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Questioning The Modality Of The Occipital Lobe

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QUESTIONING THE MODALITY OF THE OCCIPITAL LOBE

by

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ABSTRACT

This dissertation explores the occipital lobe's response to non-visual inputs, and whether this responsivity partitions into separate localization and identification pathways as seen with visual inputs. We hypothesized that occipital areas may merely prefer visual inputs, while maintaining similar task-based sensory recruitment in response to other senses. Our secondary hypothesis was that the robust occipital activation seen in late-blind participants stems at least initially from standard connections present even in the typically sighted, and that these standard connections are functionally utilized by the typically sighted in spatially relevant non-visual analyses. Our initial literature review supported our hypotheses that the occipital lobe is a highly plastic, cross-modally responsive area and that recruitment of occipital areas in the blind stems from the strengthening of existing multi-modal connections.

To further explore our topic, we conducted meta-analyses on fMRI and PET studies reporting occipital response to non-visual input in congenital/early-blind participants and/or blindfolded but otherwise typically sighted participants. Through these analyses, we noted significant extrastriate activations for blind participants beyond that seen with sighted participants, which lent support to our task-based wiring hypothesis. We also observed common activations between blind and sighted participants, notably including activation in striate cortex, which supported the notion of

functional connections to occipital lobe from other sensory inputs regardless of the presence or lack of visual input.

Finally, we conducted an fMRI study investigating the effects of short-term blindfolding on occipital responsivity to auditory stimuli in typically sighted participants. We did not observe greater activation in participants blindfolded for 45 minutes than we observed with non-blindfolded participants, but our study did further highlight the functional connections present between non-visual senses and the occipital lobe, and again supported our task-based wiring hypothesis.

Overall, we found support for the occipital lobe being multi-modally reactive, even in typically sighted individuals. We also found evidence of task-based wiring being maintained regardless of the sensory modality being responded to, and of the likelihood that these functional non-visual connections are at least initially what give rise to the widespread occipital activation observed with blind participants in response to non-visual stimuli.

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CHAPTER 1

GENERAL INTRODUCTION

Occipital lobe recruitment for visual processing is well established, with strong and consistent evidence reinforcing the link. Indeed, this area is classically considered to only respond to visual inputs, as evidenced by browsing through most undergraduate textbooks (e.g., Goldstein, 2014). However, multisensory interactions involving vision do occur, such as the McGurk and ventriloquist effects (e.g., McGurk & MacDonald, 1976; Alais & Burr, 2004), suggesting that this assumed unimodal responsiveness may not be entirely correct. Further, blind individuals and typically sighted individuals with visual input temporarily removed have been shown to functionally recruit areas of the occipital lobe to help process non-visual inputs (e.g., Weaver & Stevens, 2007; Merabet et al., 2008). Though this evidence strongly suggests that the occipital lobe is not strictly hardwired to react to visual inputs alone, it can be argued that general multisensory interactions may typically be driven by higher-level areas of association cortex (e.g., parietal areas, lobe borders), and that blind or blindfolded recruitment of occipital areas may be due to gross plastic neural rewiring rather than a strengthening of more general, standard multimodal responsivity. Thus, the question becomes whether the brain is set up to develop region-specific lobes comprising sense-specific areas (e.g., occipital lobe exclusively for vision, temporal lobe exclusively for audition), with cross-modal integration occurring in distinct higher-level areas, or if these regions merely prefer particular senses while retaining the ability to respond to and integrate information from other modalities even at lower levels of input processing.

1.1 EVIDENCE OF UNIMODAL STRUCTURING OF CORTEX

The unimodal concept seems reasonable when considering the general layout of occipital/visual areas. For instance, striate cortex/V1/primary visual cortex is critical for the experience of phenomenal/conscious vision, with damage to the area itself or the connections to the area removing conscious sight for the related visual field (see Overgaard, 2011; Walsh & Cowey, 1998). Combined with research showing that artificial stimulation can produce visual phosphenes in the related visual field (e.g., Ptito et al., 2008), it is evident that V1 is keenly linked to the visual modality.

From V1, information is sent to extrastriate areas of visual cortex (visual areas V2 through V5/MT) for further processing of particular aspects of the visual scene. In broad terms, the information sent from V1 is parsed out to these extrastriate areas along two primary streams -- the dorsal "where/how" pathway for location discrimination and action planning, and the ventral "what" pathway for identification (see, e.g., Ungerleider & Mishkin, 1982; Goodale & Milner, 1992; Milner & Goodale, 2008). Overall, the visual regions, V1 through V5/MT, show both feedback and feedforward connections amongst themselves, allowing efficient input analysis and return (see, e.g., Guo et al., 2007; Hupé et al., 1998; 2001; Pascual-Leone & Walsh, 2001; for review, see Sillito, Cudeiro, & Jones, 2006). Interestingly, each of these visual regions (including further proposed subdivisions of extrastriate cortex beyond V5/MT) contains its own retinotopically linked visual field map, further highlighting the relationship between visual processing and occipital structures (for review, see Wandell, Dumoulin, & Brewer, 2007; see also Hubel & Wiesel, 1965), and lending credence to the concept of a unimodal layout.

It should also be noted that, just as visual cortex is split into specific regions, so too are other cortical areas. The primary receptive areas of auditory and somatosensory cortex maintain designations of A1 and S1, respectively. Further secondary cortical areas within these modalities classically bear further numerically tiered divisions, though auditory cortex is often more recently referred to as comprising A1, then a surrounding area referred to as the belt, and a further area referred to as the parabelt. Regardless of the naming scheme, these designations of distinct functional sub-areas within regions of cortex known to be specially reactive to a given sensory modality support both the notion of unimodal cortical separations, as well as within-region specialization for the analysis of inputs from said sensory modality. This commonality of anatomical breakdown may be a factor in allowing plastic recruitment from non-typical sensory modalities should the initially specified sense be absent or lost later in life, retaining the notion of unimodal selectivity but with some channels allowing for otherwise unusable cortical regions to be adopted in a non-standard fashion.

Note also that the dorsal “where/how”/ ventral “what” double-dissociation of processing streams mentioned in relation to visual inputs is also evident in non-visual modalities. It is well-established in audition, with auditory location discernment and sound identification tasks eliciting the activation of separate task-specialized pathways in auditory cortex (e.g., Ahveninen et al., 2006; Alain et al., 2001; Du et al., 2015). Further evidence suggests a similar processing split for somatosensory/haptic inputs (e.g., Mishkin, 1979; Sathian et al., 2011). That the brain seems set to wire separate pathways for these gross specific task types, with unique iterations present in cortex associated with specific sensory modalities, again lends credence to the notion of a unimodal lobe structure. This allows anatomically nearby compartmentalization of specific low-level sensory functions, while potentially affording other higher-level areas to utilize multi-modal information to form a full percept of the external environment. As discussed in regards to the similarity of primary and secondary cortical region designations within visual, auditory, and somatosensory cortex, the basic similarity of compartmentalization of task-function discussed here may also speak to the other-modal recruitment plasticity seen in the absence of a given primary sense. It is viable that, should the general structure remain the same, the off-modal recruitment could also be task-based. Whether this plastic recruitment reflects more direct processing of sensory inputs, basic co-processing of input, or in the case of occipital areas, related mental visual imagery, remains to be determined.

Beyond the commonality in the division of primary and secondary processing areas, and retention of the dual-stream “what” and “where/how” pathways, similar organization to the visual retinotopic maps exists in both auditory and haptic realms. With audition, the cochlea bears an ordered tonotopic map of frequencies along its length, which further occurs in primary auditory receiving area, A1. Though this is associated with frequency instead of location, it is still a direct mapping of an external stimulus characteristic to cortex. More directly related to location-mapping, it has been shown that auditory cortex maintains networks of auditory spectral cues, utilizing information from the way sound stimuli are affected by the fold structure of the external ear, and that alteration of these folds leads to new localization patterns (e.g., Hofman et al., 1998). For somatosensory/haptic inputs, a somatosensory map of the individual parts of the body translates onto cortex, with specific parts of the body linked to specific locations of S1, the primary somatosensory area. A similar layout exists for the adjacent strip of cortex dedicated to motor control.

The above information suggests that the brain is slated to organize in such a way that specific areas of its sensory processing cortex become dedicated to specific input features and locations. It further suggests a prevalence of dedicating spatially proximal areas of cortex to a given sense, highlighting the concept of large unimodal regions (e.g., occipital for vision, temporal for audition, fronto-parietal for tactile/motor). This seems particularly relevant to the occipital lobe, as the existence of multiple retinotopic map structures throughout the region strongly implicates the lobe as being uniquely situated for visual analysis. However, evidence related in the following section suggests that cortical wiring and activation may take on a more general multi-modal approach. Beyond these concepts, the notion that the different regions of the brain seem to similarly wire for where/how and what channels of information processing is of note.

1.2 MULTIMODAL EFFECTS, CONNECTIONS, AND REGIONS

1.2.1 MULTI-MODAL INTERACTIONS

As we are able to integrate information from multiple sensory modalities into full percepts of external stimuli, it is evident that the various regions of the brain do not exist in a vacuum. Indeed, real-world stimuli tend to come with multiple facets of sensory information. For instance, movement tends to cause sound, and the presence of a given stimulus may further come with a specific scent. Running a hand along a surface can create not just tactile stimulation, but sound as well. Taste involves not just chemical properties interacting with taste buds on the tongue, but also smell and even vision. Whereas our brains may seem to develop in such a way as to process specific sensory stimuli in particular areas, they seem to adapt to these multimodal commonalities as well. This is evident through things like visual capture of a sound source, localizing (or mislocalizing) a sound as emanating from a visually salient area of activity, such as moving lips. This is further evident through the notion that a sound or visual target presented independently and below the perceptual threshold will go unnoticed, but the same sub-threshold stimuli presented together are much more likely to trigger conscious perception (e.g., Giard & Peronnet, 1999). Similar to this integrational sum being greater than its perceptual parts, we are able to determine the identity of objects through various sensory modalities, and the presence of multiple simultaneous sensory streams of information can make this identification easier. Thus, it is evident that these areas in some way form connections and share information, either directly or through mediating areas wherein their output comingles. Thus, we have interactions between the senses that must be addressed. These interactions are important to the overall exploration of this current discourse, as the particulars of how information is shared between sensory regions can inform the likelihood of sensory unimodal or domain general multimodal neural development. If the connections between regions primarily occur in distinct higher-order brain regions, this may support the notion of unimodal low-level sensory regions. Contrariwise, if these connections occur in lower-level analyses between these assumed unimodal sensory processing regions, we have evidence suggesting a more multimodal neural architecture. To investigate these connections, I will briefly discuss general studies of sensory interaction through a particular focus on multimodal illusions involving vision. Beyond this, I will relate information gained from neural connectivity studies, as well as information on known multimodal integration areas and locations where multimodally reactive neurons have been reported.

1.2.2 MULTISENSORY ILLUSIONS INCLUDING VISION

Like many things in the brain, when two senses interact in any competing fashion, one must trump the other. This can hold true with cooperative interactions as well. In general, the existing literature suggests that vision tends to be selected over audition in cases of conflicting information where spatial processing is involved, and vice versa with temporal processing (e.g., Guttman, Gilroy, & Blake, 2005). Multisensory illusions have a strong ability to inform us as to these interplays of sensory dominance and allow us to further infer general connectivity patterns.

1.2.3 MCGURK EFFECT

In the McGurk effect, a speaker is seen making the mouth-movements for a specific, simple phoneme, such as “ba” or “fa”, while a separate sound stimulus plays a separate but similar phoneme, creating disagreement between the visual and auditory domains. This typically results in the visual input modifying the auditory perception to either be heard as the visually-represented phoneme, or a novel cross between the two represented phonemes (e.g., perceiving “da” when the visual stimulus is for “ga” and the auditory stimulus is for “ba”). So here, in general, vision is acting upon audition, though with a distinct linguistic processing element on top of the typically ascribed spatial processing (McGurk & MacDonald, 1976).

1.2.4 VENTRILOQUISM EFFECT

With the ventriloquism effect, an observer’s discrimination of the source location of an auditory stimulus is shifted to coincide with a visual target from which the sound is not actually emanating, holding with the notion of spatial dominance in the visual modality (Howard & Templeton, 1966). In basic modern terms, this effect can be experienced while watching television, as we tend to localize voices to the actor speaking, rather than the hardware actually producing the sound. Further research into the ventriloquism effect gives rise to the concept of the dominating sense in a given task being related not only to temporal and spatial guidelines, but to the strength of the stimuli in the utilized sensory modalities, and even that no sense necessarily has to be selected as the dominant modality – rather, a combination of senses can be adopted to determine specific perceptual outcomes, perhaps similarly to the averaging of certain phonemes into a separate third phoneme as discussed in the McGurk effect. It has been shown that strong visual and auditory presentations tend to lead to the standard ventriloquism effect, with vision capturing (mis)localization, but also that with a heavily degraded visual stimulus, auditory location cues are more likely to trump the visual aspect, reversing the effect. With moderate degradation of the visual stimulus, it is possible for neither sense to dominate, with localization instead being perceived at a median point between the two stimuli (Alais & Burr, 2004).

1.2.5 DOUBLE-FLASH ILLUSION

The double-flash illusion is an example of auditory inputs being able to alter visual perception. In this illusion, a single flash of light presented temporally between two auditory beeps tends to be perceived as two flashes of light (Shams, Kamitani, & Shimojo, 2002; Shams, Kamitani, & Shimojo, 2000). This effect occurs with various numbers of flashes and beeps, with the illusory flashes occurring when there were more sounds than flashes. Similarly, this effect has been found to exist between auditory and tactile perception, with a series of beeps influencing the number of taps felt against a fingertip. This effect held when the auditory and tactile stimuli were presented at similar timepoints, but degraded as the taps and beeps were presented further apart, suggesting that the brain is keyed to automatically integrate crossmodal information perceived, through temporal proximity, to likely emanate from a single unified source (Bresciani et al., 2005). However, it must be noted that in the initial visual-auditory effect, spatial attention effects have been found to modulate the extra flash perception, such that specific attention to the stimulus location enhanced the neural effect associated with the perception of the illusory flash, whereas inattention degraded said effect (Mishra et al., 2007; Mishra et al., 2010).

The double-flash illusion can largely be considered a condensed iteration of the influence of auditory flutter on visual flicker perception, wherein the repetition speed of a string of auditory clicks is known to influence the perceived rate of repetition in visual light flicker. A slower auditory presentation can perceptually slow down a faster visual flicker rate, whereas a faster auditory presentation can perceptually speed up a slower visual flicker rate, with veridical alterations to the visual flicker rate bearing no notable influence on the auditory perception (Shipley, 1964).

1.2.6 RUBBER HAND ILLUSION

The rubber hand illusion (Botvinick & Cohen, 1998) arises from visual, tactile, and proprioceptive senses, and occurs when a participant’s hand is positioned out of sight and very near a visible fake hand of similar appearance and position to the occluded actual hand. The real and false hands are simultaneously brushed, often resulting in the false perception that the feeling is coming from the false hand, or even that the false hand is the participant’s actual hand (see Ehrsson, Holmes, & Passingham, 2005).

1.2.7 BOUNCE-STREAM ILLUSION

The bounce-stream illusion, based on the work of Sekuler, Sekuler, and Lau (1997; see also Ecker and Heller, 2005) occurs when two circles are shown visually crossing paths in an X pattern, with a “clack” sound, such as two pool balls colliding, occurring at the time of meeting of the visual stimuli. When the sound is not present, observers tend to report the perception of the balls moving through one another and continuing on their initial straight-line trajectories. With the sound added, observers tend to report the perception of the balls colliding with one another, altering their trajectories such that ball one takes over the path of ball two, and vice versa. In the initial experiment, it was shown that the perception of the movement of a visually rendered ball moving in a three-dimensional box could be altered by the type of sound presented – a rolling sound or the sound of a ball hitting the ground. Paired with the rolling sound, the perception tended toward the ball rolling backward in the box, whereas with the striking sound, the perception shifted to one of the ball bouncing or falling in a static box-relative location. Overall, this shows that the perception of an ambiguous visual stimulus can be directly modulated not just by concurrent auditory stimulation, but by the specific features of the auditory stimulation.

1.2.8 RELEVANCE OF MULTISENSORY EFFECTS

Taken together, these multisensory experiment findings show that the typically-wired brain, with all senses intact, will utilize information simultaneously from multiple modalities in order to determine the most likely perceptual explanation of the events being processed. It has been shown that a given sensory modality can be more likely than others to influence perception in given situations, such as vision being preferable for spatial perception, and audition for temporal perception, but it has also been shown that the quality and even content of the stimulation can shift which modality is most salient to a final perceptual assumption. Critically to the overarching intention of this paper, these findings show clear interaction between multiple sensory modalities, suggesting interaction between the neural areas primarily dedicated to each individual sense. Given these interactions, one can reasonably assume connectivity between these regions, be it direct or through higher-order sensory integration regions. This notion will now be more directly explored through relation of findings in connectivity studies.

1.3 CONNECTIVITY, MULTIMODAL REGIONS, AND MULTIMODAL NEURONS

Whereas the information on multimodal interactions put forth thus far implies plausibility of cross-modal neural wiring, it does not of itself discount the possibility of a more strictly unimodal architecture. Thus, we must look for further information as to how and where these interactions might arise. To that end, connectivity studies allow us to note where neuronal connections exist within the brain, tracing links among and between areas of cortex in order to determine general structure or the presence of processing networks.

For our current purpose, we can examine connectivity studies to look for neuronal connections among and between sensory cortical processing areas. Whereas older literature appears to focus on neuronal connections within sense-specific areas of cortex, maintaining the concept of unimodal sensory segregation, more recent connectivity studies bear out strong implication for cross-modal sensory integration even at lower levels of processing. For instance, connections to occipital cortex from both primary and parabelt auditory areas, as well as the superior temporal polysensory (STP) area, have been shown in non-human primates (Falchier et al., 2002). The prevalence of these connections varies among occipital locations, with an apparent lack in central V1 but an increasing density more peripherally in V1. Further, parietal lobe areas, particularly intraparietal sulcus (IPS) and the ventral intraparietal area (VIP), show connections from visual, sensorimotor, somatosensory, and auditory regions (Lewis & Van Essen, 2000). Whereas these IPS/VIP connections could feasibly be construed as implicating said regions as specific higher-order sensory integrational areas, critically, it was recently found that in the rat brain, direct neural projections exist between each of primary somatosensory, visual, and auditory cortices (Stehberg, Dang, & Frostig, 2014). Previously, Cappe and Barone (2005) found connections in the marmoset brain between low-level visual and somatosensory cortex, somatosensory and auditory cortex, and visual and auditory cortex. Similarly, in human participants, functional connectivity studies have shown strong links between primary auditory cortex and anterior visual cortex that remain active even during vision-specific tasks (e.g., Eckert et al., 2008), suggesting a functional role of cross-communication between these low-level regions and modalities. Functional connectivity studies have also shown links between low-level somatosensory and visual cortex in the human brain during haptic perception (e.g., Deshpande et al., 2008), particularly involving shape- (lateral occipital complex; LOC) and texture-selective areas (medial occipital cortex; MOC), with additional higher-order parietal connections leading to right LOC. These findings provide additional evidence of functional low-level bottom-up multimodal connectivity, as well as evidence for the potential of higher-order top-down influences on low-level cortex.

Given this connectivity among and between the primary sensory processing areas, it seems evident that low-level integration/modulation occurs. However, to more fully investigate this potential, we must further examine typical activations of presumed-unimodal cortex in response to other-modal sensory inputs, as well as activation patterns in multimodally reactive cortical networks.

1.3.1 HAPTIC, AUDITORY, AND VISUAL/OCCIPITAL INTEGRATION

One currently well-accepted cross-region interaction is between somatosensory input and visual cortex, wherein visual cortex tends to be recruited during tactile shape, pattern, and motion discrimination tasks, as implied in the connectivity study reported above (Deshpande et al., 2008; for review, see Sathian, 2005; Sathian & Lacey, 2007). Areas within LOC have been strongly associated with this multimodal activation, to the point of designation of the lateral-occipital tactile-visual area (LOtv). This area, LOtv, is strongly associated with determining object shape, reacting to shape information from both visual and haptic inputs, but only when this input includes shape-relevant information. This area does not appear to respond to general auditory inputs, which typically do not relate much shape relevant information, solidifying the concept of its task-specific shape discrimination role (e.g., Amedi et al., 2001; 2002; Beauchamp, 2005). However, it has been shown that this area does activate when auditory inputs do provide shape information through visual-to-auditory sensory substitution (Amedi et al., 2007). This again supports task-specificity of the region, independent of modality, further implicating the inter-region connections as functionally relevant.

Further evidence of functional relevance of auditory-visual connections has been found through neuroimaging study of the previously discussed double-flash illusion, in which two auditory beeps tend to influence visual perception of a concurrent, single flash as two flashes. It has been found that, regardless of whether the illusion is induced, activation in visual cortex is enhanced when the visual stimulus is paired with auditory stimulation, and that V1 activity is yet more strongly enhanced when the paired stimuli do elicit the perceptual illusion (Watkins et al., 2006). This succinctly shows that low-level V1 activation can be modulated by the presence of auditory stimuli, even to the point of altering environmental perception.

Compelling evidence of low-level sensory integration has also been found between haptic and auditory domains in anaesthetized macaque monkeys (Kayser et al., 2005). Beyond expected somatosensory cortex activation, haptic stimuli further elicited activation in the secondary auditory belt area, similar but weaker to that seen with purely auditory stimulation. When auditory and haptic stimuli were presented together, stronger auditory cortex activation was recorded than that seen with auditory-only stimulation, similar to the above reported auditory-visual interaction. This provides further evidence not only of multimodal activation of presumed unimodal cortex, but also of crossmodal input summing to a greater likelihood of a conscious percept. Beyond this, as the monkeys in this study were anaesthetized during testing, and the integrational neural activation occurred in an area of low-level processing, we have strong evidence of this interaction stemming from bottom-up sensory processes rather than higher-order top-down influence.

This auditory-haptic integration further helps address a potential alternate explanation for cross-modal activation involving the occipital lobe, in which it is possible that the activation seen is due to visual imagery – for instance, visualizing the three-dimensional shape of a felt stimulus. As mentally conceived images can elicit similar occipital activation to visually observed stimuli, this explanation seems credible. Indeed, it has been shown that rTMS over the MOC, a visual area implicated above as bearing haptic-visual functional connectivity and a task-function of texture-element discrimination, can interfere with visual imagery tasks involving pattern discrimination (Kosslyn et al., 1999). However, as no similar auditory imagining of haptic stimuli seems plausible, it can be reasonably assumed that auditory cortex activation in response to haptic stimulation does in fact arise through the observed low-level crossmodal projections. In conjunction with the functional connectivity studies already reported, this maintains the likelihood of similarly legitimate non-visual activation of occipital cortex.

1.3.2 MULTIMODAL NEURONS

To further examine this issue, we can turn to the behaviour of neurons themselves. Bimodal and trimodal neurons have been reported in various areas of cortex across a host of animals, particularly in superior colliculus (e.g., Wallace, Wilkinson, & Stein, 1996; Meredith & Stein, 1983) and monkey STP (for review, see Karnath, 2001), as well as monkey intraparietal areas (e.g., Lewis & Van Essen, 2000). The presence of neurons that are preferentially reactive to inputs from more than one modality not only provides a framework for how sensory integration may arise overall, but further provides compelling evidence of an underlying neural architecture capitalizing on the presence of any input that can be of use to a given perceptual task. This is particularly notable in regards to the superior colliculus, grossly responsible for orienting and eye movements, and shown to strongly react to multimodal inputs (e.g., Stein et al., 1988). As orientation tasks can result from salient information across modalities, the multimodal nature of the area is not surprising. However, based on information from the rat model it appears that, aside from specifically multimodal areas like the superior colliculus, multimodal neuron distributions are largely absent in primary sensory processing regions. Harkening back to the idea of strictly unimodal processing regions, the primary sensory receptive areas within the rat showed unimodally reactive neurons dominating almost exclusively, with only very small numbers of differently-modal neurons observed in the low-level areas. The primary anatomical locations of multimodal neuron distributions instead were found concentrated in between the primary sensory areas, with for instance, visual and auditory neurons at the junction between occipital and temporal areas (Wallace et al., 2004).

Though the apparent infrequency of other-modal neurons in presumed unimodal cortex seems to support unimodal function, it has further been shown that multimodal neurons are not necessarily the full basis of multisensory integration. Indeed, some unimodal neurons, bearing no noted response to other-modal stimuli presented in isolation, can still be modulated by these other-modal inputs when they are presented concurrently with inputs to which the neuron is set to respond (e.g., Allman & Meredith, 2007; Murray & Wallace, 2012). Interestingly, it may also be the case that even neurons set up for multimodal response only develop multimodal reactivity through life experience (e.g., Stein, Stanford, & Rowland, 2014). This provides strong implications for differences in the modal reactivity of cortical areas between congenital/early blind, late blind, and typically sighted individuals, as will be discussed in the following section.

1.4 BLIND STUDY INFORMATION AND SYNTHESIS

The information presented in the previous sections suggests that, while specific regions of the brain do appear to be largely oriented toward unimodal sensory processing tasks, this unimodality is not a hard rule of cortical isolation. Functionally relevant cross-modal interactions are behaviourally evident through the discussed illusory effects. Whereas these effects show that there is some degree of integrational communication between the senses, they do not in and of themselves tell us where, cortically, these multi-sensory effects arise. However, that there exist direct connections between sensory primary receiving areas provides us with clear evidence of neural architectural pathways through which these areas can interact even at the lowest levels of processing. This connectivity allows for the possibility of early-stage multi-sensory integration among and within the individual processing areas. The existence of areas of multimodally reactive neurons, as well as unimodally reactive neurons that can be modulated through other-modal inputs, lends further support for this possibility of low-level, direct sensory integration. Overall, these points suggest that the brain may be less likely to form strictly unimodal sensory regions than to form sensory-dominant processing areas wired to prefer a given sense, but also accept particular inputs from other senses in order to efficiently perceive the environment.

1.4.1 BLIND STUDY

In order to more fully investigate the underlying nature of neural structuring and function in the occipital lobe, we can investigate the area’s recruitment in those with absent or interrupted vision. If the occipital areas of the brain were to be wired exclusively for visual processing, one would expect the region to be largely atrophied in those blind from birth. One would similarly expect this fate if vision were lost later in life and these areas were functionally locked once developed. Fortunately for those without vision, neither of these suppositions is true. Indeed, the occipital lobes of congenitally blind individuals have been found to be structurally quite normal when compared to those of the typically sighted, with the only notable atrophy occurring in the visual pathways leading from the eye (e.g., Breitenseher et al., 1998). Similarly, those who lose sight later in life do not appear to suffer atrophy of the previously visually-ascribed areas. This lack of atrophy suggests that most, if not all of the modally-displaced lobe is indeed being recruited in some way, and that it likely retains a high degree of plasticity even later in life.

Solidifying the notions of plasticity and multimodal neural structuring, it has been shown that individuals born without a given sense (e.g., congenitally blind), or who lose use of said sense at an early developmental age (e.g., early-blind, typically reported as loss of vision within 2 to 6 years of life), recruit the neural area typically designated to the absent sense for the processing of one or more of their remaining senses (for review, see Bavelier and Neville, 2002). The resultant cortical remapping has been shown to be functionally relevant, implicated in the commonly observed perceptual gains in the spared senses experienced by those missing a sensory modality. For instance, typically visual occipital areas in the blind have been shown to be recruited for auditory (e.g., Röder et al., 1999a; 2000), haptic (e.g., Sadato et al., 1996), and olfactory (e.g., Kupers et al., 2011) processing (for review, see Amedi et al., 2005). Taste appears to be the only primary sense that does not recruit visual occipital areas in the absence of vision (Gagnon, Kupers, & Ptito, 2015).

Whereas these non-standard recruitments prove that sensory processing areas can be wired to an alternate sense from that seen with typical development, there is still the possibility that this is due to the overall high neural plasticity of early life development. In support of this notion, it has been found that typically developing newborn kittens naturally form connections between primary and secondary auditory areas to visual areas, and that these connections are pruned within the first two months of typically developing life (Innocenti & Clarke, 1984). In blind cats, these connections appear to remain, leading to functional occipital recruitment for non-visual sensory use, and highlighting the plausibility of early-plasticity providing the mechanism of non-standard recruitment (e.g., Yaka et al., 1999). However, further study indicates that plastic remapping of sensory cortex occurs even when a sense is lost much later in life, showing that late-life plasticity can remain in high degree for sensory processing areas.

Strong evidence of this late-life plasticity, both unimodal and multimodal, comes from human studies in which the particulars of visual input are altered for the typically sighted. General behavioural plasticity of the visual system through the lifespan can be observed in sighted individuals, given rapid adaptation to prism glasses that shift or invert the incoming visual image (e.g., Degenaar, 2014). Individuals in these studies are able, with practice, to rectify the perception and use of the altered image as normal, with strong implication for sensorimotor exploration impacting this normalization.

Similarly, many hemianopic patients are able to regain functional perception of imagery landing in the blind visual field through lenses extending the degree of the horizontal image reaching the spared visual field (e.g., Giorgi, Woods, & Peli, 2009). These plastic effects are similar to the previously mentioned studies on alterations of the pinnae leading to adaptation of auditory cortex to relate localization cues to the modified sound inputs (e.g., Hofman et al., 1998).

Beyond these unimodal experiences, whether or not they are aided by the influence of other modalities, evidence of strong and rapid multimodal plasticity can be seen through a set of extended-period blindfold studies, wherein typically sighted participants wore blindfolds continuously for a five day period while undergoing haptic training. Blindfolded participants showed significantly improved Braille character recognition when compared to typically sighted participants, suggesting that the oft-noted prevalence of strengthening of spared modalities was set to begin rapidly after loss of the visual sense (Kauffman et al., 2002). These behavioural gains were later linked to tactile recruitment of the medial posterior occipital lobe, V1, observable through fMRI after the five day period of constant blindfolding. This activation was further shown to be functionally relevant, as TMS disruption over occipital areas impaired tactile task performance, with no significant effect for non-blindfolded control participants. Further highlighting rapid cortical plasticity dependent on input availability, both the observed non-visual recruitment and TMS disruption effects disappeared within 24 hours of the return of vision (Merabet et al., 2008). These findings not only show that sensory recruitment shifts can still occur later in life, but also that they occur despite previous typical wiring having occurred. Overall, the evidence provided thus far seems to paint areas of low-level cortex as an opportunistically and continuously developing network.

The displayed ability of previously-wired sensory cortex to shift functional focus to another sense gives rise to the question of how this shift occurs. In general, there are two primarily plausible methods for the functional connections; either existing connections from the adopted sensory modality are strengthened, or new connections are formed. Given that we already have evidence of existing connections between sensory processing areas, coupled with the evident speed with which functional recruitment can occur, it seems likely that the former is at least initially the case – that existing pathways of connectivity strengthen with use in the absence of the area's primary sense. Indeed, as the visual imagery shifting experiments related above required exploration, training, including the use of non-visual senses to make sense of the new visual inputs, it may well be the case that even these ultimately unimodal adaptations rely on latent crossmodal connectivity.

It is further plausible that the presence of visual inputs may overshadow or inhibit the role of other sensory modalities. The rapid reversal of the functional rewiring evident in the blindfolding study (Merabet et al. 2008) – gone within 24 hours of the return of visual inputs – lends some credence to this hypothesis. Further, it has been shown that in early-blind participants, auditory and tactile stimulation can independently elicit occipital activation, but when both modalities are presented simultaneously, tactile stimulation elicits less occipital activity than when presented alone, and improvements in tactile response time are mitigated. This mitigation occurs even when attention, which would typically enhance neural firing, is specifically directed to the tactile stimulation (Weaver & Stevens, 2007). Taken together, these findings suggest that not only is the occipital lobe not necessarily a vision-specific region, but it may have a tiered preferential sensory response bias. As the occipital lobe is typically recruited for three-dimensional representation, navigation, and object identification, it is plausible that these general tasks, rather than specific-modality connections, are what is reasonably hardwired (see also Bavelier & Neville, 2002; Röder & Rösler, 2004). The visual system may provide the most salient information about local surroundings relevant to these tasks, causing the presence of visual input to largely suppress or simply overshadow inputs from other modalities. When those visual inputs are lost, auditory input may comprise the next-best modality for performing many of these tasks, causing its presence to similarly overshadow haptic input, as seen in Weaver and Stevens (2007). This uncovering of the best modality among the available inputs is also evident in the previously related shift between visual or auditory dominance in the ventriloquism effect in the presence of degraded stimuli (Alais & Burr, 2004).

Further evidence supporting both the strengthening of existing connections and task-relevant modality preference (or unmasking of existing connections) hypotheses comes from studies relating non-visual recruitment of occipital areas in typically sighted individuals. Clear evidence has been found for both auditory (e.g., Poirier et al., 2005) and tactile (e.g., Hagen et al., 2002) motion stimuli eliciting response from V5/MT, the motion-sensitive extrastriate area of visual cortex, when visual inputs are suppressed (e.g., through temporary blindfolding or simply closed eyes). Similarly, activation of inferotemporal areas in the ventral visual stream has been shown in response to haptic exploration of face and body part stimuli, in areas thought to be specially reactive to visual representations of such stimuli. Specifically, haptic face exploration evoked activation in fusiform face area (FFA), and haptic body part exploration evoked activation in the extrastriate body area (EBA). The haptically reactive regions of these areas appeared to still also react to visually-presented face and body part stimuli, suggesting again multimodal processing even in the typically sighted, with an unmasking of the othermodal activity when visual inputs are at least temporarily interrupted (e.g., Kilgour et al., 2005; Kitada et al., 2009).

Regardless of how the connections occur, we are left with an additional question of why these connections are formed or strengthened. As we have evidence that certain areas within sense-dominant cortical regions specialize in the processing of particular tasks (e.g., functional parcellation of areas of extrastriate cortex and the commonality of what/where pathways), it is evident that the brain is geared toward function-specific region building, allowing areas of specialized processing. This concept, coupled with the notion of extant multi-sensory connectivity and processing, gives rise to the possibility that it is more this functional relevance rather than strictly sensory relevance that underlies the overarching structural organization of the brain. Whether this may be true can be informed through an investigation of the particulars of non-standard sensory recruitment, here focusing on non-visual recruitment of the occipital areas. Should this recruitment retain common task-relevant region patterns, bearing out similar task processing through non-visual inputs as those observed with the fully sighted, we have strong evidence in support of a functional architecture hypothesis.

1.4.2 WHAT AND WHERE PATHWAYS REVISITED

As previously related, the visual system of typically sighted individuals comprises the ventral "what" and dorsal "where/how" pathways, with similar separations evident in auditory and somatosensory cortex. This path distinction is revisited numerous times in this discussion, as a telling piece of evidence regarding the plausibility of functional retention independent of sensory modality is that this dual-stream organization appears to be maintained in the absence of visual inputs. For instance, Ptito and colleagues (2012) found that congenitally blind participants recruited large portions of the ventral visual stream in response to a tactile shape discrimination task using a tongue-display unit. The cortical areas recruited by blind participants for this task included more regions than sighted controls recruited for the same task, with areas unique to blind recruitment including cuneus, lingual and fusiform gyri, and inferior, middle, and superior occipital gyri.

Regarding the dorsal stream, Collignon and colleagues (2011) showed that, unlike sighted controls, congenitally blind individuals preferentially recruit two areas of the occipital dorsal stream – the right cuneus and right middle occipital gyrus – in response to spatial processing of auditory stimuli. In the typically sighted, these areas are generally involved in spatial processing of visual stimuli, so here we have evidence of development of the dorsal stream without visual input, as well as maintenance of general brain area function. The study further showed, through functional connectivity analyses, that these recruited dorsal stream regions were within an audiovisual spatial discrimination network.

Perhaps more telling, Striem-Amit and colleagues (2012) showed both retention and a double dissociation of the ventral and dorsal streams in the congenitally blind through the use of visual-to-auditory sensory substitution (transforming visual information into auditory information). Here, after a single training session with the sensory substitution device lasting at most an hour and a half, both blind and blindfolded sighted control participants were shown to independently engage the ventral pathway when relating object shape, or the dorsal pathway when relating object location. Specifically, shape discrimination led to increased activity in multisensory areas (intraparietal sulcus, inferior frontal sulcus) and ventral occipital inferior temporal sulcus. Localization activated auditory regions (supramarginal gyrus, inferior parietal lobe) as well as precuneus (higher order visual dorsal stream). Importantly, the lack of previous exposure to the visual-to-auditory device and short training duration suggests a lack of training effects impacting the results. Thus, it can be reasonably concluded that the dorsal and ventral stream separations observed in the blind participants occurred naturally and independently of either visual experience or clinical/experimental intervention. Of further interest, the results of this study showed robust activation in ventral visual cortex in response to shape identification trials, extending to ventral retinotopic areas and V1. In contrast, no significant V1 activation was discerned in the location discrimination tasks, lending support to the notion that V1 activation in blind participants may be largely dependent on task characteristics.

1.5 MODALITY-SPECIFIC OCCIPITAL RECRUITMENT IN THE BLIND

In order to present a clear broad picture of occipital recruitment in the blind, further discussion in this section will center on overviews of the findings relative to each non-visual sense (barring taste, which as mentioned above, does not appear to engage occipital areas. See Gagnon, Kupers, & Ptito, 2015), as well as observed language recruitment.

1.5.1 AUDITION

Auditory processes allow us to discern various pieces of identifying and localizing information about the world around us and the objects within it. For instance, we can become aware of objects, cars, animals, other people, outside of our visual field by auditory cues indicating their presence. We can also glean information about the identity of the source of those sounds, again in gross classifications such as dog, car, person, or in finer detail, determining the full identity of an unseen person or animal based on known characteristics of their individual voice. These wide categorizations of localization and identification fit well into the dual stream “where” and “what” categorizations discussed above. Here I will discuss the particulars of occipital area recruitment for the auditory sense in those without vision.

Studies of auditory processing in the blind consistently show strong recruitment of wide areas of the occipital cortex, above and beyond the much more subdued and function-specific eliciting of occipital response to auditory stimuli seen in sighted individuals. This increased activity of brain regions typically not recruited for such tasks seems to lead to the previously mentioned and oft-cited heightened auditory discrimination and localization abilities reported for the blind. Indeed, it has been shown that early-blind individuals tend to have more cortical thickness in their occipital lobes than do sighted individuals, the degree of additional cortical thickness positively correlating with enhanced performance with auditory discrimination tasks (Voss & Zatorre, 2012). It may be that this additional cortical thickness is a reflection of the plastic rewiring of occipital areas for processing of non-visual connections. Despite the apparent view of across-the-board non-visual processing improvement associated with occipital recruitment, it seems that at least some of the observed processing benefits exist only for specific aspects of a given task. For instance, it has been shown that auditory localization gains in the congenitally blind beyond that of typically sighted individuals may exist only for sounds presented in peripheral auditory space (Röder et al., 1999b).

More recent study has shown that general auditory perception in the early blind may be at least partly enhanced by preparatory activation of medial occipital areas in response to cues indicating a pending auditory stimulus (Stevens et al., 2007). This occipital activation was accompanied by stronger activation in blind over sighted participants of typical auditory preparatory activity in temporal areas, suggesting a strengthening of typical connections as well as adopting new connections in the occipital areas. It is of note that in sighted individuals, similar occipital neural activity occurs for preparation effects toward visual stimuli as that seen here with blind individuals toward auditory stimuli. This lends further support to the notion that occipital regions may be selectively recruited for tasks that maintain their general function as ascribed in the fully sighted. Interestingly, this preservation of function appears to extend to the frontal eye-fields (FEF), which in the sighted are associated with visual attention shifts and planning of eye movements. Despite the typical vision-centric nature of FEF, congenitally blind participants were shown to strongly recruit FEF in response to auditory-target evoked spatial attention shifting (Garg, Schwartz, & Stevens, 2007).

Further study has shown that specific auditory tasks, here namely voice perception, may not specifically map to occipital areas in the blind. Voice perception is typically associated with the superior temporal sulcus (STS) in sighted individuals, and this seems to hold true for those with blindness. In a voice perception task, it was found that congenitally blind participants, but not late-blind, displayed increased activation to left STS, as well as fusiform gyrus, when compared to sighted and late-blind groups, with this STS activation correlating positively and significantly with task performance (Gougoux et al., 2009). The study did, however, find strong occipital activation in both blind groups when analyzing the neural response to all sound stimuli (voice and non-voice) compared to silence – activation absent in the sighted control participants. Thus, whereas occipital areas were indeed recruited for auditory processing, in this case, the task-specific processing of voice perception remained largely situated in the same temporal areas as are typically recruited in the sighted. This is a good indication that not all tasks in otherwise occipitally-plastic modalities must necessarily also be sideloaded into occipital areas by blind individuals. Indeed, a strengthening of the same pathways as typically used by sighted individuals (also partially seen in Stevens et al.,

2007) could plausibly also lead to behavioural task-specific performance gains, or indeed, no gain need necessarily be observed. This notion is at least tangentially relevant to differences between congenitally/early-blind and late-blind individuals, in that robustly developed typical sensory wiring may negate the utility and thus recruitment of adopting occipital areas for related tasks into the network if vision is lost later in life.

The information presented thus far regarding auditory recruitment of occipital areas highlights these areas being utilized to some degree for the given tasks, but they do not in and of themselves demonstrate cortical rewiring that leads to necessity of the areas for proper completion of the tasks. To address this, a number of studies involving transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS) have been conducted, either artificially stimulating or interrupting the function of target areas. It has been thus shown that rTMS interruption of right dorsal extrastriate cortex in the early blind, but not in sighted controls, impairs auditory spatial localization (Collignon et al., 2007). This interruption of the dorsal stream did not, however, interfere with pitch or intensity discrimination, in line with the assumption that the dorsal and ventral streams maintain their respective “where/how” and “what” specifications. In a similar study, TMS was again applied to early-blind participants over right dorsal extrastriate cortex, as well as right intraparietal sulcus (IPS), during auditory localization tasks. As right IPS is recruited by typically sighted participants in the commission of sound localization tasks, this study stood to discern not only the utility of the auditory occipital rewiring seen with blind subjects, but also the degree of functional reorganization in comparison to what is typically seen in sighted auditory processing. As before, interruption of right dorsal extrastriate cortex impaired auditory localization. However, interruption of right IPS did not impair task performance (Collignon et al, 2009). This finding suggests that the critical pathways involved in auditory localization may not just additionally recruit occipital areas in the absence of visual inputs, but may in fact alter the overall processing pathways to preferentially recruit said occipital areas.

Whereas the above-related information regarding maintenance of dorsal and ventral visual streams when applied to auditory stimulation in the blind reasonably indicate the likelihood of maintaining functional preference in an area even when recruited for a non-standard sensory modality, this could be at least in part due to overall organizational patterns of general sensory cortex, rather than a forced-retention of visual area preferences in the absence of a similar preference in the non-visual modality. In animal study of a non-visually-impaired cat, a double dissociation of where and what processing was found in auditory cortex, with interruption of the posterior auditory areas impairing auditory localization but not pattern discrimination, and the opposite effect with interruption of anterior auditory areas (Lomber & Malhotra, 2008). This suggests that the mammalian brain specifies reasonably independent pathways for localization and identification in multiple modalities, not just vision. Indeed, dorsal and ventral streams have been implicated in humans for vision, audition, and somatosensory domains (for review, see Sedda & Scarpina, 2012). Again, it is plausible that this common division across sensory modalities influences the apparent ease with which the dorsal and ventral streams of the occipital lobe can be mapped on to auditory (and as discussed next, tactile) localization and identification in blind individuals.

1.5.2 TOUCH

Tactile exploration of the environment can be used to gain gross general spatial representations, such as feeling about for obstacles in the dark, or more specifically in the blind, using a feeler cane to aid in navigation. This can also be used to discriminate finer object properties, exploring the textures, contours, and edges of objects in order to discern shape and other identification properties. As mentioned above, these spatial and identification aspects of haptic exploration divide in the somatosensory system into relatively independent pathways, essentially touch-for-action and touch-for-perception (Dijkerman & DeHaan, 2007; for review see Sedda & Scarpina, 2012). Thus, based on what has been related thus far, it stands to reason that we should see a similar breakdown in occipital recruitment for haptic analysis.

One of the most salient uses of touch-for-perception in the blind is Braille reading, which in and of itself requires a high degree of tactile discrimination ability due to the small spatial offsets between the raised dots of which the system is comprised. Increased tactile acuity in the blind reasonably seems to come as a result of general experience, regardless of the degree of vision previously afforded or experience with Braille, likely leading to enhanced recruitment of additional occipital areas compared to what can be expected in sighted individuals (Goldreich & Kanics, 2003). Indeed, in a neuroimaging study comparing late-blind individuals without Braille-reading experience to sighted controls, it was found that the late-blind individuals, but not controls, displayed occipital activation in response to a general tactile discrimination task (Sadato et al., 2004). This increased tactile acuity seems able to occur at any given stage of visual loss, and can occur quite rapidly, as uniquely evidenced by the five-day blindfolding studies reported previously. To reiterate, participants who were blindfolded for the full five day period, regardless of the intensity of training they or their non-blindfolded control cohort experienced, displayed greater performance on a Braille character discrimination task (Kauffman et al., 2002). This increased performance for blindfolded participants was later shown to be correlated with bilateral activation of occipital lobe within area V1, around the calcarine sulcus, interruption of which through rTMS impaired performance on the Braille character discrimination task (Merabet et al., 2008).

Regarding earlier-age and more permanent onset of blindness, Sadato and colleagues (1996) showed that Braille reading by congenital and early-blind individuals also triggers strong activation of medial occipital areas including V1, as well as some undisclosed extrastriate visual areas. It was further found that V1 was activated, though not as strongly, in a general shape discrimination task involving the angle of lines created by non-letter-representative Braille dots. In these same participants, passive tactile exploration of random Braille-dot patterns, with no identification task, did not trigger V1 activation. This finding highlights the recruitment of occipital areas, and indeed similar patterns of recruitment, for blind Braille reading and general haptic shape exploration. As V1 is classically known to contain low-level feature detection neurons responsive to specific orientations and properties of visual line segments, the haptic recruitment of this area seems to again belie the potential for task-based remapping of occipital areas to non-visual modalities.

Occipital activation in the blind has been shown, through both lesion and TMS study, to be functionally critical to commission of the task of Braille reading. Regarding the lesion-based evidence, an early-blind woman who was a proficient Braille reader suffered a stroke resulting in bilateral occipital lesion. With the loss of use of the occipital area, she also lost the ability to read Braille (Hamilton et al, 2000). Further evidence of the functional recruitment of occipital lobe for Braille reading through (r)TMS study has shown that temporary impairment of the mid-occipital area significantly impairs Braille reading in blind but not sighted participants (Cohen et al., 1997; Kupers et al., 2007). Relatedly, it has also been shown that TMS stimulation of the occipital lobe (in this case the entire lobe) induces only visual phosphenes in sighted controls, but tactile sensation in the fingers of blind Braille readers (Ptito et al., 2008), highlighting again the strong tactile connections to occipital areas generated in the blind.

Looking more specifically at the dorsal/ventral specific areas, Sadato and colleagues (1998) specifically showed blind-participant recruitment of ventral occipital areas, V1, and the fusiform gyri in response to non-Braille tactile discrimination tasks, coupled with deactivation of secondary somatosensory areas, whereas sighted controls displayed the opposite activation pattern (i.e. increased somatosensory activation with deactivation of occipital areas). Similarly, and again maintaining the identification characteristics of ventral stream areas, it has been shown that tactile exploration of object shape in the blind elicits activation in ventral extrastriate areas, again including the fusiform gyri. However, it was also shown that similar patterns of activation occurred in sighted participants, suggesting that tactile inputs may typically be wired to occipital and ventral stream areas regardless of whether vision is present (Pietrini et al., 2004). Similar general congruence between blind and sighted individuals of dorsal stream activation in response to tasks involving tactile-evoked spatial working memory (Bonino et al., 2008) further suggest that the ventral and dorsal pathways may to some degree be intrinsically cross-modal.

1.5.3 SMELL

The sense of smell, though largely ignored in the literature when compared to vision and audition, is nonetheless able to provide salient cues regarding the environment. This can be as basic as noting that one's hygiene is in a poor state, to recognizing specific people or even the presence of beneficial or dangerous chemicals based on known characteristic scents. More germane to the discussion at hand, crossmodal interaction between vision and olfaction has been reported, with visual aspects modulating olfaction (e.g., Zellner & Kautz, 1990; Demattè, Sanabria, & Spence, 2009), and more recently, olfaction modulating vision (e.g., Zhou et al., 2010; Kuang & Zhang, 2014).

Though not directly related to the occipital areas, it has been reported that the volume of the olfactory bulb tends to shift commensurately with changing levels of use or training, such that increased utilization leads to increased size, and vice versa. An investigation of this, as well as the notion that early-bind individuals would generally utilize olfaction moreso than would sighted controls (e.g., Cuevas et al, 2009), showed that early-bind individuals tend to display both increased olfactory performance on identification tasks and larger olfactory bulb volume than do sighted controls (Rombaux et al., 2010).

Functionally, it has been reported that congenitally blind participants engaged in an odor detection task, compared to sighted controls, elicit significantly greater neural activation throughout occipital cortex – V1 through V5/MT (Kupers et al, 2011). Task-respectively, however, the significance of these data for an odor present > odor absent condition showed significant visual-area activation in blind participants only in bilateral V2 and left-lateral V3, with a significant interaction of task and group (blind vs. sighted) resulting in only bilateral V2 activation displaying significance among the selected visual areas, with greater activation associated with blind individuals being presented with an odor. Though ventral/dorsal location was not indicated for these activations, based on provided coordinates it appears that the selected area of V2 was medially located between dorsal and ventral regions, with V3 in the ventral region. It should be noted that interpretation of this particular study may benefit from caution regarding anything beyond evidence that occipital areas can be recruited by olfaction in the blind.

Perhaps more informative, Renier and colleagues (2013) reported that both olfactory discrimination and categorization tasks elicit strong occipital responses in early-blind individuals, particularly in the right fusiform gyrus, whereas a similar identification task utilizing auditory-verbal processing preferentially recruited left ventrolateral occipital complex. A similar activation pattern dissociated by task was observed in sighted control subjects, though the degree of activation was notably less than that seen with early-blind participants, and commensurate with olfactory task performance (e.g., greater activation of right fusiform gyrus correlated to increased olfactory performance). This finding of similar functional recruitment between blind and sighted participants, split by degree of activation, is similar to that seen in above-related reports of crossmodal tactile activations of occipital lobe. This seems to suggest that the occipital lobe, particularly its ventral and dorsal pathways, may well reflect generally supramodal networks even in the typically sighted, with a tendency to become more distinct in the absence of vision.

1.5.4 LANGUAGE

Though not a sense in its own right, language nonetheless is a function generally considered both uniquely human, and from a processing standpoint, quite complex. General low-level sensory inputs must by nature be processed before higher-order linguistic processing can occur, and the overarching concept of language can be considered multimodal in that it can be experienced via auditory (e.g., spoken language, auditory Morse code), visual (e.g., visual reading, sign language, lip reading, flag semaphore, printed Morse code), or tactile (e.g., Braille) modalities, and can include crossmodal perceptual interactions such as that observed through the McGurk effect. Interestingly, though the neural correlates of language are classically thought to reside in a left-lateralized network, with more recent work implicating a broader network including some right-lateralized areas (see Price, 2000; 2010), occipital areas seem to remain absent from the discussion. However, certain aspects of language have been reported to elicit occipital activation in the blind (including the previously discussed activation associated with Braille reading), which may well make functionally relevant sense if considering the occipital pathways as containing the inherent ability to utilize multiple (or select preferential) sensory modalities for given functional tasks.

Amedi and colleagues (2003) reported strong occipital activation in congenitally blind but not sighted individuals in response to verbal memory tasks, with the degree of activation observed in V1 positively correlated with performance. Beyond V1, verbal memory elicited ventral extrastriate activation, with all occipital activations more prevalent in the left rather than right hemisphere. This study reported similar activation patterns to those found for this verbal memory task in relation to a verb-generation task, wherein participants generated a verb based on a provided noun. A similar verb-generation task conducted by Burton and colleagues (2002b) showed that both early-blind and late-blind individuals exhibited still-similar left-dominant occipital activations to those found by Amedi and colleagues, but further highlighted that late-blind individuals displayed more constricted occipital activation, mostly contained within V1 (the overall activation of which was comparable between early- and late-blind participants, though presented more medially in the late-blind), lingual and fusiform gyri. These findings suggest the plausibility of a shift in the degree of plastic occipital recruitment based on age of blindness onset, though overall similar activation between blind groups. Some slight disagreement exists between the two studies, in that Amedi et al. further reported that anterior regions of lateral occipital cortex, along with right V1, were more likely to be active during a Braille reading task, whereas left V1 and posterior lateral occipital areas were more likely to be active during verbal-memory and verb generation tasks. According to Burton and colleagues, however, the occipital activations reported for their verb-generation task were largely similar to those implicated in a Braille reading task, including V1, lingual and fusiform gyri, cuneus, lateral occipital cortex, and inferior and middle temporal gyri – largely ventral stream areas, in line with the notion that Braille reading and verb-access involve general identification processes. As the areas themselves do not differ between studies, the difference in report may simply be one of differences between congenital and early/late blind individuals, or it could be the case that the data are in actuality similar, but in one case this particular difference went somewhat unnoticed.

In a follow-up study to Amedi et al. (2003), it was shown that rTMS applied to left V1 in blind but not sighted participants interfered with a verb-generation task, typically on a semantic level (e.g., inappropriate verb selection). As with previously related studies involving (r)TMS, this finding highlights the functional, causal utility of the affected cortical area on the task (Amedi et al., 2004).

It has further been reported that the left-lateral preference of language-related occipital activation reported in the visual memory and verb-generations tasks just discussed holds for general sentence comprehension, as typically described in relation to language regions reported in sighted individuals, in the congenitally blind (Bedny et al. 2011). In order to highlight the linguistic nature of the implicated occipital regions, Bedny and colleagues presented sentence comprehension tasks alongside more difficult control tasks, reasoning that if occipital task activations remained higher for the easier language-related task than for the harder non-language task, as was reported, this would only be likely to occur if the area were preferentially keyed to language. Otherwise, the more difficult task would be most likely to elicit stronger activation. The authors further suggested a specific link between left-lateral occipital areas in the blind with language processing to the exclusion of other functions, specifically highlighting the possibility that the recruited areas take on roles mimicking that of left prefrontal cortex, for which TMS-based interruption leads to impairment of verb-generation tasks in the sighted, just as rTMS to left V1 does in blind participants (Amedi et al., 2004). As many tasks seem to target left-lateralized occipital areas in the blind, to properly test this hypothesis would require a more fine-grained look at the functional and anatomical constraints of the implicated regions than is currently provided.

A later study by Bedny and colleagues (2012) brings us to the possibility of critical/sensitive periods for functional acquisition of language, and thereby other possible recruitment tasks, in the plastic occipital rewiring observed in blind individuals. Here we have a report indicating clear qualitative functional differences in occipital lobe recruitment for language functions between congenital and late-blind individuals (the late-blind individuals in this case having lost their vision between the ages of 9 and 29 years). Specifically, participants engaged in a verbal passage comprehension task, and as control, a backwards speech sound-matching task. Congenitally blind participants alone were found to preferentially engage left occipital lobe areas for proper sentences but not for backwards speech. Late-blind participants did display some right-lateral occipital activation, but similar activation also occurred in congenitally blind participants, and is surmised to reflect response preparation.

1.6 BLIND GROUP COMPARISON

Differences in activation patterns between age-of-onset blind participant groupings, such as that related above in the language domain (Bedny et al., 2012), highlight the notion that degrees of plasticity may alter throughout the lifespan. It is thus important to keep potential group differences in mind when investigating the functional and structural neural networks of blind individuals. Congenitally blind individuals, those blind from birth, never experienced visual input, so the areas of cortex that would typically be primed to respond and map to that sense never would have been modified by that experience. This means the occipital areas of the congenitally blind would be, in essence, as clean a slate as structural, genetically driven neural growth – nature – can provide for whatever modalities and functions move in to the otherwise vacant space. The early-blind, those individuals who were not born blind, but lost phenomenal vision at an early age (again, variably reported but generally between two and six years), had some degree of visual experience, though not for long, and often of poor quality. Regardless, their visual experience still may have had some impact on neural connections. However, it is commonly found that congenitally and early-blind individuals present largely similar neural mappings and task performances to one another, with generally small differences in effect size. Despite the similarities, these differences can be significant, so it is likely wise to at least initially consider data from each group independently of the other. Late-blind individuals, those who lost their vision at some point after the cut-off for being considered early-blind, can have had a wide array of visual experience before the onset of visual loss. Many late-blind individuals thus have had their visual areas initially developed just as those of a typically sighted individual. Individuals in the late-blind grouping may be likely to show different functional patterns than those in the congenital and early-blind groups, which should not be unexpected as the degree of influence visual experience had in shaping a late-blind individual's neural function can reasonably be expected to be quite high, particularly the later in life blindness occurs. Similarly, the cortical areas dedicated to the remaining senses would have developed throughout that same time, which may lead to a reduction in task-specific neural plasticity due to the developed network being adequate as-is, and/or not bearing continued connections to other-modal cortical areas. Regardless, the changes in function after the loss of vision in this group are readily able to highlight later-life neural plasticity in the occipital lobes.

Despite the logical likelihood of differences in late-blind occipital remapping, much of the literature, including that related thus far, tends to show similar overall activation patterns across age-of-blindness-onset groupings. As related above, occipital recruitment still occurs with the late-blind for various tasks of all relevant sensory natures. However, the differences often appear to be in the degree of activation, with late-blind individuals often displaying activation in similar neural areas to those found in congenital/early-blind participants, only in more constrained overall areas or with reduced activation strength (for review, see Burton, 2003).

Like with Bedny and colleagues' language study (2012), more clear-cut differences between the blind groupings have been noted. Unfortunately, these differences may also often be confounded. Indeed, conflicting reports of areas of activation for given age-of-onset blindness groups, particularly prevalent in regards to whether activation occurs in V1, are not uncommon in the existing literature. This seems especially prevalent in relation to reports of late-blind activation patterns, and may involve characteristics of the late-blind participants recruited. For instance, as reported by Burton (2003), late-blind participants often bear some residual visual ability, as was the case in the majority of late-blind participants in a study by Sadato and colleagues (2002).

In the Sadato study, which made strong claims as to critical differences in late-blind neural activation to haptic stimuli when compared to early-blind individuals (here including those who lost vision prior to 16 years of age, itself a non-standard definition), only one of the six late-blind participants had total loss of visual experience. The remaining five late-blind subjects had either residual light perception, the ability to see only hand movement, or in one case, the ability to see the number of fingers held up at a distance of 1 meter (Sadato et al., 2002). In this study, it was concluded that a critical period existed in which V1 recruitment for haptic tasks could occur, such that after 16 years of age this recruitment could not exist. A similar study reported a critical period of 14 years, after which occipital recruitment for late-blind individuals in response to Braille reading could not occur (Cohen et al., 1999). In this study, three of the eight late-blind participants bore residual visual ability. As the extended-period blindfold study conducted by Merabet and colleagues (2008), reported earlier, showed rapid recruitment of V1 in blindfolded but otherwise typically sighted participants, all of whom were between 18 and 35 years of age, the critical period results here seem summarily disproven. Given that the blindfolded participants in the Merabet study experienced no visual input for the duration of the study, whereas the late-blind participants in the Sadato study did not experience this complete visual suppression, the differences in activation may well be due to the previously put forth notion that the presence of visual inputs can mask or suppress reactivity to other-modal input. This masking notion is again supported by the blindfold study, in that the occipital activation disappeared soon after the return of vision. Thus, it seems likely that this suppressive effect of visual input could also inhibit overall cortical remapping in the not-quite-blind.

It is worth noting that, beyond the issues related above, as related by Burton (2003), the study by Sadato and colleagues (2002) further suffered from late-blind participants achieving close to chance performance on the proscribed task, whereas early blind participants fared significantly better, and the fMRI analysis model may have been inappropriate. Highlighting this, Burton and colleagues' (2002a;b) own analyses of similar task data on late-blind individuals did indeed show activation of both low-level V1 and extrastriate occipital areas.

1.7 INITIAL CONCLUSIONS AND FUTURE DIRECTIONS

Per the information related throughout this discussion, a large amount of evidence seems to suggest that occipital recruitment in the absence of visual input tends to follow generally similar recruitment patterns regardless of the age of visual loss. Whereas some differences between congenital, early, and late-blind populations are expected, and the fine specifics of region and recruitment strength do show some difference, the overall patterns of occipital recruitment across these groups do appear to follow largely similar patterns. In general, the primary differences may relate to laterality and general breadth of activated regions. However, as occipital recruitment occurs across tasks of all primary sensory modalities (barring taste) in all age-of-onset groups, and even in those experiencing temporary visual loss, our primary hypothesis seems well-supported. The occipital lobe does indeed appear to be a highly plastic, multimodally responsive area.

Our secondary hypothesis, that the recruitment of occipital areas in the visually deprived stems at least initially from the strengthening of existing multi-modal connections, seems further supported. This support comes from the prevalence of low-level sensory cortical connections between neural areas, thickening of cortical connections in the blind, the existence of functional multi-modal interaction between the senses, some degree of use of non-visual inputs in occipital areas even in the typically sighted, and the rapidity with which occipital recruitment can be observed after the sudden loss of visual input.

We have further related evidence in support of the notion that occipital areas may well retain similar task-based sensory recruitment patterns regardless of which sensory modality the task-relevant information comes from. In particular, the common demarcation of what and where pathways is retained cross-modally, and even arises in the complete absence of vision from birth. Unfortunately, due to the discrepancies involving studies noting differences between age-of-onset recruitment patterns, the presence of study protocols not necessarily germane to the questions being asked, and in light of the prevalence of studies showing generally similar, if somewhat reduced activation in late-blind participants, a qualitative analysis of these data seems inadequate to the task of fully exploring the precise nature of potential group differences. These same reasons also negatively impact the strength with which we can conclude the above-mentioned task-based structuring of occipital areas. Instead, quantitative meta-analyses of existing fMRI and PET data seems the proper direction to elucidate the particulars of differences between blind populations, as well as to provide a stronger argument for or against modality-irrespective task-based neural wiring. Through such analyses, stronger conclusions can be made as to the nature of general occipital lobe plasticity throughout the lifespan, as well as clearer indication of task-relevant othermodal recruitment than can currently be afforded.

With this future direction in mind, I conducted a series of meta-analyses comparing and contrasting occipital activation in the congenital/early-blind and sighted participants in order to highlight occipital areas commonly and uniquely activated between these populations in response to auditory and tactile inputs. I further added an analysis grossly split by task-type (identification or localization) in order to better assess the plausibility of maintenance of the dorsal/ventral stream split for non-visual activation in occipital areas. These analyses are presented in the next section.

CHAPTER 2
META-ANALYSES OF OCCIPITAL LOBE ACTIVATION BY NON-VISUAL STIMULI

2.1 INTRODUCTION

Occipital cortex is classically considered vision-specific, with the exception that visual loss results in recruitment for non-visual tasks. However, crossmodal and multisensory research suggests that occipital activity may be modulated by non-visual inputs, particularly when vision is degraded or temporarily limited (for review, see e.g., Alais et al., 2010). It is not currently known whether this modulation occurs through low-level direct cortical connections or through higher order connectivity regions and top-down control. We do, though, know that neural connections exist between low-level primary sensory cortices in a typically developing human brain (e.g., Eckert et al., 2008). Considering this connectivity and modulation, studies comparing the connectivity patterns of blind, sighted, and blindfolded individuals may be able to provide answers as to how the brain wires based on available sensory inputs and task demands. This idea is directly relevant to our first primary question: whether the occipital rewiring seen with blind participants is more likely to stem from a unique rewiring model, or a strengthening of existing connections. Unfortunately, conflicting results are common in the existing research on blind occipital recruitment, with disagreement even as to whether primary visual cortex (V1) activation occurs. Investigating the commonalities between existing studies can shed light on whether low-level V1 activation should be expected in response to certain non-visual inputs. Should that low-level activity be found, the previously discussed low-level connections between primary sensory cortices are likely a significant contributor, which would suggest that the strengthening of existing connections model is more likely that a strict rewiring model.

To investigate the commonalities and differences of occipital lobe recruitment among congenital/early-blind and sighted participants, we combined existing research through a series of meta-analyses. These analyses involved neuroimaging studies wherein occipital activation was reported in response to non-visual inputs. These analyses allowed us to more fully determine not only the likelihood of low-level V1 activation, but also the extent of occipital activation common across studies. These commonalities were examined both for activations unique to blind participants, as well as for those similar between blind and sighted participants.

We further addressed our second primary question with these meta-analyses: whether the occipital lobe, wiring for a non-visual sense, retains its typical area recruitment based on task demands, or if wiring for a non-visual sense alters the apparent task-structure as well. We investigated this question by looking at the differences between congenital/early-blind participant neural activations in response to localization and identification tasks. We proposed that, if a task-based wiring is retained in the occipital lobe regardless of the sensory modality it responds to, the dorsal "where/how" and ventral "what" streams should retain their general dissociation. If the dorsal/ventral stream areas were not similarly separated as typically seen with visual inputs in sighted participants, we would have to conclude that the occipital lobe does not retain the same task-based recruitment in the absence of visual inputs.

2.2 METHODS

2.2.1 STUDY SELECTION

For our meta-analyses, we sought out fMRI and PET studies with congenital/early-blind and/or sighted participants wherein occipital activation was reported in response to non-visual tasks. We conducted searches through Google Scholar, EBSCOhost, and Web of Science. For our searching purposes, we used combinations of the following keywords: fMRI, PET, occipital, blind, blindness, congenital, sighted, auditory, sound, hearing, tactile, haptic, touch, spatial, localization, identification, recognition. For all analyses, studies including a number of blind participants whose loss of vision occurred more than 6 years after birth were excluded, as these participants could reasonably be considered late-blind. As later age-of-onset for blindness may elicit differences in neural connectivity from that associated with congenital/early-blindness, we did not wish to potentially confound our analyses with late-blind relative activation coordinates. Included studies were also limited to those with group statistics run on at least 5 participants, in order to limit potential skewing based on individual differences.

<u>Analysis one</u>. The first meta-analysis investigated common areas of occipital lobe recruitment in which congenital/early-blind participants displayed occipital lobe activations significantly greater than those found in sighted participants (blind>sighted contrasts), in response to auditory and/or tactile tasks. This analysis allowed us to

determine consistent areas of non-visual occipital recruitment in the early-blind, allowing us to compare the noted regions to those active during visual tasks in sighted participants (e.g., to determine if the novel areas of blind recruitment were unique activations or merely more robust activations of areas also recruited by sighted participants). This analysis helped to indicate whether low-level V1 activation was more or less likely to occur in the blind. To be included in the first meta-analysis, studies had to report PET- or fMRI-obtained neural coordinates for areas of significantly increased activity in a congenitally blind (CB) / early-blind (EB) >Sighted contrast (CB/EB > Sighted). The task eliciting the activity had to be either auditory or tactile in nature, and coordinates had to be reported in either Talairach or Montreal Neurologic Institute (MNI) space. Overall, 23 studies were included in this first meta-analysis, 15 utilizing auditory tasks, 9 utilizing tactile tasks (one study provided coordinates from both auditory and tactile tasks). The studies included in this meta-analysis are listed in Table 2.1, with the tasks associated with each study listed in Table 2.2.

Whereas a similar meta-analysis was previously conducted by Ricciardi et al. (2014), we believed that issues with their reporting and analyses justified a re-examination of the topic. Notably, they used a false data rate (FDR) correction threshold of .05, which, according to the authors of the activation likelihood estimation (ALE) software (GingerALE) used for the analysis, is generally inappropriate – a stricter FDR of .01 should be used. It was also recently revealed that older versions of the GingerALE software, including the version used in the Ricciardi et al. meta-analysis, contained issues that overestimated significant activation in regards to FDR analysis.

Thus, the existing meta-analysis results may be over-inflated due to both lax thresholding and overestimation through the algorithms used. Further, our current list of studies includes 8 relevant studies not included in the existing meta-analysis, and rejects one that was included. These additional studies bring our current list to 23 studies, as opposed to the existing study's 15. Unfortunately, it is also apparent that multiple studies used in the Ricciardi et al. meta-analysis were mis-cited, with unrelated studies reported instead of the actual studies used. Due to these issues and oversights, we felt a more conservative analysis using proper correction thresholds and updated ALE algorithms, with a larger pool of studies to draw from, was appropriate.

Analysis two. The second meta-analysis investigated common areas of occipital lobe recruitment between congenital/early-blind and sighted but blindfolded/eyes-closed (SB) participants in response to auditory and/or tactile tasks. This analysis allowed us to highlight areas activated in the CB/EB in response to non-visual task input that are similarly recruited in sighted participants when visual input is temporarily interrupted. Through limiting the sighted analysis group to blindfolded/eyes-closed participants, we were able to look at any areas of non-visual occipital activation that could uncover in a rapid fashion when visual input is removed. This criterion is further important as it has been shown that the presence of input from a given sense may mask or inhibit occipital response to other sensory input (e.g., Weaver & Stevens, 2007). Thus, full or residual visual input may limit or preclude some or all non-visual occipital response. We should further wind up with similar numbers of studies for the CB/EB study group and the SB group, as the amount of blindfolded participant studies currently appears to be on par with the number of relevant blind studies. This expected equivalence of study numbers should allow for more accurate analysis, with neither group likely to dominate the output (this will be further pursued by ensuring that all reported significant activation areas are significantly contributed to by both CB/EB and SB studies).

Occipital areas implicated in this analysis support the idea that typically developing occipital cortex maintains functional non-visual sensory connections, and that similarly located connections are strongly present in the blind. For inclusion in the second meta-analysis, studies had to report PET- or fMRI-obtained neural coordinates for areas of significant activation in response to auditory or tactile tasks, for either CB/EB or SB participants. Coordinates had to be reported in either Talairach or MNI space. For SB-participant studies, only those reporting some occipital activation in response to non-visual task inputs were used for this analysis. Overall, 31 studies were included in this second meta-analysis, 20 providing auditory-task-evoked coordinates, 14 tactile (3 studies provided separate auditory as well as tactile coordinates). The studies included in this meta-analysis are listed in Table 2.3, with the tasks associated with each study listed in Table 2.4.

<u>Analyses three and four</u>. The third and fourth meta-analyses investigated areas of occipital lobe recruitment in congenitally/early-blind participant responses relevant to spatial localization and non-spatial identification tasks, respectively. These analyses allowed us to better investigate the likelihood of a task-locked, modality-neutral neural architecture. Our reasoning was that if areas activated in the CB/EB in response to non-

visual spatial task inputs were notably different from areas activated in response to non-visual identification task inputs, particularly if a non-visual continuation of occipital lobe's typical dorsal/ventral stream delineations was uncovered, the notion of task-specific rather than modality-specific areas would be well supported. For inclusion in the third or fourth meta-analyses, studies had to report PET- or fMRI-obtained neural coordinates for areas of significant activation in response to auditory or tactile tasks for CB/EB participants. Studies reporting CB/EB performance either alone or contrasted against sighted control participants were included. Tasks had to be able to be split into localization or identification tasks. Coordinates had to be reported in either Talairach or MNI space. Overall, 8 studies were included in the localization-task meta-analysis (see Tables 2.5 and 2.6), and 19 studies were included in the identification-task meta-analysis (see Tables 2.7 and 2.8).

2.2.2 META-ANALYSES

Meta-analyses were conducted in GingerALE 2.3.6 (www.brainmap.org/ale/), utilizing Turkeltaub's non-additive activation likelihood estimation (ALE) method (Turkeltaub et al., 2012). Peak coordinates reported in the studies selected for each meta-analysis were entered into GingerALE in Talairach space. Foci from studies reporting MNI coordinates were converted to Talairach space through the software's in-built conversion function, utilizing the icbm2tal method (Lancaster et al., 2007). If a study reported converting from Talairach space to MNI space using a different conversion method, that method was used whenever possible to return those coordinates to Talairach space. For all analyses, statistical significance was determined through a non-parametric false discovery rate (FDR pN) set initially to$p < .05$. All analyses were run a second time with a more conservative $p < .01$. The initial pass ($p < .05$) was run both to account for the likelihood of small effects, as well as to compare results to an existing meta-analysis paper reporting findings with the same $p < .05$ FDR corrected significance level (Ricciardi et al., 2014). The second pass ($p < .01$) was run to determine which regions survived a stricter correction, as well as to hold with the significance thresholds suggested by the GingerALE software developers. Of the resultant found clusters, only those with a cluster size greater than the minimum recommended size calculated for each analysis were considered. Brain regions within these significant clusters that also had reported local extrema were considered significantly activated, though areas within significant clusters but without reported extrema were also considered.

2.3 RESULTS

2.3.1 BLIND > SIGHTED META-ANALYSES

At the $p < .05$ FDR level, the meta-analysis of all tactile and auditory studies reporting congenital/early-blind > sighted contrast coordinates showed significantly greater activation in the blind within bilateral cuneus, lingual and inferior occipital gyri, and right middle occipital gyrus. Further regions implicated, though without reported extrema, include bilateral fusiform gyrus, bilateral precuneus, bilateral occipital areas of the inferior temporal gyrus, left middle occipital gyrus, and right middle temporal gyrus (see Table 2.9 and Figure 2.1).

The same congenital/early-blind > sighted analysis set at $p < .01$ FDR correction returns significant coordinates corresponding with bilateral cuneus and inferior occipital gyrus, right middle occipital gyrus, and left lingual gyrus. Further regions implicated, though without reported extrema, include bilateral fusiform gyrus and bilateral occipital areas of the inferior temporal gyrus, left middle occipital gyrus, right precuneus, and right lingual gyrus (see Table 2.10 and Figure 2.1).

2.3.2 BLIND AND SIGHTED CONJUNCTION META-ANALYSES

At the $p < .05$ FDR level, the conjunction meta-analysis of all tactile and auditory studies reporting coordinates for congenital/early-blind groups and sighted participant groups showed significant areas of activation for both blind and sighted participants in bilateral cuneus and medial frontal gyrus, right lingual, postcentral, and inferior frontal gyri, right posterior cerebellar declive, left precentral and middle temporal gyri, and left inferior parietal lobule. Further regions implicated, though without reported extrema, include bilateral middle occipital and superior frontal gyri, right fusiform, inferior occipital, and middle temporal gyri, right insula, right inferior parietal lobule, left lingual, postcentral, supramarginal, middle occipital, cingulate, inferior frontal, superior temporal, and inferior temporal (both in temporal and occipital lobes) gyri, left posterior cerebellar declive, and left superior parietal lobule (see Table 2.11 and Figure 2.1).

At the $p < .01$ FDR level, the conjunction meta-analysis of all tactile and auditory studies reporting coordinates for congenital/early-blind groups and sighted participant groups showed significant areas of activation for both blind and sighted participants in bilateral cuneus, insula, and precentral gyrus, as well as right postcentral, inferior frontal, superior temporal, and inferior temporal (both temporal and occipital areas thereof) gyri, right posterior cerebellar declive, left inferior parietal lobule, and left middle temporal and medial frontal gyri. Further regions implicated, though without reported extrema, include bilateral lingual and middle occipital gyri, right inferior parietal lobule, right middle frontal, inferior occipital, fusiform, and middle temporal gyri, left claustrum, left posterior cerebellar declive, and left inferior frontal, postcentral, supramarginal, and inferior temporal (both temporal and occipital areas) gyri (see Table 2.12 and Figure 2.1).

2.3.3 BLIND PARTICIPANT LOCALIZATION META-ANALYSES

At the $p < .05$ FDR level, the meta-analysis of all tactile and auditory studies with localization-specific tasks reporting coordinates for congenital/early-blind groups (including greater than task/rest reports as well as greater than sighted participant group performance reports) showed significant areas of activation for blind participants in bilateral cuneus and precuneus, as well as occipital areas of right inferior temporal gyrus. Further regions implicated, though without reported extrema, include bilateral lingual gyrus, right superior parietal lobule, and right middle occipital and inferior occipital gyri (see Table 2.13 and Figure 2.2).

The same meta-analysis run at the $p< .01$ FDR level returns the same region breakdown as the .01 FDR meta-analysis (see Table 2.14 and Figure 2.2).

2.3.4 BLIND PARTICIPANT IDENTIFICATION META-ANALYSES

At the $p< .05$ FDR level, the meta-analysis of all tactile and auditory studies with identification-specific tasks reporting coordinates for congenital/early-blind groups (including greater than task/rest reports as well as greater than sighted participant group performance reports) showed significant areas of activation for blind participants in bilateral cuneus, middle occipital gyrus, and lingual gyrus, as well as occipital areas of right inferior temporal gyrus. Further regions implicated, though without reported extrema, include right fusiform, inferior occipital, and middle temporal gyri (see Table 2.15 and Figure 2.2).

At the $p < .01$ FDR level, the meta-analysis of all tactile and auditory studies with identification-specific tasks reporting coordinates for congenital/early-blind groups (including greater than task/rest reports as well as greater than sighted participant group performance reports) showed significant areas of activation for blind participants in bilateral cuneus, middle occipital gyrus, and lingual gyrus, as well as occipital areas of right inferior temporal gyrus, right posterior cerebellar declive, and left inferior occipital gyrus. Further regions implicated, though without reported extrema, include right fusiform, inferior occipital, and middle temporal gyri, and occipital areas of left inferior temporal gyrus (see Table 2.16 and Figure 2.2).

2.4 DISCUSSION

2.4.1 CONGENITAL/EARLY-BLIND > SIGHTED

The meta-analysis run on the congenital/early-blind > sighted contrast coordinates populated by studies across auditory and tactile sensory tasks revealed a number of early visual occipital areas more strongly activated in the blind population than in sighted controls. Taken together, the revealed early-blind occipital activation network, responding to non-visual inputs, provides strong evidence that the same areas that are classically recruited in sighted participants during visual tasks are strongly utilized by the blind during non-visual tasks. As these non-visual tasks are essentially spatially discriminatory in nature (e.g., spatial localization, object identification, motion processing), a likely explanation for this non-visual activation is that the occipital lobe is largely tasked with responding to these types of tasks, using whichever modality provides the most relevant information. That visual input in general is exceptionally well-suited to spatial discrimination, with the organization of visual information mapped spatio-topically in cortex, means a strong preference for such inputs in spatially-relevant occipital areas should be expected. That fully sighted individuals often display decreased activation in occipital areas in response to non-visual stimuli suggests that, with all senses present, classically respective sense-specific areas are more locally set up to handle these tasks. If a task is primarily auditory, without task-relevant visual input, it would make little sense to spend limited cognitive attentional resources on excess visual processing, but rather make good sense to increase the utilization of areas strongly associated with auditory processing.

Indeed, existing literature suggests that vision tends to be selected over audition in cases of conflicting information where spatial processing is involved, and vice versa with temporal processing (e.g., Guttman et al., 2005). However, as the preference may just be useful spatial information, maintaining spatially-relevant inputs from non-visual inputs makes sense in case the generally-preferred modality, here vision, is ever impaired or simply unavailable. Studies on the lateral-occipital tactile-visual area (LOtv) support this spatial-wiring hypothesis, as LOtv is strongly associated with determining object shape, and typically responds to visual and haptic input, but only when that input includes shape-relevant information (e.g., Amedi et al., 2001; 2002; Beauchamp, 2005). Similarly, LOtv does not appear to respond to general auditory inputs, which typically do not relate shape-relevant information, but has been shown to respond to shape-relevant auditory input through visual-to-auditory sensory substitution (Amedi et al., 2007).

Behavioural evidence from crossmodal sensory illusions fits well with the useful inputs assumption touched on above -- for example, the ventriloquism effect. In this effect, given strong visual and auditory inputs, the visual system tends to mislocalize the source of speech to an object, such as a ventriloquist’s dummy, making gross “mouth” movements in time to the auditory input while the actual speaker visually displays no vocal motor cues. Given a heavily degraded visual stimulus, however, auditory location cues become more useful and the effect reverses. With moderate degradation of the visual stimulus, it is possible for neither sense to dominate, with localization of the sound instead being perceived at a median point between the visual and auditory stimuli (Alais & Burr, 2004).

Again considering crossmodal visual illusions, we can infer that connections exist between the classically sense-specific cortical regions. Whereas these interactions could take place subcortically, or in higher cortical regions, leaving sensory areas unimodal and isolated from one another, low-level connections have been shown to exist between auditory, tactile, and visual cortex in both non-human (e.g., Falchier et al., 2002; Lewis & Van Essen, 2000; Stehberg et al., 2014; Cappe & Barone, 2005; see also Sathian, 2005, Sathian & Lacey, 2007) and human participants (e.g., Eckert et al., 2008; Deshpande et al., 2008) through connectivity analyses. Considering these connections, alongside studies showing occipital activation to non-visual stimuli in blindfolded or eyes-closed sighted participants, it seems likely that these direct connections between sensory regions may give rise to the more robust non-visual occipital recruitment seen in blind participants. Given the loss of a sense, the cortical areas primarily responsible for processing its input would only be able to utilize information from the remaining senses. If connections to those remaining senses either already existed or were to be formed regardless, it is viable that these same connections would be strengthened through use, similar to the rapid switch to occipital activation for non-visual input seen in degraded visual input studies (e.g., Kauffman et al., 2002; Merabet et al., 2008), or area V5/MT segregating into both multisensory and vision-specific regions in sighted individuals, but utilizing the entire area for non-visual processing in congenitally blind individuals (Ricciardi et al., 2007). To more widely test this assumption, we conducted a second primary meta-analysis on neural areas commonly recruited for both congenital/early-blind and sighted individuals with temporarily restricted vision during auditory and haptic spatial tasks, expecting a number of occipital areas to be highlighted.

2.4.2 CONGENITAL/EARLY-BLIND AND SIGHTED CONJUNCTION

The conjunction meta-analysis combining auditory and tactile task studies revealed common occipital activations in bilateral cuneus and occipital areas of right inferior temporal gyrus, with bilateral lingual gyrus and middle occipital gyrus, as well as occipital areas of left inferior temporal gyrus, right inferior occipital gyrus, and right fusiform gyrus included in significant clusters, though without specifically reported extrema (see Figure 2.1, Table 2.11, and Table 2.12). This consistent inclusion of occipital areas across modalities suggests that auditory and/or somatosensory inputs can indeed recruit occipital cortex for non-visual processing, even in sighted individuals. That these areas are similarly utilized by both blind and sighted participants suggests that the pre-existing non-visual occipital connections within sighted participants likely exist in similar fashion in blind populations for the implicated areas. Considering that cuneus, lingual gyrus, middle and inferior occipital gyrus, and occipital areas of inferior temporal gyrus were also revealed as significant activation areas in the blind>sighted meta-analysis (see Figure 2.1, Table 2.9, and Table 2.10), it does seem likely that a strengthening of these pre-existing non-visual occipital connections occurs in these areas for blind populations, likely resulting in broader, more robust recruitment of these regions for the blind. As some extents of occipital areas beyond that seen in the conjunction meta-analysis were seen in the blind>sighted meta-analysis, it is plausible that there are also relatively unique non-visual occipital connections formed in occipital areas of blind individuals, lending potential support to the notion that some of this recruitment may stem from neurogenesis that would not occur in sighted individuals.

Thus, both primary theories of the origins of non-visual occipital recruitment -- strengthening of typical connections and/or formation of entirely new connections -- hold merit through our findings. However, it is further possible that the unique connectivity is further branching of the strengthened connections, which our analyses cannot here address.

The similarity of the recruited areas in sighted participants and those whose vision was lost early in life further suggests that occipital cortex may be organized for processing inputs relevant to specific functions regardless of modality, with a tiered preference for which modality is utilized. This could indicate that blind/blindfolded recruitment of occipital areas for non-visual stimuli occurs via an unmasking or strengthening of typically existing standard multimodal wiring, as opposed to strict neurogenesis and rewiring. This unmasking model is supported by research showing that auditory and tactile stimulation can independently elicit occipital activation, but when both modalities are presented simultaneously, occipital tactile activation is largely washed out by the presence of even task-irrelevant auditory stimuli (Weaver & Stevens, 2007). Coupled with the ability of sighted occipital areas to activate for non-visual inputs, but generally only measurably when vision is absent through blindfolding or closed eyes (as seen in the sighted occipital activation studies used for the conjunction meta-analysis), it is viable that occipital areas are in fact wired with a tiered preference for which sensory modality commands the most robust and utilized connectivity.

2.4.3 V1 ACTIVATION

Referring back to Figure 2.1, it is notable that little to no V1 activation is present in the blind > sighted contrast meta-analysis. This finding is concerning in regards to the strength of the hypothesis that functional low-level connectivity in occipital lobe to non-visual inputs should be robust in blind participants. However, V1 activation is clearly present in the conjunction meta-analysis, which suggests not only that the aforementioned functional low-level connectivity does indeed exist, but that this connectivity also exists in sighted individuals. It is of note that the clusters showing V1 activation for this analysis were reported as being significantly contributed to by both blind and sighted coordinate studies, so this is not a case of clustering blind-only or sighted-only results, but rather a proper conjunction. This commonality of the ability to elicit V1 activation to non-visual stimuli in both the blind and the sighted, coupled with the lack of notable V1 activation in the blind > sighted meta-analysis, sheds light on a plausible explanation as to the V1-based discrepancies among blind studies. If V1 activity is occurring in response to non-visual inputs for both blind and sighted participants, even if at differing degrees, that makes it that much less likely to note significantly greater V1 activation to non-visual inputs in the blind as compared to sighted controls. In other words, the lack of V1 activation reported in some studies may well be due to the control group displaying unexpected V1 activation as well.

2.4.4 TASK-SPECIFIC COMPARISON

The results of the third and fourth meta-analyses suggest that blind human recruitment of the occipital lobe does indeed retain a task-based delineation. As seen in

Figure 2.2, the localization and identification results have some similar areas of activation, but further clearly unique areas of activation. Of particular note is the parietal/precuneus activation unique to the localization-task meta-analysis. This dissociation of regions by task type follows the dorsal/ventral stream pattern, here with localization recruiting dorsal stream areas in the parietal lobe, and identification relying more on ventral areas and inferotemporal cortex – a similar pattern to that seen in sighted participants using visual information to conduct localization and identification tasks.

Whereas this finding does lend support to the hypothesis that the occipital lobe is sensory modality agnostic, more grossly preferring useful inputs for specific task types rather than from specific senses, it must be noted that there were comparatively very few studies included in the localization meta-analysis. Though it seems likely that the addition of further studies as they become available would strengthen our initial conclusions and expand on dorsal/localization specific structures in the blind, we cannot be certain until those data become available. Thus, we cautiously consider these results as support for our hypotheses.

2.5 CONCLUSIONS

Taken together, our findings coupled with the discussed studies strongly indicate that not only is the occipital lobe not a vision-specific region, but it may well have a tiered preferential sensory response bias. Further, we have promising support for the notion that the occipital lobe wires based on task demands, regardless of the sense providing the input. As the occipital lobe is typically recruited for three-dimensional representation, navigation, and object identification, it is plausible that these general tasks, rather than specific modality connections, are what is reasonably hardwired (see also Bavelier & Neville, 2002; Röder & Rösler, 2004). The visual system may provide the most salient information about local surroundings relevant to these tasks, causing the presence of visual input to largely suppress or simply overshadow inputs from other modalities. When those visual inputs are lost, auditory input may comprise the next-best modality for performing many of these tasks, causing its presence to similarly overshadow haptic input, as seen in Weaver and Stevens (2007). This uncovering of the best modality among the available inputs is also evident in the shift between visual or auditory dominance in the ventriloquism effect in the presence of degraded stimuli (Alais & Burr, 2004), as well as the apparent segregation of V5/MT based on available inputs (Ricciardi et al., 2007).

Table 2.1. Studies Included in the Blind > Sighted Meta-Analysis

Study	Participants	Imaging	Modality
Amedi et al. (2010)	8CB, 8S	1.5T MRI	Tactile
Anurova et al. (2015)	12EB, 12S	3T MRI	Auditory
Arno et al (2001)	6EB, 6S	PET	Auditory
Bauer et al. (2015)	8EB, 7S	3T MRI	Tactile
Collignon et al. (2011)	11CB, 11S	3T MRI	Auditory
deVolder et al. (2001)	6EB, 6S	PET	Auditory
Fiehler et al. (2009)	12CB, 12S	1.5T MRI	Tactile
Gizewski et al. (2003)	9CB, 3EB, 12S	1.5T MRI	Tactile
Kitada et al. (2013)	17EB, 22S	3T MRI	Tactile
Klinge et al. (2010)	10CB, 10S	3T MRI	Auditory
Lewis et al. (2011)	10CB, 14S	3T MRI	Auditory
Noppeney et al. (2003)	4CB, 7EB, 12S	2T MRI	Auditory
Poirier et al. (2006)	6EB, 6S	2T MRI	Auditory
Ptito et al. (2005)	5CB, 1EB, 5S	PET	Tactile
Renier et al. (2010)	12EB, 12S	3T MRI	Both
Roeder et al. (2002)	10CB, 11S	1.5T MRI	Auditory
Sadato et al (1998)	3CB, 3EB, 10S	PET	Tactile
Vanlierde et al. (2003)	5EB, 5S	PET	Auditory
Voss et al. (2008)	12EB, 7S	PET	Auditory
Watkins et al. (2012)	5EB, 6S	3T MRI	Auditory
Watkins et al. (2013)	5EB, 6S	3T MRI	Auditory
Weeks et al. (2000)	9CB, 9S	PET	Auditory
Wolbers et al. (2011)	7EB, 7S	MRI	Tactile

CB = congenitally blind; EB = early blind; S = sighted

Table 2.2. Blind > Sighted Meta-Analysis Study Tasks

Study	Task
Amedi et al. (2010)	Object recognition
Anurova et al. (2015)	Sound identification, localization
Arno et al (2001)	Auditory substitution
Bauer et al. (2015)	Symmetry perception
Collignon et al. (2011)	Spatial localization, pitch discrimination
deVolder et al. (2001)	Mental imagery
Fiehler et al. (2009)	Guided hand movement
Gizewski et al. (2003)	Braille
Kitada et al. (2013)	Object identification
Klinge et al. (2010)	Mood/vowel identification
Lewis et al. (2011)	Sound source identification
Noppeney et al. (2003)	Semantic discrimination
Poirier et al. (2006)	Motion discrimination
Ptito et al. (2005)	Orientation discrimination
Renier et al. (2010)	Localization, identification
Roeder et al. (2002)	Language discrimination
Sadato et al (1998)	Non-Braille discrimination
Vanlierde et al. (2003)	Visuo-spatial imagery
Voss et al. (2008)	Auditory localization
Watkins et al. (2012)	Naming, reversed speech
Watkins et al. (2013)	Passive listening
Weeks et al. (2000)	Localization, delayed matching
Wolbers et al. (2011)	Scene/object exploration

Table 2.3. Studies Included in the Blind and Sighted Conjunction Meta-Analysis

Study	Participants	Imaging	Modality
Alain et al. (2001)	15S	1.5T MRI	Auditory
Amedi et al. (2010)	8CB, 8S	1.5T MRI	Tactile
Anurova et al. (2015)	12EB, 12S	3T MRI	Auditory
Arnott et al. (2005)	15S	1.5T MRI	Auditory
Burton et al. (2002)	9EB	1.5T MRI	Tactile
Collignon et al. (2011)	11CB, 11S	3T MRI	Auditory
James et al. (2002)	6S	4T MRI	Tactile
Kim et al. (2011)	9S	3T MRI	Both
Lambert et al. (2004)	6CB, 6S	2T MRI	Auditory
Lewis et al. (2011)	10CB, 14S	3T MRI	Auditory
Linden et al. (1999)	5S	1.5T MRI	Auditory
Maeder et al. (2001)	18S	1.5T MRI	Auditory
Matteau et al. (2010)	8CB	1.5T MRI	Tactile
Merabet et al. (2007)	12S	3T MRI	Tactile
Miquée et al. (2007)	18S	3T MRI	Tactile
Poirier et al. (2005)	6S	2T MRI	Auditory
Poirier et al. (2006)	6EB, 6S	2T MRI	Auditory
Ptito et al. (2012)	7CB, 1EB	3T MRI	Tactile
Rämä et al. (2000)	8S	1.5T MRI	Auditory
Renier et al. (2010)	12EB, 12S	3T MRI	Both
Ricciardi et al. (2006)	6S	1.5T MRI	Tactile
Ricciardi et al. (2008)	3CB, 1EB, 7S	1.5T MRI	Tactile
Saito et al. (2003)	11S	3T MRI	Tactile
Stevens et al. (2007)	12B	3T MRI	Auditory
Voss et al. (2008)	12EB, 7S	PET	Auditory
Weaver et al. (2007)	9EB	3T MRI	Both
Weeks et al. (2000)	9CB, 9S	PET	Auditory
Wu et al. (2007)	13S	4T MRI	Auditory
Zhang et al. (2005)	20S (E1), 22S (E2)	1.5T (E1), 3T (E2) MRI	Tactile
Zimmer et al. (2005)	16S	3T MRI	Auditory
Zimmer et al. (2006)	16S	1.5T MRI	Auditory

CB = congenitally blind; EB = early blind; S = sighted

Table 2.4. Blind and Sighted Conjunction Meta-Analysis Study Tasks

Study	Task
Alain et al. (2001)	Localization, pitch discrimination
Amedi et al. (2010)	Object recognition
Anurova et al. (2015)	Identification & localization
Arnott et al. (2005)	Localization, identification
Burton et al. (2002)	Braille
Collignon et al. (2011)	Spatial localization, pitch discrimination
James et al. (2002)	Priming, exploration
Kim et al. (2011)	Shape discrimination
Lambert et al. (2004)	Mental imagery
Lewis et al. (2011)	Sound identification
Linden et al. (1999)	Sound discrimination
Maeder et al. (2001)	Recognition, localization
Matteau et al. (2010)	Motion discrimination
Merabet et al. (2007)	Roughness discrimination
Miquée et al. (2007)	Shape exploration and encoding
Poirier et al. (2005)	Motion discrimination
Poirier et al. (2006)	Motion discrimination
Ptito et al. (2012)	Shape discrimination
Rämä et al. (2000)	Mood discrimination
Renier et al. (2010)	Localization, identification
Ricciardi et al. (2006)	Working memory
Ricciardi et al. (2008)	Motion perception
Saito et al. (2003)	Match/different discrimination
Stevens et al. (2007)	Backward recognition
Voss et al. (2008)	Monaural/binaural localization
Weaver et al. (2007)	Target/non-target discrimination
Weeks et al. (2000)	Localization, delayed matching
Wu et al. (2007)	Attention shifting
Zhang et al. (2005)	Orientation discrimination (E1) Orientation and spacing discrimination (E2)
Zimmer et al. (2005)	Localization
Zimmer et al. (2006)	Localization

Table 2.5. Studies Included in the Localization Meta-Analysis

Study	Participants	Imaging	Modality
Anurova et al. (2015)	12EB, 12S	3T MRI	Auditory
Collignon et al. (2011)	11CB, 11S	3T MRI	Auditory
Matteau et al. (2010)	8CB	1.5T MRI	Tactile
Poirier et al. (2006)	6EB, 6S	2T MRI	Auditory
Renier et al. (2010)	12EB, 12S	3T MRI	Both
Ricciardi et al. (2008)	3CB, 1EB, 7S	1.5T MRI	Tactile
Voss et al. (2008)	12EB, 7S	PET	Auditory
Weeks et al. (2000)	9CB, 9S	PET	Auditory

CB = congenitally blind; EB = early blind; S = sighted

Table 2.6. Localization Meta-Analysis Study Tasks

Study	Task
Anurova et al. (2015)	Sound localization
Collignon et al. (2011)	Spatial localization
Matteau et al. (2010)	Motion discrimination
Poirier et al. (2006)	Motion discrimination
Renier et al. (2010)	Localization
Ricciardi et al. (2008)	Motion perception
Voss et al. (2008)	Auditory localization
Weeks et al. (2000)	Localization, delayed matching

Table 2.7. Studies Included in the Identification Meta-Analysis

Study	Participants	Imaging	Modality
Amedi et al. (2010)	8CB, 8S	1.5T MRI	Tactile
Anurova et al. (2015)	12EB, 12S	3T MRI	Auditory
Arno et al (2001)	6EB, 6S	PET	Auditory
Bauer et al. (2015)	8EB, 7S	3T MRI	Tactile
Burton et al. (2002)	9EB	1.5T MRI	Tactile
Collignon et al. (2011)	11CB, 11S	3T MRI	Auditory
Gizewski et al. (2003)	9CB, 3EB, 12S	1.5T MRI	Tactile
Kitada et al. (2013)	17EB, 22S	3T MRI	Tactile
Klinge et al. (2010)	10CB, 10S	3T MRI	Auditory
Lewis et al. (2011)	10CB, 14S	3T MRI	Auditory
Noppeney et al. (2003)	4CB, 7EB, 12S	2T MRI	Auditory
Ptito et al. (2005)	5CB, 1EB, 5S	PET	Tactile
Ptito et al. (2012)	7CB, 1EB	3T MRI	Tactile
Renier et al. (2010)	12EB, 12S	3T MRI	Both
Sadato et al (1998)	3CB, 3EB, 10S	PET	Tactile
Stevens et al. (2007)	12B	3T MRI	Auditory
Watkins et al. (2012)	5EB, 6S	3T MRI	Auditory
Weaver et al. (2007)	9EB	3T MRI	Both
Wolbers et al. (2011)	7EB, 7S	MRI	Tactile

CB = congenitally blind; EB = early blind; S = sighted

Table 2.8. Identification Meta-Analysis Study Tasks

Study	Task
Amedi et al. (2010)	Object recognition
Anurova et al. (2015)	Sound identification
Arno et al (2001)	Auditory substitution
Bauer et al. (2015)	Symmetry perception
Burton et al. (2002)	Braille
Collignon et al. (2011)	Pitch discrimination
Gizewski et al. (2003)	Braille
Kitada et al. (2013)	Object identification
Klinge et al. (2010)	Mood/vowel identification
Lewis et al. (2011)	Sound identification
Noppeney et al. (2003)	Semantic discrimination
Ptito et al. (2005)	Orientation discrimination
Ptito et al. (2012)	Shape discrimination
Renier et al. (2010)	Identification
Sadato et al (1998)	Non-Braille discrimination
Stevens et al. (2007)	Backward recognition
Watkins et al. (2012)	Naming
Weaver et al. (2007)	Target discrimination
Wolbers et al. (2011)	Scene/object exploration

Table 2.9. Blind > Sighted Contrast Meta-Analysis Results (Auditory and Tactile, FDR < .05)

	Min. Cluster Size: 471		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 4712 mm^3: -26,-96,-4 to -2,-74,38 center -13.4,-84.8,15.2						
	L Lingual Gyrus	18	-6	-82	0	L Mid. Occipital Gyrus
	L Cuneus	18	-14	-86	20	L Precuneus
	"	17	-6	-82	10	
2: 2144 mm^3: 24,-84,-8 to 48,-62,8 center 37.8,-72.2,-1.2						R Inf. Temporal Gyrus (Occipital)
	R Inferior Occipital Gyrus	19	42	-70	-2	
	"	19	32	-76	-2	R Fusiform Gyrus
	R Middle Occipital Gyrus	18	30	-82	6	R Lingual Gyrus
	--	--	--	--	--	R Mid. Temporal Gyrus
	--	--	--	--	--	
3: 1440 mm^3: 2,-88,6 to 24,-76,32 center 16.4,-82.9,22.5						
	R Cuneus	18	18	-82	26	R Precuneus
	"	18	6	-86	10	
	R Middle Occipital Gyrus	18	18	-86	14	
4: 512 mm^3: -48,-80,-10 to -42,-64,0 center -45.2,-70.2,-5.3						L Mid. Occipital Gyrus
	L Inferior Occipital Gyrus	19	-44	-68	-6	L Fusiform Gyrus
	"	19	-46	-78	-2	L Inf. Temporal Gyrus (Occipital)
	--	--	--	--	--	
5: 472 mm^3: 4,-88,-4 to 22,-74,4 center 11.1,-81.4,-.4						
	R Lingual Gyrus	17	8	-86	0	
	"	N/A	18	-76	0	

Table 2.10. Blind > Sighted Contrast Meta-Analysis Results (Auditory and Tactile, FDR < .01)

	Min. Cluster Size: 39		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 1800 mm^3: -22,-92,10 to -10,-78,32 center-15.5,-85.9,20.3						
	L Cuneus	18	-14	-86	20	L Mid. Occipital Gyrus
2: 696 mm^3: 38,-74,-6 to 46,-64,2 center 42.4,-68.5,-2.5						R Inf. Temporal
	R Inferior Occipital Gyrus	19	42	-70	-2	Gyrus (Occipital)
	--	--	--	--	--	R Mid. Occipital Gyrus
	--	--	--	--	--	R Fusiform Gyrus
3: 552 mm^3: 16,-86,22 to 22,-78,32 center 19,-81.8,26.7						
	R Cuneus	18	18	-82	26	R Precuneus
4: 480 mm^3: -10,-88,-2 to -4,-76,4 center -6.7,-81.6,.6						
	L Lingual Gyrus	18	-6	-82	0	L Cuneus
5: 152 mm^3: -46,-70,-8 to -42,-66,-4 center -44.4,-68.1,-6.1						L Fusiform Gyrus
	L Inferior Occipital Gyrus	19	-44	-68	-6	L Mid. Occipital Gyrus
	--	--	--	--	--	L Inf. Temporal
	--	--	--	--	--	Gyrus (Occipital)
6: 120 mm^3: 30,-78,-4 to 34,-74,0 center 31.5,-76.3,-2						
	R Inferior Occipital Gyrus	19	32	-76	-2	R Mid. Occipital Gyrus
	--	--	--	--	--	R Lingual Gyrus
7: 48 mm^3: 28,-84,4 to 30,-80,6 center 29,-82,5						
	R Middle Occipital Gyrus	18	30	-82	6	

Table 2.11. Conjunction Meta-Analysis Results (Auditory and Tactile, FDR < .05)

	Min. Cluster Size: 823		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 3280 mm^3: -54,-56,34 to -30,-22,50 center -42,-38.4,41.8						
	L Inferior Parietal Lobule	40	-50	-26	46	L Postcentral Gyrus
	"	40	-36	-46	38	L Supramarginal Gyrus
	"	40	-46	-38	42	L Sup. Parietal Lobule
2: 3144 mm^3: -10,-94,-12 to 22,-76,18 center 1.1,-85.4,4.4						
	L Cuneus	17	-4	-86	6	L Lingual Gyrus
	R Cuneus	18	10	-88	14	L Mid. Occipital Gyrus
	"	17	4	-86	6	R Mid. Occipital Gyrus
	"	17	18	-86	8	L Post. Cerebellar
	R Post. Cerebellar Declive	N/A	2	-82	-10	Declive
	R Lingual Gyrus	17	6	-86	2	
3: 2016 mm^3: -58,-68,-6 to -44,-48,8 center -50.6,-58.7,-.5						L Mid. Occipital Gyrus
	L Middle Temporal Gyrus	37	-52	-60	-2	L Inf. Temporal Gyrus
	--	--	--	--	--	(Temp. & Occip.)
	--	--	--	--	--	L Sup. Temporal Gyrus
4: 1456 mm^3: 40,-32,40 to 50,-20,52 center 44.9,-25.5,45.7						
	R Parietal Postcentral Gyrus	2	44	-26	46	R Inf. Parietal Lobule
5: 1080 mm^3: -8,-4,44 to 10,10,56 center -1.5,3,50.3						
	L Medial Frontal Gyrus	6	-4	0	52	L Sup. Frontal Gyrus
	"	32	6	4	50	R Sup. Frontal Gyrus
	R Medial Frontal Gyrus	6	-4	6	46	L Cingulate Gyrus
6: 944 mm^3: 40,-70,-6 to 50,-58,2 center 43.9,-63.8,-2.6						R Mid. Temp. Gyrus
	R Inferior Temporal	37	44	-64	-2	R Inf. Occipital Gyrus
	Gyrus (Occipital areas)	--	--	--	--	R Mid.Occipital Gyrus
	--	--	--	--	--	R Fusiform Gyrus
7: 896 mm^3: 42,2,16 to 52,10,30 center 46.7,5.7,22.3						
	R Inferior Frontal Gyrus	9	46	4	20	R Insula
8: 864 mm^3: -56,-2,26 to -48,10,42 center -52.2,2.1,31						
	L Precentral Gyrus	6	-52	2	30	L Inf. Frontal Gyrus
	"	6	-52	0	38	

Table 2.12. Conjunction Meta-Analysis Results (Auditory and Tactile, FDR < .01)

	Min. Cluster Size: 69		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 1288 mm^3: -58,-66,-6 to -46,-50,4 center -51,-59.5,-.9						L Inf. Temporal Gyrus
	L Middle Temp. Gyrus	37	-52	-60	-2	L Mid. Occipital Gyrus
2: 1056 mm^3: -48,-52,34 to -32,-32,46 center -39.9,-42,40.4						
	L Inferior Parietal Lobule	40	-36	-46	38	L Supramarginal Gyrus
	"	40	-46	-38	42	
3: 856 mm^3: 40,-32,42 to 50,-20,52 center 44.9,-25.6,46						
	R Par. Postcentral Gy.	2	44	-26	46	R Inf. Parietal Lobule
4: 576 mm^3: -8,-92,4 to 6,-82,12 center -4.5,-86.2,7.1						L Lingual Gyrus
	L Cuneus	17	-4	-86	6	R Lingual Gyrus
	R Cuneus	17	4	-86	6	L Mid. Occipital Gyrus
5: 464 mm^3: 42,2,18 to 50,10,28 center 46.7,5.3,21.9						
	R Inferior Frontal Gyrus	9	46	4	20	R Insula
6: 432 mm^3: -54,-30,42 to -46,-22,48 center -49.6,-25.3,45						
	L Inferior Parietal Lobule	40	-50	-26	46	L Par. Postcentral Gy.
7: 424 mm^3: 40,-70,-6 to 48,-60,0 center 43.7,-64.2,-2.7						R Mid. Temporal Gy.
	R Inferior Temporal	37	44	-64	-2	R Fusiform Gyrus
	Gyrus (Occipital)	--	--	--	--	R Inf. Occipital Gyrus
8: 352 mm^3: -34,14,8 to -28,20,16 center -30.7,16.7,12.4						
	L Insula	13	-30	16	12	L Claustrum
9: 256 mm^3: 60,-26,4 to 66,-22,12 center 62.6,-23.9,7.5						
	R Sup. Temporal Gyrus	42	62	-24	8	
10: 216 mm^3: 28,-10,50 to 34,-4,54 center 30.3,-7,51.9						
	R Precentral Gyrus	6	30	-8	52	R Mid. Frontal Gyrus
11: 208 mm^3: -56,0,26 to -50,6,32 center -52.8,2.5,29.3						
	L Precentral Gyrus	6	-52	2	30	L Inf. Frontal Gyrus
12: 176 mm^3: 0,-82,-12 to 4,-78,-2 center 1.6,-80.6,-7.4						R Lingual Gyrus
	R Post. Cereb. Declive	N/A	2	-82	-10	L Post. Cereb. Declive
	--	--	--	--	--	L Lingual Gyrus
13: 160 mm^3: 8,-90,10 to 12,-86,16 center 10.2,-88.3,13.5						
	R Cuneus	18	10	-88	14	R Mid. Occipital Gyrus
14: 128 mm^3: -6,-2,50 to -2,4,54 center -4.5,.9,51.6						
	L Medial Frontal Gyrus	6	-4	0	52	
15: 88 mm^3: 30,16,10 to 32,18,14 center 31.1,16.9,11.8						
	R Insula	13	30	16	12	

Table 2.13. Blind Participant Localization Meta-Analysis Results (Auditory and Tactile, FDR < .05)

	Min. Cluster Size: 116		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 832 mm^3: 12,-88,4 to 28,-80,12 center 20.6,-84.3,8.2						R Mid. Occipital Gyrus
	R Cuneus	17	22	-84	8	R Lingual Gyrus
2: 424 mm^3: -10,-88,0 to -4,-82,10 center -6.2,-84.3,4.7						
	L Cuneus	17	-6	-84	4	L Lingual Gyrus
	"	17	-6	-84	8	
3: 368 mm^3: 16,-72,40 to 24,-64,46 center 20,-67.7,43.1						
	R Precuneus	7	20	-68	44	R Sup. Parietal Lobule
4: 352 mm^3: 38,-72,-6 to 46,-64,0 center 42,-67.9,-2.4						
	R Inferior Temporal	N/A	42	-68	-2	R Inf. Occipital Gyrus
	Gyrus (Occipital)	--	--	--	--	R Mid. Occipital Gyrus
5: 160 mm^3: -22,-74,38 to -16,-70,42 center -19.3,-72.7,39.8						
	L Precuneus	7	-20	-72	40	

Table 2.14. Blind Participant Localization Meta-Analysis Results (Auditory and Tactile, FDR < .01)

	Min. Cluster Size: 9		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 416 mm^3: 16,-88,4 to 26,-82,12 center 21,-84.4,8.4						R Mid. Occipital Gyrus
	R Cuneus	17	22	-84	8	R Lingual Gyrus
2: 168 mm^3: 18,-70,42 to 22,-66,46 center 20.1,-68.1,43.4						
	R Precuneus	7	20	-68	44	R Sup. Parietal Lobule
3: 144 mm^3: -8,-86,2 to -4,-82,10 center -6.1,-84,4.7						
	L Cuneus	17	-6	-84	4	L Lingual Gyrus
	"	17	-6	-84	8	
4: 104 mm^3: 40,-70,-4 to 44,-66,0 center 41.7,-68.2,-2.6						
	R Inferior Temporal	N/A	42	-68	-2	R Inf. Occipital Gyrus
	Gyrus (Occipital)	--	--	--	--	
5: 24 mm^3: -20,-74,40 to -18,-72,40 center -19.3,-72.7,40						
	L Precuneus	7	-20	-72	40	

Table 2.15. Blind Participant Identification Meta-Analysis Results (Auditory and Tactile, FDR < .05)

Cluster	Min. Cluster Size: 420 Region	BA	Peak (Talairach) X	Y	Z	Other Areas
1: 3584 mm^3: -28,-100,-4 to -2,-76,24 center -12.1,-88,9.4						
	L Middle Occipital Gyrus	18	-16	-90	10	
	L Cuneus	18	-8	-96	10	
	L Lingual Gyrus	18	-6	-82	0	
2: 3072 mm^3: 2,-94,-2 to 18,-78,26 center 9.5,-86.1,10.8						
	R Lingual Gyrus	17	8	-86	2	
	R Middle Occipital Gyrus	18	12	-90	14	
	R Cuneus	18	10	-82	22	
3: 624 mm^3: 40,-72,-8 to 48,-62,0 center 43.5,-65.7,-3.5						R Inf. Occipital Gyrus
	R Inferior Temporal	37	44	-66	-4	R Fusiform Gyrus
	Gyrus (Occipital)	--	--	--	--	R Mid. Occipital Gyrus
	--	--	--	--	--	R Mid. Temporal Gy.

Table 2.16. Blind Participant Identification Meta-Analysis Results (Auditory and Tactile, FDR < .01)

	Min. Cluster Size: 36		Peak (Talairach)			
Cluster	Region	BA	X	Y	Z	Other Areas
1: 1632 mm^3: 2,-92,-2 to 16,-80,26 center 9.1,-86.1,10.3						
	R Lingual Gyrus	17	8	-86	2	
	R Middle Occipital Gyrus	18	12	-90	14	
	R Cuneus	18	10	-82	22	
2: 1120 mm^3: -22,-98,6 to -6,-84,20 center -13.8,-90.4,11.6						
	L Middle Occipital Gyrus	18	-16	-90	10	L Lingual Gyrus
	L Cuneus	18	-8	-96	10	
3: 280 mm^3: -8,-84,-4 to -4,-78,6 center -6.3,-81.4,-.1						L Cuneus
	L Lingual Gyrus	18	-6	-82	0	
4: 272 mm^3: 40,-70,-6 to 46,-62,0 center 43.5,-65.8,-3.6						R Inf. Occipital Gyrus
	R Inferior Temporal	37	44	-66	-4	R Fusiform Gyrus
	Gyrus (Occipital)	--	--	--	--	R Mid. Occipital Gyrus
	--	--	--	--	--	R Mid. Temporal Gy.
5: 80 mm^3: 12,-62,2 to 16,-58,4 center 14.6,-60.6,2.8						
	R Lingual Gyrus	19	14	-60	2	
6: 56 mm^3: 26,-70,-14 to 30,-68,-12 center 28.3,-69.1,-12.6						
	R Post. Cerebellar Declive	N/A	28	-68	-12	
7: 56 mm^3: -50,-78,-2 to -48,-76,0 center -49.1,-77.2,-1.1						L Mid. Occipital Gyrus
	L Inferior Occipital Gyrus	18	-50	-78	0	L Inf. Temporal
	--	--	--	--	--	Gyrus (Occipital)

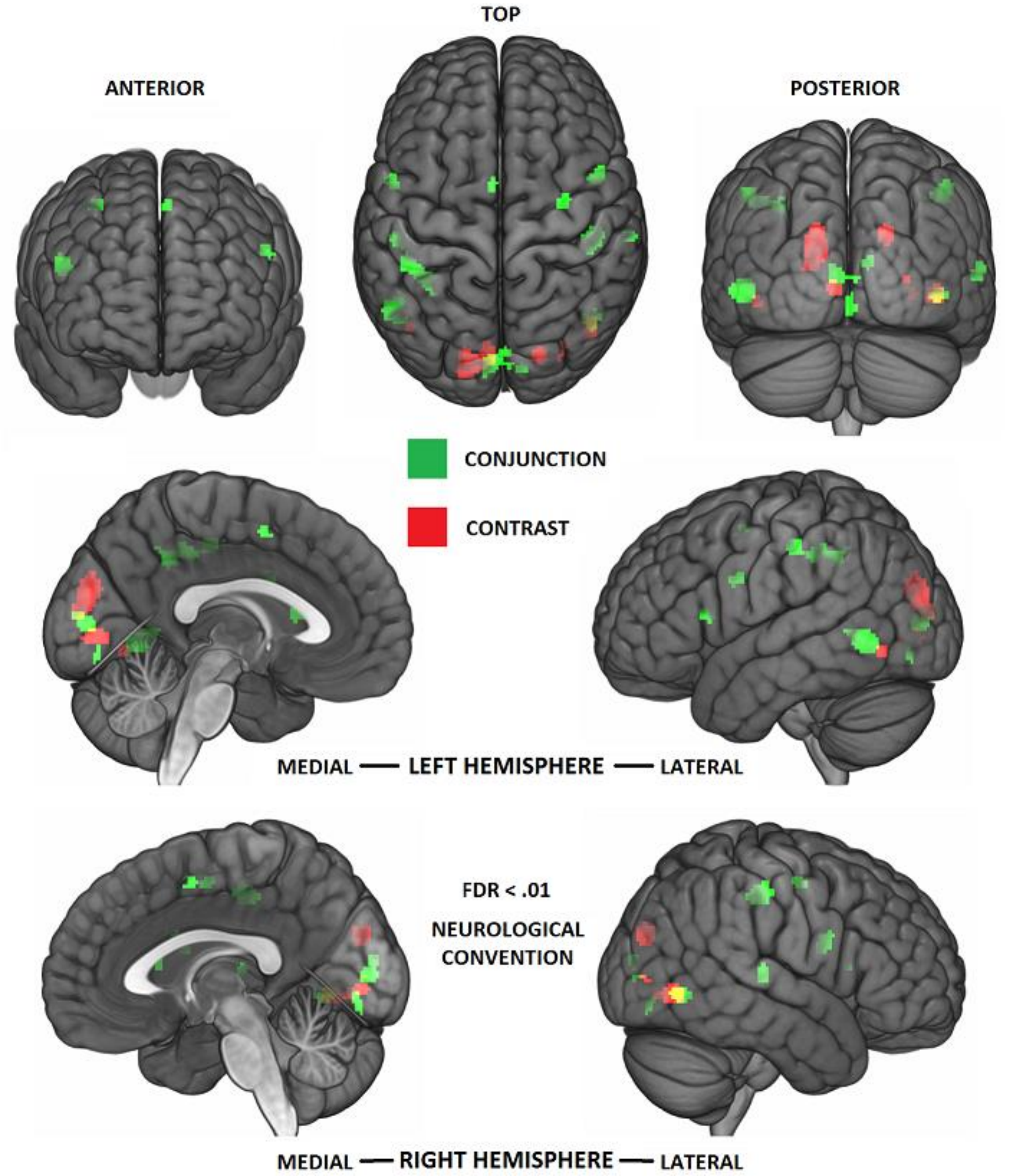

Figure 2.1. Contrast and Conjunction Meta-Analysis Results. Activation clusters significant at the $p < .01$ FDR correction threshold are presented in red for the contrast meta-analysis (blind > sighted) and in green for the conjunction meta-analysis (blind and sighted). All images displayed in neurological convention (left = left).

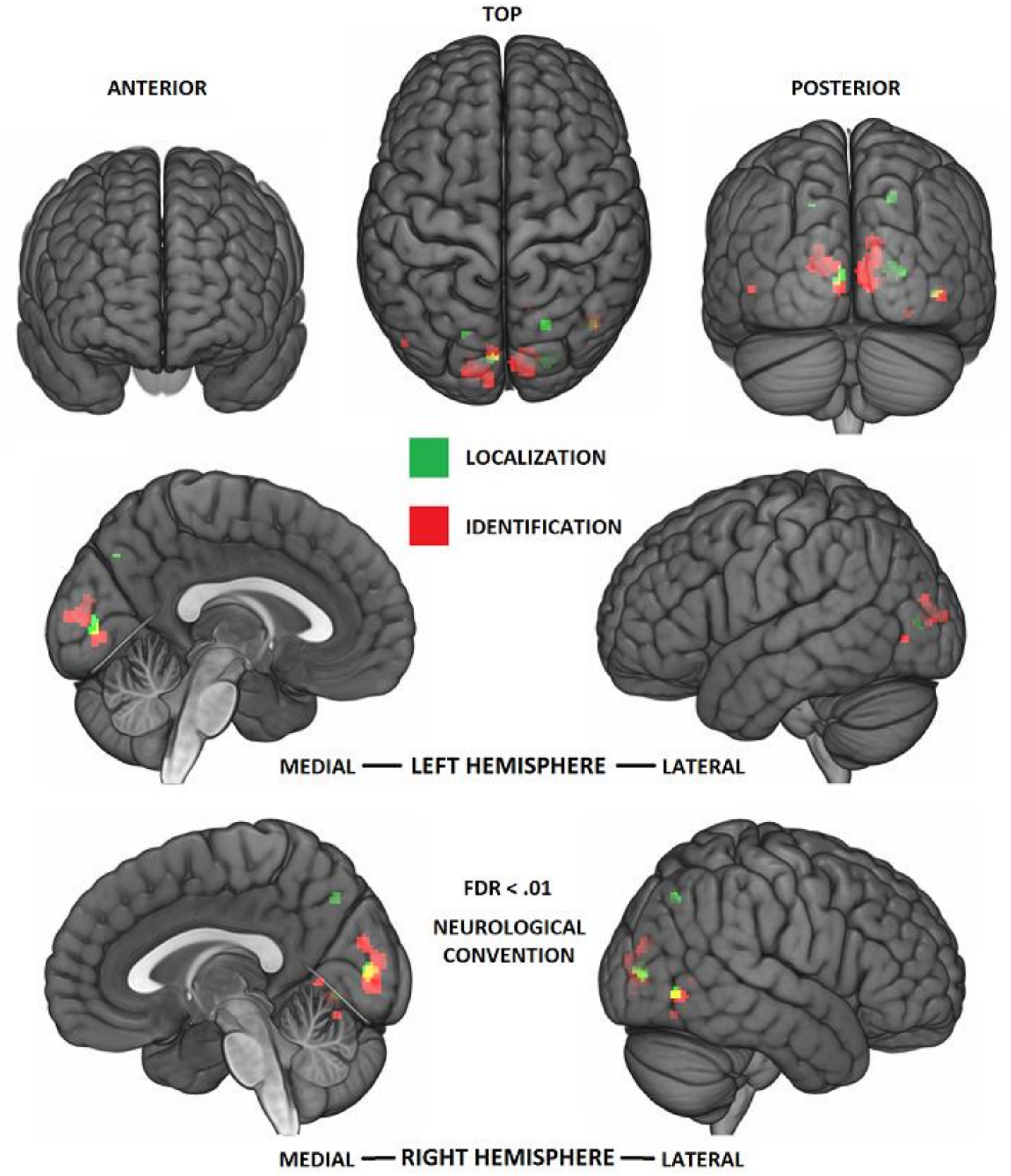

Figure 2.2. Localization and Identification Task Meta-Analysis Results. Activation clusters significant at the $p < .01$ FDR correction threshold are presented in red for the identification task meta-analysis and in green for the localization meta-analysis. All images displayed in neurological convention (left = left).

CHAPTER 3

OCCIPITAL ACTIVATION DURING AUDITORY LOCATION, FREQUENCY, AND DURATION DISCRIMINATION: AN fMRI STUDY

3.1 INTRODUCTION

We have suggested above that cortex may be wired to respond to task-specific, rather than merely modality-specific, demands. As it has been suggested that visual input generally excels at providing spatial information (consider, for instance, the visual gestalt principles for determining object continuity and relative location), and auditory input at providing temporal information (consider, for instance, the minute timing differences involved in auditory localization), if the cortical structures most associated with those inputs wire more to the task than to the sensory modality, spatially/temporally relevant input from a non-primary sense should recruit similar areas as commonly seen with primary sense input.

We also relayed evidence that non-visual recruitment of occipital lobe may be suppressed when visual input is present, and that auditory input may further suppress occipital responses to tactile information (e.g., Weaver & Stevens, 2007). This evidence sets the stage for the notion of tiered preferential responsivity – a given brain area generally having the connections to and ability to respond to inputs from various senses, and a prioritization preference based on which sense typically provides the most useful information for the area's task(s). This notion further shows how it could be inferred, though we believe erroneously, that the most typically useful sense for a given area is what is actually being wired for – occipital lobe as a visual area, temporal as auditory, as opposed to being more robust task-oriented areas.

We further have evidence that relatively short durations of blindfolding can result in behavioural (e.g., Lewald, 2007; Facchini & Aglioti, 2003) and functional (Weisser et al., 2005; Lazzouni et al., 2012; Poirier et al., 2005; see also Boroojerdi et al., 2000) changes in non-visual occipital processing. This evidence, coupled with studies showing connections between low-level primary sensory areas, seems to further support the concept of a more global connectivity for sensory inputs, suggesting an as-needed functional unmasking of these extant connections rather than, say, rapid connective neurogenesis. To wit, it is unlikely that robust new sensory connections could be made in rapid fashion, or that they should. Considering vision, even if it were possible, it would likely be maladaptive to generate robust new connections to alternate sensory inputs if visual input was impaired for only a matter of hours. Rather, it seems likely that existing connections should be maintained to allow integrative problem-solving based on the best available inputs for current conditions.

Thus, to investigate our overarching hypothesis of task-based wiring, examining cortical responses to spatial information in the absence of visual input seems relevant. If task-based wiring occurs, and occipital lobe is indeed a largely spatial processing area, interruption of visual input should result in auditory spatial tasks notably recruiting occipital structures, whereas time-judgment tasks may not.

Indeed, we found some support for this hypothesis through the results of our preceding meta-analyses, wherein localization tasks elicited unique dorsal stream activations, and identification tasks elicited unique ventral stream activations. Based on this support, conducting a more direct investigation of the task-specific wiring hypothesis seemed sound. To test this hypothesis, we conducted an fMRI study wherein sighted participants and blindfolded but otherwise typically sighted participants responded to spatial and non-spatial auditory tasks. These tasks involved 1-back comparisons of sound location, duration, and pitch. Each of these stimulus features were pseudo-randomized on every trial, with a basic staircase design used to titrate difficulty. For each run, participants responded to only one of the three features. We hypothesized that, after a period of blindfolding, we would be able to note increased cortical activity in occipital areas for spatial but not time-based tasks. We did not anticipate significant occipital recruitment for non-spatial tasks, hypothesizing instead that any differences in neural recruitment for such tasks between the sighted and blindfolded groups would likely remain in temporal lobe structures.

3.2 METHODS

3.2.1 PARTICIPANTS

We recruited 26 participants (13 blindfolded, 13 control) from the University of South Carolina SONA research pool. All participants were free of neurological or auditory impairment, and gave informed consent. One blindfolded participant was excluded from all analyses due to non-completion of all tasks, leaving 12 blindfolded and 13 sighted control participants. Though not blindfolded, sighted control participants were instructed to keep their eyes closed during scan tasks because the presence of input from a given sense may mask or inhibit occipital responses to other sensory inputs (e.g., Weaver & Stevens, 2007), as put forth in the previous meta-analysis.

3.2.2 STIMULI

Task stimuli included sound clips of single-frequency tones with varied duration, frequency, and location, generated as-needed by the experiment delivery software, Presentation. Location changes were handled via a simple pan function, with no elevation alterations presented. Each of these features was independently varied based on participant task-performance, using a staircase procedure with a goal of ~70% to 75% accuracy on 1-back recognition tasks for each feature. Titration was based on performance over series of 16-trial blocks. Within each block, only 4 possible frequencies, 4 possible durations, and 4 possible locations were presented, centered around a static base value and shifted higher and lower based on a titrated step size. The static base values were a frequency of 1750 Hz, a duration of 375 ms, and a central location (numerically represented as a pan value of 0 on the range of -1 to 1, or full left to full right). Initial step sizes were 100 Hz, 200 ms, and a pan of 0.5. The stimulus features used for each block were calculated as (base +/- 0.5 * current step size) and (base +/- 1.5 * current step size). Thus, the initial presentations would be combinations of 1600, 1700, 1800, or 1900 Hz, 75, 275, 475, or 675 ms, and a pan of -0.75, -0.25, 0.25, or 0.75. Minimum step sizes were 10 Hz, 10 ms, and a pan of 0.01. Maximum step sizes were 500 Hz, 220 ms, and a pan of 0.66.

3.2.3 EXPERIMENTAL DESIGN

Trials consisted of one auditory tone being played at the start of a 1500 ms trial duration. After each trial, the next trial began immediately.

Participants engaged in 9 runs of 1-back tasks (1 practice and 2 experimental runs for each of the three stimulus features), responding via button press on each trial to indicate whether the specified target feature (frequency, duration, or pitch) was repeated. At the start of each run, a 32-second instructional audio clip was played, describing the task and reiterating which feature was to be attended to for the run. For each run, participants responded to a single target feature, but all three stimulus features varied throughout all trials regardless of run type. All features were able to change such that the stimuli for each run type were the same, with the only notable difference having been what feature was attended to. For example, as in Figure 2.1 below, if the first trial in a pitch run had a 1000 Hz tone presented at the far left for 200 ms, and the second trial had a 1000 Hz tone presented at the far right for 300 ms, the correct response would be a button press as the same frequency was presented. If the third trial had a 1030 Hz tone presented at the far right for 300 ms, the correct response would be no button press, as the frequency changed from the previous trial.

Within each run there were 8 blocks of 16 trials each, for 128 trials per full run. After each block was a 13 second long break, including after the last block of each run to fully model the hemodynamic response function. This made each run an average of 5.5 minutes long. Run type was indicated verbally by the experimenter, as well as through the instruction sound file, at the beginning of each run. The order of run-type presentation was counterbalanced across participants. The target stimulus feature (based on run-type) was pseudo-randomly presented to ensure between 3 and 4 repeat trials in each block. The non-target features (e.g., duration and location if the target feature was frequency) were randomly selected for each trial.

3.2.4 PROCEDURE

All participants in the blindfold group were fitted with a blindfold (Mindfold Relaxation Mask; Mindfold, Inc., Durango, CO) upon completion of informed consent, demographic information forms, and de-metaling. The blindfold remained in place until the end of the experiment. Participants were then seated in front of a computer and engaged in practice runs of the task for each of the three stimulus features – again, frequency, duration, and location. These practice trials ensured task comprehension and provided us with stable ~70% to 75% accuracy performance levels for each participant prior to beginning scanning. Participants were then led into the scanner bay.

After setup in the scanner, participants completed 6 experimental runs (two for each relevant feature) while having BOLD signal data recorded. Each run had the participant responding specifically to one of the three feature types, and was comprised of 8 blocks of 16 trials each. All participants also underwent a T1 anatomical scan. Sighted participants, who were instructed to keep their eyes closed during scan tasks, had their T1 recorded after the third task run. Blindfolded participants had their T1 recorded before the task scans, in order to extend their pre-task time blindfolded.

3.2.5 IMAGE ACQUISITION

MRI scans were acquired using a Siemens Prisma 3T MRI system (Siemens Medical, Erlangen, Germany) with a 20-channel head coil. During scanning, we acquired a T1-weighted 3D MPRAGE sequence with GRAPPA R=2, FoV = 256x256mm, with 208 0.8 mm sagittal slices, 8° flip angle, TI=1060 ms, TR=2400 ms, and TE=2.24 ms. The fMRI sequence, repeated for each of the six experimental runs, used a T2*-weighted, gradient-echo (GE) echo-planar imaging (EPI) sequence with a multi-band acceleration factor of 4, a 208x208 mm field of view (FoV), and 65° flip angle. We used a TR of 1200 ms, TE=37 ms, and 60 interleaved anterior-to-posterior acquired axial slices for 280 volumes. Slice thickness=2 mm, resulting in a volume with 2x2x2 mm between voxel centers.

3.2.6 PREPROCESSING AND WHOLE-BRAIN ANALYSIS

Neuroimaging data were analyzed using the MarsBaR (http://marsbar.sourceforge.net) and Statistical Parametric Mapping 12 software (SPM12: http://www.fil.ion.ucl.ac.uk/spm/software/spm12), running via MATLAB (http://www.mathworks.com/products/matlab/). Functional imaging data were preprocessed using motion correction and slice-timing correction. The resulting mean functional image was co-registered to the T1 scan and then normalized to stereotaxic space using the unified normalization-segmentation method. This spatial normalization was then applied to the functional data, warping the size, shape and orientation of each individual's brain to standard Montreal Neurological Institute (MNI) space. The data were smoothed with an 8mm Full-Width Half-Maximum Gaussian kernel.

Statistical analyses were performed initially with MarsBaR, examining activation values elicited by the different feature tasks when compared to rest, and when compared to each other, both by group (blindfolded or sighted) and again with all participant data together after no significant group differences were noted. Activation values were generated for five separate regions of interest (ROIs) related to our hypotheses, defined in MarsBaR using the AAL anatomical atlas. These regions (with the AAL areas included in parentheses) were striate (calcarine), extrastriate (lingual, superior occipital, middle occipital, inferior occipital), dorsal (precuneus, superior parietal, inferior parietal), ventral (fusiform, inferior temporal), and auditory (heschl, superior temporal). The activation values for these ROIs were then input into the JASP statistical software package (jasp-stats.org) and ANOVAs were run to examine group and task differences. Further statistical analyses were conducted using the general linear model (GLM) as implemented in SPM12. We performed analyses in SPM on three main contrasts: spatial (location >rest; duration; pitch), time (duration >rest; location; pitch), and pitch (pitch >rest; location; duration). These analyses were first conducted with a small volume correction applied to limit the search for significantly activated voxels to occipital areas, as defined by a mask based on the AAL atlas anatomical definitions. Parametric blood oxygenation-level dependent (BOLD) activation maps were derived from linear contrasts between these conditions. First-level statistical analyses were run for each participant, followed by second-level analyses for the sighted and blindfolded groups independently. Group comparison contrasts were conducted to note any differences between the sighted and blindfolded groups in all contrasts. As with the MarsBaR activation analyses, another set of second-level contrasts were run on both groups together after no significant group differences were discerned. All analyses were initially examined with a family-wise error correction $p <$ .05 alpha criterion, and again at an uncorrected $p < .001$. Uncorrected analyses were used in order to further explore the data to ensure no interesting potential activation areas were overlooked due to lack of power/small effects.

3.2.7 SMALL VOLUME CORRECTION

Small volume correction analyses were conducted using anatomical regions derived from the AAL atlas. We selected anatomical regions to restrict the analysis to occipital regions, though some degree of proximal parietal/temporal overlap exists. Analyses were again conducted using SPM12.

3.3 RESULTS

3.3.1 BEHAVIOURAL RESULTS

As briefly mentioned above, no notable significant differences in BOLD activation were observed between sighted and blindfolded groups for any contrast or for any of the MarsBaR analyses. Similarly, no significant differences between sighted and blindfolded participants were noted in response times for correct or incorrect responses in the location, pitch, or duration conditions (all $F(23,1) < 1.137$, $p> 0.297$. However, for the location task only, there was a significant interaction effect of group * correctness ($F(1,23) = 16.271$, $p< 0.001$) wherein blindfolded participants displayed longer response times for trials they responded to incorrectly ($M = 859.5$ ms, $SD = 102.2$ ms) than did sighted participants ($M = 804.3$ ms, $SD = 86.7$ ms) when compared to the notable lack of difference in response times for trials answered correctly between blindfolded (*M* = 794.3 ms, *SD* = 86.5 ms) and sighted (*M* = 799.2 ms, *SD* = 79.6 ms) participants. We do not believe this result impacts the decision to collapse further analyses across groups, particularly as a follow-up t-test comparing the response times for incorrect trials between blindfolded and sighted participants showed no significance ($t(23) = 1.461$, $p = 0.158$).

Response accuracy similarly did not significantly differ between sighted and blindfolded participants for any of the conditions (all $F(23,1) < 0.324$, $p > 0.575$), and the staircase procedure worked as-intended. Sighted participants achieved an average accuracy of 71.6% on duration trials, 71.1% on frequency trials, and 72.6% on location trials. Blindfolded participants achieved an average accuracy of 73.2% on duration trials, 74.2% on frequency trials, and 73.4% on location trials.

Due to the overall lack of significant differences between the sighted and blindfolded groups, all analyses of interest reported below were conducted on the combined group of all 25 participants.

It should be noted that, for the localization task, all participants ended with a step size titrated at 0.66 (i.e., the maximum step size, with pan values for the four locations of -1, -0.33, 0.33, and 1). As performance accuracy remained within the target percentage, however, and accuracy for the location task was not significantly different between the task conditions, we do not feel that this impacts our comparison of the location task to the frequency and duration tasks.

3.3.2 MARSBAR ROI ANALYSES

Through MarsBaR, we created region of interest (ROI) files using the AAL anatomical atlas for five different areas of cortex relative to our hypotheses: striate (calcarine), extrastriate (lingual, superior occipital, middle occipital, inferior occipital), ventral (fusiform, inferior temporal), dorsal (precuneus, superior parietal, inferior parietal), and auditory (heschl, superior temporal). Again through MarsBaR, we determined the activation values within these ROIs relative to our fMRI data contrasts, in particular the feature > rest contrasts (L>R, F>R, D>R) and feature vs. other features contrasts (L>FD, F>LD, D>FL). ANOVAs run on the resultant contrast values showed no significant main effect of group (blindfolded or sighted) within any of these ROIs. Similarly, no significant interaction effect involving group was noted within any of these ROIs (see Table 3.1). This lack of significant group differences may be due to lack of sufficient power in our analyses, or it could simply be that the amount of time blindfolded was not sufficient to induce neural activation pattern changes between the groups.

Due to the lack of significant group differences, further analyses were conducted with the blindfolded and sighted groups combined in order to examine feature task effects. The feature vs. rest (see Figure 3.2) and feature vs. other features (see Figure 3.3) contrasts were re-run with the combined group. Through these analyses, we noted a significant effect of the feature task when compared to rest within the ventral ($F(1.571,37.693) = 13.849$, $p < .001$) and dorsal ($F(2,48) = 5.448$, $p = 0.007$) ROIs. It should be noted that, for the ventral ANOVA, Mauchly's test of sphericity indicated a violation of the assumption of sphericity (W=0.727, *p*=0.025), so a Greenhouse-Geisser correction was conducted. Post-hoc comparisons using t-test with Bonferroni correction indicated that, for the ventral ROI, the mean activation value for the location task (*M* = -0.622, *SD* = 0.652) was significantly lower than the frequency (*M* = -0.058, *SD* = 0.465, *t*(24) = -4.933, *p*< .001) and duration (*M* = -0.044, *SD* = 0.634, *t*(24) = -3.751, *p* = 0.003) task values. The frequency and duration task values did not significantly differ from one another (*t*(24) = -0.140, *p* = 1.000). For the dorsal ROI, the mean activation value for the location task (*M* = -0.023, *SD* = 0.771) was significantly higher than the frequency (*M* = -0.389, *SD* = 0.760, *t*(24) = 3.026, *p* = 0.017) and duration (*M* = -0.325, *SD* = 0.996, *t*(24) = 2.804, *p* = 0.030) task values, and the frequency and duration task values did not significantly differ from one another (*t*(24) = -0.508, *p* = 1.00).

A significant effect of the feature vs. other feature analyses was also noted for the dorsal ROI (*F*(2,48) = 5.448, *p* = 0.007), but not for the ventral ROI (*F*(2,48) = 0.158, *p* = 0.854). No other ROIs showed significant effects for either the feature task vs. rest or feature vs. other feature analyses (all *F*(2,48) < 0.792, *p*> 0.459). Post-hoc comparisons using t-test with Bonferroni correction indicated that, for the dorsal ROI, the mean value for the location > frequency and duration contrast (*M* = 0.334, *SD* = 0.478) was significantly greater than the frequency > location and duration (*M* = -0.215, *SD* = 0.555, *t*(24) = 3.026, *p* = 0.017) and duration > frequency and location (*M* = -0.119, *SD* = 0.502, *t*(24) = 2.804, *p* = 0.030) contrast values. The frequency > location and duration and duration > frequency and location values did not significantly differ from one another (*t*(24) = -0.508, *p* = 1.000).

Through the above results, we can note that the location task elicited significantly different neural activation when compared to the frequency and/or duration task(s). This activation presented as greater activation during location tasks in dorsal areas, and lesser activation during location tasks in ventral areas. To further investigate these activations, we conducted small volume corrected fMRI analyses in SPM, restricting analysis to occipital areas, and followed these up with whole brain analyses as warranted.

3.3.3 FMRI ANALYSES

Considering the results of our MarsBaR ROI analyses, our primary analyses of interest for further investigation were those contrasts comparing BOLD activation in response to the location task to that of the duration task. However, we ran contrasts to compare the activation patterns between all three feature tasks against one another (location vs. duration, location vs. frequency, frequency vs. duration) as well as each feature task vs. rest. Small volume correction analyses were initially used to investigate significant areas of occipital activation for these contrasts, with follow-up whole-brain analyses run as-warranted.

3.3.3A FEATURE VS. REST

We compared the BOLD activation for each feature task to rest, using a small volume correction to restrict the analysis to occipital areas. All comparisons were conducted with a $p< .05$ family-wise error correction. No positive activation was noted in relation to any of our three feature tasks, but region-similar negative activations were noted for each (see Tables 3.2 through 3.4).

For all feature tasks, areas of bilateral middle occipital, superior occipital, and middle temporal gyri, bilateral precuneus, left inferior temporal gyrus, and left cuneus displayed significantly lower activation than rest. The frequency and duration feature tasks further elicited decreased activation in left fusiform gyrus. The location and frequency feature tasks further elicited decreased activation in right inferior temporal gyrus and left inferior occipital gyrus, and the location task feature alone further elicited decreased activation compared to rest in right inferior occipital gyrus (see Figures 3.4 through 3.6).

3.3.3B LOCATION VS. DURATION

Comparing the activation observed for the location task to that observed for the duration task was anticipated to be our most telling contrast. For our location > duration contrast, we initially conducted small volume correction analyses, restricting the analysis volume to occipital areas as defined in the AAL brain atlas. Significant results were only returned for positive activation, showing that some occipital areas were activated more strongly in response to the location task than for the duration task, and that no occipital areas were more strongly activated in the duration task than in the location task. For the small volume corrected location > duration contrast run with an alpha criterion of .05, family-wise error corrected (see Table 3.5), we report significant activation in right middle occipital gyrus and right angular gyrus.

The location > duration small volume correction contrast was also run with an uncorrected alpha criterion of .001, again with only positive activations returned (see

Table 3.6). The areas implicated in this analysis included bilateral middle occipital and angular gyri, bilateral precuneus, left cuneus, and left inferior parietal lobule.

We further conducted whole brain analyses with a $p < .05$ family-wise error correction (see Figure 3.7 and Table 3.7) to further investigate the location > duration contrast, and noted significant positive activation in bilateral precuneus, right middle occipital gyrus, left cingulate gyrus, right angular gyrus, and left middle frontal gyrus. No significant negative activations were noted for this location > duration contrast at the .05 alpha level.

Looking at the same whole brain location > duration contrast with an uncorrected .001 alpha criterion, positive activations (see Figure 3.7 and Table 3.8) include bilateral areas of precuneus, cingulate gyrus, middle occipital gyrus, angular gyrus, inferior parietal lobule, supramarginal gyrus, middle frontal gyrus, superior frontal gyrus, middle temporal gyrus, and inferior temporal gyrus, as well as left cuneus, right superior occipital gyrus, and right superior temporal gyrus.

Negative activations for the location > duration contrast with an uncorrected .001 alpha criterion (see Table 3.9) show attention to stimulus duration, rather than location, led to increased activation in mostly frontal areas. Specifically, we observed activation in bilateral areas of inferior frontal gyrus, precentral gyrus, and supplementary motor area, along with right hemisphere sections of middle frontal gyrus, insula, and caudate, and left hemisphere sections of superior frontal gyrus and cerebellum.

3.3.3C LOCATION VS. FREQUENCY

We also compared the activation observed for the location task to that observed for the frequency task. We anticipated that this contrast would be less likely to show differences in occipital areas than the location vs. duration contrast due largely to the possibility of frequency information priming thoughts of spatial height (e.g., Rusconi et al., 2006; Chiou & Rich, 2012). Small volume correction analyses on the location > frequency contrast, limiting the scope to occipital areas, returned no significant positive or negative activations at a .05 family-wise error corrected alpha level, nor any significant negative activations at an uncorrected .001 alpha level. Positive activations at an uncorrected .001 alpha level (see Table 3.10) included right middle occipital and angular gyri.

In a follow-up whole-brain analysis for our location > frequency contrast, no significant positive or negative activation clusters were noted at a *p* < .05 family-wise error corrected alpha criterion. The whole brain location > frequency contrast run with an uncorrected alpha criterion of .001 (see Figure 3.8 and Table 3.11) showed positive activations in bilateral areas of precuneus, inferior parietal lobule, superior parietal lobule, supramarginal gyrus, middle occipital gyrus, and angular gyrus, as well as left areas of inferior temporal gyrus, middle temporal gyrus, and middle frontal gyrus.

Negative activations for the location > frequency whole brain contrast at uncorrected alpha of .001, signifying areas of greater activation during the frequency rather than location task (see Figure 3.8 and Table 3.12), included right inferior frontal gyrus and right middle frontal gyrus.

3.3.3D FREQUENCY VS. DURATION

Rounding out our contrasts, we compared the activations observed for the frequency task to that observed for the duration task. We anticipated the possibility of a somewhat similar but likely muted activation pattern for the frequency >duration contrast as seen with the location > duration contrast. For our frequency > duration contrast, using small volume correction to limit the area of examination to occipital regions, no significant positive or negative activation clusters were noted at either $p < .05$ family-wise error correction or $p < .001$ uncorrected alpha criteria. Similarly, in a follow-up whole brain analysis with a $p < .05$ family-wise error corrected alpha criterion, no significant positive or negative activation clusters were noted.

The whole brain frequency > duration contrast run with an uncorrected alpha criterion of .001 (see Figure 3.9 and Table 3.13), however, showed positive activations in bilateral cingulate gyrus, right precuneus and inferior frontal gyrus, and left middle and superior frontal gyri.

Negative activations for the frequency > duration whole brain contrast at uncorrected alpha of .001, signifying areas of greater activation during the frequency rather than duration task (see Figure 3.9 and Table 3.14), included bilateral areas of cerebellum.

3.4 DISCUSSION

In this study we investigated the likelihood of and differences in occipital activation in response to auditory stimuli in the absence of vision. Our primary hypothesis was that we would uncover evidence that occipital lobe wires in a task-based rather than modality-based fashion, with dorsal stream occipital areas activating preferentially for location-based auditory tasks.

We did note significant dorsal-stream area activations in the combined-groups data, preferentially for the auditory location task, in support of our hypothesis. Particularly of note were the results of the initial MarsBaR ROI analyses for the dorsal and ventral areas, wherein the location feature tasks elicited significantly greater activation in the dorsal areas, and significantly lower activation in the ventral areas, than did the frequency or duration feature tasks. Indeed, the frequency and duration feature tasks elicited statistically similar activation patterns in occipital areas to one another. These results are well in line with a task-based neural wiring, wherein dorsal areas are more active for spatial relation tasks, and ventral areas more active for identification tasks. As our stimuli were purely auditory, our results show strong evidence that this dorsal/ventral split is maintained in areas classically recruited for visual tasks when recruited for auditory tasks. Parietal and occipital areas, particularly occipital areas on the parieto-occipital border, were significantly recruited. This result potentially lends further support to the notion that such inter-lobe areas are more likely to be engaged for cross- or other-modal tasks, rather than for other-modal tasks to recruit brain areas classically ascribed to a given sense. However, the same activation highlights the pre-existing data streams to the recruited areas – even regularly sighted participants who simply close their eyes appear readily able to have purely auditory location information utilize these classically visual dorsal stream areas. Thus, it remains entirely plausible that lobe border area structures have a tendency to be wired for multiple sensory inputs. On the other hand, our meta-analysis results from chapter 2 clearly showed occipital V1 activation shared between blind and sighted individuals, so it seems more likely that a generally robust functional connectivity between sensory inputs and occipital lobe exists, beyond just lobe border areas.

Regardless, we do here have evidence for the retention of task-based recruitment in occipital areas when responding to spatially relevant non-visual stimuli. In particular, the consistently higher degree of activation observed in right middle occipital gyrus during location tasks falls well in line with previous research. Indeed, it has been shown that right middle occipital gyrus maintains a notable preference for spatial input, regardless of stimulus modality, in the early blind. Further, as in our results, the area was shown to be more active in sighted controls during non-visual spatial rather than non-visual non-spatial tasks (Renier et al., 2010). Middle occipital gyrus and cuneus, another occipital region implicated in our location contrasts, are both also implicated as auditory spatial processing regions in the congenitally blind, though classically considered visuospatial (Collignon, et al., 2011).

Precuneus activation also seems fairly consistent in response to our location tasks, the area being associated with visuospatial mental imagery and spatial attention (for review, see Cavanna & Trimble, 2006). As posterior cingulate cortex is strongly linked to precuneus (e.g., Fransson & Marrelec, 2008), the cingulate activation is not surprising – especially as posterior cingulate cortex is associated with spatial attention (e.g., Small et al., 2003). Similarly, the inferior parietal lobule/supramarginal gyrus/angular gyrus activations are not surprising, the areas implicated in left/right discrimination and sustained attention (e.g., Hirnstein et al., 2011; Husain & Nachev, 2007; Karhson, Mock, & Galob, 2015; Lee et al., 2013)

3.4.1 STUDY LIMITATIONS AND FUTURE DIRECTIONS

Though the initial intent was to examine differences in activation between participants who had been blindfolded for approximately 45 minutes and participants who had not, our analyses showed no significant behavioural or neural differences between the groups. Thus, we combined the sighted and blindfolded group data to more robustly investigate common patterns of activation in response to the tasks. Though unexpected, and potentially due to a lack of power, this lack of group differences nonetheless can be explained given the existing literature – some studies report discernible neural changes from blindfolding in rapid fashion (e.g., Poirier et al, 2007), whereas others may only detect small yet significant BOLD activation changes after 5 full days of blindfolding, including directed blindness training (e.g., Merabet et al., 2008). Considering the similarity in activation patterns observed between our participant groups, It is possible that our task may not have been conducive to encouraging enhanced occipital area recruitment – considering the similarity in activation patterns observed between our participant groups, it instead appears plausible that our task recruited a standard degree of occipital recruitment that could be expected from any typical sighted individual with their eyes closed. This standard recruitment possibility is given merit through studies showing that the presence of a given sense can mask or inhibit activations from another sense that would otherwise be discernible (e.g., Weaver & Stevens, 2007) – the unmasked connections hypothesis.

Further investigation along this particular line could be conducted with similar task data collected from sighted participants with their eyes open during the task.

It is also possible that our tasks simply were not difficult or long enough to elicit the anticipated occipital alteration/additional unmasking. As performance on the location task in particular was highly invariant between groups, it may be that a more robust task, possibly involving elevation changes, or focusing more heavily on location-tasks in general would be better able to elicit between group differences. It is also possible that the amount of blindfolded time simply was not enough to elicit changes beyond those that might arise with simply closed eyes, as we observed. Since sighted participants were instructed to keep their eyes closed during functional scans, this may help explain why sighted and blindfolded participants showed similar performance and activation. Further, the only practice either group received on the tasks was a single run for each feature (frequency, duration, and location). More directed/lengthy training/practice, particularly on the location task, may well have helped elicit differences in neural recruitment between the groups. It is plausible that, with longer blindfolding time, a more robust location-based task, and longer, more directed location-task practice, significant group differences and perhaps further occipital recruitment may be observed.

Limitations aside, whereas engagement with our location-based auditory task did preferentially elicit dorsal stream occipital activations, a future investigation into more ventral-stream relative tasks would shed more light on the extent of occipital lobe’s task-based delineations. Just as more robust location-based tasks may elicit further dorsal occipital recruitment, a robustly engaging identification task may well elicit the same in ventral areas, rounding out the classic double dissociation.

3.5 CONCLUSIONS

All told, though these data cannot directly address the question of how and when more robust non-visual functional connections are formed in the occipital lobe, they do provide further compelling evidence that the occipital lobe is indeed wired in a task-based fashion that is more modality-agnostic than previously believed.

Table 3.1. Results of the group ANOVAs.

Feature vs. Rest contrasts

ROI	Within/Between		*F*	df	*p*
Striate	Within	Feature * Group	0.284	(2,46)	0.754
	Between	Group	0.557	(1,23)	0.463
Extrastriate	Within	Feature * Group	0.698	(2,46)	0.503
	Between	Group	0.389	(1,23)	0.539
Ventral	Within	Feature * Group	1.140	(1.57,36.15)	0.320
	Between	Group	0.013	(1,23)	0.911
Dorsal	Within	Feature * Group	0.056	(2,46)	0.946
	Between	Group	0.766	(1,23)	0.390
Auditory	Within	Feature * Group	0.129	(2,46)	0.880
	Between	Group	1.737	(1,23)	0.200

Feature vs. Other Feature Contrasts

ROI	Within/Between		*F*	df	*p*
Striate	Within	Contrast * Group	0.284	(2,46)	0.754
	Between	Group	-0.056	(1,23)	1.000
Extrastriate	Within	Contrast * Group	0.698	(2,46)	0.503
	Between	Group	0.006	(1,23)	0.938
Ventral	Within	Contrast * Group	0.970	(2,46)	0.387
	Between	Group	-4.5e-5	(1,23)	1.000
Dorsal	Within	Contrast * Group	0.056	(2,46)	0.946
	Between	Group	-0.044	(1,23)	1.000
Auditory	Within	Contrast * Group	0.129	(2,46)	0.880
	Between	Group	-0.007	(1,23)	1.000

Table 3.2. Location > Rest occipital SVC analysis results, *p* < .05 FWE, negative activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates				Peak *p* (FWE)
		X	Y	Z	*t*(23)	
530	Middle Occipital, Superior Occipital,	36	-85	31	11.29	< .001
--	Inferior Occipital, Middle Temporal,	24	-85	40	10.44	< .001
--	and Inferior Temporal Gyri	45	-79	25	9.11	< .001
575	Middle Occipital, Superior Occipital,	-39	-88	19	11.07	< .001
--	Inferior Occipital, Middle Temporal,	-42	-76	28	9.26	< .001
--	and Inferior Temporal Gyri	-18	-88	37	8.29	< .001
37	Cuneus and Precuneus	-9	-61	25	9.98	< .001
15	Precuneus	-6	-61	19	8.47	< .001
--	--	-15	-64	19	6.49	0.002
17	Precuneus	15	-61	25	7.49	< .001

Table 3.3. Frequency > Rest occipital SVC analysis results, *p* < .05 FWE, negative activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates			*t*(23)	Peak *p* (FWE)
		X	Y	Z		
564	Middle Occipital, Superior Occipital,	-45	-79	28	13.88	< .001
--	Inferior Occipital, Inferior Temporal,	-42	-67	25	10.08	< .001
--	and Middle Temporal Gyri	-39	-76	40	8.33	< .001
329	Middle Occipital,	48	-76	25	11.74	< .001
--	Superior Occipital, and	42	-82	28	10.77	< .001
--	Middle Temporal Gyri	33	-85	34	11.42	< .001
90	L Cuneus,	-6	-61	28	10.04	< .001
--	Bilateral Precuneus	12	-61	25	8.81	< .001
20	Precuneus	-6	-61	19	8.52	< .001
--	--	-15	-64	19	7.70	< .001
11	Fusiform Gyrus	-36	-43	-14	6.54	< .001
--	--	-27	-49	-14	5.59	0.013
14	Inferior Temporal Gyrus	51	-70	-8	6.42	0.003

Table 3.4. Duration > Rest occipital SVC analysis results, *p* < .05 FWE, negative activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates			*t*(23)	Peak *p* (FWE)
		X	Y	Z		
386	Middle Occipital,	-45	-79	28	13.88	< .001
--	Superior Occipital, and	-42	-67	25	10.08	< .001
--	Middle Temporal Gyri	-33	-82	40	8.33	< .001
96	L Cuneus,	-6	-64	25	11.74	< .001
--	Bilateral Precuneus	15	-61	25	10.77	< .001
361	Middle Occipital,	48	-76	25	11.42	< .001
--	Superior Occipital, and	48	-67	25	10.04	< .001
--	Middle Temporal Gyri	24	-85	40	8.81	< .001
19	Precuneus	-6	-61	19	8.52	< .001
50	Fusiform and	-33	-46	-11	7.70	< .001
--	Inferior Temporal Gyri	-39	-52	-14	6.54	0.002
--	--	-54	-61	-8	5.59	0.012
13	Middle Temporal Gyrus	-57	-70	1	6.42	0.002
--	--	-51	-79	4	5.27	0.023

Table 3.5. Location > Duration occipital SVC analysis results, *p* < .05 FWE, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (FWE)
31	Middle Occipital Gyrus	45	-73	31	6.67	0.002
--	Angular Gyrus	39	-79	37	6.16	0.005

Table 3.6. Location > Duration occipital SVC analysis results, *p* < .001 uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (uncorr.)
77	Mid./Sup. Occipital Gyrus	45	-73	31	6.67	< .001
--	Angular Gyrus	39	-79	37	6.16	< .001
12	Cuneus, Precuneus	-12	-61	28	5.03	< .001
46	Mid. Occipital Gyrus	-42	-67	25	4.22	< .001
--	Angular Gyrus	-39	-79	31	4.16	< .001
--	Inf. Parietal Lobule	-33	-67	37	3.84	< .001

Table 3.7. Location > Duration whole brain analysis results, *p* < .05 FWE, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates				Peak *p* (FWE)
		X	Y	Z	*t*(23)	
261	Precuneus (Bilateral)	9	-49	43	8.89	< .001
--	Cingulate Gyrus (Left)	-6	-40	43	8.6	< .001
--	--	-3	-70	46	7.38	0.003
23	Middle Frontal Gyrus	-30	29	40	7.8	0.001
24	Middle Occipital Gyrus	45	-73	31	6.67	0.010
--	Angular Gyrus	39	-79	37	6.16	0.028

Table 3.8. Location > Duration whole brain analysis results, $p < .001$ uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates			$t(23)$	Peak p (uncorr.)
		X	Y	Z		
1806	Bilateral: Precuneus, Cingulate Gyrus	9	-49	43	8.89	< .001
--	L: Cuneus, Mid. Occipital Gyrus	-6	-40	43	8.6	< .001
--	L: Angular Gyrus, Mid. Temporal Gyrus	-3	-70	46	7.38	< .001
173	Mid. Frontal Gyrus	-30	29	40	7.8	< .001
--	Sup. Frontal Gyrus	-24	41	40	6.55	< .001
--	--	-24	47	28	3.88	< .001
507	Angular Gyrus, Supramarginal Gyrus, Mid./Sup. Occipital Gyrus, Inf. Parietal Lobule, Inf./Sup. Temporal Gyrus	45	-73	31	6.67	< .001
--		51	-49	28	6.39	< .001
--		39	-79	37	6.16	< .001
104	Mid./Sup. Frontal Gyrus	27	29	46	6.19	< .001
31	Supramarginal Gyrus, Inf. Parietal Lobule	-63	-37	40	4.61	< .001
26	Bilateral Cingulate Gyrus	0	23	13	4.56	< .001
--	--	0	20	22	4.03	< .001
12	Mid./Sup. Frontal Gyrus	27	8	49	4.56	< .001
46	Mid. Temporal Gyrus	-60	-61	-5	4.42	< .001
--	Inf. Temporal Gyrus	-57	-52	-2	4.21	< .001

Table 3.9. Location > Duration whole brain analysis results, *p* < .001 uncorrected, negative activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (uncorr.)
161	Inf. Frontal Gyrus	54	11	22	5.41	< .001
--	Precentral Gyrus	54	11	4	4.56	< .001
47	Inf. Frontal Gyrus, Precentral Gyrus	-45	11	22	4.7	< .001
14	Inf. Frontal Gyrus	-39	29	4	4.64	< .001
20	Cerebellum	-3	-79	-23	4.49	< .001
11	Caudate	12	2	19	4.2	< .001
22	Sup. Frontal Gyrus	-6	23	46	4.13	< .001
--	Bilateral Supplementary Motor Area	--	--	--	--	--
25	Bilateral Supplementary Motor Area	3	8	61	4.12	< .001
18	Mid./Inf. Frontal Gyrus	45	41	16	4.05	< .001
18	Insula	30	23	1	3.98	< .001

Table 3.10. Location > Frequency occipital SVC analysis results, *p* < .001 uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (uncorr.)
18	Mid. Occipital Gyrus, Angular Gyrus	42	-73	34	4.53	< .001

Table 3.11. Location > Frequency whole brain analysis results, *p* < .001 uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (uncorr.)
87	Inf. Parietal Lobule	-33	-43	43	5.76	< .001
580	Bilateral Precuneus	-9	-67	55	5.74	< .001
--	Bilateral Superior Parietal Lobule	3	-55	49	5.24	< .001
--	--	9	-61	64	4.13	< .001
26	Supramarginal Gyrus/Inf. Parietal Lobule	54	-34	34	4.55	< .001
29	Mid. Occipital Gyrus, Angular Gyrus	42	-73	34	4.53	< .001
21	Mid. Frontal Gyrus	-33	32	37	4.24	< .001
53	Inf. Parietal Lobule/Supramarginal Gyrus	-60	-37	37	4.24	< .001
19	Mid. Temporal Gyrus	-60	-61	-8	4.18	< .001
--	Inf. Temporal Gyrus	-54	-58	-2	4.1	< .001
27	Mid. Frontal Gyrus	-30	2	52	4.18	< .001
10	Mid. Occipital Gyrus, Angular Gyrus	-33	-67	37	4	< .001

Table 3.12. Location > Frequency whole brain analysis results, *p* < .001 uncorrected, negative activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (uncorr.)
47	Inf. Frontal Gyrus	42	11	22	5.29	< .001
44	Inf. Frontal Gyrus	51	38	4	4.11	< .001
--	Mid. Frontal Gyrus	42	29	13	3.72	0.001

Table 3.13. Frequency > Duration whole brain analysis results, $p < .001$ uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	*t*(23)	Peak *p* (FWE)
15	Inf. Frontal Gyrus	21	14	-17	5.16	< .001
53	Sup. Frontal Gyrus	-15	47	34	4.47	< .001
--	Mid. Frontal Gyrus	-24	32	40	3.83	< .001
61	Bilateral Cingulate Gyrus	3	-40	40	4.04	< .001
--	Right Precuneus	3	-31	40	4.01	< .001
--	--	3	-40	31	3.79	< .001

Table 3.14. Frequency > Duration whole brain analysis results, $p < .001$ uncorrected, positive activations.

Size (Voxels)	Structures Within Cluster	Peak MNI Coordinates X	Y	Z	$t(23)$	Peak p (FWE)
33	Cerebellum	-27	-64	-29	4.57	< .001
--	--	-39	-58	-32	3.84	< .001
--	--	-27	-49	-32	3.82	< .001
15	Cerebellum	42	-58	-32	4.32	< .001

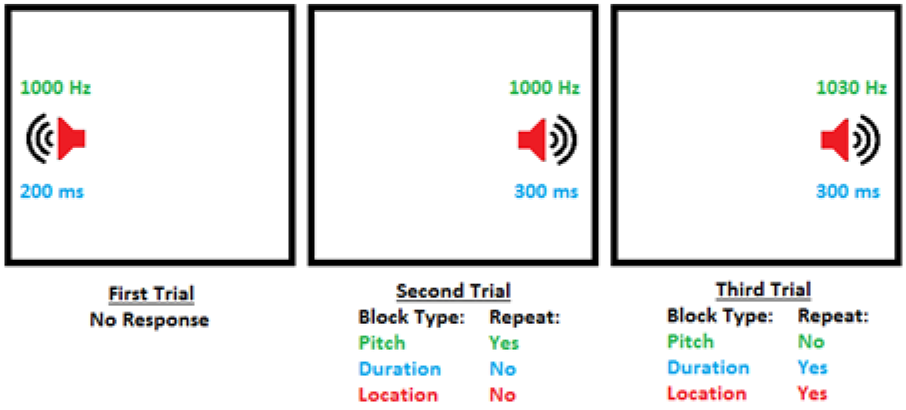

Figure 3.1. Example of correct trial responses by run type.

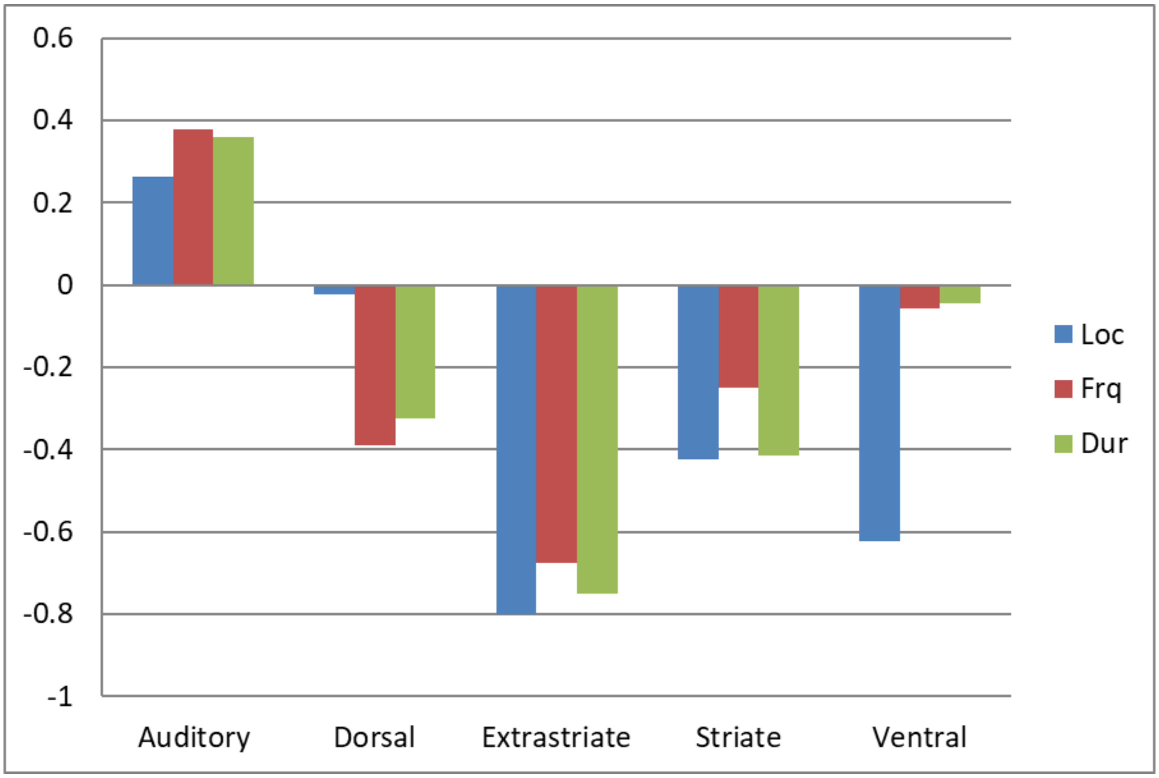

Figure 3.2. Average ROI activation values for feature vs. rest contrasts.

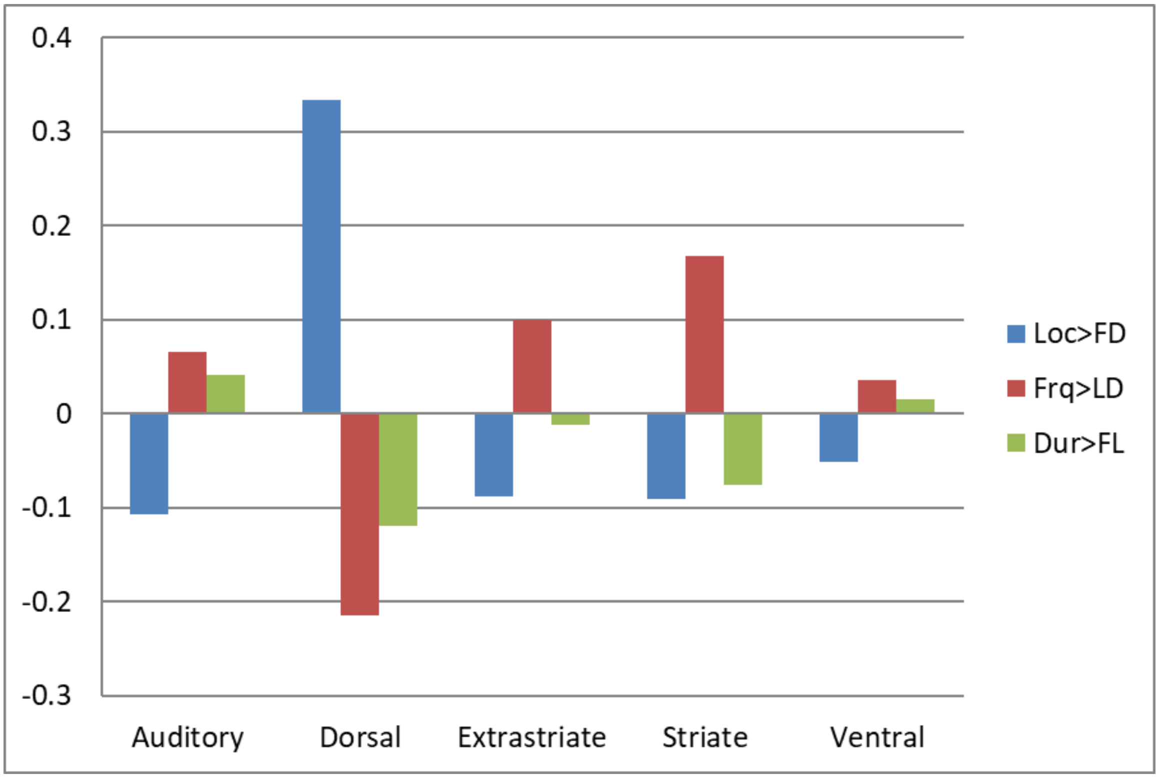

Figure 3.3. Average ROI activation values for feature vs. other features contrasts.

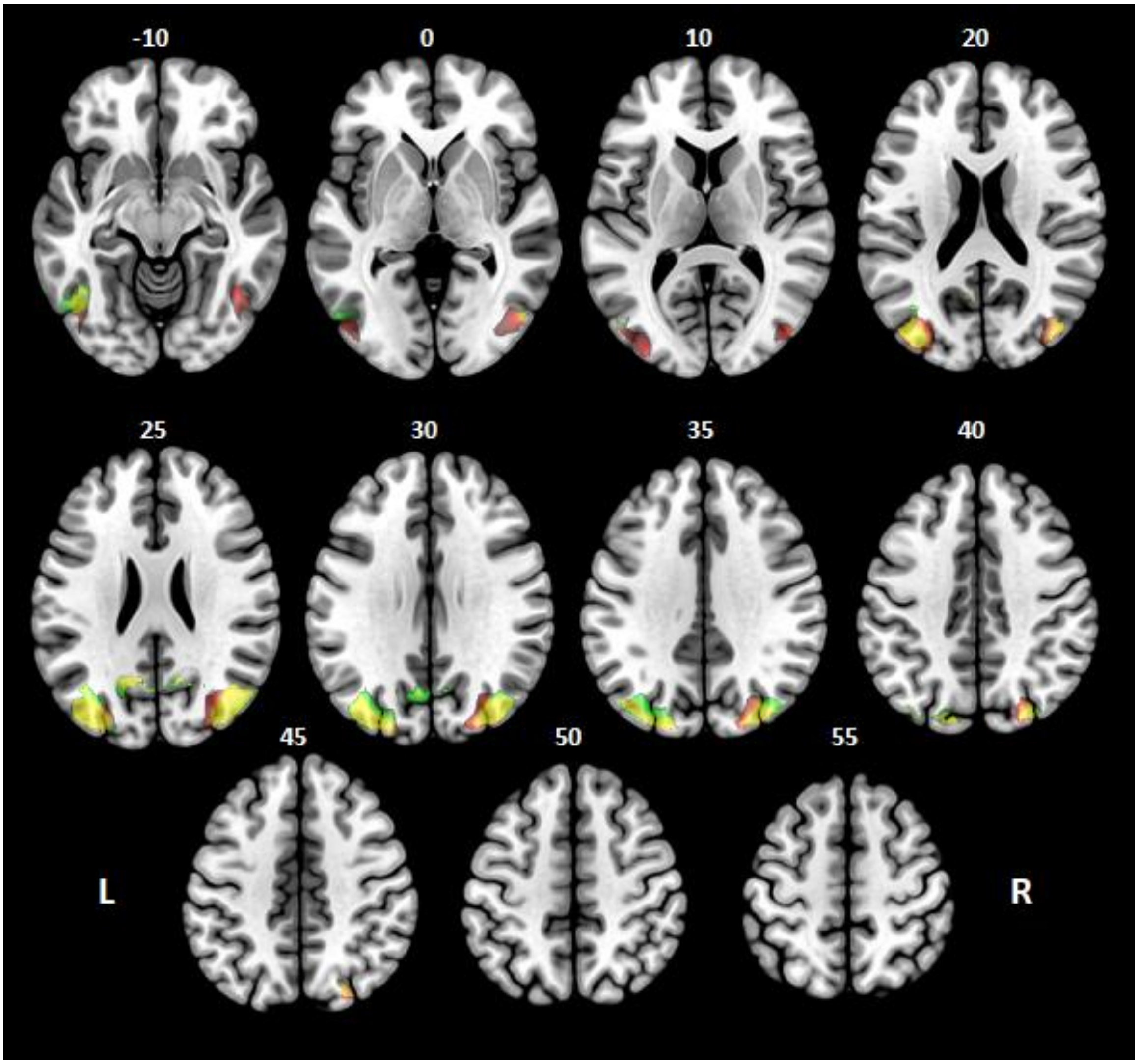

Figure 3.4. Negative occipital activation for the location feature > rest (red) and frequency feature > rest (green) contrasts significant at the *p* < .05 FWE correction threshold under small volume correction with an inclusive occipital mask. Overlapping areas are displayed in yellow. All images displayed in neurological convention (left = left).

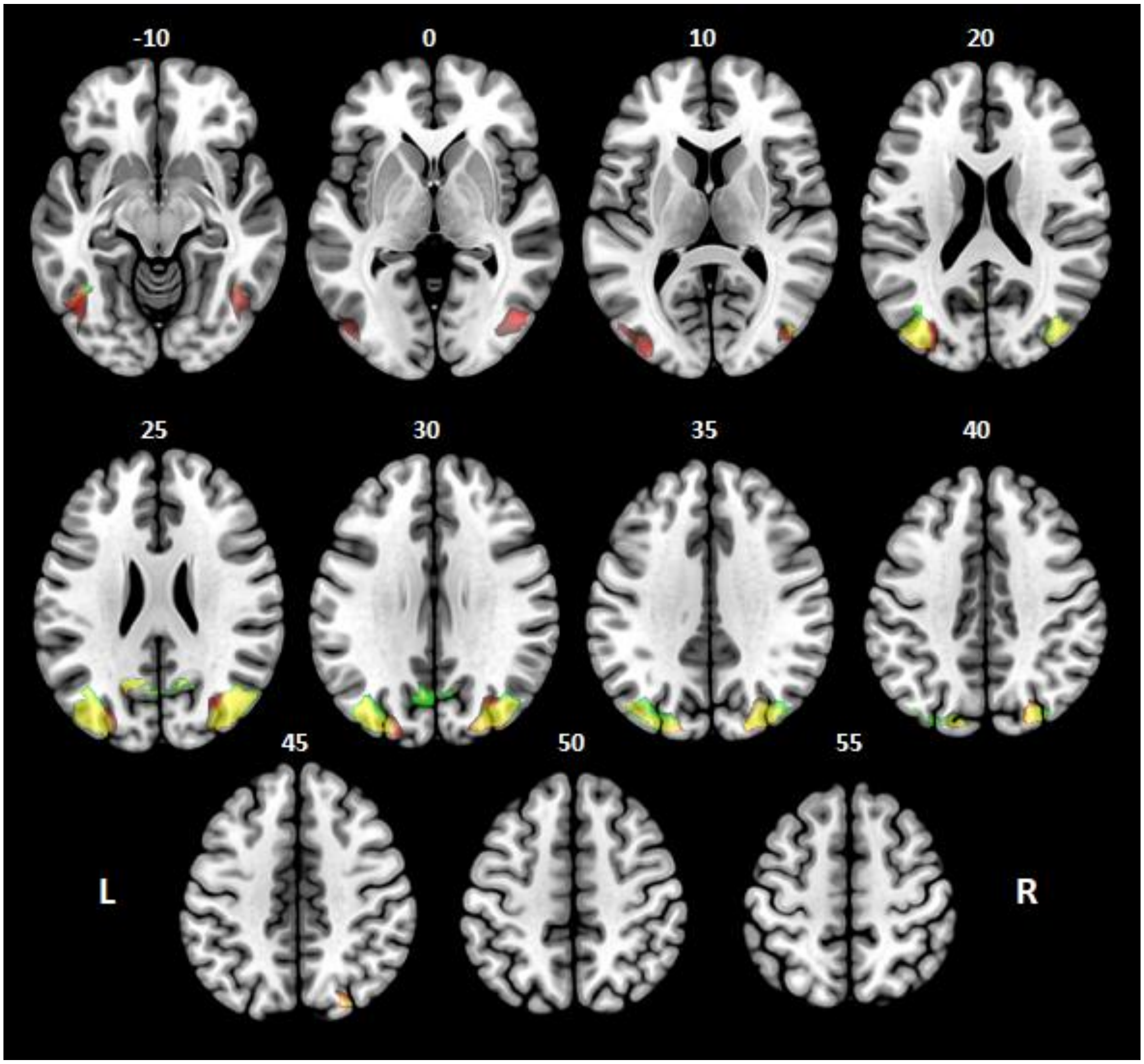

Figure 3.5. Negative occipital activation for the location feature > rest (red) and duration feature > rest (green) contrasts significant at the $p < .05$ FWE correction threshold under small volume correction with an inclusive occipital mask. Overlapping areas are displayed in yellow. All images displayed in neurological convention (left = left).

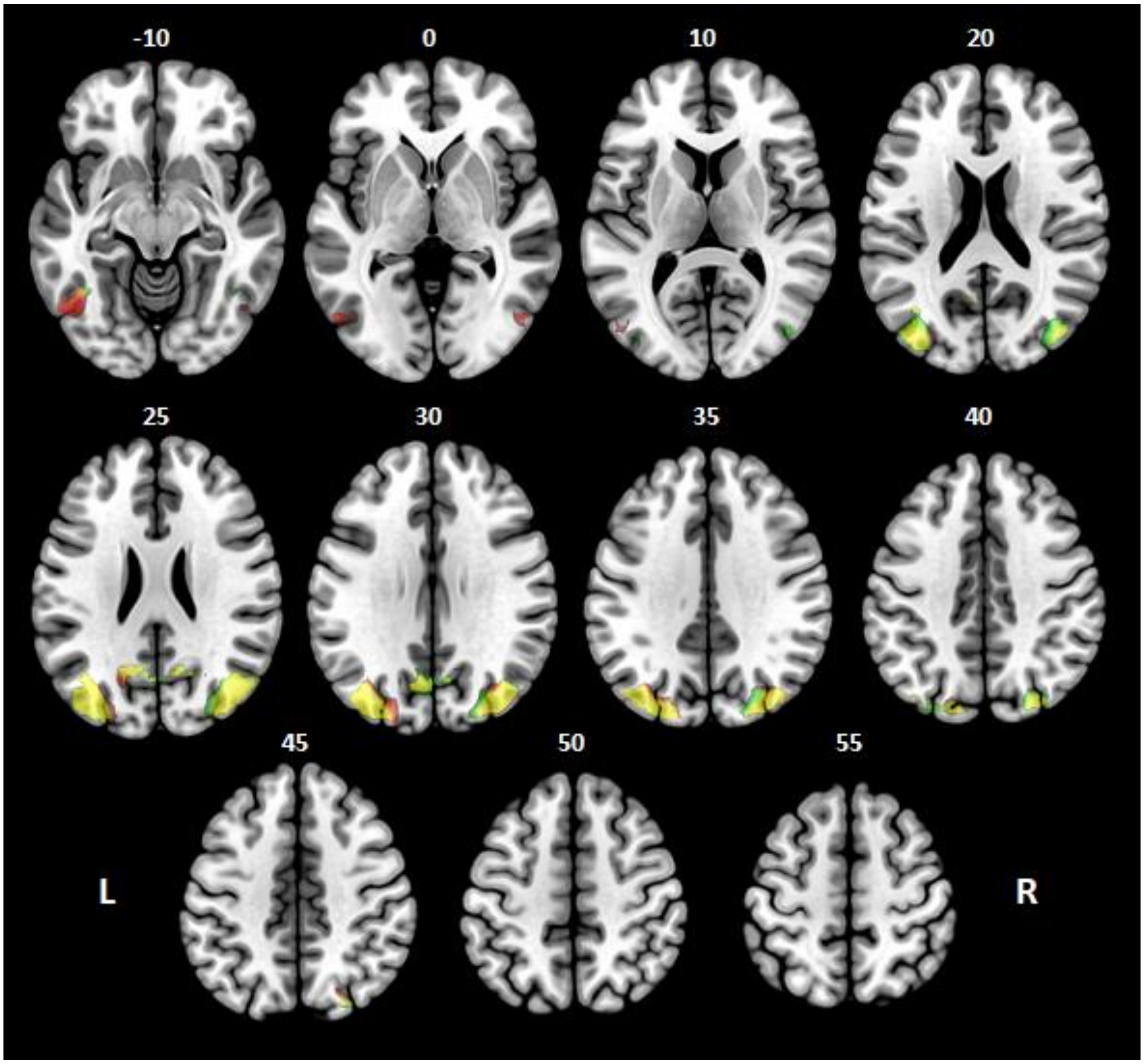

Figure 3.6. Negative occipital activation for the frequency feature > rest (red) and duration feature > rest (green) contrasts significant at the $p < .05$ FWE correction threshold under small volume correction with an inclusive occipital mask. Overlapping areas are displayed in yellow. All images displayed in neurological convention (left = left).

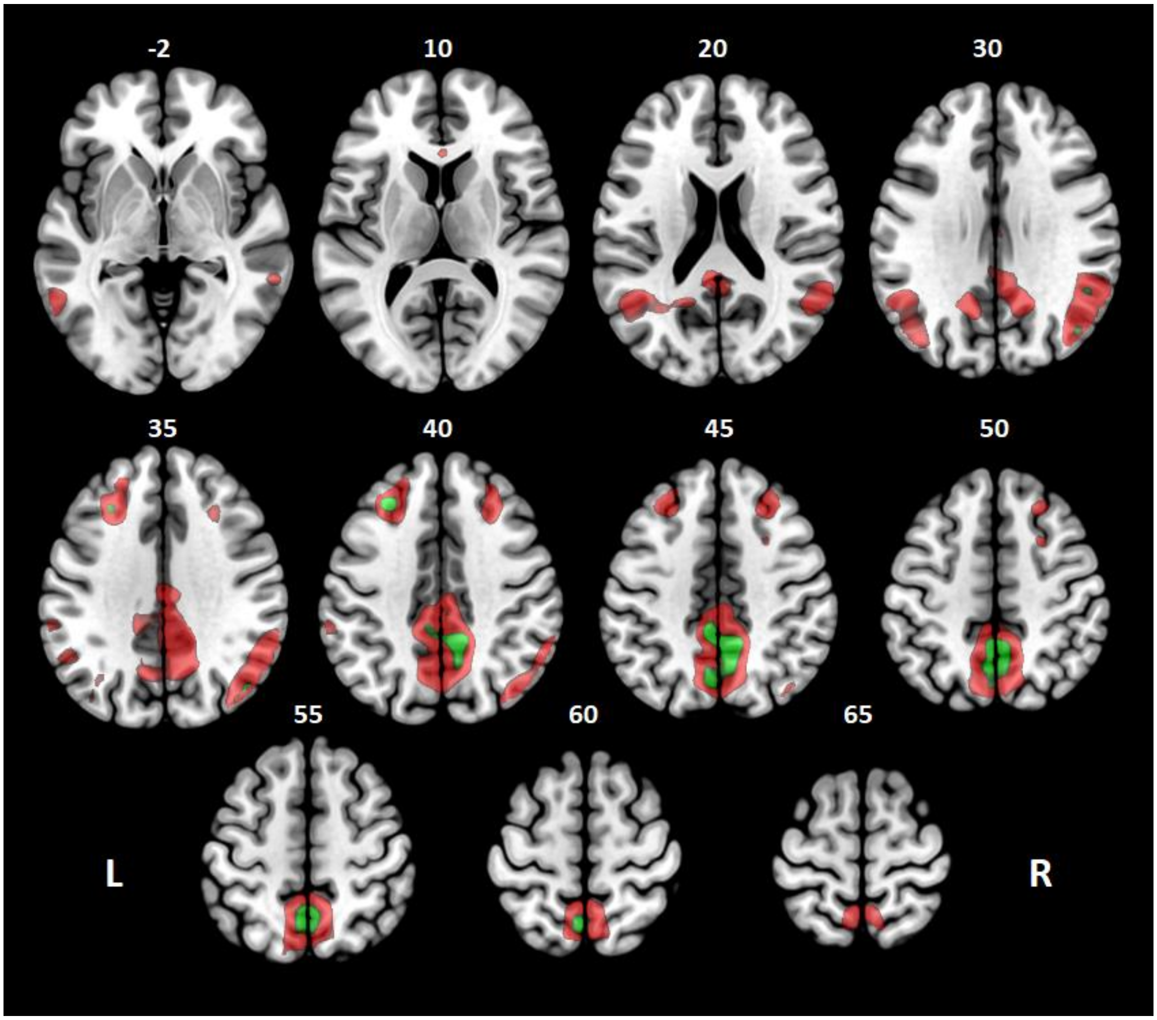

Figure 3.7. Positive whole-brain activation for the location > duration contrast. Clusters shown in green are significant at the 0.05 alpha level under family-wise error correction. Clusters shown in red are significant at the 0.001 uncorrected alpha level. Numbers represent the axial location of the slice in millimeters.

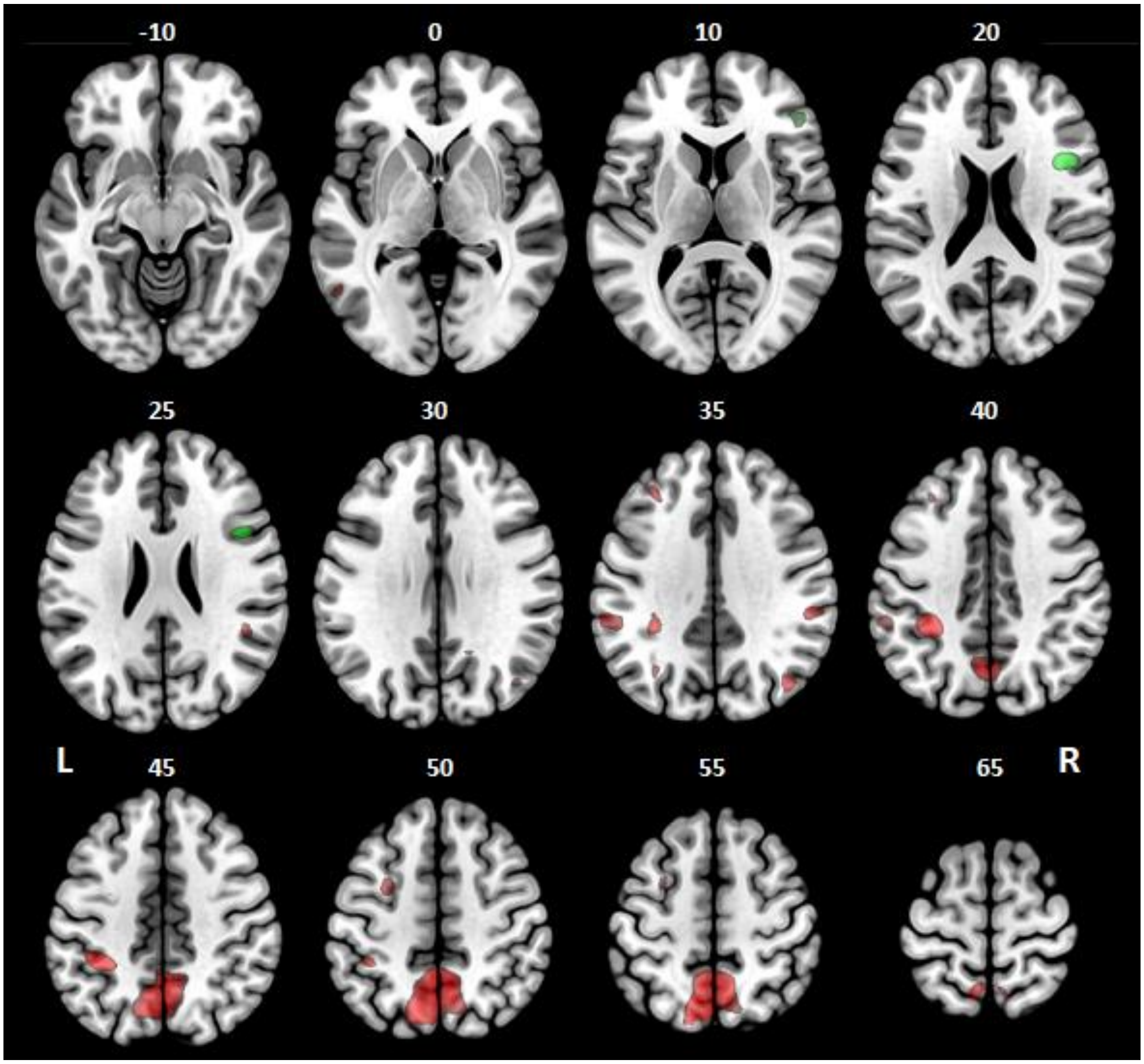

Figure 3.8. Whole-brain activation for the location > frequency contrast at the 0.001 uncorrected alpha level. Positive activation clusters are shown in red, and negative activation clusters are shown in green. Numbers represent the axial location of the slice in millimeters.

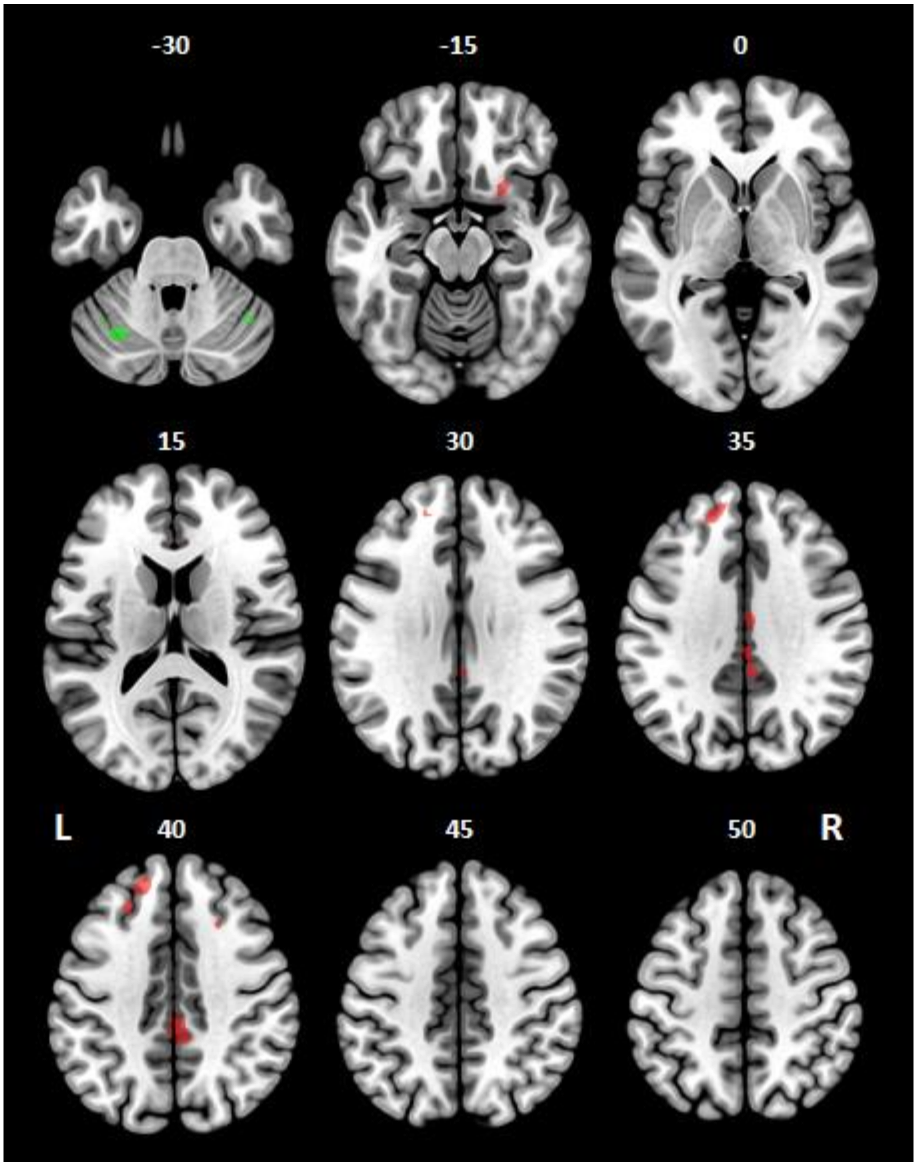

Figure 3.9. Whole-brain activation for the frequency > duration contrast at the 0.001 uncorrected alpha level. Positive activation clusters are shown in red, and negative activation clusters are shown in green. Numbers represent the axial location of the slice in millimeters.

CHAPTER 4

OVERALL CONCLUSIONS

In this dissertation, we set out to investigate occipital lobe function – in particular, whether this classically-visually-ascribed area was actually a modality-agnostic, task-specific neural area as opposed to being essentially unimodal in nature. Our secondary item of interest was to ascertain whether the robust occipital activation seen in late-blind individuals is likely to, at least initially, stem from typically-active connections in occipital regions that are utilized by the typically sighted in spatially-relevant, non-visual analyses.

Through our investigations, we have provided evidence in support of both of these notions. Regarding the occipital lobe being modality agnostic, we initially related information from previous studies showing the existence of connections between primary sensory cortical areas in the typically developing brain, as well as multi-modal effects supporting the utility of said connections. We further related evidence of strong recruitment of occipital areas for non-visual processing in the blind, and rapid recruitment of occipital areas for non-visual processing in typically sighted individuals whose vision is experimentally inhibited. Our review of the literature further provided evidence supporting the notion of occipital areas retaining the typical what/where ventral/dorsal pathway split cross-modally, and that this task-type dissociation even arises in the congenitally blind – without the influence of vision.

We then conducted a series of meta-analyses in order to more quantitatively investigate the existing data in relation to our hypotheses. Through this, we uncovered evidence of both unique occipital recruitment for non-visual stimuli in the blind, as well as evidence of common occipital recruitment for non-visual stimuli shared across both blind and typically sighted individuals. This evidence strongly reiterates the notion of existing neural connections between sensory areas, as well as the active functionality of these connections. Further, though indirectly, this evidence lends support to the idea that these same pre-extant connections would be initially capitalized on if vision were lost later in life, allowing for rapid expansion of the occipital lobe's role in processing non-visual stimuli. Whereas our meta-analyses also showed some support for task-based wiring in the occipital lobe in response to non-visual stimulus processing, the low number of studies available for the related analyses limited our ability to more confidently address that issue. However, as our own fMRI study provided some evidence of task-based wiring, we feel that as more studies become available for inclusion in the localization and identification specific meta-analyses, the general results will more clearly indicate the double-dissociation between these task types for non-visual processing as we've come to expect from visual tasks.

Lastly, we conducted a novel fMRI study, examining the occipital response of blindfolded and typically sighted individuals to auditory stimuli that varied in response to perceived location, auditory frequency, and duration of presentation. Neural activation was recorded while participants engaged in 1-back tasks while focusing their attention on one of the three shifting stimulus features, allowing us to compare occipital activation patterns in response to the feature-based tasks' purely auditory stimuli. Though we did not note any statistically significant group differences between the blindfolded and sighted group participants, our analyses on the combined participant data revealed strong evidence of task-based recruitment in the occipital lobe in response to auditory stimulus processing. Specifically, the location discrimination task elicited significantly greater activation (or less inhibition, considering all observed occipital activation for our tasks was negative when compared to rest) in the occipito-parietal dorsal/where pathway than did the frequency or duration tasks. As the location task was the only task of the three that was truly spatially relevant, this unique utilization of the dorsal stream fits with the notion of spatial processing recruiting similar pathways regardless of the modality the spatially relevant stimulation originates from. As the participants involved either simply had their eyes closed or were blindfolded for less than an hour prior to the start of our experiment, this investigation also provided further evidence of the rapid availability of occipital processing for non-visual stimuli, highlighting again the utility of the low-level connections between sensory modalities and implicating them as likely sources of initial adaptation of occipital areas in the case of visual interruption.

A further item of interest that can be examined with our data is that of V1 activation to non-visual tasks. There does not appear to be a consensus across existing studies as to whether V1 activation of this sort should be expected, and our own fMRI study shows a lack thereof. However, considering the meta-analysis results, we can note that whereas the blind > sighted contrast did not display V1 activation, the conjunction contrast did. This suggests that even sighted individuals, given the right task, will utilize V1 in response to non-visual input processing. From this observation we can further postulate that the lack of V1 activation in some studies reporting blind > sighted contrasts may well be due to an unexpectedly higher degree of V1 activity in the sighted group due to latent low-level sensory connections. This activation would make it more difficult to note additional activation in the area in blind participants, and may be a contributing factor, beyond the limitations previously noted, to the lack of differences we observed between our blindfolded and sighted-eyes-closed participant groups in our fMRI study.

Though our investigations are not without their limitations – the meta-analyses for task-based recruitment require more available studies to allow for stronger claims, and our fMRI experiment would benefit from extension regarding improvements to help elicit differences between blindfolded and sighted participants, as well as the inclusion of a robust ventral/what pathway identification task – we believe the case has nonetheless been made that the occipital lobe is not a unimodal area. Instead, it does indeed appear to be a plastic, multi-modally reactive area with specifically-wired task-based processing pathways.

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