reports that stimuli tend to fade, blink and dim prior to disappearing and that they may be nearly faded but return if the eye moves. Habituation occurs via attentional mechanisms that normally inhibit redundant sensory information; much the same way one habituates to noises and smells after a short period of time.

The second study supported earlier theories that TF involved a complex visual processing system. The results of the second study allowed us to propose a more comprehensive model of the complex visual attention system. We propose that a stimulus is perceived and maintained within the PC pathway located in the posterior temporal cortex, which resists image fading when working efficiently. The left hemisphere may play a greater role in this process than the right. If this region is damaged then the PC pathway is less efficient at resisting image fading and the stimulus disappears at a quicker rate. The parietal cortex contributes to the length of time it takes for images to fade via feedback mechanisms that serve to refresh or update the visual image, which creates the perception that the stimulus is blinking or fading in and out prior to disappearing. The right hemisphere may be dominant for aspects of stimulus processing that retard TF, such as being more sensitive to movement. When this system is damaged, the feedback mechanisms are no longer refreshing or updating the image and image fading accelerates. Attentional mechanisms in the DLPF habituate to redundant stimuli in the environment and serve as a filter to inhibit the resistance of the PC pathway thus leading to image fading. The parietal cortex enhances and directs attention toward a stimulus. When the frontal lobe is inhibited or damaged, the parietal cortex may be released from inhibition and better able to detect movement. The results of this study uniquely demonstrate the interplay

between PC processing and TF and laterality effects on both TF and tasks designed to be sensitive to PC and MC processing. They suggest that the complexities of TF might be understood in terms of the ventral and dorsal visual processing streams and attentional systems that gate percepts in and out of consciousness.

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APPENDIX

INSTITUTIONAL REVIEW BOARD APPROVAL FORMS

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and expires on October 26, 2010. The Assurance number is FWA00005960.

Principal Investigator:	TAYLOR-COOKE, PATRICIA
Co-Investigator(s):	
Protocol Number:	**X050907003**
Protocol Title:	*A Retrospective Data Analysis of the Contribution of Magno/Parvo Pathways to Visual Attention in Simulated Lesions*

The IRB reviewed and approved the above named project on 8-01-08. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.

IRB Approval Date: 8-01-08

Date IRB Approval Issued: 8-01-08

Marilyn Doss

Marilyn Doss, M.A.
Vice Chair of the Institutional Review
Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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Principal Investigator:	TAYLOR-COOKE, PATRICIA
Co-Investigator(s):	
Protocol Number:	**X050713005**
Protocol Title:	*Contribution of Magnocellular and Parvocellular Pathways to Visual Attention*

The IRB reviewed and approved the above named project on 7-23-08. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

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