Seeing the Meaning: Higher-Order Neuroplastic Changes in the Time Scale of Processing within Early Visual Areas in the Congenitally Blind

ALANA D’ALFONSO

Princeton University

This thesis was submitted to Princeton University in partial fulfillment of the requirements for the degree of Bachelor of Arts in Psychology.

April 2011
HONOR PLEDGE

I pledge my honor that this paper represents my own work in accordance with University regulations.

-------------------------------
Alana D'Alfonso
Acknowledgements

This experiment would not have been possible without the help of a number of individuals. First and foremost, I would like to express many thanks to my two advisors, Uri Hasson (Psychology/Neuroscience) and Adel Mahmoud (Global Health and Health Policy). Thank you Professor Hasson for believing in me and being willing to let me take on my own project examining a population with which you do not usually work. This was really an amazing experience and I learned so much along the way. Thank you for answering all of my lengthy emails and for imparting on me your research expertise during our many, many meetings. And, thank you for teaching me so much and being patient with me when necessary. This project wouldn’t have been possible without your guidance. Professor Mahmoud, thank you for all of your wisdom and support, both in terms of the global health portion of this thesis and also in so far as life plans. Thank you for all of the expert advice regarding research and medicine and for reminding me to take one step at a time. You were always so encouraging and willing to take time out of your day to talk to me, of which I am extremely appreciative. Both of you have inspired me to want to continue to incorporate research into my career—Professor Hasson from the experience I gained through working in your lab and Professor Mahmoud through your class and our many research-related discussions.

I also cannot thank enough Chris Honey, Yulia Lerner and Lauren Silbert in my lab. Chris was so incredibly helpful in writing scripts, assisting me with the technical aspects of analysis and also giving me feedback on the final paper. He did not hesitate to offer to help me on weekends or to answer my phone calls while I was scanning at Georgetown and having technical troubles. Yulia was also an amazing teacher. She showed me how to complete the pre-processing and provided me with so much feedback and assistance over the course of the project, which was very helpful given that this study paralleled her previous study. Lauren was really great in showing me how to approach the post-processing this summer when I was first learning and was always willing to help when I asked. She even drove one of my subjects to and from New York. I really can’t thank you three enough! Thank you also to Matt Johnson and Chris Thompson whose workstations were near mine in the lab. They were always willing to stop by and chat with me to see how I was doing and offer any insight that they could.

Many thanks to the Georgetown lab with whom I collaborated on this project, including Josef Rauschecker, Paula Plaza, and Laurent Renier. Josef, the head P.I., took the time to meet with Professor Hasson and I and to thoroughly consider our project proposal. Without his help and agreement to collaborate, finishing this project would not have been possible. Laurent Renier was instrumental in obtaining IRB approval for the study at Georgetown. Paula helped me run the actual subject scans and scheduled all of the subjects’ visits. Thank you very much to Paula for answering my numerous questions via email and being instrumental in helping me coordinate my research trips.

This research would also not have been possible without funding. Thank you so much to the Henry Luce Fellowship (Professor Dan Osherson), Psychology Department (Tamara Thatcher), and the Center for Health and Wellbeing (Kristina Graff) for your generosity. Thanks also to Carol Agans in the Psychology Treasury Department for helping me handle the transfer of funds to Georgetown.

In addition, thank you to those who assisted in helping me gain approval for this study. Thanks to RoseMarie Stevenson who personally sat with me and went over all of the necessary steps for IRB approval and human subjects training when I decided to start my study early in the
spring of my junior year. Thank you to Professor Todorov, the IRB chair at the time, who corresponded with me via email regarding my study approval. Similarly, many thanks to Joe Broderick, IRB secretary who updated me on my application and issued me expedited approval to protocol changes when needed.

In regards to running the study, thank you to Ray Lee, our Princeton Neuroscience Institute Technical Director, who worked with me and allowed me to start my scanning time slot early. Also, thank you for all of the blind organizations that took the time to find out more about my study and sent out information advertising the experiment to their members, especially the New Jersey Foundation for the Blind. Also, thank you to the Kauffman’s at Vision Ventures for all of your help in subject recruitment. Thank you to all of the study participants, some of whom traveled from fairly long distances.

I also have many friends and family to thank. Thank you to my friends Dhruv and Sidak for letting me stay with them while I was researching at Georgetown. And last but not least, thank you to my family (Mom, Dad, Jared), Dave, and friends (especially Marina and Marianna) for being there for me and helping me when I was stressed.
ABSTRACT

The function of blind striate and extrastriate cortices is a highly contested topic among researchers. Prior studies suggested that the occipital cortex in congenitally blind individuals can adopt new functions, such as the processing of tactile and auditory information. However, the exact nature of these neuroplastic changes is still debated. While some researchers argue that striate and extrastriate cortices continue to process low-level sensory information (albeit in novel sensory modalities), others argue that these areas in the blind may process higher-order auditory and language information. In this study, we tested whether the visual cortex in the congenitally blind responds reliably to a spoken narrative, comparing conditions in which the higher-order narrative structure is intact or disrupted. While undergoing functional magnetic resonance imaging (fMRI), 8 congenitally blind participants listened to unaltered recording of a real life story as well as to versions of the story that had been segmented and scrambled at the time-scales of ‘words’ (0.7±0.5s) and of ‘sentences’ (7.7±3.5s). The reliability of responses evoked by the intact and scrambled stimuli was assessed within and between sighted and congenitally blind individuals. Three primary results were found: (i) left-lateralized extrastriate cortex in congenitally blind (but not sighted) individuals demonstrated reliable activity in response to the real-life story; (ii) the reliable responses were observed only for the intact story but not for the scrambled versions of the story; (iii) regions within the classic auditory and language network (e.g., superior temporal gyrus, Broca’s area) in the blind demonstrated similar response profiles as those seen in sighted individuals exposed to the same auditory narratives. These results suggest that early visual cortex in the blind responds most reliably when higher-order information (unfolding over many seconds) is preserved, as in the intact story. In sighted individuals, the same dependency on information accumulated over long time scales is observed, but only in higher-order extra-linguistic areas. The present results suggest that early visual cortical circuits are greatly altered in congenitally blind individuals, and their function shifts from low-level sensory processing (as is typical in sighted individuals) toward the processing of high-level structure as found in complex real life stories.

The neuroimaging portion of this study served to further elucidate the nature of the blind occipital lobe which, in turn, could provide a stronger basis of knowledge in the area of blindness rehabilitation. Blindness affects millions around the world, with most cases occurring in developing nations and being easily preventable. Among other methods, there currently exists in the area of rehabilitation both echolocation and gene therapy. However, the question is, just because we have these techniques that may bring those who are blind closer to visually navigating the world, should we be using them? Is sight always a gift? In the United States, there is a strong blindness culture. Being blind means being a part of a community and restoring vision could lead to feeling ostracized. The cases of Virgil Adamson and Mike Mays provide examples of what it is like for someone who had only lived his or her life as a blind person up until receiving rehabilitative treatment as an adult. Their stories suggest that blindness rehabilitation techniques are more disruptive than helpful in certain cases within developed nations. In developing countries, the story is somewhat different. There is certainly more stigma and sight restoration offers many individuals a chance at a new life. In these cases, human rights and economic motives may outweigh the negatives.

The final portion of this study was comprised of a separate social connectedness survey, which
was completed by all study participants. The survey results suggested an elevated degree of social connectedness, which could in turn be associated with greater overall health. This ability of these blind individuals to better connect with others may be linked to better complex language-related comprehension abilities acquired as a result of blind visual cortex reassignment. However, a small subject pool and confounding factors prevent any concrete conclusions from being drawn in this area. Also mentioned by the subjects was the amount of attention paid in the U.S. to the link between blindness and mental illnesses, such as depression and anxiety. This stands in stark contrast to conditions found in developing countries, where discussing mental illness is taboo, especially within the context of blindness which is already viewed as a "weakness." It may be possible that too much attention is paid to what is "wrong" with blind individuals in the United States and not enough to the unique aspects of blindness culture.
TABLE OF CONTENTS

Acknowledgements 3

Abstract 5

Chapter 1 Introduction 7
  1. Existing research on the neuroplasticity of blind visual cortex 8
  2. Present study 11

Chapter 2 Method 14
  1. Participants 14
  2. MRI acquisition 16
  3. Experiment and stimuli 16
  4. Data processing 17
    4.1 Pre-processing 17
    4.2 Intersubject correlation analysis 18
  5. ROI Analysis 19

Chapter 3 Results 20
  1. Responses to naturalistic stimuli in the blind as a function of temporal scrambling 20
  2. Comparison of responses between the sighted and the blind 21
  3. Profile of early visual areas in the blind 23

Chapter 4 Discussion 23
  1. V2/V3 in the congenitally blind as a higher-order language area 24
  2. The language network outside visual cortex and implications of non-plasticity 28
  3. Conclusion 30

Chapter 5 Global health and health policy certificate chapter 30
  1. Blindness around the world 30
  2. Applications of study results: Blindness rehabilitation 32
    2.1 Echolocation and the blind 32
    2.2 Gene therapy 35
    2.3 Should we work towards blindness rehabilitation? 36
      2.3.1 Evidence from the U.S. 36
      2.3.1 Evidence from developing nations 40
  3. Social connectedness survey component of this study 43

References 48

Figures 53
Seeing the Meaning: Higher-Order Neuroplastic Changes in the Time Scale of Processing within Early Visual Areas in the Congenitally Blind

It was once widely accepted that the structure and function of neural networks were fixed properties. This has been proved otherwise in a plethora of literature on neuroplasticity produced since the 1970s. Neuroplasticity is defined as the ability of neurons to alter their connectivity and function following changes in neural and environmental contexts; environmental changes may include lesions, alterations in sensory input or the process of development (Rugnetta, 2011). The concept of neuroplasticity has been applied to many neuroscientific phenomena including phantom limb pain, cognitive reserve in Alzheimer’s, seizure-induced changes in epilepsy, and stroke rehabilitation (e.g. Flor et al., 2006; Whalley et al., 2004; Scharfman et al., 2002; Bracewell et al., 2003). In this study, we investigate neuroplasticity in response to sensory deprivation.

Congenital blindness is an ideal setting for the study of neuroplasticity following sensory deprivation. Contrary to the “use it or lose it” maxim, the visual cortex in those born blind is both present and functional. Anatomical MRI scans have revealed an intact and morphologically normal occipital lobe in this blind population (Wanet-Defalque et al. 1988; Breitenseher, 1998). PET studies have shown not only that there is blood flow present in blind visual cortex but also that the blood flow is increased relative to sighted controls at baseline (Phelps et al., 1981). Prior studies have given conflicting results on neuroplasticity in the congenitally blind, as will later be further detailed. In light of such debate, the goal of this experiment is to work towards finding an answer to the question of whether the neural networks in early visual regions in the congenitally blind retain their low-level properties or are reassigned to function as higher-order areas. The design of this experiment provides a unique approach that sets it apart from previous studies, most notably through its use of complex, naturalistic stimuli.
Existing Research on the Neuroplasticity of Blind Visual Cortex

Studies over the past two decades suggest that the visual cortex in the congenitally blind can maintain its activity by developing novel functions, such as the processing of linguistic-related information within early visual areas (e.g. striate and extrastriate cortex). The visual cortex in the blind has been found to show reliable responses to linguistic tasks such as Braille reading, verbal memory, and semantic/syntactic processing (e.g. Sadato et al., 1996; Amedi et al., 2003; Roder et al., 2002).

These plastic functions of visual cortex in the congenitally blind parallel behavioral deficits that disappear with age. According to Mills (1993), blind children may show evidence of language delays and frequently substitute similar sounding words due to lack of visual input. However, these sound production problems do not persist as blind children enter adolescence. Additionally, like autistic children, blind children tend to demonstrate “pronoun reversal,” meaning that it is common for blind children to use a first or second person pronoun when a third person pronoun is appropriate and vice versa (Chiat, 1986). However, this also is not a lifelong trend and elevated rates of pronoun reversal are noticeably reduced by age 5 (Perez-Pereira & Castro, 1992). The meaning that words hold for blind children may differ as well, a deficit that presents itself in the form of verbalism. For example, if one were to ask a congenitally blind child to describe grass, it would not be atypical if he or she said “green,” despite the fact that this child has never seen colors and does not attach the same significance to these visual concepts. In fact, studies have shown that over 50% of responses given by young blind children, if asked for the first descriptive word that comes to mind, are visually based (Cutsford 1951, as cited in Perez-Pereira & Conti-Ramsden, 1999). Nevertheless, this verbalism does not appear to last as blind children come into their teen years (Harley, 1963).
As congenitally blind children mature, not only are their lingual deficits overcome but also superior language abilities may be developed. A comprehensive study by Brieland (1950, as cited in Perez-Pereira & Conti-Ramsden, 1999) involving over 160 participants examined verbal abilities in a variety of categories, including verbal memory, lip movement, corresponding body gestures, and vocal pitch variation in both the blind and sighted. In addition to matching the performance of sighted teens in almost all categories of a verbal production task, blind adolescents also demonstrated superior pitch variation and verbal memory. In a similar vein, Neimeyer and Starlinger (1981) noted the superiority of speech discrimination in the blind in a study using electric response audiometry. Blind individuals showed greater ability to discriminate speech on all levels (words, short phrases, complete sentences), both when noise was and was not present. Some hypothesized that this speech processing enhancement may be attributable to better hearing in the blind. But, Neimeyer and Starlinger (1981) observed no differences in hearing acuity between blind and sighted subjects.

With the knowledge that most lingual deficits in the blind are surmounted and enhanced language abilities are developed, some researchers have attempted to link the behavioral changes in the blind with neuroplastic changes in early visual cortex. However, the nature of the plastic changes in early visual areas in the blind is still under debate. Although it is agreed upon that the visual cortex is recruited in blind individuals engaged in Braille reading, verbal memory, and language processing tasks involving syntactic reasoning and semantic judgments, the exact role of visual cortex in completing these linguistic tasks is not certain.

There is serious disagreement amongst researchers as to whether blind early visual cortex is a low or high-level area. Some researchers claim that although the sensory input received by early visual areas is changed in blind individuals (e.g. auditory or tactile instead of visual input),
the level at which this processing is occurring remains characteristic of low-level sensory areas. It was proposed, for example, that early visual areas are used to decode low-level somatosensory information during Braille reading. A PET study by Sadato et al. (1996) examined visual cortex activation in the congenitally and early blind in response to various types of tactile stimulation. Three conditions were employed: touching without tactile discrimination, tactile discrimination of a random dot pattern, and Braille reading. In sighted controls, deactivation of occipital cortex was seen during tactile processing. In blind individuals, both types of tactile discrimination activated striate and extrastriate visual cortex but simple touch did not; more visual activation was seen for Braille reading than in the random dot discrimination task. Others have examined what happens to Braille reading abilities in the blind when early visual regions are no longer properly functioning. A Transcranial Magnetic Stimulation (TMS) study by Cohen et al. (1997) compared disruption of the occipital cortex during the reading of both Braille letters and embossed Roman letters. Early blind and sighted subjects were asked to identify the letters while TMS was applied to both striate and extrastriate cortex. Sighted subjects were still able to accurately identify the embossed Roman letters by touch when TMS was applied to the mid-occipital lobe. The same could not be said for the early blind participants, as identification of both Braille and Roman letters was disrupted.

Other researchers have investigated the possibility that the plastic changes within early visual cortex may allow the visual region to engage in higher-order functions. In sighted individuals, low-level sensory information is received from the retina and processed in the early visual stream. In blind individuals, this bottom-up processing is disrupted due to lack of visual input. Thus, early visual regions in the blind instead receive top-down information from higher cortical regions, which may change the type of processing performed in these areas. In particular,
the early visual regions in the blind may act more like higher-tier cortical areas. Exploring this possibility, Amedi (2003) examined verbal memory in ten congenitally blind individuals and matched controls with hopes of elucidating the topography of the blind visual region. A verbal memory task that probed higher-order function, and a Braille discrimination task that probed low-level tactile processing, were used in separate experiments. The results revealed a hierarchical mapping: areas that were further posterior within blind visual cortex, including striate and extrastriate cortex, responded to verbal memory stimuli. By contrast, more anterior regions such as the lateral occipital cortex (LOC), where other higher-order visual areas would typically exist, responded to Braille reading. Interestingly, better verbal memory performance correlated with greater activation within primary visual cortex in the blind. Sighted individuals, including those with superior verbal memory skills, did not demonstrate this activation within the occipital lobe. Based on these results, Amedi suggested a reverse hierarchy within blind visual cortex. In a typical sighted person's occipital lobe, as one moves from posterior regions, such as V1, to more anterior regions, such as the LOC, the level of processing becomes more abstract. Here, we see the reverse order in blind subjects, as verbal memory function was discovered in the posterior early visual regions, while Braille reading function was found to be present in more anterior visual regions.

Present Study

Taking the described disagreement amongst researchers into account, this experiment was conducted to address that which had not yet been covered in the stimuli and protocol of previous studies. In this study, we will test whether early visual areas in the blind respond to the low-level properties of naturalistic linguistic stimuli such as the words, the intermediate properties such as the structure of a sentence, or the high-level properties such as the structure of
an entire story. Unlike this experiment, most other research studies involving auditory listening tasks in the congenitally blind have used relatively simplistic stimuli at the word or sentence level (e.g. Roder et al., 2002, Amedi et al., 2003). This study also differed from previous research in that the stimuli here were presented within the context of an entire narrative. Prior studies have presented stimuli in isolation, without the context of other words or sentences within a larger framework. In using naturalistic stimuli, we are brought closer to examining the real world responses of blind individuals to language tasks.

This experiment is based on the Lerner et al. (2011) experimental design. In the Lerner et al. (2011) study, a real-life story was scrambled at the word level, sentence level and paragraph level and was also played backward. All scrambled versions of stimuli consisted of the same audio; only the arrangement of this audio was altered on the order of words, sentences, and paragraphs. Subjects were told to listen carefully to each condition and response reliability was measured using fMRI. Correlation of the BOLD (blood oxygen level dependent) signal across subjects within defined regions of interest (ROIs) was calculated and used to determine response reliability. Responses within early auditory regions (e.g. early auditory cortex, A1+) were reliable for all conditions, indicating that such activation was not dependent on the temporal structure of the stimuli. On the other hand, responses in higher-order language areas (e.g. areas along the temporo-parietal axis) did vary as a function of temporal structure, forming a response gradient from A1+ to the TPJ (Figure 1A).

Similar results were found in a prior study in the visual cortex of sighted individuals. In this study by Hasson et al. (2008), sighted subjects watched a movie sequence which was randomly scrambled at three different time scales: short (4±1 sec), intermediate (12±3 sec), and long (36±4 sec). The results revealed differences in response reliability when the temporal
structure of the stimulus was disrupted. In parallel with the results seen in auditory cortex, response reliability in early visual areas (e.g. V1, V2, V4) and MT in sighted individuals was essentially invariant to temporal scrambling. This suggests that the responses in early visual areas are driven mainly by momentary visual input regardless of the coherence of the temporal structure. In contrast to early visual areas, response reliability in several higher-order brain areas (e.g. FEF, TPJ) depended on information accumulated over longer time scales (Figure 1B).

Based on these results, Hasson et al. (2008) proposed that a parallel could be drawn between the way in which the brain integrates information over space and time. Spatial receptive fields (SRFs) allow for the mapping of a corresponding position within the space of the visual field to specific neuronal responses (Schwartz, 1980). The size of SRFs increases within the visual cortex relative to the level of processing occurring, varying with eccentricity (Smith, 1989). By analogy with the SRF concept, Hasson et al. (2008) suggested the concept of temporal receptive windows (TRWs). The TRW of a neuron is defined as the amount of time during which information is gathered from sensory and/or cognitive input before a response is generated. In neurotypical individuals, it was put forth by Hasson et al. (2008) and reaffirmed by Lerner et al. (2011) based on their above-mentioned results that primary sensory areas have a short TRW and cognitive regions have a long TRW.

Thus, by framing this study using the concept of TRWs, we will be able to characterize the time scale of processing within early visual areas in the congenitally blind. As noted above, previous studies have found that the visual cortex in congenitally blind individuals responds to linguistic information. However, it is still under debate whether these early visual areas process low-level properties of linguistic stimuli (e.g. identifying single letters or words over short time scales using haptic or auditory information) and hence preserve their low-level sensory
characteristics, or whether these areas process high-level properties of linguistic stimuli (e.g. processing the story’s narrative over long time scales) and are therefore higher-order integrative regions. By measuring the time scales of processing in congenitally blind individuals using the exact same protocol as used in Lerner et al (2011), we will be able to determine if the functional properties of neural networks within these early sensory regions are persevered (i.e. have a short TRW) or are altered (i.e. have an intermediate or long TRW).

Finally, this protocol will allow us to compare directly the responses across congenitally blind and sighted subjects in nonvisual areas. It is possible that the way in which linguistic information is processed in language areas outside of the occipital lobe is also altered in the blind and undergoes neuroplastic changes. This alternative hypothesis has been pointed to in other studies that have demonstrated symmetrical as opposed to lateralized responses to language in the blind (e.g. Karavatos, 1984; Roder et al., 2000).

Methods

Participants

A total of 10 congenitally blind individuals (mean age: 53, range of ages: 37-61 years) participated in this study. Data from two of the subjects were excluded due to scanner quality issues during the one scan and the subject’s request to leave during the other scan. All subjects were completely blind with no light sensitivity and did not have other noticeable impairments. Every subject became blind at birth: seven were classified as having a condition known as Retinotopy of Prematurity (ROP); the remaining subject had glaucoma. At least four of the participants were noted to have remarkable music abilities, three of whom perform as paid professional musicians. All subjects were proficient Braille readers and exhibited hearing within
the normal range. Seven were right-handed and one subject described herself as either ambidextrous or left-handed.

Subject recruitment was conducted in the following way: blind organizations in New Jersey, New York, and Pennsylvania were contacted, and if after the purpose of this study was communicated and the organization was interested in assisting, a written description of the study was provided that could be sent out to their members. Any interested participant could then inquire further about the study. This required a thorough discussion of the project with various administrators at each organization, including secretaries and directors. Over 30 organizations were contacted in the tri-state area, including the American Foundation for the Blind, VISIONS Services for the Blind and Visually impaired, National Association for the Visually Handicapped, New Jersey Foundation for the Blind and its various chapters, New Jersey Commission for the Blind, National Federation of the Blind Pennsylvania, among others. Despite these efforts, the number of potential participants who presented themselves was very limited. There also were a few blind individuals who inquired but did not meet the study requirements of congenital blindness and no residual vision. Given the small subject pool in the Princeton and surrounding areas, we initiated collaboration with Josef Rauschecker at Georgetown University. Five subjects were scanned at Georgetown and all five were included in the data analysis. Three research trips to Georgetown were conducted to record data and to minimize variability in experimental parameters across sites. All subjects were screened and provided informed consent prior to scanning under protocol that had been approved by the Princeton University Committee on Activities Involving Human Subjects and/or the Georgetown Institutional Review Board. Subjects received monetary compensation for their participation in the study and were also
reimbursed for any incurred travel expenses. Funding for this experiment was provided by the Henry Luce Scholarship, the Psychology Department and the Center for Health and Wellbeing.

**MRI Acquisition**

The study was conducted using scanners at both Princeton University and Georgetown Medical Center. At Princeton, a Siemens Allegra 3T scanner was used along with a Nova head coil. Anatomical scans were acquired using a T1-weighted MPRAE image (TR = 2500 ms, TE = 4 ms, 160 volumes). Slicing was set at 1 mm with 0 mm spacing. Functional scans were acquired using T2*-weighted imaging (TR = 1500 ms, TE = 30 ms, 300 volumes). An interleaved order was used for slice acquisition, with slices set at a 3 mm thickness and 1 mm spacing. MRI-safe headphones were utilized for the duration of the scan and extra padding was placed around the head of the subjects to limit motion. At Georgetown, a 3T Siemens Tim Trio scanner was used with a 12-channel phased-array head coil. Anatomical scans were acquired using a T1-weighted MPRAGE image (TR =1900 ms, TE =2.52 ms, 176 volumes). Slicing was set at 1 mm with 0 mm spacing. Functional scans were acquired using T2*-weighted imaging and the same parameters as followed while scanning at Princeton (TR = 1500 ms, TE = 30 ms, 300 volumes, 3 mm slice thickness, 1 mm spacing). As at Princeton, MRI-compatible headphones were used and extra head padding was provided to minimize head motion.

**Experiment and Stimuli**

The study by Lerner et al. (2011) provided the sighted control data used in this experiment. The stimuli and protocol in this study with congenitally blind individuals were nearly identical to those used by Lerner et al. (2011). In Lerner et al.’s study, a 7-minute real-life story was presented to subjects through MRI-safe headphones. It was a comedic narrative titled
“Pie Man” that was told by Jim O’Grady at a storytelling event in New York. The story was manipulated temporally to generate the following four conditions: full forward story (7 minutes), scrambled at the sentence level (7.7±3.5s), scrambled at the word level (0.7±0.5s), and the reverse story. The reverse condition was included in the stimuli set for this study but largely discarded from the results due to unreliable responses (a possible reason being that subjects may not have paid attention during this condition, which was always presented at the end of the scanning session). Each condition was presented twice and the order of runs was varied for the second presentation. Each stimulus started with 12 seconds of music and ended with 15 seconds of clapping and silence; these time periods were cropped out during preprocessing. Before the start of the study and between runs, subjects were told to listen very carefully and to pay attention to the audio, even if it seemed somewhat nonsensical. A survey was administered at the end of the experiment on the topic of social connectedness for the purpose of linking this study to more direct public health applications. The specific survey content did not include questions concerning the story narrative (for survey details and results, see Fig. 9 and the Global Health and Health Policy Certificate section).

Data Analysis

Pre-processing.

Data was pre-processed using BrainVoyager QX (Brain Innovation) and scripts written in MATLAB (Mathworks). Pre-processing procedures within BrainVoyager QX used in the creation of each VTC included 3D motion correction, high and low pass trend removal, and slice scan time correction. VTC-post processing included spatial smoothing using a Gaussian-filter of 6 mm as well as de-spiking and global projection in MATLAB (to mitigate motion and other artifacts). VTCs were then cropped to remove the music and silence present in each run, as
mentioned above. Next, because the same stimuli start trigger could not be used at both scanning sites for technical reasons, alignment of the data had to be addressed. Audio correlation analysis was employed for the purpose of alignment. RTC files representing the audio in the full and scrambled conditions were generated and then utilized to create correlation linear regression maps. The lag was adjusted appropriately and the time course was exacted from A1+ for each subject in each condition. A cross-correlation was then performed that calculated the correlation of the BOLD signal within A1+ across subjects for each condition (full, sentences, words). By examining the resulting cross-correlations and their relative shifts from zero, it was possible to align the data from both scanner sites by cropping data points from the start and end.

**Intersubject correlation analysis.**

Intersubject correlation (ISC) represented the primary type of analysis employed for this study. Using this method, the BOLD response within an ROI was compared across subjects. A high ISC indicated response reliability between subjects within that ROI. This method allowed for the assessment of the similarity of responses in each brain area within the congenitally blind individuals, the sighted individuals, and between the sighted and blind groups.

The ISC for this study was calculated in two ways. One method, here called Run-averaged ISC, involved calculating for each subject the average response time course in each voxel across the first and second runs. These averaged time courses for each subject were then correlated by comparing each subject’s averaged time course to the mean of all other time courses for all other subjects within each condition (full, sentences, words). A second type of ISC, labeled Cross-run ISC, involved calculating the average responses across all subjects in the first run and the average responses across all subjects in the second run. These two averages of run1 and run2 were then correlated within each condition.
Intergroup correlation was also determined between the blind and sighted groups. The average response time course for all blind subjects within a condition was calculated and then correlated with the average response time course for all sighted subjects within the same condition.

Maps were created using Cross-run ISC and intergroup correlation. To create the Cross-run ISC maps that are depicted in this paper, correlation coefficients were calculated using a voxel-by-voxel comparison across all subjects within a condition. The correlation coefficient $C(r_1, r_2)$ was calculated for each voxel, where:

$$C(r_1, r_2) = \frac{r_1(t) \cdot r_2(t)}{\sqrt{(r_1(t) \cdot r_1(t))(r_2(t) \cdot r_2(t))}}.$$  

In this equation, $r_1(t)$ was the response time course of a voxel to the first presentation of the condition (full, sentences or words) averaged across subjects and $r_2(t)$ was the response time course of a voxel to the second presentation of the same condition averaged across subjects. To create the intergroup correlation maps, the $C(r_1, r_2)$ was calculated for each voxel where $r_1(t)$ was the response time course of a voxel to a condition in the blind averaged across all subjects and $r_2(t)$ was the response time course of a voxel to the same condition in the sighted averaged across all subjects.

**ROI analysis.**

The ROIs used in this experiment were defined in the following ways. The A1+ ROI was previously defined in Lerner et al. (2011) using a story from Stephens et al. (2010) as a localizer. The remaining ROIs (STG, TPJ, Precuneus, MPFC, V2) were defined anatomically using identified sulci and gyri as references. These ROIs were identified using anatomical markers.
while viewing the full condition ISC map, which may have caused some selection bias in favor of the full condition.

Results

Responses to Naturalistic Stimuli in the Blind as a Function of Temporal Scrambling

Cross-run intersubject correlation maps were generated on a voxel-by-voxel basis for each condition (full story, sentences, and words). The Cross-run ISC was calculated by averaging run1 from every subject within a condition and then correlating this mean BOLD response in each voxel with the average of run2 from every subject within the same condition (see Methods). Reliable responses were evoked by all conditions, including the reverse story, in early auditory cortex (A1+). Such responses in A1+ independent of the scrambling of the input (words, sentences, or intact story) indicate a short TRW. Even though it was previously noted (see Methods) that the reverse condition results were mostly not used due to unreliability, the activity demonstrated in A1+ specifically in response to the reverse condition can be considered to be reliable for a couple of reasons. One reason is that Lerner et al. (2011) also reported reliable responses within A1+ in the sighted to the reverse condition. As will be later detailed, there is considerable overlap between the blind and the sighted in the time scales of processing within nonvisual regions, including A1+ (see Figure 4). Another reason is that tonotopy studies have revealed a preserved tonotopic organization within early auditory areas in the blind (Stevens, 2009). Areas further along the temporo-parietal axis demonstrated reliable responses that were dependent on temporal structure. The superior temporal gyrus (STG) responded reliably only to the words, sentences, and full conditions, thus suggesting that the STG has an intermediate TRW. Regions such as the medial prefrontal cortex (MPFC), and precuneus responded reliably
only when subjects listened to the full story; this dependence on the presence of input that contains long time scales signifies the existence of long TRWs within these brain regions. In addition, we observed in blind individuals reliable responses in extrastriate cortex (adjacent but not overlapping with striate cortex; here labeled V2/V3) (Fig. 2). Such response reliability found in early extrastriate cortex was unique to the congenitally blind subjects and was not found in the sighted controls who participated in the study by Lerner et al. (2011). It also should be highlighted that this response reliability was only evoked by the full story, not by any of the other conditions (see bottom of Figure 6).

**Comparison of Responses Between the Sighted and the Blind**

In addition to characterizing the neural responses to temporally varied naturalistic stimuli in the visual cortices of blind individuals, we also investigated whether the responses within nonvisual areas were similar to or differed from those seen in the sighted. In line with this objective, ROI profiles were examined in the sighted and the blind. Time courses were extracted from the same ROIs (A1+, STG, Right TPJ, and precuneus) in both the blind and the sighted, and Run-average intersubject correlations were calculated separately within each ROI for each condition. The Run-average ISC was determined using the method of averaging each subject’s runs 1-2 within a condition and then correlating this average with the mean of all other subjects within the same condition (see Methods). In both the sighted and blind groups, A1+ showed a high level of correlation for all conditions, including the reverse story. The STG exhibited a reliable response to the full, sentences, and words conditions in both populations. In contrast, the RTPJ and Precuneus demonstrated high levels of correlation only for the full condition (Fig. 3). In agreement with the abovementioned results (Fig. 2), this suggested the presence of short (A1+), intermediate (STG) and long (RTPJ, Precuneus) TRWs.
To further answer this question, intergroup correlation maps were created that examined the correlation of BOLD responses between all averaged blind runs and all averaged sighted runs within a condition in each voxel (see Methods). The resulting sighted-blind correlation map represents those areas of reliable responses within each condition that were shared across sighted and blind participants. These shared regions and the resulting hierarchical gradient of temporal receptive windows can be seen in Figure 4. Areas that reliably responded to only the full story are shown in blue, while areas that responded to input at the sentence time scale or above are depicted in green; regions that responded to all conditions, including words, are shown in red. This sighted-blind correlation map can be compared to the gradient map produced when computing the intersubject correlation for the sighted only (labeled “sighted” in Fig. 4). The same general trend of a temporal hierarchy along the temporo-parietal axis can be seen in both the sighted-blind and sighted maps. More specifically, the same regions show high levels of BOLD correlation for the different conditions in the sighted-blind maps as compared to the sighted maps. This demonstrates that the nonvisual areas of activation that are shared between the blind and sighted subjects in response to the specified stimuli have similar time scale characteristics to those areas that show responses in the sighted subjects.

ROI analysis was completed to further investigate the correlation found between the sighted and blind participants in the full story condition (as this was the only condition in which reliable responses had been demonstrated in both the blind and sighted in all defined ROIs). Time courses were extracted from the A1+, STG, RTPJ, and precuneus ROIs. Figure 5 depicts the resulting intergroup correlation within each ROI. As seen in the chart, there is a high level of correlation between the sighted and blind responses to the full condition within the A1+, STG, RTPJ, and precuneus regions (ranging from an intergroup correlation value of 0.5 to 0.75).
contrast, minimal correlation is seen between the sighted and blind responses to the full condition within V2/V3 (intergroup correlation value of <0.1).

Together, these results demonstrate that highly similar responses to naturalistic stimuli scrambled at varying time scales are evoked in both the congenitally blind and the sighted in nonvisual language areas. Also, it is notable that responses of areas within the visual cortex do not show correlation between the blind and the sighted.

**Profile of Early Visual Areas in the Blind**

We will now turn our attention specifically to the V2/V3 ROI. As previously pointed out, activation in this area was found only in response to the full condition in the congenitally blind (Fig. 2). The exact location of V2/V3 is depicted in Figure 6 as it appears in both the 2-D and 3-D maps. As shown in these Cross-run ISC maps, this ROI is found in the posterior portion of the occipital lobe but adjacent to the expected position of V1. An ROI analysis was also performed in which the activation profile of V2/V3 was determined. The time course for each condition within V2/V3 was extracted and the Cross-run ISC was calculated within blind participants. As shown on the plot in Figure 6, reliable responses were only seen in this ROI when subjects listened to the full story and not for the sentences or words conditions. This suggests that V2/V3 in the congenitally blind reliably processes information that is conveyed in the intact story but not in the scrambling conditions. Such a response profile is indicative of an area that has a long TRW (see for example the TPJ and Precuneus in Figure 3) and, therefore, may be considered to be acting as a higher-order area.

**Discussion**

In this experiment, we investigated the functional nature of early blind visual cortex as it relates to low-, intermediate-, and high-level processing using naturalistic stimuli. Reliable
responses in the congenitally blind evoked by a real-life story were measured as functions of varying temporal structure. Two main findings were uncovered; the first was that activation in area V2/V3 was demonstrated in response to only the full intact story condition (not words or sentences) in the blind. High levels of intersubject correlation were found within early visual cortex in the blind. By contrast, high levels of intergroup correlation were not found between the blind and the sighted within visual cortex. The second major finding was that a similar hierarchy of temporal receptive windows was found in both the blind and sighted (Lerner et al., 2011) outside of visual cortex along the temporo-parietal axis and also included other higher-order areas often associated with language tasks, such as the precuneus and medial prefrontal cortex. Just as in sighted individuals, early auditory regions in the blind were found to process information over very short scales, while higher-order language areas were found to integrate information over increasingly longer time scales. High levels of blind-sighted intergroup correlation were demonstrated within ROIs in the classic language network.

**V2/V3 in the Congenitally Blind as a Higher-Order Language Area**

In the sighted population, the hierarchical organization of visual cortex reveals a gradient consisting of sensory areas in the most posterior regions and more complex processing areas further anterior. In contrast, our results demonstrated a reverse hierarchy where high-level processing in response to naturalistic stimuli is evoked in early visual areas in the congenitally blind. More specifically, this area (labeled V2/V3) showed a long time scale of processing that corresponded to the length of a full story. These results of blind early visual cortex activation within the context of temporal receptive windows and the use of real-life stimuli represent novel findings.
These novel findings are consistent with the larger pattern of results from linguistic experiments in the congenitally blind and studies of functional connectivity. In particular, visual cortex activation in response to nonvisual linguistic-related stimuli such as Braille reading, semantic versus syntactic processing, and verbal memory has previously been demonstrated in the blind (e.g. Sadato, 1996; Roder et al., 2002, Amedi et al., 2003). The classification of early visual regions in the blind as higher-order areas specifically is also reasonable within the framework of previous work. Other studies have demonstrated early visual cortex activation in the congenitally blind in response to high-level tasks involving verbal memory, verb generation, and semantic retrieval (Amedi et al., 2003; Noppeney et al., 2003). Functional connectivity studies in the blind also support the existence of a higher-order area within blind extrastriate cortex. For example, increased cortical connections between the frontal language areas and visual areas in the blind have been reported (e.g. Liu et al., 2007). This finding is compatible with the results of our study, as reliable responses were generated within both early visual areas and frontal language areas while subjects listened to the intact story. Frontal-occipital coupling has been demonstrated by other linguistic neuroimaging studies in the blind as well, including a study by Noppeney et al. (2003) that involved a semantic retrieval task.

What is the mechanism by which these suggested extensive neuroplastic changes in blind visual cortex might occur? The ability of blind visual cortex to take on new functional roles like complex language processing may be related to the concept of early synapse formation. In neurotypical individuals, occipito-temporal connections that project from extrastriate areas to regions in anterior temporal cortex do exist but are very limited due to competition for synaptic space (Catani, 2003). Owing to the lack of visual input in the blind, there is less competition during synapse formation, which allows for the creation of more cross-modal connections. The
proportional increase in the number of feedback pathways thus allows for greater neural plasticity and suggests that the blind occipital lobe may be able to participate in other nonvisual functions such as the language processing found here. Animal studies, although not directly applicable, also support this viewpoint. Sutured-lid and enucleation experiments in monkeys and kittens have demonstrated that a high percentage of neurons in the visual region become responsive to other sensory modalities such as touch. Synaptic re-wiring was also noted: a significantly higher percentage of thalamo-cortical connections within early visual areas were found to exist in these visually deprived animals (Hyvarinen et al. 1981; Berman et al., 1991).

There are also studies (e.g. specific studies concerning Braille reading) that seem, on the surface, to disagree with our results. For example, studies of Sadato et al. (1996) and Cohen et al. (1997) have implicated early blind visual cortex as a region associated with Braille reading (low-level processing). However, these studies recruited participants who were early blind, not congenitally blind like in this study. Other experiments have also pointed out potential flaws in these oft-cited studies, such as the labeling of subjects in the Sadato study; some subjects were described as “early blind” despite their technical status of “late blind.” This is an important distinction, as the visual cortex in those who are late blind may undergo different plastic changes (Buchel, 1998). Nevertheless, there have been certain experiments in which a congenitally blind population was studied and activation within early visual cortex was demonstrated in response to tactile stimuli (e.g. Buchel, 1998). One way to explain this discrepancy is through the idea of lateralization. Our study found reliable responses while subjects listened to the intact story only in the left early visual cortex. This is consistent with the neurotypical lateralization of language areas to the left hemisphere and also with results found by other blind linguistic fMRI studies, such as the experiment by Amedi (2003) that demonstrated activation within left hemispheric
early visual areas in response to verbal memory tasks. In line with this theory, activation of blind visual cortex during Braille reading studies and TMS studies involving the stimulation of primary somatosensory cortex has primarily been demonstrated in the right hemisphere (Buchel, 1998; Whittenberg, 2004).

Our finding of left lateralized blind early visual cortex as being representative of a higher-order language area that processes information over long time scales has certain implications. Demonstration of high-level processing within would-be sensory areas such as extrastriate cortex indicates that the functional properties of these neural networks are able to change based on received input from higher-tier areas; the innate properties of these sensory regions are not preserved. This indicates that there is an extensive amount of plasticity demonstrated by blind visual cortex. Such changing of innate properties is also consistent with what we know about development: early on in life, cerebral cortex is very similar across the entire brain before specialization occurs (Hepper, 2005).

Parallels to behavioral data concerning language function in the blind can also be extrapolated. As mentioned earlier, the blind display deficits in areas such as word substitution, pronoun reversal, and verbalism, which are eventually overcome (e.g. Chiat, 1986; Perez-Pereira & Castro, 1992). Over time, the blind develop better verbal memories and speech discrimination skills than sighted individuals (Brieland, 1950, as cited in Perez-Pereira & Conti-Ramsden, 1999; Neimeyer & Starlinger, 1981). A higher-order language area within visual cortex that processes temporally complex input could potentially be useful in correcting for these shortcomings and assisting in the development of enhanced lingual abilities.

By referring to early visual cortex in the blind as a higher-order language region, this does not mean that only lexical or grammatical properties of the stimuli are being processed.
Blind V2/V3, as we have defined here, could also be responding to the extra-linguistic properties of stimuli, such as understanding the narrative and the use of situation models. Essentially, by using the term “higher-order language area” we are referring to both linguistic and extra-linguistic processing. Extra-linguistic regions process both meaning and in-context information.

In the sighted (Lerner et al., 2011), these areas include the MPFC, precuneus, and inferior frontal gyrus. V2/V3 in the blind could also be acting as an extra-linguistic area in this sense. As a potential application of this idea, V2/V3 could be used in mentally keeping track of the state of the world. Internally attending to and following the state of their environment is an important and necessary focus in the lives of blind individuals. This could be an interesting research question for more studies involving the congenitally blind population.

The Language Network Outside Visual Cortex and Implications of Non-Plasticity

If V2/V3 serves as a higher-order language area in the congenitally blind, what are the implications for the functions of other language areas? Are these classic language areas functioning in the same way as found in the sighted population? Are additional areas outside of the occipital lobe recruited? Our results showed that nonvisual language areas in both the blind and sighted demonstrated similar reliable activity within the same regions in response to the words, sentences, and full story conditions. This suggests that properties of language areas outside of the visual cortex in the blind remain the same, a result that is supported in various ways by the existing literature and explored below.

Even though behavioral abilities in the blind could suggest altered functioning of the classical language network, a large bulk of research studies suggest otherwise. Other neuroimaging studies that examined responses to stimuli processed at an intermediate linguistic level, such as auditorily presented individual sentences, have noted an overlap of the blind and
sighted response topographies in language areas outside of the occipital lobe. Overlapping areas included the middle frontal gyrus, inferior parietal regions, medial temporal gyrus, among others (Roder et al., 2002; Bedny et al., 2011). Information processed at the higher-level, such as verb generation in response to noun cues, also generated similar responses in blind and sighted participants in areas other than visual cortex. Specifically, similar activation was seen in the left inferior frontal cortex, dorsolateral prefrontal cortex, left posterior superior temporal gyrus, etc (Burton, 2002). Lastly, studies in the blind demonstrating an intact theory of mind (ToM) network may also lend support to these findings of a largely unaltered classic language network in the blind. Linguistic experience is widely cited as a pre-requisite for ToM development (e.g. Garfield et al., 2001). It is noted that there is considerable overlap between the extended language network (ELN) and the ToM network. The extended language network refers to language comprehension put in context, such as language within a text. The ELN typically involves the recruitment of right hemispheric language areas as well (Ferstl, 2008). Such a language network is comparable to that seen in this study, as all stimuli were presented within the overall context of a real-life story. In-context language processing and ToM are often linked as involving similar tasks. The blind appear to be able to be able to carry out ToM tasks normally and have shown neurotypical responses in areas including the MPFC, STS, TPJ, and precuneus; also similar to sighted individuals, responses were not seen in visual cortex in the blind (Bedny, 2009).

The implications of these high levels of same-region correlation between the sighted and the blind extend to the general realm of neuroplasticity and blindness. To what extent does neuroplasticity affect the functioning of various brain regions in the blind? As we have discussed, the area of most interest amongst most researchers is the visual cortex. But, what
about the other brain areas? As we have defined here, neuroplastic changes in the blind as related to language processing over different time scales appear to be mostly limited to the visual cortex.

**Conclusion**

In summary, major plastic changes occur in the visual cortex of the congenitally blind that alter the function of underlying neural networks. Our study demonstrated a reverse hierarchy, showing that early visual cortex in the blind functions at a very high level and processes complex speech information over long time scales. It also was shown by our results that areas outside of blind visual cortex within the classic language network do not undergo the same plastic changes and remain similar in function to the language areas in sighted individuals.

**Global Health and Health Policy Certificate Chapter**

**Applications of Study Results: Blindness rehabilitation**

This study focused on the concept of language processing in the congenitally blind within early visual regions. The goal of this study, like others in the field of blind neuroplasticity, was to further understand the nature of the occipital lobe in the blind. Having a more thorough understanding of the neuroplastic changes within blind visual cortex allows for the application of this information to the field of blindness rehabilitation. Here we will examine the link of this study’s results to potential rehabilitative knowledge while exploring the broader health and health policy implications, noting how distinct economic and social contexts should be considered in deciding how (and whether to) treat blindness.

**Blindness Around the World**

Globally, about 39 million people are blind. Another 245 million are not technically blind but suffer from low-level vision (WHO Visual Impairment and Blindness, 2011). Cataracts represent the leading cause of blindness around the world, accounting for 48% of cases;
glaucoma is the next leading cause at 12% (Vision2020 Report, 2007). Sadly, almost 9 out of every 10 cases of blindness worldwide could have either been prevented or easily cured if the proper resources were available (WHO Visual Impairment and Blindness, 2009).

Most instances of avoidable blindness occur in developing nations: over 90% of those who are visually impaired live in third world countries (WHO Visual Impairment and Blindness, 2011; see Figure 7). In fact, 75% of the world’s blind population lives in Asia and Africa alone (Thylefors, et al., 1995). The most common causes of blindness in developing countries include cataracts, trachoma, and xerophthalmia. Cataracts, as mentioned above, are the leading cause of world blindness and can form due to a variety of factors, ranging from inherited to environmental influences. Trachoma, which develops as a result of a chlamydial eye infection, leaves 6 million blind each year. Treatment involves the use of antibiotics, but prevention efforts are key, as trachoma is thought to develop from poor hygiene and contaminated drinking water. Xerophthalmia affects almost 10 million children each year and has been shown to be due to a lack of Vitamin A (Sardegna, 2002).

Even though the majority of the burden is seen in developing countries, industrialized nations also demonstrate an alarming number of cases. In Australia, for instance, almost half a million people over age 55 have some form of visual impairment (Facts on Eye Health: Australia, 2010). Indigenous populations within Australia are especially at risk, as they are 6 times as likely to be blind in comparison to local non-indigenous people. Major causes of blindness amongst this population include diabetic eye disease with 94% of cases being preventable (Taylor, 2010). In other developed nations, such as the U.S., age-related macular degeneration and diabetic retinopathy are the major causes of vision loss. Age-related macular
degeneration is the third leading cause of visual impairment worldwide (WHO Priority Eye Diseases, 2010).

Various organizations have been formed at both the national and global level in an attempt to address this major health problem. Unite for Sight, for instance, is a non-profit organization that places a strong emphasis on working towards providing more cataract surgeries, defining their success in terms of number of cataract surgeries performed. Similarly, the Global Initiative for the Elimination of Avoidable Blindness (GIEAB) centers its goals around treatment, advocating that a primary objective should be to increase the number of ophthalmologists in each country (Thylefors, 1998). While these are important objectives, they are also primarily magic bullet approaches. What about prevention? What about the downstream factors like clean water and adequate food? The relationship between poverty and blindness is cyclical. Those living in poverty are at greater risk of being exposed to contaminated water and living in unsanitary environments. These conditions can lead to certain forms of blindness. In turn, being blind in these countries makes the prospect of getting a job and being able to live above the poverty line much less likely, thus reinforcing the cycle (Vision2020 Report, 2007). Some organizations, like Vision2020, are addressing these downstream factors by incorporating educational information and involving the local community in their efforts. However, these integrated approaches are not nearly as common or as heavily funded as simpler, magic bullet solutions. More needs to be done to address this serious issue of preventable blindness in developing nations.

**Past Blindness Rehabilitation Work**

Here, we will explore the past and current efforts in blindness rehabilitation within the areas of echolocation and gene therapy. The question will also be raised of whether pursuing
blindness rehabilitation is more harmful than helpful, an important but often overlooked consideration.

**Echolocation and the blind.**

A number of auditory location studies have been conducted with the congenitally and early blind that show activation in visual cortex and also superior performance. One such study by Kujala et al. (1992) examined the ERPs elicited as subjects either attended or ignored sounds of a particular frequency presented from different locations. Attended sounds corresponded to an N2b component positioned further posterior in the blind than in the sighted; the specific area of distribution was located in the occipital cortex in the blind. Perhaps attributable to their neuroplastic occipital cortex, blind individuals have been found to surpass sighted controls in echolocation tasks. In a study by Schenkman et al. (2010), blind and sighted individuals had the task of identifying the location of sounds and determining whether or not a reflective object was present. Blind subjects performed this task with significantly more accuracy at all distances; notable differences in precision were noted as the distance increased to greater than 2 meters away.

Creators of various rehabilitative aids have used the concept of this unique echolocation ability in their design. Ifukube (1991) created a device that emits downswept frequency-modulated ultrasound signal from a transmitter and then transforms the frequency of the reflected signal through a receiver in a way that is similar to, and as quick as, the method used by bats. A main advantage of this device over other prior devices is the fine level of size discrimination that is possible. A later device by Arno et al. (1999) utilized the concept of frequency-pixel association as it relates to echolocation. Essentially, with this auditory substitution device, blind individuals are able to mentally construct visual patterns by hearing...
sounds of particular frequencies. The device and others like it created by the Arno lab utilizes a camera that captures a scene and then produces a specific pitch for each pixel (Capelle et al., 1998). This type of apparatus is still being developed, as the Rauschecker lab at Georgetown with whom I worked for example, is now also conducting a study concerning frequency-pixel technology. These devices show what is possible when the knowledge of neuroplasticity within blind visual cortex is applied for rehabilitative purposes.

However, some blind individuals do not need actual devices to utilize their superior abilities in echolocation. Daniel Kish, now 44, became completely blind around the age of one due to retinoblastoma. He has taught himself to echolocate and has famously become known as a “human bat” (Austin, 2010). Daniel utilizes rapid tongue clicks, the sounds of which reflect off his nearby surroundings. In this way, Daniel is able to “see” through the use of sound. His abilities have attracted the attention of neuroscience researchers who are now conducting fMRI studies with Daniel that examine the activations produced when he echolocates in response to naturalistic stimuli. Their study is looking to explore the cross-modal plasticity in Daniel’s visual cortex, an interesting study design since Daniel is a trained expert in echolocation (Austin, 2010).

Because of his increased independence relative to other blind individuals who do not echolocate, Daniel is able to get around fairly easily on his own and is well accomplished. He has obtained higher education degrees in psychology and has even started World Access for the Blind, his own training group in which he shows other blind persons how to effectively use echolocation. Some blind individuals are not as impressed by Daniel as others, saying that he is making the blind community appear “abnormal” (Finkel, 2011). This is an important question on
which later there will be further reflection: Do the blind want to be singled out for rehabilitation? Is not offering a “fix” an indication that something is “wrong” with them?

A teenager named Ben Underwood represents another example of a blind individual who uses echolocation to navigate the world around him. Ben, like Daniel, lost his eyes to retinoblastoma at a very young age. Now as a teenager, he has perfected his use of echolocation and is known to be a tough competitor in foosball and videogames. Ben claims that his motivation to use this echolocation ability came from the positive attitude put forth by his mother, who reminded him growing up that he might not have his eyes, but he still has his other four senses. She often reminds him, “There’s nothing you can’t do” (Schorn, 2009). For the blind community, having this support network is extremely important in learning to cope and achieve.

**Gene therapy.**

 Revolutionary work in the area of using gene therapy to restore sight to the congenitally blind has recently taken place in the lab of Albert Maguire and Jean Bennett at the University of Pennsylvania. Maguire and Bennett used recombinant adeno-associated virus to deliver a healthy copy of defective retinal gene RPE65 (Maguire et al., 2008). The viral vector was injected into a 3mm³ area on the retina using a surgery technique that had been practiced thousands of times prior in the lab. Maguire and Bennett treated 6 individuals who suffer from Leber’s Congenital Amaurosis (LCA), a condition in which the retina is not able to process light. One patient in the study who was interviewed extensively was noted prior to surgery to have superior language skills and also to be an excellent skier. This patient’s surgery went well, and weeks after the operation, she had increased visual acuity, pupil restriction in response to light, and mobility. While she could see colors, overall shapes, and letters, she could not recognize faces or read words (Walters, 2008).
Essentially, the surgery helps to restore some vision, but is far from perfect. How is it possible to explain to patients the benefits of the surgery without the risk of setting their hopes too high? Also, how is it possible to realistically describe what life will be like for the patients following surgery, given that only those who have had their vision restored would be able to provide such a description? Is the sight that these individuals possess post-operation similar to the vision of a sighted person? The answer to this question, in many respects, is no. On the other hand, is it ethical to not offer the opportunity of having the surgery if we have the technology, despite these shortcomings? Such questions will now be further explored.

**Should we work towards blindness rehabilitation?**

At first glance, one would not question whether or not we should work towards creating technologies that provide sight to the blind. After all, vision is of great importance to and highly emphasized within the sighted population. However, some factors need to be considered when deciding whether or not sight would represent a positive change in the lives of the blind, such as blind culture, difficulty adjusting to a visual world, psychological factors, etc. Essentially, is sight a gift? Answering this question requires the consideration of the cultural climates in developed versus developing nations.

**Evidence from the U.S.**

Sometimes, questions at the macro level can be further elucidated by examining those questions at the level of the individual. Here, we will explore case studies of blind persons in the U.S. who were the recipients of sight restoration techniques.

A well-known case is that of Virgil Adamson who was studied by Oliver Saks, a famous neurologist known for his tendency to take on difficult, but interesting neurological cases. Virgil became blind as a young boy due to retinitis pigmentosa. He grew up in Kentucky, where he fell
victim to a triple-pronged illness comprised of meningitis, polio, and cat-scratch fever. Complications from this illness caused Virgil to develop cataracts and to, eventually, become completely blind. Virgil’s life changed in ways that did not just reflect his vision: his personality, which was once lively, became subdued. He also experienced changes in his memory, as his ability to remember facts became almost encyclopedic. As a young adult, Virgil trained as a masseur and moved to Oklahoma. There, he met his wife, who encouraged him to explore visual restoration options. His wife’s doctor, Dr. Hamlin, performed Virgil’s surgery, which involved removal of his cataracts. Unfortunately, there was already extensive damage to his macular field of vision. Thus, cataract removal could only improve his vision to a certain extent (Sacks, 1995).

After surgery, it was difficult to tell exactly what Virgil could and could not do. At times, Virgil gave colors the wrong names, for example, calling green “red.” It was hard to tell if Virgil was suffering from color agnosia or anomia, or if it was a matter of lack of practice in matching a color to its name. At times, he would claim that he could not see anything, but would correctly navigate around objects and reach for objects if asked; he seemed to not be consciously aware of his seeing abilities but would behave as if he was seeing. Conversely, Virgil would at other times display signs of a complete lack of visual behavior but would claim that he could see (Sacks, 1995). This could have potentially been very stressful for someone like Virgil. It could have been stressful as well for his friends and family members who were unsure of how to help him. Also, what would one say to Virgil while he was acting as if he was seeing when he actually wasn’t? Would it be possible to phrase such remarks in a way that wasn’t discouraging?

What some may not realize about Virgil’s newfound sight is that he had to learn to see. Virgil had difficulty recognizing size and shapes but eventually could identify objects after a period of time. He had to painstakingly figure out how everything was put together on a part-by-
part basis. He had trouble recognizing faces and words, even though he could individually distinguish parts of a face and letters. Like an infant, Virgil had to “visually construct” the world (Sacks, 1995). Virgil also completely lacked confidence in what he was seeing. Having sight actually made it more difficult to complete everyday actions, such as crossing the street. Additionally, Virgil had a hard time connecting visual and tactile modalities. For instance, he was able to know a hill by the feeling he had as he walked up it but could not tie this experience to recognizing the visual shape of a hill (Sacks, 1995). He was skilled in navigating his tactile world—by adding a visual component, it was almost as if he was going backwards in some respects.

Virgil’s mental health was also affected by his surgery. Post-operation, he experienced fear, depression, anger, and general psychological stress. He found walking to be frightening and noted how disgusted and saddened he was to see the bodies of his massage clients. However, he was elated upon seeing his family, whose faces he had not gazed upon since he was a young boy. He also felt angry that he had been thrust into this situation and could not help himself resolve the conflicts that he had come across. For instance, at times, Virgil experienced extreme blurriness of vision. It was difficult to tell if these periods without sight were due to psychological or neurological causes, as the episodes only occurred at very specific stressful times, such as when Virgil’s family visited. It is possible that it was a case of cognitive overload, and hence of neurological causes. It is also possible that Virgil did not want to see at those moments and that his psychological stress manifested itself in a physical way. By the end of his life, Virgil became blind once again due to health complications. Virgil actually felt relieved as his vision faded, noting that he was now “allowed not to see” (Sacks, 1995).
Mike Mays, another blind patient to whom sight was restored in the U.S., had a mostly similar experience to that of Virgil’s. For Mike, his concerns were less related to the technical difficulties of his new sight and more focused on the fact that he had been happy being blind. He became blind at the age of 3 after an unfortunate chemical spill that burned his eyes. His mother was determined to give Mike as normal of an experience as possible: she had him participate in the same activities as his brothers and sisters, including sports and household chores. Like Ben who was mentioned earlier, Mike had a mother who also encouraged him and told him that anything was possible. Mike learned how to ride a bike, played soccer, and became an extreme downhill skier, winning gold medals at the Para-Olympics. He was always pushing limits, even speaking of becoming a crossing guard as a child. He received stem cell surgery to restore his vision at the encouragement of his wife and children. Mike said he was skeptical at first, since he was very comfortable with his blindness and felt as if surgery was a way to say that how he had been living was “incorrect” (Blackston, 2008). After his operation, he claimed that he now felt afraid while skiing and as if he was going to crash into things that were not actually close to him. Like Virgil, Mike had to learn to use his vision and had difficulty recognizing faces, 3D shapes, and perspective. Mike noted that his sight was most analogous to “guessing” (Fine et al., 2003). He did believe that sight also had benefits, such as being able to see his kids play (Blackstone, 2008).

From these stories of Mike and Virgil, one can receive a glimpse into the lives of blind individuals who have taken advantage of blindness rehabilitation technology. Their stories reveal the complexity of blindness and sight restoration. While being able to partially distinguish the features of loved ones proved to be a joyful aspect of sight, other stressful components also accompanied their everyday lives. For those like Virgil and Mike who had received support as
blind individuals and in turn possessed strong blind identities, gaining sight also meant losing part of their previous sense of self. There is something to be said for blind culture in developed nations such as the United States, where there is not as much stigma surrounding visual impairment. More support and resources are provided in places such as the U.S., enabling blind individuals to not only accept their condition but to be proud. Given this environment, blindness rehabilitation may not be as welcomed by some within the blind community of developed countries.

**Evidence from developing countries.**

The described outcomes of patients in developing countries tend to be relatively positive. A woman in Kenya, for example, seemed elated after her operation, noting that she can now talk with others in her village. Before, she was not able to trust others in her conversations, saying that she could never be sure if their facial expressions matched their words (Unite for Sight Module 11, 2010). Congenitally blind individuals in other developing countries have also stressed encouraging outcomes from surgery. A well-studied patient known as S.R.D grew up blind in India until her congenital cataracts were removed at age 12. After her surgery, she went through a learning period but was eventually able to recognize objects, match 3-D shapes, and even roughly identify faces of family members. She was also able to work as a maid, find a husband, and have a child. Should she have remained blind, the possibility of accomplishing such life milestones would have been much less likely in her country of origin (Ostrovsky, 2006).

Pawan Sinha, the ophthalmologist and M.I.T. researcher who studied S.R.D’s case, initiated a project in India called Project Prakash that aims to treat those who suffer from congenital blindness. Hundreds of thousands of children in India are blind and most cases are
preventable. Additionally, most cases are also treatable. But, in developing nations such as India, treatment is often not available (Sinha, 2007). Given the knowledge that S.R.D. had a readily treatable disease but unfortunately lived in an area in which treatment access was limited, she may have felt frustrated. Having the surgery could have relieved some of this frustration and have seemed like a welcomed option to S.R.D. at the time. Sinha set out to change this unfortunate situation in India and has demonstrated the difference that a single person can make in the lives of others (Ostrovsky, 2006).

Even though the cases of Virgil and Mike have pointed out some of the negative aspects of blindness rehabilitation, if there is a great need for treatment in these developing areas, is it wrong of Sinha to help? As briefly referenced, following her surgery, S.R.D. could segment images, match basic shapes, identify faces, etc. She was described by Sinha as being “well integrated into mainstream society” and to be able to “effectively” use her vision (Ostrovsky, 2006). Sinha has also given numerous other examples in his academic lectures of children whom they have treated through Project Prakash and their positive progress in the areas of spatial navigation and object segmentation (Sinha, 2009). Based on these results, Sinha advocates treating blindness whenever possible and notes that we have a duty to do so if we are able to (Ostrovsky, 2006).

However, a few caveats should be noted. One is that only the relatively positive results are detailed in the case study of S.R.D and in the cases of the treated patients described in Sinha’s lectures. Is it possible that those treated in India are not sharing with others the more negative sides of their treatment? Mike and Virgil may have felt able to talk openly about their struggles, but the environment in India is different in many ways. Stigma surrounding blindness in developing countries like India is strong. Being blind is viewed as a weakness and such stigma
even prevents those who are blind from seeking treatment. Even though quality of life for a blind individual in developing nations is considerably lowered in many respects, including the areas of employment and romantic relationships, those who are blind often do not want treatment and deny that their vision is poor. Reasons for not seeking treatment include fatalism, believing that a higher power has willed it to be so, and not wanting to be a burden to others. Slightly less than half surveyed in a particular study who refused treatment presented co-morbid mental health issues and rejected the notion that there was anything wrong with their vision (Fletcher et al., 1999). Similar attitudes toward treatment exist in South Africa. A study by Rotchford et al. (2002) revealed that fatalism and fear represented the greatest barriers to seeking treatment for blindness, not cost.

In addition to the human rights motive advocated by Sinha, there is an economic motivation as well for the implementation of blindness rehabilitation programs in developing countries. Cataracts, for instance, the leading cause of blindness worldwide, pose a great economic burden. Treating cataracts with surgery has an average cost per Disability Adjusted Life Year (DALY) saved of $10-$40 and thus represents a very cost effective option (Vision2020 Report, 2007). However, the number of these surgeries performed in developing nations is much lower than in developed countries due to upfront cost and availability of qualified surgeons (see Figure 8).

Other organizations in India, in addition to Project Prakash, have been established to address the disparities in blindness rehabilitation, such as Narayana Nethralaya (NN). This hospital is well integrated and representative of the needs of the Indian population. Their motto “where faith heals you” and stressed principles, such as “donate your eye without fear; it won’t leave you blind in your next birth” emphasize the relative importance of spirituality and religious
values to the Indian community. Narayana Nethralaya acts as an accessible center where quality eye care is available. According to Dr. Shetty, Chairman of NN, around 2 million infants each year are at risk of developing Retinotopy of Prematurity (ROP), a major cause of congenital blindness. Through screening by NN, about 10% of infants, on average, tested for ROP are found to have the disease. The organization has set up a satellite group called Project ROP that has brought care to various rural districts in India. NN has also become a leader in bringing cutting-edge technology to India. Telemedicine software is being used in the rural clinics. Images can be sent directly to NN doctors’ phones should an expert physician not be available at a rural site. The doctor can then diagnose and quickly report back (Shetty, 2010).

Thus, given the knowledge that blindness represents more of a barrier to having a high quality of life in developing nations, perhaps the negative aspects of blindness restoration should not be as heavily weighed as in developed countries. That is not to say that the physical and mental difficulties suffered by those like Virgil and Mike should not be taken into consideration. However, if not having sight means not being able to have a job and hence food, clothing, and shelter in developing nations, survival must be put first. Also, a question that was raised earlier should be taken into account as well—is it really ok to not offer treatment to those who desire it if we have the technology to do so? Should we not let the individual decide? At what point does it become acceptable for a higher-authority to withhold a form of treatment from a patient population? Does anecdotal evidence that includes mental health aspects provide a strong enough case? What about if the treatment helps some but hurts others? These are all interesting aspects to reflect upon in relation to designing and offering blindness rehabilitation treatment.
Social Connectedness Survey Component of this Study

In addition to the fMRI portion of this study, there was a survey presented to each subject at the end of the experiment. This survey represented a component that was more directly applicable to public health aspects of blindness. The topic of the survey was that of “social connectedness;” it was originally developed by Professor Richard Lee of the University of Minnesota (side note: permission was obtained directly from Dr. Lee prior to the experiment to use this survey). Using such a survey topic was suggested during a conversation about this project with Professor Glatt of the Princeton Psychology department. The survey consisted of 20 questions that the interviewee answered on a scale of strongly disagree (score of 1) to strongly agree (score of 6). Questions from the survey included those such as “I feel understood by the people I know” (for exact survey, see Figure 9). Positively phrased questions were scored normally, while negatively phrased questions were reverse scored. Given the number of questions and range of scores for each question, the minimum possible total score was -50, while the maximum was 50.

Nine out of the ten subjects were surveyed. Geographically, three were from New Jersey, two were from New York and four were from Washington D.C. and its surrounding areas. The set of scores was the following: -31, -18, -4, 11, 28, 29, 33, 37, 50. The average score was 14.33; the median was 28. The average and median were both above zero, suggesting an elevated degree of social connectedness, but it should be emphasized that the subject pool is quite small. The range of values also included three values less than zero, so the results were not completely conclusive.

The idea behind this survey was that if blind participants do demonstrate activation within visual cortex to the full story condition, this means that they have an extra area that
processes complex language in comparison to sighted individuals. In turn, this could mean that they are able to better engage in social communication. In fact, it has been shown by behavioral studies that a higher percentage of speech of the blind as compared to their sighted counterparts is devoted to social communication (Dunlea, 1989). If the blind are able to better socially communicate with others, they may have an elevated sense of social connectedness. A stronger sense of social connectedness could have many implications, including those related to mental health and wellbeing.

Regardless of whether or not these results can be trusted and the number of confounding factors that could potentially be lurking beneath the surface, asking these survey questions opened a dialogue with the blind participants and allowed them to talk about their own life experiences. Subject R.P. did think that it was plausible that blind individuals are able to better socially communicate and connect based on her own personal experiences. She recounted how she typically holds her conversation partner’s hand to feel closer to him or her. Employing the use of an additional sensory modality such as the physical sensation of touch may indeed add to feelings of mental connectedness.

Other good points were raised regarding the type of population that was surveyed. M.P. noted that when working with the congenitally blind, it is important to remember that they have never seen, so going through life is a matter of “just learning to adjust.” This compares with those who are late blind and are coping with that which was lost. However, coping is still necessary for all blind individuals. As mentioned earlier, much of how a blind person views his or her blindness depends upon the nature of the environment in which he or she was raised and how much support was received. Subject S.L. spoke of living in a tough city environment and seeing herself as a loner who was not well supported by her family. But, being a loner though
was not always interpreted as something that was “negative” when completing the survey. Another subject noted that, like many people, sometimes she just likes to have her space. Besides support from family and friends, having outlets also represents a major contributing component to the level of achieved coping and overall happiness. Outlets for the subjects interviewed included music and spirituality for the most part. In fact, the majority of subjects were heavily involved in music. Some were singers, others jazz musicians, still others avid music listeners; three subjects even had their own released music records. Some subjects also remarked that they regularly find a sense of inner peace through prayer and spiritual rituals.

A better sense of social connectedness with others could be extrapolated to potentially correlate with better mental health. Some of the subjects thought of this possible correlation while answering the survey questions, noting that the questions shared similar components with mental health survey questions. Subject N.Y. noted that blind individuals are “always asked these kinds of questions” and another volunteered information regarding her experience with psychotherapy for anxiety related to her blindness. These responses were interesting for a few reasons: one reason is that it shows that in America, the support for those who are blind is ample and there is a high likelihood that they will be offered help for related problems. Also, it has been determined by various studies that there is a potentially strong connection between blindness and mental illnesses such as depression and anxiety; these subjects provided further confirmation of this notion in their comments (e.g. Brennan & Cardinali, 2000; Cimarolli, 2006). Apparently, based on information gathered from these blind subjects who represent direct sources on this topic, this connection between blindness and mental health is often recognized by healthcare providers in the U.S. The same cannot be said for developing countries where stigma surrounding both mental illness and blindness is more severe (e.g. Fletcher et al., 1999).
There is still some residual stigma in the United States. One subject brought up the fact that social connectedness as a result of social communication is a two-way street. Sometimes, other people are afraid to talk to them because they’re blind. There also is a lack of respect—as if they are less human because they are lacking vision. Subject R.P. told me a story of how she has experienced situations in which she was talking to someone and the other person walked away mid-conversation. She was then left talking to what appeared to be herself, which she noted was embarrassing. This brings me to my last and final point regarding the prospect of sometimes-unwelcome rehabilitation in the United States. Blindness is a culture and even asking questions about their blindness or focusing on their blindness in any way can be insulting to certain blind individuals who do not wish to be treated abnormally. Perhaps this feeling can best be summarized with a line that one subject has told Paula, the post-doctoral researcher with whom I work at Georgetown, in the past, “Nothing is wrong with me. I’m just blind.”
References


Shetty, K. B. (2010, April). Childhood blindness is not given importance in India. *The Times of India*.


Figure 1. An integrated view of the proposed hierarchy of time scales in visual and auditory modalities. This was a figure in the Lerner et al. (2011) paper depicting a summary of results from their auditory TRW study in conjunction with results from the visual TRW study by Hasson et al. (2008). The figure shows primary sensory areas, such as A1 and V1, to have short TRWs, while long TRWs are found in regions such as the TPJ and IPS. Areas outlined in yellow indicate areas of overlap. CS, central sulcus; LS, lateral sulcus; STS, superior temporal sulcus; TPJ, temporo-parietal junction; IPS, inferior parietal sulcus.
Fig. 2 Intersubject correlation in the congenitally blind for natural stimuli. Inflated brain maps representing Cross-run intersubject correlation (ISC) in the three conditions (full, sentences, words) are depicted. Lateral, medial, and posterior views are shown. Each map encompasses areas of activation present in maps of shorter time scales, plus additional areas. For example the full condition map (long time scale) contains areas such as A1 and the STG found in the sentences map (intermediate time scale), along with other areas such as the TPJ and V2/V3+. A, anterior; P, posterior; A1, primary auditory cortex; STG, superior temporal gyrus; TPJ, temporo-parietal junction; V2/V3+, extrastriate cortex. MPFC, medial prefrontal cortex.
Figure 3. Activation profiles of selected ROIs in the congenitally blind and sighted. Each individual chart represents the Run-average intersubject correlation within a particular ROI. Selected ROIs include those along the A1-TPJ axis (A1+, STG, RTPJ) and also the Precuneus. A1+ demonstrated reliable responses for all conditions including nonsensical sound (reverse condition; not shown), denoting a short TRW. The STG generated reliable activity for the full, sentences, and words condition, suggesting an intermediate TRW. The TPJ showed evidence of reliable responses to only during the full condition, which corresponds to a long TRW. Similarly, the precuneus also exhibited a long TRW. A1; primary auditory cortex; STG, superior temporal gyrus; RTPJ, right temporo-parietal junction.
Figure 4. Intergroup sighted-blind correlation. The sighted 3D surface maps (top) represent the sighted intersubject correlation demonstrated in the study by Lerner et al. (2011). The sighted-blind 3D surface maps (bottom) show the intergroup correlation found between the congenitally blind subjects in this study and the sighted subjects in the Lerner et al. study. Voxels that were above a set threshold in all intersubject correlation maps were given the label of “word scram.” Similarly, voxels that were above a set threshold in all intersubject correlation maps except word scram were given the label of “sentence scram.” Lastly, voxels that were above a set threshold in only the full intersubject correlation map were given the label of “full story.”
Figure 5. Intergroup blind-sighted correlation within selected ROIs. This figure shows the correlation for the full condition between data from the sighted (Lerner et al., 2011) and the congenitally blind. The intergroup correlation was calculated using averaged data across subjects within an ROI. High levels of correlation were seen in A1+, the STG, the TPJ, and the precuneus. A1, primary auditory cortex; STG, superior temporal gyrus; TPJ, temporo-parietal sulcus.
Figure 6. Closer examination of the V2/V3 ROI. The top figure shows the Cross-run intersubject correlation for the full condition as depicted for both the 2D map and the posterior view of the 3D surface map. The area enclosed in each blue circle denotes the V2/V3 ROI that was identified as showing reliable responses within the full condition. The plot below the map shows the Cross-run intersubject correlation within the V2/V3 ROI in each condition; the full condition shows the highest and clearest correlation within V2/V3. COR, coronal plane; SAG, sagittal plane; TRA, transverse plane.
Figure 7

PREVALENCE OF BLINDNESS

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Figure 8

Cataract Surgery Rate 2006

Disclaimer: © World Health Organization. The boundaries and names shown and the designations used on this map do not imply the expression of an opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

**Figure 9**

### SOCIAL CONNECTEDNESS SCALE-REVISED

**Directions:** Following are a number of statements that reflect various ways in which we view ourselves. Rate the degree to which you agree or disagree with each statement using the following scale (1 = Strongly Disagree and 6 = Strongly Agree). There is no right or wrong answer. Do not spend too much time with any one statement and do not leave any unanswered.

<table>
<thead>
<tr>
<th>Strongly</th>
<th>Disagree (1)</th>
<th>Disagree (2)</th>
<th>Mildly Disagree (3)</th>
<th>Mildly Agree (4)</th>
<th>Agree (5)</th>
<th>Strongly Agree (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I feel comfortable in the presence of strangers...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>2. I am in tune with the world...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*3. Even among my friends, there is no sense of brother/sisterhood...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>4. I fit in well in new situations...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>5. I feel close to people...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*6. I feel disconnected from the world around me...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*7. Even around people I know, I don't feel that I really belong...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>8. I see people as friendly and approachable...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*9. I feel like an outsider...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>10. I feel understood by the people I know...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*11. I feel distant from people...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>12. I am able to relate to my peers...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*13. I have little sense of togetherness with my peers...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>14. I find myself actively involved in people's lives...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*15. I catch myself losing a sense of connectedness with society...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>16. I am able to connect with other people...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*17. I see myself as a loner...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*18. I don't feel related to most people...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>19. My friends feel like family...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>*20. I don't feel I participate with anyone or any group...</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

* reverse score

Collaboration in Senior Thesis Work
The Relationship between the Senior Thesis and Earlier Work

Please use this form to indicate the relationship between previous work and your senior thesis and to indicate whether your thesis involved collaboration with others.

Indicate below whether there is any overlap between your senior thesis and earlier work that you did for junior reports, junior papers, or papers for various courses.

Overlap       ___X____
No overlap    _______

If you checked the box indicating that there is overlap between your senior thesis and previous work, please describe the overlap on a separate page, and include it within the thesis after this form.

Readers of your thesis may, if they choose, ask to see earlier papers that you indicate have some overlap with your senior thesis.

Indicate below whether all or part of your thesis resulted from work done collaboratively with one or more other people.

Collaboration   ______
No collaboration ___X____

If you checked the box indicating that your thesis work was done entirely, or in part, in collaboration with other people, describe the nature of the collaboration and what resulted from it on a separate page, and include it within the thesis after this form.
**Description of overlap with previous work:** There is some overlap in this paper with my third fall JP and my spring JP from junior year. But this overlap is not extensive, as my JPs consisted of literature review and this is an experimental study. The overlap mostly occurs in the introduction section called “Existing Research on the Neuroplasticity of Blind Visual Cortex.” Some of those sources come from my two JPs. However, for the most part, I tried to go back and re-read the original papers and to write up the background information based on these re-readings.
Did your Senior Thesis involve research with human subjects? Yes / No

If your Senior Thesis DID involved research with human subjects, please indicate your IRB Case Number below.

#___ 4143__________ Approval Date ___March 15, 2010_________