INVESTIGATING VISUAL TO AUDITORY CROSSMODAL COMPENSATION IN A MODEL FOR ACUTE BLINDNESS

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ABSTRACT

This study examined neural integration of the sensory modalities of vision and hearing. The objective is to investigate whether an effect of cross-modal compensation of visual to auditory networks in human participants occurs with the deprivation of visual input. This model for acute blindness had a novel design that attempted to imitate true blindness. The experiment involved 10 participants wearing opaque contact lenses that blocked visual feedback for a total of five hours. The duration of the total experiment was approximately eight hours, and involved seven sessions. The overall accuracy across time did not improve in blind individuals (p = 0.586), however, there was a significant finding in speaker accuracy (p<0.000), and a significant interaction between session and speaker (p=0.004). Reaction time generated a main effect of session (p<0.000) and a significant main effect of speaker (p<0.000), but no significant interaction between session and speaker with respect to reaction time.

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1.0 INTRODUCTION

It has previously been reported that blind individuals have superior auditory and tactile skills compared to individuals with regular or corrected sight, especially in spatial acuity, which suggests a cross-modal plasticity due to experience (Ashmead et al. 1991; Goldreich & Kanics 2003; Lessard et al 1998; Van Boven et al. 2000). Neuroimaging has been used to explore crossmodal compensation from the visual to the auditory network, showing activation in many occipital cortex areas while early and late blind humans complete auditory or tactile tasks (Alho et al. 1993; Amedi et al. 2003; Sadato et al. 2004). Currently, a ‘true’ model of acute blindness has not been used to investigate crossmodal compensation from the visual to the auditory networks. This study explored how visual deprivation impacts the ability of participants to perform an auditory localization task in order to draw conclusions on the putative plasticity associated with acute blindness. Using opaque contact lenses, as opposed to ski masks and blindfolds, this study was able to use a true model for acute blindness to explore how long-term visual deprivation impacts the ability of participants to perform an auditory localization task. Long-term blindness was defined as a duration exceeding 90 minutes, currently the longest time of deprivation in normally sighted individuals. The sound localization task employed was modeled after a study done by Lewald (2007) and an experimental setup similar to Hoover (2012); both studies will be described in further details.

In order to develop an in depth understanding of how this experimental design evaluates the ability to localize sounds, it is important to understand the (1) auditory and (2) visual systems.
1.1 THE AUDITORY SYSTEM

The focus of this study will solely be on binaural sound localization; individuals who are able to localize sound to a spatial position using two acoustic sensors. In the case of the Homo sapien, this entails two normally functioning ears (Stern 2006). There are two types of cues used for sound localization: monaural cues and binaural cues. Monaural cues refer to cues where only one ear is required as the head-ear shape and torso act as direction-dependent frequency filters for the eardrum that receives a sound wave (Stern 2006). The latter involves the use of both ears as well as direction-dependent frequency filters. The first broad analysis of binaural perception was the ‘duplex theory’, presented by Lord Rayleigh, and for the most part, remains valid to this date (Strutt 1907). With the exception of a sound source that is precisely in front or directly behind the head, sound is impacted by time and intensity with respect to the physical location of the sound source. The phenomenon of Interaural Time Difference (ITD) is defined as a delay in sound arrival. It takes slightly longer for sound to reach the more distant ear. Similarly, interaural Level Difference (ILD) is defined as a difference in sound arrival between the two ears because the head blocks some of the energy for the ear further away, particularly at higher frequencies. This is due to a ‘shadowing’ effect of the head, preventing some of the incoming sound energy from reaching the ear that is turned away from the direction of the source of sound (Keating P & King AJ 2015).

1.1.1 The Auditory Mechanism

The auditory stimulus we know as ‘sound’ is converted into neural impulses by the cochlea, which contains a million moving parts (Garrett 2009).
In order for sound to convey information and have meaning, it must be translated for recognition in the auditory cortex. Sound waves travel from the outer ear to the middle ear, where they are converted to vibrations and continue to the inner ear, where nerve signals are sent to the auditory cortex. The outer part of the ear, known as the pinna, channels sound, selecting sounds from the side and front and blocking sound coming from behind, and funnels it into the smaller area of the auditory canal (Brown 1987; Kiang et al. 1982; Spoendlin 1969; Wangemann 2006). As a result, the tympanic membrane (or eardrum) of the middle ear section vibrates and thereby transmits sound energy to the ossicles. The ossicles are tiny bones that function as a lever and further transfer the vibrations to the cochlea. The ossicles are compiled of three small parts: the malleus (hammer), incus (anvil), and stapes (stirrup). The stirrup is adjacent to a flexible, thin membrane known as the oval window, located on the face of the vestibular canal, which is where the sound energy enters the cochlea. The tympanic canal is connected to the vestibular canal at the far end of the cochlea; this opening is referred to the helicotrema. The helicotrema eases the transition for the pressure waves traveling through the cochlear fluid into the tympanic canal (Figure 1). Sensory cells sitting on top of the membrane known as hair cells move up and down and bumping against the membrane tilting side to side, causing channels on the bristle surface to open up. This results in an electrical signal, and the auditory nerve carries the signal to the brain, where it is translated into sound (Wangemann 2006; Brown 1987; Kiang et al. 1982; Spoendlin 1969).
**Figure 1: The Anatomy of the Ear;** This image presents the anatomy of the outer, middle, and inner ear of a human being. The outer ear is called the “pinna” and is made of ridged cartilage covered by skin. The inner ear consists in part of the cochlea, where sound is transformed into nerve impulses to travel to the brain. Image from Geisler 1998.

1.1.2 The Auditory Cortex

The auditory nerves are the eighth cranial nerves, and enter the brain stem from each side, crossing over to the opposite hemisphere (Winer & Lee 2007; Hackett et al. 2001; Romanski & Averbeck 2009). The pathway takes them from the inferior colliculi, to the medial geniculate nucleus of the thalamus, and then to the auditory cortex in each temporal lobe. Although neural impulses generally travel to the opposite hemisphere, they also travel to the same side. The auditory cortex is topographically organized; thereby neurons that are from adjacent receptor locations were projected to adjacent neurons within the cortex (Figure 2). More specifically, the spatial arrangements of where sounds of different frequencies are processed in the brain are arranged in proximity with respect to closeness of tones to each other in terms of frequency. Close tones are also represented in topologically neighbouring regions of the brain. In each hemisphere, the auditory cortex is located on the superior gyrus of the temporal lobe (Garrett 2009).
1.1.3 Sound Localization

The auditory neuroepithelium cannot directly code the location of a sound source. Instead, sound localization is evaluated based on binaural comparisons of timing and intensity (ITD & ILD). Monaural frequency analysis is computed in the dorsal cochlear nucleus, which provides a fairly direct, tonotopically organized projection onto the contralateral primary auditory cortex (A1) (Malmierca 2003). Again, this pathway first moves to the inferior colliculus, and then the medial geniculate nucleus. Unlike the dorsal cochlear nucleus, the ventral cochlear nucleus projects second-order neurons both ipsilaterally and contralaterally to the superior olivary complex in the brainstem. The neurons in the medial superior olive (MSO) are commonly excited by stimuli from either ear (Cant & Casseday 1986). However, they respond most frequently when a tone is presented to the two ears with a delay in one ear to the other.
Cells that are in the lateral superior olive are excited by the ipsilateral ventral cochlear nucleus, and cells from the contralateral ventral cochlear nucleus are projected across the midline, forming synapses in the medial nucleus of the trapezoid body (MNTB). The MNTB (contralateral sound) inhibits neurons in the lateral superior olive, but these neurons are excited by the ipsilateral sound, therefore allowing the detection of differences in sound intensity between the two ears (Blauert 1982; Brungart et al. 1999; Moore & Caspary 1983).

1.2 THE VISUAL SYSTEM

The outer part of the eye is the cornea, which is transparent (Purves et al. 2004). Immediately behind the cornea is the anterior chamber, filled with aqueous humor, a clear-watery liquid that provides a supply of nutrients (Figure 4). Aqueous humor is produced in the posterior chamber, which is the space between the lens and the iris, and flows through the pupil into the anterior chamber. The ciliary muscles are responsible for an extensive volume of fluid production (Purves et al. 2004).

Figure 3: The Anatomy of the Human Eye; Image obtained from Neuroscience 3 ed 2004.
The ciliary muscles attached to the lens can stretch, since the lens is a flexible tissue, allowing for focus on distant objects, or the muscle can relax for objects that are near. This is a process known as accommodation. In other words, observing objects at a distance results in thinning of the lens, as it becomes flat and has the least refractive power. If an object is observed close-up, the lens is made thicker and rounder and has the most refractive power (Figure 5) (Purves et al. 2004).

The lens inverts the object in view onto the retina. The retina is the only part of the eye that has neurons with the capability of transmitting visual signals to central targets. The iris partially covers the lens, and gives our eyes their colour. The opening of the iris is what composes the pupil, controlling the amount of light that enters the eye with contractions and relaxations, based on bright or dim light, respectively (Purves et al. 2004).

The light-sensitive structure of the retina is made up of two main types of receptor cells, rods and cones. There are also natural cells that are connected to these light-sensitive receptor cells.

1.2.1 The Visual Pathway

The optic nerve does not contain any photoreceptors and is insensitive to light, producing what is known as the blind spot. Axons in the optic nerve run a straight course to the optic chiasm, where 60% of the fibers cross in the chiasm and the remaining 40% continue towards the thalamus and midbrain targets of the same side. The optic tract however, contains fibers from both sides, unlike the optic nerve. There is a decussation (or partial crossing) of ganglion cell axons at the optic chiasm, which permits approximately the same cortical site of each respective hemisphere to process information from corresponding points of the two retinas (Purves et al. 2004). The ganglion cell axons in the optic tract target the diencephalon and midbrain, in particular the
dorsal lateral geniculate nucleus of the thalamus. The neurons found in the lateral geniculate nucleus send axons to the cerebral cortex using the internal capsule, more specifically, a region called the optic radiation (Figure 6). These axons terminate in the primary visual cortex (V1) or the striate cortex, located within and along the calcarine fissure in the occipital lobe. This may be referred to the retinogeniculostriate pathway or the primary visual pathway. If there is damage anywhere along this pathway, it may result in serious visual impairment (Purves et al. 2004).

Figure 4: Visual Areas; Central projections of the retinal ganglion cells terminate at (i) the lateral geniculate nucleus of the thalamus, (ii) the superior colliculus, (iii) the pretectum, and the (iv) hypothalamus. This image shows the crossing axons of the right eye.

1.2.2. Eye-Head Coordination

The head and eye move in coordination in order to achieve what is perceived as ‘gaze orientation,’ which consists of saccadic eye movement towards the target and a near-simultaneous movement of the head (Bizzi et al. 1971; Bizzi et al. 1972; DeSouza et al. 2011; Morasso et al. 1973; Zambarbieri 1997). As the saccade is completed, the head movement falls behind and there is a counter rotation of the eyes in order to make up for the lag and maintain accurate gaze orientation. It is vastly agreed upon that the vestibular-ocular reflex (VOR) plays a role in the head and eye motor system coupling. A true concomitant eye and head movement
occurs towards targets that are large, whereas the remaining head displacement is executed once a target has already been reached for smaller target positions (Zambarbieri 1997). The study done by Zambarbieri (1997) concluded that although the strategy is similar, there are varying quantitative and qualitative outcome parameters of the eye-head coordination.

1.2.3 Light Adaptation

Ganglion cells are particularly important for light adaptation (Purves et al. 2004). A light spot’s intensity will impact the response rate of a ganglion cell when it is in its receptive field. As a result of the discrepancy between the narrow range of the ganglion cell discharge rates and the large range of light intensities over which we can see, an adaptation mechanism is required. The ganglion cell’s response to level of illumination presents the entire dynamic range of a neuron’s firing rate, which encodes information about the intensity differences across a range of luminance values that are a priority for a particular visual scene (Purves et al. 2004). The retinal ganglion cells have an antagonistic center-surround organization, which downplays the signal sent for the background level of illumination, a potential explanation as to why the relative brightness of objects remains much the same over a range of lighting conditions (Purves et al. 2004).

1.3 SOUND LOCALIZATION

There have been studies that indicate that early blind (EB) subjects have a superior ability to localize sounds compared to normally sighted individuals (Lessard et al. 1998; Kujala et al. 1997; Rice 1970). The theory that acuity is enhanced in the remaining senses in an individual experiencing blindness has long been investigated (Ashmead et al. 1991; Goldreich & Kanics 2003; Lessard et al 1998; Van Boven et al. 2000). An assumption is that recruitment of neural
processing from visual areas, such as primary visual cortex, for non-visual functions results in superior auditory and tactile performance of blind compared to sighted humans (Lewald 2007). Generally, these studies attribute the greater ability to localize sounds to reorganizations in neuronal populations that are involved in processing cues for localization of sounds, or additionally, to improved learning. The superior and inferior colliculus, and the primary auditory cortex are involved in spatial analysis and may cause neural compensation due to the increased use of spectral information between or within the structures (Chalupa & Rhoades 1977; King 1993; Middlebrooks & Knudsen 1984; Spitzer & Semple 1991; Stumpf et al. 1992; Toronchuk et al. 1992; Zambarbieri 1997). By measuring event-related potentials (ERP), Kujala (1992; 1995) was able to show increased use of parietal or occipital brain areas in blind individuals in response to auditory stimuli during sound localization tasks, compared to normally sighted individuals. They suggested that crossmodal reorganization provoked the effect of dormant but preexisting auditory connections to the visual cortex, as well as better learning strategies (Butler 1987).

The two primary methods for investigating sound localization include psychophysical studies involving an auditory task and a measure of behavioural performance, and neuroimaging studies involving an auditory task and a measure of activation, which has commonly been done so through the use of functional magnetic resonance imaging (fMRI).

1.3.1 Psychophysical studies

There are three major types of sound localization tasks that are used in these studies. (1) Head restrained; a head-centered axial system, (2) manual pointing; body-limb-centered segmental system using visuomanual coordination, and (3) free-field; no swivel or mount (axial system) for
the participant’s head, participant moves freely in horizontal and vertical plane and may be asked
to point, button-press or move head.

Lewald (2007) explored whether accuracy of sound localization improves when people
experience short-term light deprivation. Participants were blindfolded and the non-deprived
group removed the blindfold between sessions, compared to the deprived group, which kept the
blindfold on between the sessions. Subject’s heads were fixed by a swivel-mount, allowing the
head to rotate along the azimuthal plane as they responded to a sound localization task. Lewald
(2007) showed that when using a task of head pointing to acoustic targets as a measurement, the
accuracy of sound localization was increased after a short-term light deprivation of 90 minutes.
However, the increase of accuracy reverts to pre-deprivation values after 180 minutes of re-
exposure to light. This effect was only true for constant error, defined as systematic deviations
from target positions, which was reduced after light deprivation, however, there was no noted
change in the general precision of head pointing. The mean slope of the pointing responses
plotted as a function of eccentricity for both groups indicated that actual sound locations were
undershot (Lewald 2007). The researcher drew the conclusion that non-visual inputs to the visual
cortex exist in normally sighted individuals, and are not due to non-reversible reorganizational
processes from light deprivation (Lewald 2006). Lewald (2007) suggests that visual calibration
of the neural representation of auditory space during light deprivation may be required in
normally sighted individuals for precise sound localization. The idea of visual calibration has
been supported by studies that have reversibly induced a constant error in sound localization by
exposure to a consistent spatial disparity of auditory and visual stimuli using visual space (Canon
1971; Zwiers et al. 2003). This has also been done by manipulating the auditory localization cues
(Held 1955; Kalil & Freeman 1967), or by the presentation of synchronized spatially disparate
repetitive sound bursts and flashing light spots in total darkness (Lewald 2002b; Recanzone 1998). Essentially, all of these experiments involved systematically shifting sound localization to correct for deviation of sound from visual positions following the adaptation period. Therefore, the assumption is that with the absence of visual calibration during light deprivation, there may be some alteration of the geometry of the auditory space (Lewald 2007).

Hoover et al. 2012 looked for evidence of auditory-visual crossmodal compensation by measuring binaural and monaural sound localization in people with vision in one eye and compared it to normally sighted controls. One-eyed individuals showed significantly better binaural sound localization than controls for central sounds, but that significance was lost in the peripheral locations (Hoover et al. 2012). Moro & Steeves (2012), on the contrary, showed no dominance between visual and auditory processing in people with one eye.

There are numerous psychophysical studies that compare blind individuals to sighted individuals, and demonstrate auditory and tactile superiority (Ashmead et al. 1991; Goldreich & Kanics 2003; Lessard et al 1998; Roder et al 1999; Van Boven et al. 2000). Ashmead et al. (1991) showed auditory superiority by testing sound localization and sensitivity to ITD in human infants. There was no change in sensitivity to ITD across ages of 16 weeks, 20 weeks, and 28 weeks according to Ashmead et al. (1991). However, there was an increase in sensitivity to free-field, measured by the minimum audible angle localization performance. Participants in a study by Goldreich and Kanics (2003) experienced enhanced tactile acuity in blindness. This experiment was conducted by observing passive tactile acuity of blind and normal-sighted participants on an automated grating orientation task. This task required subjects to distinguish between two stimuli differing only in spatial orientation otherwise identical with respect to area, pressure and force. The grating orientation task tests passive tactile spatial acuity. A multivariate
Bayesian data analysis was used to determine predictors of acuity, and showed significantly
superior acuity in blind participants. This finding was independent of the degree of childhood
vision, light perception level, or Braille reading, leading to the authors suggesting their findings
were due to crossmodal plasticity (Goldreich & Kanics 2003).

A study performed in 1998 by Lessard et al. credited early-blind human participants with
improved ability to localize sounds compared to normally sighted individuals. Lessard (1998)
focused on how an ecologically critical function, like 3-D spatial mapping, is done by early-blind
individuals with or without residual vision. The participants experienced both monaural and
binaural listening conditions and the study found that early-blind participants can map the
auditory environment either equally or in a superior manner compared to normally sighted
participants (Lessard et al. 1998). Early-blind participants are also able to correctly localize
monaural sounds, but early-blind individuals with residual peripheral vision are unable to
localize sounds as precisely as normally sighted participants and participants that are completely
blind. Through this, they concluded that compensation might vary dependent on the extent of
blindness (Lessard et al. 1998).

1.3.2 Neuroimaging Studies

Jiang et al. (2014) designed an fMRI based experiment to test auditory motion processing for
early blind individuals. He tested early blind versus sighted individuals using a coherent and
incoherent stimulus, presented through MRI-compatible stereo headphones. The stimuli
contained “dynamic ITD” and “ILD” as well as Doppler shifting. The Doppler Effect, also
known as the Doppler Shift, is a change in frequency of a sound wave for an observer that is
moving relatively to the source (Poessel 2011). The regions of interest (ROI’s) were the left and
right human middle temporal complex (hMT+), the right and left planum temporale (PT), and left and right primary auditory cortex (PAC) (defined as the contiguous cluster of voxels in Heschl’s gyrus showing the most significant activation to 100% coherent motion versus silence using the auditory localizer stimulus). Jiang et al. (2014) found that EB individuals had significantly better behavioural performance in the identification of the direction of unambiguous motion of fairly naturalistic stimuli. They also showed significant blood oxygenated-level dependent (BOLD) responses to auditory motion in the hMT+, compared to individuals with normal sight who did not show any significant BOLD responses. They concluded that in EB individuals, the auditory hMT+ responses are associated with auditory motion. The PT region did not successfully decode the auditory motion stimulus, and thereby, the multimodal responses of the hMT+ in EB individuals were not driven by connections from that region. Plasticity that is observed in EB individuals tends to appear in the auditory regions of the cortex (Jiang et al. 2014). There have been other studies that show activation of true visual occipital cortex areas, of both early and late blind participants, during tactile or auditory tasks (Burton et al. 2004; Sadato et al. 2004; Amedi et al. 2003; Burton et al. 2002; Weeks et al. 2000; Buchel et al. 1998; Sadato et al. 1998; Sadato et al 1996; Alho et al. 1993).

Studies have also looked at different structures of the brain, comparing early visually deprived individuals to late visually deprived individuals. Shi et al. (2015) specifically looked at the structure of the corpus callosum by combining surface tensor-based morphometry with thickness profile. They found that reorganization is more significant in individuals with congenital blindness, compared to individuals with late blindness and sighted controls (Shi et al. 2015).
1.3.3 Crossmodal Compensation

Multisensory processing is also known as multimodal integration, and observes how information from different sensory modalities are integrated into the nervous system (Chan & Dyson 2014). The “modality-shifting effect” is used to show the relationship that may be associated between responding to two elements across a task that involves two modalities, in comparison to responding to a task consisting of only one modality (Spence et al. 2001). This experiment showed that reaction times (RT’s) were slower when participants were asked to respond to ‘unexpected’ modalities, defined as a mixture of two stimuli (i.e. 50% auditory, and 50% visual). They concluded that RT’s positively benefitted when the modality was expected (i.e. 75% Auditory, and 25% Visual). Chan and Dyson (2014) did a three-way repeated measures analysis of variance (ANOVA) using the factors of Condition (baseline, intramodal, intermodal), Modality (same, different), and Response (first, second). They found a within-modality preference pattern, and significantly slower RT’s for different-modality trials compared to same-modality trials (Chan & Dyson 2014). They also found strengthening within-modality retrieval, but that strengthening was not associated with a benefit for different-modality responding, but instead, it disrupted same-modality responding.

The origin of crossmodal plasticity was at the synaptic level (Goel et al. 2016; Petrus et al. 2014). At the synaptic level, plasticity reduced postsynaptic strength of excitatory synaptic transmission in two thirds of the layer in auditory cortex (A1) compared to the increase in strength of excitatory synapses of the deprived visual cortex (V1) (Petrus 2014). This may be characteristic of homeostatic adaptation in the non-deprived sensory cortices (Whitt et al. 2013). There have been some studies that indicate thalamocortical (TC) plasticity in the V1; however, it is said that these TC inputs experience less plasticity as individuals continue to age (Hensch
2005; Katz & Crowley 2002). Other studies demonstrated TC plasticity in older participants with the deprivation of a sense, or due to peripheral nerve transection (Montey & Quinlan 2011; Oberlaender et al. 2012; Yu et al 2012). Petrus et al. (2014) were able to show that the response properties of A1 changed proceeding light deprivation in mice. More specifically, they recorded single unit responses of pure-tone stimuli in mice that were deprived of light for 6-8 days, measuring frequency by evaluating the presented sound frequency against the resulting frequency response area (FRA) function as a plot. Higher rates of spontaneity were found in animals deprived of light, and shorter first spike latencies were found in normal mice, emulating an increase in response promptness and excitability (Petrus et al. 2014).

1.3.4 Head turning versus manual pointing

Whether the participant is asked to locate a target via manual pointing or via head turning influences auditory perceptual performance and additionally, influences performance patterns. Normally sound localization towards a source position in a free-field movement involves the pinna acting as a directionally dependent spectral filter, as it produces prominent peaks and notches in a free-field sound spectrum. Binaural room impulse response (BRIR) is the spectral filtering properties of ears and head and any room reverberation that is captured. Head turning uses a head-centered axial system, and manual pointing uses the body-limb-centered segmental system (Goldstein 2014; Pinek & Brouchon 1992; Paillard 1987; Wolfe et al. 2012; Yantis 2013). Although the oculovestibular reflex is said to compensate for undershooting, head turning towards visual targets still results in undershooting as the target location becomes more peripheral (Bratz 1966; Biguer et al. 1985). Participants that have the freedom to move their head have more accurate sound sourcing than when their heads are fixed (Thurlow et al. 1967; McAnnally & Martin 2010; Perrett & Noble 1997; Jongkees & Veer 1958), even resulting in
confusion in differentiating front or back sound location (Wightman & Kistler 1999). Our ability to hear sounds appears to be mainly in one definite direction, and it is believed that this is due to head movements during sound perception. Head motion alters the position of the aural axis and the angle between the axis and the sound direction. This change of lateral angle can define the direction of the source of the sound (Wallach 1940).

Manually pointing at visual targets uses visuomanual coordination, essentially, an integration of segment position information, target position with respect to the body and hand, and proprioceptive body information (Prablanc et al 1979; Cordo & Flanders 1989). Pinek and Brouchon (1992) concluded that there is dissociation between manual localization and head orientation for auditory stimuli. They found that their data provided evidence that left or right-handed manual pointing came predominantly from a unilateral distributed process, versus a bilateral neurologically distributed process for head turning. This was found for both normal participants and those with right parietal damage, additionally indicating that right parietal lesions have little or no effect on audiomanual deficits in a systematic way (Pinek & Brouchon 1992).

1.3.5 Sound localization around an azimuth array

Some sound localization studies done in as free-field tasks are analyzed along an “azimuth” (Ashmead et al. 1991, Bratz 1966; Lewald 1998a; Lewald 1998b; Lewald et al. 2000; Lewald 2007; MacPherson & Middlebrooks 2002; Middlebrooks & Green 1991; Morgan 1978; Preblanc et al. 1979; Roder et al. 1999; Tannazzo et al. 2014; Toronchuk et al. 1992; Voss et al. 2015; Zambbarieri et al 1997; Zimmer et al. 2004). The azimuth is known as angular measurements that are located spherically from the origin (a vector) of the observer along the coordinate
system, this measurement is of particular interest when investigating the difference in arrival times between the ears. These measurements are generally established in the form of angles, however, not all experiments are performed using the measurements of degrees. Many are also done along a spherical coordinate system, with the observer as the origin, and measurements taken in cm. The measurements used are dependent on the equipment and the study, but measurements of angles or in cm are an acceptable method for sound localization studies.

1.3.6 Effect of vision on horizontal and vertical planes

There may be a bias when comparing the performance of blind to blindfold individuals that are normally sighted in order to draw conclusions regarding plasticity (Tabry et al. 2013). This is particularly true with congenitally blind and early blind individuals, but may also be true for late blind individuals. Sighted individuals are at a disadvantage when having to suddenly perform a sound localization task without vision. Tabry et al. (2013) compared blindfold vs. non-blindfold in the horizontal vs. vertical planes with two different pointing methods, hand vs. head. They discovered that all three factors influenced the average absolute deviation error. Mostly, head-pointing in the horizontal plane was affected. Blindfolding showed a tendency to undershoot eccentric positions during the head-pointing task, but not during the hand pointing. The conclusion of these findings indicated that hand-pointing accuracy remained sufficient without visual feedback, however, the absence of visual feedback resulted in less accurate head-pointing (Tabry et al. 2013).

1.3.7 Eccentricity

Eccentricity refers to an ‘object’ that is not placed centrally, and in the context of this study refers to speakers not placed centrally in front of the participant. It is known that eccentricity
influences sound localization via transformations of the auditory spatial coordinates from a craniocentric to an oculocentric frame of reference within neural maps of space (Lewald 1998). Different studies had varying setups for their sound localization speakers, for instance, a study with 25 speakers ranged from -90° to +90°, and with 16 speakers it ranged from -45° to +67.5° (Tabry et al. 2013). Another study has 21 speakers between -80° to 80° (Lewald 2007). There is no clear definition of how far eccentric compared to centric locations are, as many studies use different locations. However, in summary of reviewed literature, the centric locations are approximately between 0° to 30-50°. Lewald (2007) defined centric speakers to be 0-40° and eccentric speakers to be 40-80°. Studies that examined the effect of eccentricity during visual or auditory tasks and perceptual grouping across eccentricity have found that eccentric viewing produces thresholds that are elevated for movement detection, acuity, stereopsis, critical flicker fusion, letter recognition, orientation discrimination, and lateral stimulus facilitation (Tannazzo et al. 2014). Higher order functions such as facial and word recognition, object detection in natural scenes, and biological motion identification are shown to decrease in performance. A study done by Lewald et al. (2007) investigated the ability of participants to localize eccentric sounds, and reported systematic underestimation when relaying on the median plane of the head as the sole reference. This experiment was done in darkness, and required subjects to turn their head towards the sound. When the experiment was repeated with a laser pointer attached to the head as a point of visual marker, sound localization was fairly accurate (Lewald et al. 2007). Participants also compared head pointing in darkness to hand pointing in light, and these results also showed systematic errors in accuracy. Overshooting responses resulted when the head remained aligned with the trunk (Lewald et al. 2007). This study credits their findings to neural
processes in the posterior parietal cortex, which is responsible for transforming visual and auditory spatial coordinates into a frame of reference that is trunk-centered (Lewald et al. 2007).

1.4 RESEARCH QUESTIONS AND HYPOTHESIS

This study examined the impact of visual deprivation on auditory localization in order to analyze crossmodal plasticity from the visual to the auditory network. When the brain is deprived of one sensory modality, plasticity becomes compensatory. This entails alterations in brain structure and function that impact neural interactions within the network and possibly behavioural outcomes. It has previously been stated that blind individuals are either equal to or better at performing sound localization tasks than normally sighted individual. Particularly, it is changes in the occipital cortex function that become activated in response to non-visual information. This topic has been investigated with normally sighted individuals wearing blindfolds/ski masks as well as congenitally blind, late and early blind individuals. This study will take an alternative and novel approach in examining the impact of visual deprivation on performance in an auditory task for a prolonged period of blindness. The HYPOTHESIS, based on previous literature, is that performance of auditory localization will improve with prolonged visual occlusion. Unlike the previously mentioned literature review, this study had participants experience visual deprivation by wearing occluding contact lenses, compared to a blindfold (Lewald et al. 2007) or a ski mask (Landry & Shiller 2013). Opaque contact lenses were used in order to achieve absence of visual feedback and have participants experience the effects of true blindness. A true model of blindness in research is defined as setting up the experiment so the participant is as blind as is possible. In addition to opaque lenses, this study will also involve participants in stimulating tasks, such as walking, eating, and listening to music while their visual input is blocked during their 1st (90 minute) and 2nd (180 minute) breaks. This was done in attempt to achieve a true
blindness model by stimulating the remaining senses and creating a natural environment for the participant. The aims of the study prioritize in (1) performing a sound localization task in participants wearing occluded lenses to collect data for the purpose of analyzing accuracy as well as observational data. (2) To have participants with long term visual deprivation that exceeds 90 minutes perform the sound localization task.

2.0 METHODOLOGY

2.1 PARTICIPANTS

A total of 12 participants (7 female, mean age = 26.25, range = 21-45) were tested in the present study. Participants had a varying range of contact lens experience, ranging from no experience to 12 years. Two participants were excluded due to technical difficulties with faulty equipment, and results are based data from 10 participants (7 female, 3 male, mean age = 26.1). All participants had normal or corrected-to-normal vision, and had no history of hearing impairment. No hearing assessment was performed on participants. While they participated in the “Light” trials, participants with corrected vision wore their prescription glasses. There was no direct monetary compensation, but all participants were provided with a lunch and snacks throughout the day. All participants gave informed consent. The experiment was conducted with approval from the Human Participants Review Committee, York University’s Ethics Review Board and conforms to the standards of the Canadian Tri-council Research ethics guidelines.

2.2 EQUIPMENT SETUP

Two PC computers were connected through a serial cable. Computer 1 was a Dell Optiplex gx270, Intel Pentium 4 (x86 Family 15 Model2 Stepping 9 GenuineIntel ~2793 MHz). Computer 2 was a Dell Optiplex gx260, Intel Pentium 4 (x86 Family 15 Model 2 Stepping 7 GenuineIntel
~1992 MHz). Both ran on Windows XP, and had 768MB memory capacity. Computer 2 was connected to a relay box through a parallel port. The relay box was custom designed, and functioned with a switch that opens and closes circuits to the speakers, depending on the instruction from the computer. If the switch was open the speaker was disconnected, and if it was closed the speaker was connected. The relay box was also connected to an amplifier (Cambridge Soundworks Desktop Theatre 5.1). The amplifier had 5 outputs, but only one was used for the speakers. The amplifier was connected to the relay box using VGA connectors. There were 16 speakers (MAX Fidelity, model T26AFF5NEOBMFF) that were wired and connected using DIN connectors to the relay box.

Computer 1 was connected to a Wiimote (Model RVL-003, Nintendo) motion controller via Bluetooth, which was attached to a helmet worn by the participants (Figure 7). Attached to the helmet was a laser pointer that could be powered on/off depending on requirement. The laser pointer was turned on during the localization task, but turned off for the remainder of the baseline and all further testing. The Wiimote used 2 AA batteries and had a 16 KiB EPROM chip (16.3 kilobytes of storage). Using three infrared sensors, digital buttons 1 and 2 of the Nunchuk RVL-004 that accompanies the Wiimote system were used to pair with the computer and signaled speaker selection and a new trial, respectively (other buttons include A, B, -, + Home, 1, 2, POWER, but were not used). Two of the external sensors were Wii Wireless Sensor Bars (CAT.NO:ND-GWII1125, Nintendo) and the third sensor was a NYKO Wireless Sensor Bar (ITEM# 877005-E14 4X AA). The infrared sensors were used to triangulate the precise spatial dimensions (X, Y, and Z) of the Wiimote. This is done using the accelerometer situated in the circuit board of the Wiimote. Computer 1 recorded this information.
The experiment was performed in a sound-attenuated room (2 x 2.24 x 2.4m) lined with 3.8cm of sound-absorbing foam. Sixteen speakers were attached to a semicircular metal frame (height = 112 cm from the floor) that was labelled with a continuous scale (cm) from left to right (total length = 369.6 cm). Speakers were placed 4 cm apart. Participants were seated 100 cm from the centre, left and right of the semicircle (Figure 7). Sixty-nine red dots were positioned along the semicircle 3 cm apart, with three dots between each speaker. Two points were added before the first speaker (point 1 and point 2) and after the last speaker (point 68 and point 69) to ensure that a location was recorded if the participant moved beyond these points. These red points are used as reference markers across the semicircle to calculate the difference between where the participant perceived the sound is coming from with the actual location of the sound. The red dots were placed along the semicircle on locations 3 cm apart and were used in the initial localization/calibration task to determine reference points for identifying sound location. The speakers were distributed as follows:

**Table 1: Speaker number and associated value on semi-circle**

<table>
<thead>
<tr>
<th>Spk</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point</td>
<td>3</td>
<td>7</td>
<td>11</td>
<td>15</td>
<td>19</td>
<td>23</td>
<td>27</td>
<td>31</td>
<td>39</td>
<td>43</td>
<td>47</td>
<td>51</td>
<td>55</td>
<td>59</td>
<td>63</td>
<td>67</td>
</tr>
</tbody>
</table>
Figure 5: Speaker and participant arrangement: participant sits a 100 cm from the centre and a 100 cm from the far left (speaker 1) and far right (speaker 16) speakers.

Between points 32 to 38, there is no speaker. This is the centre of the semicircle, where the middle sensor is located and where participants begin each trial of the experiment by looking straight ahead before moving to their target, signaling their response with the Nunchuk, and returning to centre before they begin the next trial. The response is recorded using the Wiimote system, which records the location in which the participant is pointing at with their head (further explained in Section 2.3).

2.3 EXPERIMENTAL DESIGN

All participants filled out a demographic questionnaire, and performed an eye dominance test (Appendix I). The design of the experiment involves a localization/calibration task and six experimental sessions. During all of the sessions, the participant was asked to sit upright in the chair, in a comfortable position, facing the centre of the semicircle (Figure 8). For each trial, the participant starts off with their head position located at centre, wearing a helmet with the Wiimote attached. A sound is then played for 2 seconds, and the subject then points their head to the perceived location of the sound, selects their desired location by pressing button 1 on the Nunchuk, returns their head position to centre, and presses button 2 to signal the next trial.
Figure 6: Participant in sound lab; (a) shows the Wiimote attached to the participant’s helmet, as well as the Nunchuck and the position they maintain during the duration of the experimental trials, (b) shows the arrangement of the room in which the participant performed the sound localization tasks; the participant sits in a straight position in front of the semi-circle and reports to sound localization tasks. The speakers are labeled for quick reference and the labels remained intact during the duration of the experiment.

Session 1 of 6

For the localization task, which is categorized as part of Session 1, the participant is asked to turn their head to direct the Wiimote laser-pointer attached to their helmet at each red dot across the semicircle, and press button 1 on the Nunchuk. This records the 69 points across the full semi-circle. The participant then does the sound localization task baseline. The baseline consists of a full run with the lights on (Light run) and a run with the lights off (Dark run, Session 2). Each run consists of three blocks with ten trials per block (30 trials in each run). During the Light run, the laser pointer is turned off to prevent visual feedback of the Wiimote location.


**Session 2 of 6**

Session 2 consists of the Dark run performed during the second part of the baseline. The lights are turned off, and the participant is wearing a blindfold and is asked to keep their eyes closed. The Dark run was completed during the baseline task because it was consistently used in other psychometric studies (Lewald et al. 2006) and will serve as a comparison for sound localization blindfolded versus the novel task of performing sound localization with the lack of visual feedback.

Following the end of Session 2, the participant inserts the first contact lens into their dominant eye. The participant then inserts the second contact lens into their non-dominant eye.

**Session 3-5**

For Session 3 only, the participant completes a practice run of two blocks with 16 trials per block (32 trials total), and then performs the first blind experimental run, which consists of ten blocks with 16 trials per block (160 trials total). The practice runs are to allow for accommodation to performing the task with opaque contact lenses. The practice trials are not taken into consideration for the analysis, but rather to allow time for the eyes to adjust to having large lenses. Sessions 3 to 5 are performed identically (i.e., blind runs with 160 trials), with the participant wearing opaque contact lenses, the lights turned off, and the door closed.

There is a 90-minute break at the end of Session 3, during which the participant engages in conversation with experimenters, listens to music/videos, takes a walk on a predetermined route outside the lab, and interacts with their environment. Other activities may include, but are not limited to, eating, washroom breaks, locating items on their desk, and attempting to write an email on a desktop computer. A researcher is present at all times. There is a 180-minute break at
the end of Session 4, which follows the same procedure as the 90-minute break, after which the participant performs Session 5.

Following the end of Session 5, the participant removes the non-dominant contact lens first, then the dominant contact lens, and immediately performs Session 6.

**Session 6-7**

Session 6 and 7 are performed in the same manner as Sessions 2-4, but the contact lenses are removed, the lights are on, and the Wiimote laser pointer is turned off. There is a practice run of two blocks with 16 trials per block (32 trials total) before the experimental run, which is ten blocks with 16 trials per block (160 trials total). The practice trial is run to provide individuals with time to return to adjust to light sensitivity and having their vision returned.

Between Session 6 and 7 there is a 60-minute break. During this break, the participant has regular vision. They continue to engage in conversation with experimenters and are taken on the same predetermined walk they were exposed to during blindness. The completion of Session 6 marks the end of the experiment (Figure 7).

![Figure 7: Temporal sequence of experimental design; this is an outline of the experimental procedures. It shows how the participant will spend their time during the course of the experiment.](image)
For the insertion of contact lenses, a total of 30 minutes have been allocated. The total time for the experiment is approximately 8 hours. Participants varied in the amount of time they required to insert and remove the contact lenses, and the experiment lasted an average of 5 hours and 44 minutes (524.3 minutes, SD=44.34). The average time to insert the first contact lens was 6 minutes, and 3.1 minutes for the second lens. The average time to remove the first contact lens was 4 minutes and 3 minutes for the second lens. There was no monetary compensation, however, lunch was provided.

2.4 DATA ANALYSIS

The data has been analyzed with respect to individual participant performance of accuracy and Reaction Time (RT) and compared across speakers. A complete analysis of all participants was run using SPSS 22 (IBM, Armonk, NY).

Each participant performs the sound localization task (baseline control) and Sessions 6 and 7 without contact lenses, and Sessions 3 to 5 with opaque contact lenses causing visual impairment across time (experimental condition). The localizer is used to compute the accuracy of a participant’s ability to localize sounds emitted from the 16 target (i.e., speaker) locations relative to each of the 69 points (Figure 5) marked along the semicircle. Since there are three sensors covering the semicircle in order to encompass the entire range, two of the three sensors at a time are reporting X, Y, and Z locations of each of the 69 points (i.e., either the left and middle sensor, or the right and middle sensor). Using the X values from each sensor, the sound location the participant selected was matched up with the most comparable point along the 1-69 range on the semicircle. This point is then used in the accuracy calculation along with the actual point
location, which are speakers 1 through 16 (their exact point locations are described in Section 2.2 and are noted in Figure 7).

A head movement graph was computed for each perceived point of each participant, in order to verify whether they correctly located a speaker to the left or the right (Figure 10). The y-axis on the graph consists of the position of the sensor (scale = 0 to 1), and the x-axis is the position across time. This is done for each X location the participant selected, to ensure that the head movements are being reported in the correct direction. A movement across the graph towards 1 denotes a head movement towards the left side of the semicircle, and a movement across the graph towards 0 denotes a head movement towards the right side of the semicircle.

**Figure 8: Head movement graphs:** All 10 trials are shown moving towards position 1. A steep drop that shows the trial trails off and restarts again moving upwards toward position 1 indicates that for this head movement the participant made a movement to the left towards speaker 1.
Once the perceived positions have been matched (perceived X1 and X2 to the localizer), a point along the semicircle is obtained. This point is used as a reference to calculate the accuracy score: the perceived point against actual target speaker. The equation is as follows:

$$\text{Accuracy} = |\text{actual} - \text{perceived}|$$

The absolute value is taken into consideration in order to obtain an accuracy score. A large accuracy score indicates that the amount of difference between the perceived and the actual target speaker was large and indicates less accuracy, and a lower score indicates more accuracy.

**Accuracy**

An average accuracy score was computed for each speaker, for each session, resulting in 16 averages per session, per participant. In the case of a missing value due to technical glitches, an average of the other values was taken and used as the missing value. In total we had 7 missing values. The value distribution table can be seen in Table 1.

**Table 2: Value distribution for response accuracy**

<table>
<thead>
<tr>
<th>Session</th>
<th>Blocks</th>
<th>Total Trials (X trials x 16 speakers)</th>
<th>Total Trials in Experiment (Total Trials x 10 participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>48</td>
<td>480</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>48</td>
<td>480</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>160</td>
<td>1600</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>160</td>
<td>1600</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>160</td>
<td>1600</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>160</td>
<td>1600</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>160</td>
<td>1600</td>
</tr>
</tbody>
</table>

**Total trials of all speakers/sessions/participants = 8960**
**Reaction time**

The second dependent variable was reaction time (RT) and was computed as the duration between the onsets of speaker sound to button press for selecting the perceived speaker location. This was done using Matlab (Version 7.10.0.99 R2010a, The Mathworks, Inc., Natick, MA), in which a program was created to obtain the time of speaker sound and the time of button press, and then subtract time of button press by speaker sound in order to get the RT. The participants were not aware that we would be measuring reaction time as it was not a planned analysis prior to administering the experiment.

**Reaction Time = button press time – speaker sound time**

**Degree Measurements**

There are 69 points along the semicircle, of which 16 have speakers attached. All of the 69 points are spaced 3 cm apart from one another. Using this information, along with the radius of the semicircle (100 cm), each point was given a radian measure (\(\theta\)) using the following formula:

\[
\theta = \frac{s}{r} = \frac{\text{length of subtended arc}}{\text{length of radius}}
\]

Where ‘s’ is the distance/circumference location (cm) from the center of the semicircle (point 35). Once the radians at each point were calculated, the conversion to degrees was calculated in Excel. All points to the left of the center were given a negative degree value, and those to the right were given a positive degree value. This method resulted in the degree value points ranging from -55° to 55° with 0° having no speaker. The layout is as follows:
Figure 9: **Speaker and participant angle arrangement**: this image shows the angular distribution

### Mean Signed Error

\[
\theta = \frac{\sum_{i=1}^{n} \hat{\theta}_i - \theta_i}{n}
\]

Where \(\hat{\theta}_i\) is an estimate or observed value and \(\theta_i\) is the actual or theoretical value. Each speaker has only one theoretical \((\theta_i)\) value, which is measured in degrees. The numerator \((\hat{\theta}_i - \theta_i)\) is the definition of directional error within the experiment. Therefore, the Mean Signed Error (MSE) is the average of directional errors. For each trial, a corresponding directional error was computed. Then the MSE was calculated for each speaker for each session across all test subjects. This provided 112 MSE values in total divided into 7 groups (i.e. 7 sessions x 16 speakers = 112 MSE values).

### Absolute Error

Absolute Error = \(|\theta_i - \hat{\theta}_i|\)
Where $\theta_i$ is the actual or theoretical value and $\hat{\theta}_i$ is an estimate or observed value.

For each trial, a corresponding absolute error was computed. The average absolute error was then calculated for each speaker in each session across all test subjects. This provided a total 112 average absolute error values divided into 7 groups (i.e. 16 speakers x 7 sessions = 112 absolute error values).

**Standard Deviation of Directional Errors**

Standard deviation measures the variation of observed values from matching theoretical values.

For each trial, a corresponding directional error was computed. The standard deviation was then calculated for each speaker in each session across all test subjects. This provided a total 112 average standard deviation values divided into 7 groups (i.e. 16 speakers x 7 sessions = 112 standard deviation values).

Using the observed values compared to that of directional errors for each trial resulted in the same standard deviation values. This is because the variance did not change within these two sets of data.

**3.0 RESULTS**

**3.1 DATA ANALYSIS: ACCURACY**

A repeated measures ANOVA comparing accuracy with the factors of session (7) and speaker (16) was done and showed no main effect of session ($F(6,54) = 0.784, p = 0.59, \eta^2 = 0.080$), but revealed a significant main effect of speaker ($F(15,135) = 9.390, p < 0.01, \eta^2 = 0.511$). Appendix A shows the significant main effect of speaker in pairwise comparisons with Bonferroni correction. There was also a significant interaction between session and speaker ($F(90,810) =$}
1.470, \( p = 0.01, n^2 = 0.140 \). Appendix B shows the significant pairwise comparison of Session * Speaker without Bonferroni correction.

The significant main effect of speaker reports that speaker 16 is less accurate than speaker 7, 8, and 10-15, speaker 15 was less accurate than speaker 11 and 14 (Appendix A). However, speaker 1 was less accurate than speakers 2-6. The overall trend is shown in Figure 11.

**Figure 10: Mean response accuracy;** during Sessions 1 to 7 across all 16 speakers mean accuracy scores of each speaker within each session were analyzed using a repeated measures ANOVA. For sessions 1 & 2, there was 3 blocks per speaker (16) for a total of 48 trials per session across speakers. There were 10 blocks per speaker (16), per sessions 3-7, for a total of 160 trials per session across speakers.

A repeated measures ANOVA on accuracy scores comparing the factors of session (7) by eccentricity (4) was also performed. Left eccentric speakers were speakers 1-4 (Ecc_L (Quadrant 1)), right eccentric speakers were speakers 13-16 (Ecc_R (Quadrant 4)), left centered speakers
were speakers 5-8 (C_L (Quadrant 2)), and right centered speakers were speakers 9-12 (C_R (Quadrant 3)). The speakers were divided as follows:

![Speaker Quadrants Diagram](image)

**Figure 11: Speaker Quadrants**: the speakers were divided into 4 quadrants. Quadrant 1 is speaker 1-4 (-55° to -34°), quadrant 2 is speakers 5-8 (-28° to -7°), quadrant 3 is speakers 9 – 12 (7° to 28°), and quadrant 4 is speakers 13-16 (34° to 55°).

There was a significant main effect of centricity ($F(3,27) = 8.257, p < 0.01, n^2 = 0.478$) (Appendix C), as well as a significant interaction between session by eccentricity ($F(18,162)= 1.815, p = 0.03, n^2 = 0.168$) (Appendix D). Speakers in the right eccentric quadrant (4) were less accurate than speakers in the left center quadrant (2) ($p < 0.01$), as well as less accurate than the right center quadrant (3) ($p < 0.01$). A pairwise comparison with Bonferroni correction of session by centricity revealed that quadrant 4 was less accurate than quadrant 2 and 3 during session 1, 2, 5, 6 and 7, and quadrant 4 was less accurate than quadrant 2 during session 3. This significant interaction was lost during session 4. A clear centric pattern is visible in Figure 12.
Figure 12: Accuracy in centricity by speakers; Sessions are grouped together and show a clear pattern of increased accuracy for centricity for the respective speakers. Accuracy is defined as proximity to actual location, with a higher accuracy score indicating a less accurate result, and lower accuracy scores (towards 0) indicate less deviation from the actual location.

3.2 DATA ANALYSIS: REACTION TIME

A repeated measures ANOVA on RT comparing the factors of session (7) by speaker (16) was done and showed a main effect of session (F(6,54) = 20.890, p < 0.01, n² = 0.699), (Figure 13), with pairwise comparison shows in Appendix E. There was also a significant main effect of speaker (F(15,54) = 12.809, p < 0.01, n² = 0.587), with pairwise comparisons shown in Appendix C. The session and speaker interaction showed no significance (F(90,810) = 1.201, p = 0.11, n² = 0.118). The pairwise comparisons indicated that with the exception of session 2, all other sessions (3-7) had a faster reaction time than session 1 (See Appendix E). Similarly, nearly
all sessions, but namely 4-7, had a faster reaction time than session 2. Only session 6 had a faster reaction time than session 4.

The pairwise comparison suggests that participants took longer to react to selecting speaker 15 rather than speaker 5 (p < 0.03). Participants were faster to react to speaker 7 rather than speaker 3 (p < 0.05) and faster in reacting to speaker 10 than speaker 6 (p < 0.21).

**Figure 13: Reaction time (RT);** mean reaction time is plotted for Sessions 1 through 7 across 16 speakers. Reaction time is defined as time of button press subtracted by the speaker sound time, in order to obtain the length of time required to respond to sounds across sessions.

### 3.3 DATA ANALYSIS: MEAN SIGNED ERROR

A linear regression was conducted on each session, which showed a significant main effect of speaker, session (1) (F(1,14) = 410.664, p < 0.01, R² = 0.967), session (2) (F(1,14) = 120.400, p < 0.01, R² = 0.896), session (3) (F(1,14) = 254.421, p < 0.01, R² = 0.948), session (4) (F(1,14) =
451.452, p < 0.01, $R^2 = 0.970$), session (5) ($F(1,14) = 334.683$, p < 0.01, $R^2 = 0.960$), session (6) ($F(1,14) = 483.951$, p < 0.01, $R^2 = 0.972$), and session (7) ($F(1,14) = 291.409$, p < 0.01, $R^2 = 0.954$), (Appendix G).

**Figure 14: Mean Signed Error (MSE);** mean signed error is plotted for Sessions 1 through 7 across 16 speakers. Mean signed error is defined as the average distance between the localization points, in degrees. Localization points can be defined as the actual location and the estimated location.
Each individual regression suggests that amongst all sessions, participants were more accurate in localizing sounds in the center speakers compared to that of eccentric speakers. This indicates the MSE is significantly impacted by the placement of the speakers.

Figure 15: Mean Signed Error (MSE) per speaker across all sessions; mean signed error is plotted per speaker for Sessions 1 through 7. This graph indicates the direction in which the participants reported to the speakers. A positive MSE means the head movement is to the right, and a negative MSE means the head movement is to the left. If the participant is reporting to speakers 1-8 and they have a positive MSE, they are underestimating speaker locations closer to 0°. If they are reporting to speakers 9-16 and they have a negative MSE, they are underestimating speaker locations closer to 0°.

A repeated measures ANOVA comparing the factors of sessions 3, 4 and 5 across all 16 speakers was conducted and showed a main effect of sessions (F(1,92) = 9.545, p < 0.01), (Figure 16).

This indicates that each session was significantly impacted by reduced blindness. The individual ANOVA testing for sessions 3, 4 and 5 produced the following statistics:
Session 3: $F(1,14) = 254.421$, $p < 0.01$,

Session 4: $F(1,14) = 451.452$, $p < 0.01$, and

Session 5: $F(1,14) = 334.683$, $p < 0.01$.

Although the order of the highest to lowest significance per session would be Session 4, Session 5 then Session 3, all of the $F$ and $p$ values are extremely significant within each session. To order them by significance in this way does not provide any additional information since the values computed were extreme in all sessions.

**Figure 16: Mean Signed Error (MSE) per speaker across sessions 3-5;** this is a closer look at the sessions during which the participant was blind. This graph shows the directional error or MSE across time of blindness from $T = 0$ to $T = 5$ hours.
3.4 DATA ANALYSIS: ABSOLUTE ERROR

A linear regression was conducted on each session, which did not show a significant main effect of speaker, session (1) (F(1,14) = 3.083, p > 0.10, R² = 0.180), session (2) (F(1,14) = 1.861, p > 0.10, R² = 0.117), session (3) (F(1,14) = 0.037, p > 0.80, R² = 0.003), session (4) (F(1,14) = 0.001, p > 0.90, R² = 0.000), session (5) (F(1,14) = 0.598, p > 0.40, R² = 0.041), session (6) (F(1,14) = 0.273, p > 0.60, R² = 0.019), and session (7) (F(1,14) = 1.951, p > 0.10, R² = 0.122).
Figure 18: Absolute Error; absolute error is plotted for Sessions 1 through 7 across 16 speakers. Mean signed error is defined as the distance between the localization points, in degrees. Localization points can be defined as the theoretical location and the estimated location.

The regressions were unable to determine if absolute errors are significantly impacted by the placement of speakers. A closer look at Sessions 3, 4 and 5 is shown in Figure 19.
Figure 19: Average Absolute Error per Speaker across Session 3 – 5: comparing all 16 speakers across the blind sessions 3, 4, and 5.
Figure 20: Average Absolute Error per Quadrant across Session 3 – 5; looking at the absolute error of eccentric compared to centric quadrants. Centricity effect is evident in the lower absolute error value in quadrant 2 and 3.

3.5 DATA ANALYSIS: DIRECTIONAL ERROR

A linear regression was conducted on each session, which did not show a significant main effect of speaker, session (1) (F(1,14) = 0.193, p > 0.60, R² = 0.014), session (2) (F(1,14) = 0.531, p > 0.40, R² = 0.037), session (3) (F(1,14) = 1.470, p > 0.20, R² = 0.095), session (4) (F(1,14) = 10.828, p < 0.05, R² = 0.4361), session (5) (F(1,14) = 3.780, p > 0.07, R² = 0.213), session (6) (F(1,14) = 0.106, p > 0.75, R² = 0.008), and session (7) (F(1,14) = 2.098, p > 0.10, R² = 0.130).

The regressions were unable to determine if the deviation of directional errors are significantly impacted by the placement of speakers. Each session had low F-stats and high p-values (greater
than 5%), except for Session 4. This does not indicate if the standard deviation is significantly impacted by the placement of the speakers. Session 4 produced a low $p$-value of 0.005, even though its $R^2$ and F-Stat were also low.

![Graph: Standard Deviation of Directional Errors](image)

**Figure 21: Standard Deviation of Directional Errors:** standard deviation of directional errors is plotted for Sessions 1 through 7 across 16 speakers. Standard deviation is defined as the variance between localization points. Localization points can be defined as the theoretical location and the estimated location.

### 3.6 QUALITATIVE OBSERVATIONS

There were various similarities among participants with respect to observations made by the researchers. When participants inserted the first contact lens, all participants felt slight irritation in their eyes. They described the feeling as “unusual,” “weird,” “dryness,” “numbness,” and/or “discomfort”. Importantly, none of the participants reported any pain or needed to discontinue
the experiment after insertion of contact lenses. After approximately 5 minutes, participants reported that their dominant eye (with the opaque contact lens inserted) had become accustomed to the lens and the aforementioned feeling had either completely disappeared, or nearly disappeared. All participants stated they were “shocked” or “surprised” when the first, and particularly second contact lens was inserted. They reported feeling “surprised” or “shocked” because their one eye was in complete darkness. Although it was indicated to participants that their vision would be obstructed, they still felt uneasy for the first few minutes and were reluctant to stand up. Four out of ten participants panicked when they first inserted both contact lenses, and felt fairly uneasy. For these participants, the experiment was delayed for a few minutes (approximately 5 minutes). All participants agreed to continue with the experiment. No participants reported being able to see any light, with the exception of when they first inserted the lens as it was still dry, and it moved when they blinked. However, once the participant became accustomed to the lens and used an eye drop, this was no longer an issue.

All participants preferred to use the researcher’s/assistants’ hand as a guide to get from the chair to inside the sound room. Initially, they also preferred to use a hand as a guide as they did their “scheduled” walks (2x during the 90 minute break and 4x during the 180 minute break). As the experiment went on, some individuals attempted to walk alone for a longer period of time, but all participants at least attempted to walk independently.

Participants were asked to perform numerous tasks during their five hours of visual deprivation. Each participant was asked to identify numerous items in the room, including office supplies, toys and figurines, eat a meal, use the bathroom and listen to some type of audio stimulation (i.e. music, TED Talks, a TV show). The common observation included confusion about the height of ceiling; they “ducked” down closer to towards the floor, appearing in a hunched over position as
they walked to avoid “hitting the ceiling with their head.” Some participants reported feeling “smaller/shorter” while they walked, feeling the need to look up as though they need to look past something to regain their vision, and they reported feeling nauseous when they did not have support from the wall and/or an assistant’s hand. Participants had trouble recognizing individuals they knew by the sound of their voice, unless they were extremely familiar, and often looked at a spot just beside the person they were talking to. Most stated that standing in one spot made them feel “uneasy,” as though they might fall over. This can be described as symptoms resembling “vestibular disorders,” such as vertigo and dizziness.

As participants were blind for a longer amount of time, they experienced improvement and higher confidence with balance, hand-face coordination, and independence in completing tasks. This study is unable to draw conclusions about whether this was a result of crossmodal compensation, learning, or an alternate unknown effect. However, based purely on researchers’ observations, the participants appeared to be adjusting to completing tasks without sight across time. It should be noted that all participants felt more tired as the experiment went on, and expressed feeling “dryness” in their eyes from their contacts. Each participant felt tired at the end of the 8 hour experiment and felt a sense of relief when they had their vision returned to them. They were given the opportunity to slowly adjust to light exposure and felt a sense of relief and less tired. This will be further addressed in the discussion section.

4.0 DISCUSSION

The goal of this thesis was to explore the possibility of crossmodal compensation in participants who experienced blindness. The main findings, based on analyzing accuracy, indicated a significant main effect of speaker (p<0.000) and a significant interaction between session and
speaker (p=0.004). However, there was no significant main effect of session (p = 0.586), and therefore no significant improvement in accuracy across time in individuals wearing opaque contact lenses. Reaction time yielded a main effect of session (p<0.000) and a significant main effect of speaker (p<0.000), but no interaction. This study encompassed a novel design that blocked visual feedback using opaque contact lenses and had participants perform a free-field sound localization task. Other studies that reported an increase in acuity of other senses when participants are blinded (Ashmead et al. 1991; Fieger et al. 2006; Goldreich & Kanics 2003; Lessard et al 1998; Lewald 2006, Van Boven et al. 2000) involved slightly different designs that did not test true vision loss, as done with opaque lenses. These studies involved early blind participants, ski masks and blindfolds, and a comparison between a blindfolded (“deprived”) group and non-a group that had their blindfold removed between sessions (“non-deprived”). In comparison to some of the existing literature, this study showed significantly different findings, particularly since participants have no visual feedback with the opaque contact lenses. Without any light entering their eyes, they experience a sensation different from a ski mask and blindfold that is much closer to an individual who is legally blind. No significant main effect of session revealed no improvement in accuracy of sound localization across time. Our findings may be attributable to a few potential explanations, including ability to use free-field sound localization as opposed to fixed along the azimuthal angle of a swivel, and absence of visual calibration.

4.1 FREE-FIELD SOUND LOCALIZATION

Free-field sound localization may not be as sensitive to ITD’s, perhaps due to the fact that free-field localization involves the coordination of many movements and other cues apart from ITD’s
(Ashmead et al. 1991). This could partially contribute to *the lack of significance* found in session accuracy. The overall spatial impression requires an integrative process, and multiple cues may change as the participant’s head moves, in comparison to fastening a participants’ head and removing the requirement of coordination (Ashmead et al. 1991). No significant main effect of session could be explained partially due to the fact that participants were asked to free-field localize sounds, involving the coordination of their ITD and ILD’s with head movements without visual feedback. Additionally, there may be a need to recalibrate ITD’s with the loss of vision. ITD’s are important as they are used to determine the azimuthal or horizontal plane during sound localization (King 1999). Neural adaptation has been credited to play a key role in initial processing of ITD’s, which is significant considering that ITD’s are a prevailing cue for sound localization in human beings (Stange et al. 2013). Neural adaptations occur when our sensory systems encode information about patterns of activity in the environment across neurons of population (Clifford et al. 2007). Sound localization is said to adapt to recent stimulus history at the level of the superior olivary complex. More recent studies claim that binaural adaptation may be occurring earlier on in the binaural system, specifically, the ILD’s are adapting through a gain-control mechanism mediated by retrograde GABA_B receptor signaling (Stange et al. 2013).

In order to obtain a representation that is cohesive, ITD and ILD are both used in combination to provide enough information for sound source localization (Salimen et al. 2015; Middlebrooks & Green 1991). When frequencies are low, ITD is the prevailing cue for horizontal sound source localization. However, for higher frequency, ILD cues are dominant (Middlebrooks & Green 1991; Wightman & Kistler 1992; Macpherson & Middlebrooks 2002). Studies have shown that a listener’s head movements are a crucially important method for achieving correct sound
localization. Binaural time and level disparity cues from a listener’s head are key for accuracy in horizontal sound localization (Honda et al. 2013).

Even though the participant is under complete visual feedback block, and thereby experiencing their surroundings like a blind individual, they have not had as much interaction with their environment as long-term blind individuals, and we see no short-term adaptation. This experiment aimed to place participants in a scenario that was as realistic as possible to a true-blind person, but without numerous years of blindness. In the study done by Lewald et al. (2007), participants showed an improvement in constant error after 90 minutes of light-deprivation. This study involved participants leaving opaque contact lenses in their eyes for approximately 5 hours of blindness. The participant was not restrained and was encouraged to partake in their environment, as they would have with regular vision. There is a possibility that adapting to numerous competing changes (i.e. coordination, voice recognition, touch) had an impact on the level of improvement in sound localization. Other factors may play a role in their ability to experience an improvement in localizing sound with the loss of vision.

Current studies are exploring the potential that neural processing is rapidly updated as the sensory conditions undergo changes (Keating & King 2015). Spatial processing is prevalently studied by evaluating compensation from the switch that occurs when participants respond to a monaural cue compared to binaural cues. These studies have allowed conclusions to be drawn regarding neuronal ILD and ITD sensitivity, and how the auditory space can temporarily be impacted and reversed, drawing the conclusions that perhaps the importance lies within the relative sound location rather than the actual position of a sound source (Keating & King 2015). A study by Hildebrant et al. (2015) found that the actual position of the onset of a stimulus may be preserved in the neural response to the stimulus onset. Keating and King (2015) also argue
that the reweighing of spatial cues is in accordance with specific dominant sensory conditions, particularly, when visual information is available. When participants are asked to respond to the sound localization tasks, their accuracy improves with the availability of visual information due to audio-visual calibration. It is possible, that the lack of audio-visual calibration in participants who are experiencing new vision loss, may have an impact on their inability to perform a sound localization task with improved accuracy.

4.2 ABSENCE OF VISUAL CALIBRATION

The absence of visual calibration may be a possible explanation for the lack of increase in accuracy across sessions in an acute model of blindness. In contrast to studies that suggest that long-term visual deprivation may lead to generally better performance in all aspects of auditory spatial perception (Ashmead et al. 1991; Lessard et al. 1998; Roder et al. 1999). Perhaps this viewpoint is slightly simplistic and may need to reconsider how widespread these enhancements are. In contrast to spatial information in the visual or somatosensory modalities being received by receptor epithelia, the auditory system synthesizes its representation of space using localization cues for its complex computation. The main cues are established from interaural differences in time of sound arrival and sound-pressure levels. It also consists of spectral content of the sound, which is shaped by the effects of the head and pinnae (Blauert, 1997). The auditory space may require supplementary development of its topography, which is demonstrated at the perceptual level, most likely performed by the visual system rather than genuine auditory factors (Lewald 2002b).

Other studies have shown a reversed improvement in constant error (defined as deviations from target, and interchangeable with accuracy) in sound localization through three different types of
tasks: (i) Distortion of visual space using lenses (Canon 1971; Zwiers et al. 2003), (ii) manipulating auditory localization cues (Held 1955; Kalil & Freedman 1967) and (iii) synchronized spatially distinct repetitive sound bursts and flashing light spots in complete light obstruction (Lewald 2002; Recanzone 1998). In all the aforementioned studies of the three sound localization tasks that showed improvement in constant error, sound localization was systematically shifted. This was done in order to account for the deviation of the sound from the visual positions during the prior occurring adaptation period (Lewald 2006; Recanzone 1998). This results in the reasonable assumption that the complete absence of visual calibration during darkness can have an effect on the auditory space geometry. This could mean greater deviations of auditory localization than from visual localization. According to Redding and Wallace (2001), calibration is determined by limb starting position visibility and alignment is in turn determined by the available visual feedback. A recent study done by Voss et al. (2013) also indicated similar findings, poorer performance of head pointing in the horizontal plane in blindfolded individuals compared to non-blindfolded conditions. Essentially, having visual orientation of personal space with respect to location and proximity may reduce the feedforward movement planning, and could be a contributing factor to the lack of significance in the main effect of accuracy across sessions.

4.3 CROSSMODAL COMPENSATION

In the study done by Lewald et al. (2007), participants showed an improvement in constant error after 90 minutes of light-deprivation. This study involved participants leaving opaque contact lenses in their eyes for approximately 5 hours of blindness. To our knowledge, this is the longest duration of “blindness”. There have been some neuroimaging studies in the last decade that showed functional significance of the non-deprived visual cortex in auditory space perception.
Although retinal coordinates play a major role on visual spatial information, the auditory system extracts sound information based on its location relative to head position. If there is a deviation of the eyes from the central position, it impacts the retinal visual and head-centered auditory coordinates. Meaning, that the eccentric eye position with perceptual alignment of visual and auditory spaces may require processes of coordinate transformation that use the signals of the orbital eye positions. These neural correlates have been established both in cortical and subcortical levels (Zimmer et al. 2004). For instance, in primate inferior colliculus, changes in eye position were found to impact the neuronal responses of auditory stimuli, without shifting their spatial tuning (Groh et al, 2001). In summary, Zimmer et all (2004) was able to show activation of the primary visual cortex that was evoked by sound lateralization with eccentric eye position. This may not necessarily indicate that auditory information is processed in the V1/V2, but it does suggest that there is an involvement of the visual areas in transforming auditory spatial coordinates of eccentric eye position. Reviewing studies that involve tasks for visual localization versus sound localization, found that there is greater accuracy in visual localization tasks than sound localization tasks as well as an involvement in the visual cortex (Gouguoux et al. 2005; Weeks et al. 2000). Early loss of vision has been reported to weaken the aptitude of the central nervous system’s ability to integrate multisensory cues (Putzar et al. 2007; Wallance et al. 2004). If sensory function is restored early enough, for example cochlear implants within the first 2-3 years of life for congenitally deaf children, synthesis of auditory and visual information can be achieved (King 2009; Schorr et al. 2005). In a report by Lazzouni and Lepore (2014), the importance of time in compensatory plasticity is discussed. Although short-term deprivation with the use of blindfolds shows cortical excitability of the visual cortex in
adults, reorganization remains more prominent in the congenitally blind (Lazzouni & Lepore 2014).

These findings could offer a potential explanation for the lack of significant improvement in accuracy in a model of true blindness. Perhaps there is already neural processing that occurs in regularly sighted individuals and crossmodal compensation enhancements from visual to auditory processing are not yet clearly understood.

4.4 IMPROVEMENT IN ACCURACY OF CENTRIC LOCATIONS

The significant main effect of centricity and significant interaction of centricity indicates that participants were generally more accurate in responding to speakers on the center of the semicircle rather than on the far left and right quadrants. More specifically, quadrant 4 was less accurate than the two center quadrants during all sessions, with the exception of session 4. A study by Wood and Bizley (2015) evaluated the relative sound localization abilities in humans and found that a participant’s ability to localize sounds decreased as they reported to locations further down their peripheral (eccentric locations). They were also able to prove that sound detection improved when the shifts between sounds were centrally located, rather than the far peripheral sound shifts. There was a limited availability of ILD cues compared to ITD cues at the peripheral location (Wood & Bizley 2015). It is of importance to note, that one study done by Brang et al. (2015) was able to show, using electrocorticography, that when participants respond to sounds in their peripheral, it activates the visual cortex. Although participants were free to move their heads, we can infer that their head movements in the vertical axis was limited as depicted in the head movement graphs (an example of one of these graphs is Figure 10). Though previously mentioned studies have reported activity in the visual cortex during sound localization, this particular experiment showed rapid activation for eccentric sound locations.
(Brang et al. 2015). These findings are similar and consistent with a vast amount of current literature, in which participants experience underestimation in locating eccentric sounds, and thereby assist in confirming an appropriate sound localization methodology (Lewald et al. 2007; Lewald et al. 2000; Morgan 1978; Wood & Bizley).

4.5 EYES CLOSED, BLINDFOLD, AND CONTACT LENSES

There are a number of varying approaches to observing the behaviour and interconnectivity enhancements in individuals who have their vision deprived. Commonly these studies are performed with a blindfold (or blacked out ski mask), not as often, participants are asked to report to sound localization tasks with their eyes closed, and lastly, participants have occluded lenses inserted in their eyes. To our knowledge, no study has observed long-term visual deprivation (defined as an experiment longer than 90 minutes of visual deprivation) with occluded lenses. This study has a period of blindness that is an excess of 5 hours, and so an experiment with eyes closed was not explored.

It is very unlikely to have an individual comply to continuously close their eyes during an experiment of prolonged visual deprivation. Since it is a natural reflex to open your eyes at any sign of insecurity, there would not be a sufficient amount of time to allow for any short-term changes in plasticity. Having your eyes closed is a volitional, or intentional, behavior and you have sensory feedback on your face. If you are consciously making an effort for a motor control it differs from experiencing blindness caused by blocking your cornea from visual input.

However, in order to achieve a model of true blindness, visual deprivation was implemented with the use of occluded contact lenses. A true model of blindness has been defined as an experiment where the participant is as blind as possible and as naturally as possible. The occluded lenses are
a mimic of contact lenses used for sight-correction and participants are able to accommodate to having them on their eyes within minutes. This is in comparison to a ski mask or blindfold, which is felt on the face throughout the experiment and can be accidently moved, allowing light to enter the eyesight. A blindfold still allows for sensory cues on your face. If contact lenses are worn, the participant feels more “naturally” blind, and begins to interact differently with their environment in comparison to with a blindfold on, particularly a loss of security is experienced as one would except if vision was truly lost. This may be due to the fact that the participant has nothing on their face, but see’s complete blackness when they blink, but feel nothing covering their eyes. Your corneal nerves habituate to the sensory information, but you have no somatosensory feedback on your face. This could be a potential explanation for explanation for the dramatic differences in the behaviour of participants with contact lenses compared to blindfolds.

There is no research that involves participants being scanned with opaque contact lenses as they contain iron oxide, which is a source of artifact on MRI. In treating amyloidosis, an eye-patch and opaque contact lenses have the same affect, but with the latter being reported as faster in some studies and as more aesthetically pleasing (Anderson et a. 2006; Collins et al. 2008). This may infer that there are fairly similar pathways, but have some differences that may be relatable to Late Blind (LB) and Congenitally Blind (CB). Individuals with a blindfold may experience increased activation in the ventral premotor area, anterior insula and the operculum parietal, compared to participants with contact lenses who may experience increased activation in the superior parietal cortex and operculum parietale. Both blindfold and contact lens wearers may experience activity in multimodal integration cortices, cortical hubs and unimodal sensory
cortices. However, the difference in these regions is not as large compared to normally sighted individuals (Ortiz-Teran et al. 2016).

4.6 ACCURACY vs PRECISION

In the experiment, accuracy is expressed as how close each test subject’s observed localization point was to the actual/theoretical point along the semicircle. Precision is how close the observed localization points were to one another. The statistical methods used to measure accuracy and precision are Mean Signed Error (MSE) and standard deviation, respectively. The lower the MSE, the more accurate the test subject is, and comparably, the lower the standard deviation, the more precise the test subject is.

When comparing regression analyses for each session across all test subjects for both MSE and standard deviation, MSE showed values that represent a strong fit to the data. Each regression showed decreasing MSEs as the localization points moved closer to the middle of the semicircle. This indicates that test subjects were more accurate in their estimates with speakers close to or directly in front versus to the sides. The regression analyses for standard deviation showed no significance, and therefore unable to verify the level of precision.

4.7 DIRECTIONAL ERROR

Looking at the directional error (MSE) in comparison to accuracy, the results are similar with respect to peripheral field. There was less variability in directional error when participants were asked to report to speakers located in the central locations. When individuals have normal sight, the peripheral vision is a key player in controlling direction, which is known as the two channel model (Paillard & Amblard 1985). This model states that movement direction is processed in the kinetic visuomotor channel from the visual periphery. Central vision is said to have an influence on directional accuracy (Khan et al. 2004). It is interesting to note that in Figure 14 (as well as
Appendix G), the line of best fit has two different slopes, one on the left and one on the right. This nonlinear effect near the origin may be a result of no speaker in the centre location.

4.8 LIMITATIONS AND FUTURE DIRECTIONS

The limitation of this study is a small sample size (n=10). However, the study had a duration of approximately 8 hours, and repetitive trials. When comparing improvement of sound localization, there may be differences individually that we are unable to account for in a sample of this size. It would be suggested to continue collecting data on more participants and pool the data to have a substantially larger cohort. This would account for deviations among participants.

Another limitation was that some individuals who had never had any practice with the use of contact lenses experienced some troubles while inserting the lenses and had anxiety that may or may not have impacted their performance. There was no known or feasible method for us to measure whether their fear and anxiety impacted their ability to focus on the experiment and localize the sounds during the task. With further data collection, perhaps participants can be analyzed in two groups, experienced users and less experienced users.

The participants performed the sound localization task without receiving feedback. A study by Honda et al. showed that during free-field movement, sound localization performance improved and decreased angular errors on the horizontal plane during proprioceptive feedback for sound localization. They found that listeners with auditory, visual (during non-blind experiments), and proprioceptive feedback regarding the target locations improve the localization accuracy (Zahorik et al. 2006). If subjects were receiving feedback, there may have been improvement in eccentric locations. Since individuals were walking and becoming accustomed to their environment, they were learning to behave as though they were blind. Perhaps feedback
regarding correct (or close) and incorrect (too far) speaker location would have assisted in accuracy performance, particularly for speakers in eccentric locations.

Some participants experienced fatigue during the experiment, and it is possible that it may have influenced their performance. Based on notes from participants, the majority stated they felt tired on and off, but more towards the end when they were nearing 5 hours of blindness. This would be a difficult factor to avoid since the fatigue is brought on by their contact lenses and feeling like they are preparing themselves for sleep. Although the experiment was never performed too early (approximately at 9:00 am), since their eyes had no visual input when they blinked, participants experienced fatigue. Some participants did not use eye drops, and no participant used them constantly, only when they first inserted the contacts. Perhaps using eye drops once an hour would relieve some of the feeling of fatigue.

Similarly, the participants may have been impacted by boredom. Their activities are limited with the loss of vision, and this could contribute to their performance. There was an attempt to fill up most of the two breaks with some activities (i.e. walking, identifying objects, attempting to type an email, and eating). Participants were also listening to Ted Talks or listening to other podcasts online. Perhaps more interactive activities can be planned to keep the participant more active.

With an opportunity to perform this experiment again, some future suggestions would include using eye drops for participants, comparing performance of participants who are experienced contact users and novice or new users, comparing performance of experiment with feedback for sound localization and with a head restraint.
5.0 CONCLUSIONS

Although there is considerable evidence that the deprivation of one sense may crossmodal brain reorganization that directly influences the enhancement of another sense, it is unclear how widespread these enhancements are. The results of the present study suggest that there is no increase in accuracy across time in participants performing a sound localization task in a model of acute blindness. There is a main effect of speaker, correlating to the main effect of centricity, which suggests that eccentric locations were localized with less accuracy. The findings of significant main effect of centricity are comparable to current literature and emphasize in favour of this study’s methodology used to investigate crossmodal compensation, which make the lack of main effect of accuracy in session across time an interesting finding. These findings are a key addition to existing literature in crossmodal compensation of visual to auditory networks. With a novel design and model for acute blindness, this study showed unique results that pose questions in visual-auditory calibration in sound localization in normally sighted individuals. Contrary to some previous research, this study did not show improvement in accuracy across sessions of sound localization, which is possibly explained by absence of visual calibration. Additionally, these results may be due to the fact that there is neural processing in the visual cortex and transformation of auditory spatial coordinates that plays a role in perceptual alignment of audition and vision in regularly sighted individuals. This research study may show some insight for how late-blind individuals learn to adapt to their non-sighted environment, and that enhancements are perhaps not as quickly induced as we may have previously believed. For future research, it could be valuable to explore the neural mechanisms that occurring in a novel design of acute blindness that has not previously been explored, in comparison to effects that are seen in normally sighted individuals of existing literature.
6.0 REFERENCES


Tabry V, Zatorre RJ, Voss P. 2013. The influence of vision on sound localization abilities in both the horizontal and vertical planes. Front Psychol. 12


APPENDIX A

**Significant Main effect of Speaker Accuracy:** PAIRWISE COMPARISONS with Bonferroni correction. If Mean Difference is negative, then (J) is less accurate than (I). Yellow denotes that (J) is less accurate than (I).

<table>
<thead>
<tr>
<th>(I) Speaker</th>
<th>(J) Speaker</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>1.576*</td>
<td>0.013</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>3.289*</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>3.810*</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>4.919*</td>
<td>0.002</td>
</tr>
<tr>
<td>1</td>
<td>6</td>
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<td>0.028</td>
</tr>
<tr>
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<td>4</td>
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<td>0.036</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>3.343*</td>
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<td>7</td>
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<td>0.005</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>-6.759*</td>
<td>0.034</td>
</tr>
<tr>
<td>10</td>
<td>16</td>
<td>-6.830*</td>
<td>0.015</td>
</tr>
<tr>
<td>11</td>
<td>15</td>
<td>-4.190*</td>
<td>0.048</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
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<td>0.003</td>
</tr>
<tr>
<td>12</td>
<td>16</td>
<td>-4.980*</td>
<td>0.004</td>
</tr>
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<td>13</td>
<td>16</td>
<td>-4.031*</td>
<td>0.001</td>
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<td>16</td>
<td>-3.423*</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>15</td>
<td>16</td>
<td>-1.886*</td>
<td>&lt;0.000</td>
</tr>
</tbody>
</table>

~ If Mean Difference is –ve, then (J) is less accurate than (I)  
~ Yellow denotes that (J) is less accurate than (I)
## APPENDIX B

Significant Interaction between Session x Speaker in Accuracy: PAIRWISE COMPARISON w/out Bonferoni

<table>
<thead>
<tr>
<th>Speaker</th>
<th>(I) Session</th>
<th>(J) Session</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
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</thead>
<tbody>
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<td>1</td>
<td>6</td>
<td>-2.097*</td>
<td>0.034</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>5</td>
<td>-3.810*</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>2</td>
<td>3.810*</td>
<td>0.031</td>
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<tr>
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<td>1</td>
<td>5</td>
<td>-3.193*</td>
<td>0.041</td>
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<td>2</td>
<td>4</td>
<td>-1.837*</td>
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<td>-2.590*</td>
<td>0.047</td>
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<td>0.039</td>
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<tr>
<td>2</td>
<td>4</td>
<td></td>
<td>-1.757*</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td></td>
<td>-2.157*</td>
<td>0.040</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>4</td>
<td>-1.403*</td>
<td>0.045</td>
</tr>
<tr>
<td>7</td>
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<td>4</td>
<td>-1.620*</td>
<td>0.024</td>
</tr>
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<td>1</td>
<td>2</td>
<td>-1.533*</td>
<td>0.037</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>6</td>
<td>1.437*</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td></td>
<td>1.617*</td>
<td>0.020</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>7</td>
<td>-1.677*</td>
<td>0.014</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>6</td>
<td>0.700*</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>7</td>
<td>-0.980*</td>
<td>0.024</td>
</tr>
</tbody>
</table>
### APPENDIX C

Significant Main Effect of Centricity: PAIRWISE COMPARISONS w/ Bonferoni

<table>
<thead>
<tr>
<th>(I) Centricity</th>
<th>(J) Centricity</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4</td>
<td>-4.246*</td>
<td>0.004</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>-3.887*</td>
<td>0.005</td>
</tr>
</tbody>
</table>

~ If Mean Difference is –ve, then (J) is less accurate than (I)
~ Yellow denotes that (J) is less accurate than (I)
APPENDIX D

Significant Interaction between Session x Centricity: PAIRWISE COMPARISON w/ Bonferoni

<table>
<thead>
<tr>
<th>Session</th>
<th>(I) Centricity</th>
<th>(J) Centricity</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>4</td>
<td>-4.759*</td>
<td>0.042</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>-3.967*</td>
<td>0.013</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>4</td>
<td>-4.367*</td>
<td>0.017</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>-4.225*</td>
<td>0.009</td>
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<td>3</td>
<td>2</td>
<td>4</td>
<td>-3.488*</td>
<td>0.044</td>
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<td>5</td>
<td>1</td>
<td>2</td>
<td>4.758*</td>
<td>0.010</td>
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<td>3</td>
<td>4</td>
<td>-3.477*</td>
<td>0.026</td>
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<td>6</td>
<td>2</td>
<td>4</td>
<td>-4.708*</td>
<td>0.007</td>
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<td></td>
<td>3</td>
<td>4</td>
<td>-4.342*</td>
<td>0.030</td>
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<tr>
<td>7</td>
<td>2</td>
<td>4</td>
<td>-5.780*</td>
<td>0.005</td>
</tr>
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<td></td>
<td>3</td>
<td>4</td>
<td>-4.383*</td>
<td>0.024</td>
</tr>
</tbody>
</table>

~ If Mean Difference is –ve, then (J) is less accurate than (I)
~ Yellow denotes that (J) is less accurate than (I)
**APPENDIX E**

**Significant Main effect of Speaker Reaction Time:** PAIRWISE COMPARISONS with Bonferroni correction. If Mean Difference is negative, then (J) has a slower reaction time than (I).

<table>
<thead>
<tr>
<th>(I) Speaker</th>
<th>(J) Speaker</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>7</td>
<td>0.0273*</td>
<td>0.048</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
<td>-0.0187*</td>
<td>0.027</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>0.209*</td>
<td>0.011</td>
</tr>
</tbody>
</table>
**APPENDIX F**

*Significant Main effect of Session Reaction Time: PAIRWISE COMPARISONS with Bonferroni correction. If Mean Difference is negative, then (J) has a slower reaction time than (I).*

<table>
<thead>
<tr>
<th>(I) Session</th>
<th>(J) Session</th>
<th>Mean Difference (I-J)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>0.666*</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.721*</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.916*</td>
<td>0.016</td>
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<td>6</td>
<td>0.964*</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.947*</td>
<td>0.005</td>
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<tr>
<td>2</td>
<td>4</td>
<td>0.360*</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.555*</td>
<td>0.034</td>
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<tr>
<td></td>
<td>6</td>
<td>0.603*</td>
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<td>0.586*</td>
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</tr>
<tr>
<td>4</td>
<td>6</td>
<td>0.243*</td>
<td>0.031</td>
</tr>
</tbody>
</table>
APPENDIX G

SESSION 1 (Predicted Y, Mean Signed Error vs. Degrees)

SESSION 2 (Predicted Y, Mean Signed Error vs. Degrees)
SESSION 3 (Predicted Y, Mean Signed Error vs. Degrees)

SESSION 4 (Predicted Y, Mean Signed Error vs. Degrees)
SESSION 7 (Predicted Y, Mean Signed Error vs. Degrees )
APPENDIX H

EYE DOMINANCE TEST

All participants received the following instructions for performing the eye dominance test:

(i) Hold your hands out at arm’s length in front of you, palms facing forward

(ii) Make a triangle with your hands by combining both of your thumbs to be roughly perpendicular to the rest of your hands and allowing your index fingers to touch.

(iii) Using the space between your hands as a viewing window find a mark on the wall that stands out to you and fits within the parameters of your viewing window, and focus on it with both eyes open.

(iv) Alternate closing each eye to see when the object moves out of the center of the triangle. When you close your dominant eye, the object will move out of vision. For example, if you close your left eye and the object remains in sight, but you close your right eye and the object moves out of sight, then you are right eye dominant.
APPENDIX I

PARTICIPANT DATA COLLECTION FORM

<table>
<thead>
<tr>
<th>Date:</th>
<th>Time:</th>
<th>Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>Sex:</td>
<td>Corrected vision: yes/no</td>
</tr>
</tbody>
</table>

Experimenters present:

Matlab Codes run:
- Computer 1: LaserLocalizer.m & headmovetrial3 (2 or 10, depending on trial number using)
- Computer 2: soundtasktrial3 (2 or 10, depending on trial number using)

1. Have you previously worn contact lenses? Yes / No
   - If yes, do you were them: regularly / occasionally / not very often at all / you only tried them once or twice / other: (please specify use, i.e., year(s))

2. Have you experienced any hearing loss?
   - If yes, please specify.

4. **Eye dominance:** Extend both arms in front of your body and place your hands together so as to make a small triangle between your thumbs and the first knuckle. With both of your eyes open, look through the triangle and focus on a specific small object. Close your left eye. If the object remains in view, you are right eye dominant. If your hands appear to move off the object and move to the left, then you are left eye dominant: **Right-eye dominance / Left-eye dominance.**

Can you wink with both eyes? R Yes/No L Yes/No

5. Sound Localization Task
   ** Note: #1-3 = Session 1 **

81
<table>
<thead>
<tr>
<th>Task</th>
<th>Description and Notes</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Localization</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Practice with lights ((x3))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Dark trial ((x3))</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Put in contact into dominant eye:**

Which eye 1\(^{st}\): ________

Do you feel any numbness, sagginess, and/or any other weird/unusual feeling?

**Put in contact in other eye:**

Which eye 2\(^{nd}\): ________

Do you feel any numbness, sagginess, and/or any other weird/unusual feeling?

<table>
<thead>
<tr>
<th>Task</th>
<th>Description and Notes</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Practice trial ((x2))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Session 2 ((x10))</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**90 min break** *(describe things person does)*
-Participant may engage in conversation with experimenters, listen to music, or an audio-book.

-Participant will be guided to walk around by experimenters (guide participant around the halls, allowing them to listen for sounds, and encourage them to interact with the environment)

Time:____________

<table>
<thead>
<tr>
<th>Task</th>
<th>Description and Notes</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Practice trial (x2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Session 3 (x10)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**180 min break (describe things person does)**

-Participant may engage in conversation with experimenters, listen to music, or an audio-book.

-Participant will be guided to walk around by experimenters (guide participant around the halls, allowing them to listen for sounds, and encourage them to interact with the environment)

Time:____________
<table>
<thead>
<tr>
<th>Task</th>
<th>Description and Notes</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>8. Practice trial (x2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>9. Session 4 (x10)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Remove nondominant contact lens</strong> first</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you feel any numbness, sagginess, and/or any other weird/unusual feeling? L/R eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you feel any numbness, sagginess, and/or any other weird/unusual feeling? L/R eye</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>10. Practice trial (x2)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>11. Session 5 (x10)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>60 min break (with vision) (describe things person does)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Participant may engage in conversation with experimenters, listen to music, or use their computer/phone, washroom break.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time:______________________</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Task</td>
<td>Description and Notes</td>
<td>Time</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------------</td>
<td>------</td>
</tr>
<tr>
<td>12. Practice trial (x2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Session 6 (x10)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Additional Notes:
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
______________________________________________________________________________
APPENDIX J

CONSENT FORM

Informed Consent Form

Study Name: Investigating multimodal interactions within the human brain

Researchers: Nevena Savija – Graduate, Department of Biology, York University – nsavija@yorku.ca

Dr. Joseph DeSouza, PhD - Department of Psychology, York University - desouza@yorku.ca

Purpose of the Research: We hope to investigate the neural integration of sensory modalities (specifically, vision and hearing; vision and touch; and vision and motor control) in humans when faced with the removal of visual input. Our proposed research path will investigate the effects of altering visual inputs upon auditory localization, sensitivity to touch, and motor control of the face. The final results of these investigations will be published in a scientific journal.

What You Will Be Asked to Do in the Research: Subjects will be fitted with black occluding contact lenses in both eyes for approximately 6 hours of the total 8 hour session. Subjects will be given 3 different tasks at various intervals spanning the length of the session. During the auditory localization task, subjects will be seated in a room where auditory stimuli (i.e., a tone) will sound from various locations and subjects will be asked to point to the origin of the sound. The index finger of subjects’ dominant hand will be affixed with a sensor to detect their localization response. During the touch sensitivity task, the experimenter will use a Two-Point Aesthesiometer, a calibrated ruler affixed with two movable plastic tips, to evaluate changes in acuity thresholds by tapping predetermined areas of the body. A video will be taken of the facial motor control tasks, during which subjects will be asked to alternate winking with their right and left eye for a set number of winks. Each of these tasks will done once prior to putting in the black contact lenses to familiarize subjects with the procedures, several times at various intervals after insertion of the contact lenses, and at least once following removal of the contact lenses. While subjects are wearing the black contact lenses, they will be in the constant company of an experimenter(s) who will guide them between task stations and provide any assistance required with performing the tasks or other normal functions like walking, sitting, drinking, eating lunch, washroom breaks (a same-sex experimenter will accompany subjects for washroom breaks), etc.
Time commitment for experiment: Length of the total session may vary minimally across subjects, but is estimated to be 8 hours. We hope to expand this behavioural test in the future by utilizing fMRI technology to elucidate patterns of referred sensation as facilitated by multimodal neurons. If subjects choose not to participate in this subsequent study, their involvement in the present study will not be influenced in any way.

Compensation: Subjects will be paid $10 for each hour of participation for a total of $80 for the 8 hour session. Lunch and a snack will also be provided for subjects.

Risks and Discomforts: We do not foresee any risks or discomfort from your participation in the research. However, due to the novel experience of losing visual input, it is possible that some subjects may experience initial fear or uneasiness following insertion of the contact lenses. Also, if subjects are not accustomed to wearing contact lenses on a regular basis, they may experience some discomfort when inserting, wearing, or removing the contact lens. Subjects are free to leave the experiment at any time due to any discomfort; their decision to do so will not affect their relationship with the researchers, York University, or any other group associated with this project.

Benefits of the Research and Benefits to You: Through the present research study, we will gain a better understanding of the complex relationship among multiple senses and how we form perceptions of the changing world around us. This research will also allow us to infer the adaptations made by the brain when it is suddenly deprived of vision for an extended period of time, thus offering insight into neural plasticity. Subjects will benefit from participating in this study by contributing to our scientific outcomes and experiencing temporary, short-term neural plasticity first-hand. Subjective experiences provided during this study may also provide subjects with elevated insight and compassion for others whose loss of vision is less transient.

Withdrawal from the Study: You may stop participating in the study at any time, for any reason, if you so decide. If you decide to stop participating, you will still be eligible to receive the promised pay for agreeing to be in the project and any data gathered as a consequence of your participation will be destroyed and omitted from our analyses. Your decision to stop participating, or to refuse to perform particular tasks, will not affect your relationship with the researchers, York University, or any other group associated with this project. In the event you withdraw from the study, all associated data collected will be immediately destroyed wherever possible.

Confidentiality: Subjects will be identified on all task results by a subject code only. Videos will be taken of subjects’ faces during the motor control task. Videos will be analyzed and referenced using the subject code only. Any videos or pictures taken will be strictly used for analytical purposes, and will not be used in any publications unless consent has been given below. Your data (task results and all photographs) will be stored indefinitely in a locked facility, in a locked file cabinet, on password-protected computer(s) and password protected files with access by
selected research staff. Coded data will be used to prepare publications (journal articles, review articles, news releases, grant applications and thesis reports). Confidentiality will be provided to the fullest extent possible by law.

___ Please initial here to provide consent for using your videos and/or pictures in a future publication and/or report.

___ Please initial here if you would like to be contacted for involvement in a future study.

**Questions about the Research?** If you have questions about the research in general or about your role in the study, please feel free to contact me (nsavija@yorku.ca) or my supervisor - Dr. Joseph FX DeSouza - either by telephone at (416)736-2100 extension 22946 or by e-mail (desouza@yorku.ca). This research has been reviewed and approved by the Human Participants Review Sub-Committee, York University’s Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, please contact the Sr. Manager & Policy Advisor for the Office of Research Ethics, 5th Floor, York Research Tower, York University (telephone 416-736-5914 or e-mail ore@yorku.ca).

**Legal Rights and Signatures:**

I, _______________, consent to participate in 'Investigating multimodal interactions within the human brain' conducted by Nevena Savija and Dr. Joseph DeSouza. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

**Signature** _______________  **Date** _______________

Participant

**Signature** _______________  **Date** _______________

Principal Investigator