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"The role of perceptual consolidation in auditory perceptual processing and cognition"

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The Role of Perceptual Consolidation in Auditory Perceptual Processing and Cognition

Masters Thesis

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Abbreviations

AB	Attentional Blink
ABRM	Auditory Backward Recognition Mask
ACC	Anterior Cingulate Gyrus
ANOVA	Analysis of Variance
ASRM	Auditory Simultaneous Mask
AUC	Area Under the Curve
BMI	Backward Mask Intensity
BOLD	Blood Oxygen Level Dependent
CC	Cingulate Cortex
CMP	Cross-modal Plasticity
DLPFC	Dorsolateral Prefrontal Cortex
DTI	Diffusion Tensor Imaging
EB	Early Blind
EPI BOLD	Echo-Planar Imaging Blood Oxygen Level Dependent
FA	Flip Angle
fMRI	functional Magnetic Resonance Imaging
FOV	Field of View
GLM	General Linear Model
ISI	Inter-stimulus Interval
IPL	Inferior Parietal Lobule
IPS	Intraparietal Sulcus
LB	Late Blind
MOD	Mask Onset Delay
ms	Millisecond
NT	No Trial
PCC	Posterior Cingulate Cortex
PET	Positron Emission Tomography
PFC	Prefrontal Cortex
PPL	Posterior Parietal Lobe
ROI	Region of Interest
RSVP	Rapid Serial Visual Presentation
SC	Sighted Counterpart
SOA	Stimulus Onset Asynchrony
SPL	Superior Parietal Lobule
STG	Superior Temporal Gyrus
STM	Short-term Memory
TE	Echo Time
TOJ	Temporal Order Judgment
TR	Time of Repetition
TST	Tone Span Task
T1/ T2	First Target, Second Target
VFC	Ventral Frontal Cortex
V1	Primary Visual cortex

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Abstract

In the auditory information-processing stream, sound is first transduced into pre-perceptual sensory traces. Over time, analysis of the sensory traces leads to perceptual recognition of the original stimulus event. The process of integrating pre-perceptual sensory traces into a perceptual representation for use in cognition is *perceptual consolidation.* Early blind (EB) individuals, who were born blind or became blind before 2 years of age, show faster perceptual consolidation and enhanced auditory memory abilities when compared to sighted counterparts (SC) and late onset blind individuals (LB; lost vision after visual maturity). Previous work has suggested that the faster perceptual consolidation process may be a mechanism that increases auditory perceptual abilities in the EB. This thesis examined whether a relationship exists between perceptual consolidation and auditory memory, and whether the perceptual consolidation process could be improved with training in the SC and LB. Additionally, this thesis characterized the changes in functional brain activity that accompanied improvements in perceptual consolidation speed.

The results reveal a novel relationship between the speed of perceptual consolidation and auditory short-term memory (STM) capacity. Individuals who demonstrated a fast rate of perceptual consolidation on an auditory backward recognition mask (ABRM) task had a large auditory STM capacity on a tone span task (TST). Furthermore, perceptual consolidation was improved after five days of training in both SC and LB individuals. Performance gains in the LB were similar to the SC, and reached an asymptote similar to that of non-trained EB who performed the same task. If perceptual consolidation is correlated with STM capacity, improving perceptual consolidation may increase STM capacity. This thesis examined the degree to which perceptual consolidation training would generalize to increase STM capacity, and found that generalization did not consistently increase STM capacity.

This thesis used functional magnetic resonance imaging (fMRI) to demonstrate that decreases in the volume of functional brain activity accompanied improvements in ABRM performance after training. Conditions were devised to examine brain activity related to task difficulty and brain activity related to sensory stimulation. A reduction in the overall volume of activity was observed in the same regions of interest (ROI) in both SC and LB groups. When pre- and post-training activity was overlaid on one another, common fronto-parietal brain regions were active when task difficulty was held constant. However, there was no such overlap when task difficulty was not held constant. This suggests that the activity of fronto-parietal areas, associated with attention and cognition, is related to the degree of attention required to perform a task at a certain level of difficulty.

Cross-modal plasticity (CMP) has been associated with superior sensory perceptual processing and memory abilities in the EB. The question of whether the LB demonstrate CMP during non-visual tasks is a matter of debate. Functional MRI results from this thesis demonstrated that CMP was not observed in the LB before or after auditory training. LB subjects showed patterns of brain activity more similar to SC than the EB. Since CMP was not observed in the brain of our LB subjects and their behavioral performance did not reach the level of the EB, our results indirectly support a functional role for CMP in the EB.

Chapter 1: General Introduction

Efficient sequential processing of information in audition is critical to perceive, identify, and recognize an auditory event. Unlike vision in which eye fixation can keep available the spatial information required for perception, auditory input changes over time and the information may not remain available (Massaro, 1972, a). Spectral-temporal organization must be preserved in order to retain the identity of each stimulus (Winkler & Näätänen, 1992, Näätänen & Winkler, 1999). Thus accurate auditory recognition relies on swift and organized processing to avoid interference from subsequent stimuli. Information-processing models have proposed a two-stage hierarchy in which sensory information is first transduced into a large-capacity system, and then certain information is selected for further analysis within a small-capacity system (Broadbent, 1958; Näätänen, 1988; Chun & Potter, 1995). In the auditory information-processing stream, a stimulus is first transduced into sensory traces that are held in a pre-perceptual store. The analysis of the sensory traces occurs over time and leads to perception of the original stimulus event (Kallman & Massaro, 1983).

The integration of pre-perceptual sensory traces into a durable perceptual representation for use in cognition has been termed *perceptual consolidation* (Stevens & Weaver, 2005; Kohout & Stevens, 2006). When perceptual consolidation is disrupted, sensory traces are not transformed into a perceptual representation. A fast perceptual consolidation process ensures auditory representations will be protected from being disrupted by subsequent auditory stimuli. Thus, representations could reach cognitive mechanisms such as STM faster and be used to direct behavior. Certain populations show enhancements in auditory capabilities. EB individuals show faster perceptual consolidation rates (Stevens & Weaver, 2005) and better cognitive abilities such as auditory STM (Röder et al., 2001) compared SC and LB individuals. It is not known whether SC or LB individuals may be able to acquire enhanced auditory processing and cognitive abilities indicative of the EB. Understanding the mechanisms that underlie enhanced auditory perceptual abilities could be applied to populations that don't show these advantages.

The first aim of this thesis was to determine if a relationship exists between perceptual consolidation rate and STM capacity. We hypothesized that faster perceptual consolidation would lead to more stimulus representations in memory and a greater STM capacity. The second aim was to examine whether training could increase perceptual consolidation rate in SC and LB individuals. We hypothesized that both groups would show increased perceptual consolidation rates with five days of training. Finally, fMRI was used to characterize the training-related changes in brain activity associated with training on the ABRM task. As the training literature in SC is mixed and no study has trained LB subjects on an auditory task before, we did not draw any *a priori* hypotheses about the pattern of change in brain activity after training. Identifying potential changes in functional brain activity associated with training could be used to devise training tasks that increase auditory processing and perceptual abilities in sighted individuals with language dysfunction, as well as for LB individuals who become more dependent on the auditory system.

Speed of auditory information processing

ABRM tasks have been used to examine the time course of auditory perceptual processing (Massaro, 1972, a). Subjects first learn to differentiate between two tones that were of just noticeable difference in frequency (e.g. 770 and 870 Hz; duration 20 ms). The original design of an ABRM trial consists of one of the tones (test stimulus) followed by a masking stimulus at variable silent intervals (Massaro, 1970, 1975). The mask stimulus is usually the same frequency of the test stimulus and played at the same intensity. The goal is to determine which of the two learned tones was played. Recognition performance is asymptotic when the tones are presented alone. However, when presented simultaneously with the mask stimulus, recognition performance is at chance level (i.e. 50/50). The masking stimulus can be presented at various mask onset delays (MOD) after the offset of the test stimulus. The MOD at which the mask no longer disrupts recognition of the test tone can be considered the time required for auditory stimuli to reach a stable perceptual state. Auditory perception requires the integration of different stimulus elements (frequency, duration, etc.) into a perceptual representation, which has been termed perceptual consolidation (Stevens & Weaver, 2005). The time for the perceptual consolidation process varies between individuals, but does not seem to exceed 250 milliseconds (ms) (Massaro, 1972, a; Kallman & Morris, 1984; Stevens & Weaver, 2005). The combined results demonstrate that a certain amount of uninterrupted processing time is required for perceptual consolidation of a stimulus.

It is possible however, that the duration of the test stimulus presentation (e.g. 20 ms in Massaro, 1970), rather than processing time, could be a factor that interferes with perceptual processing of the test stimulus. Massaro (1972, b) varied test tone duration while processing time was held constant and found that increasing the duration of the test tone had very little effect on tone recognition. In contrast, increasing available processing time independent of duration of the test tone improved recognition performance. This important result suggested that the speed of consolidation is the variable that most accurately predicts perceptual recognition of an auditory stimulus.

Recent ABRM designs have made use of more complex auditory stimuli such as tone-pairs that require the perceptual integration of sensory information from individual tones (Stevens & Weaver, 2005; Kohout & Stevens, 2006). A typical trial presents two tone-pair stimuli followed by a mask that is a combination of the frequencies in the tone-pairs. Presentation of two tone-pairs in a single trial eliminates the retrieval of the learned test tones from long-term memory. A two-alternative forced-choice procedure forces the subject to report whether the tone-pairs were played in the same or different order. In this design the time for perceptual consolidation of the second tone-pair is measured using various MODs, and results have suggested that the process takes no longer than 250 ms (Stevens & Weaver, 2005; Kohout & Stevens, 2006; Stevens & Kohout, in preparation), which is consistent with previous work (Efron 1963; Massaro, 1972, a; Kallman & Morris, 1984).

Psychophysical experiments over the years have attempted to explain how the masking stimulus retroactively disrupts processing and recognition of the test stimulus. One such experiment examined whether the masking stimulus simply disrupted the subjects attention and reduced recognition performance (Kahn & Massaro, 1971). The authors demonstrated that a visual masking stimulus did not interfere with auditory tone recognition performance regardless of the MOD, whereas an auditory masking stimulus affected tone recognition at short MODs. A more recent study has demonstrated a similar result using auditory and visual stimuli in a rapid serial presentation paradigm (Duncan, 1997). Thus, when the masking stimulus is in the same modality as the test stimulus, recognition of the test stimulus is impaired. These results indicate that sensory traces preserve the acoustic information of the test tone after its presentation (Massaro, 1972, a). Thus the presentation of a non-overlapping masking stimulus after the offset of the test tone interferes with the pre-perceptual feature traces of the test tone. This again highlights the importance of speed of processing in the auditory system. If pre-perceptual sensory traces of the test tone are perceptually consolidated before the onset of the next auditory stimulus, they are not masked and a perceptual representation is available to cognition.

Neural mechanisms that underlie ABRM

Various theories have been proposed to identify the neural mechanisms that underlie backward recognition masking. The integration theory suggests that the auditory system is like a long exposure snapshot, and that sensory representations of the two stimuli in a trial are perceptually consolidated together into a single blended representation. The interruption theory posits that the perceptual consolidation process of the first stimulus is interrupted and abandoned in favor of processing the second stimulus. Electrophysiological studies have attempted to determine which theory better explains backward masking. Neural responses to tones in auditory cortex are comprised of a fast excitatory component followed by inactivity and then a late excitatory component (Brosch & Schreiner, 1997). Microelectrode recordings of neural activity in male Macaque auditory cortex have demonstrated that the latter of the two components was suppressed by the initial component generated by a masking stimulus (Brosch et al., 1998). Importantly, the magnitude of the neural response to a single tone was always greater than the response to the combined tone and mask. This result suggests that the mask stimulus interrupted the neural activity caused by the first stimulus rather than integrating with it (Brosch et al., 1998). More recently, visual masking and rapid serial visual presentation (RSVP) studies have extended the interruption theory into what is called the competition theory. The competition theory is based on the principle of temporal overlap in the neural representations of both stimuli, even if the stimuli themselves are never overlapped in time (Keysers & Perret, 2002). These overlapping neural representations will compete as the neural response to the first stimulus decreases and the neural response of the second stimulus increases. The stronger of the two neuronal responses wins at the point in time when they overlap. The competition theory differs from the interruption theory because it is not temporally defined and can account for backward and forward masking, whereas the interruption theory is temporally defined and can only account for backward masking (Keysers & Perret, 2002). Thus, competition theory can account for the speed of processing in a larger variety of perceptual tasks.

A hierarchical organization of the auditory system exists where pre-processing of auditory information (i.e. analysis of frequency, location, etc.) occurs in subcortical brain areas and post-processing of auditory information (i.e. integration of frequency, location, etc.) involves non-primary association areas of cortex (Hall et al., 2002; Wessinger et al., 2001). The larger network of neural systems underlying performance in the ABRM task has been studied (van Dijk et al., 2003). Using fMRI, which measures the change in the ratio between oxygenated and deoxygenated blood of an area of the brain in response to neural activity, van Dijk and others (2003) demonstrated significant activity in temporal, parietal and frontal cortices during the ABRM task. Specifically, the posterior superior temporal gyrus, anterior temporal gyrus, inferior parietal lobule (IPL), inferior frontal cortex, middle frontal cortex, anterior cingulate cortex (ACC), and the putamen were active. Similar areas of activation in temporal, parietal, and frontal cortices were found from an ABRM task using tone-pair stimuli followed by a single mask stimulus (Stevens & Snodgrass, in preparation). The observed activity in non-auditory related brain areas during the ABRM tasks may be attributed to other mechanisms. For example, parietal and frontal lobe regions are considered the core regions of attentional networks where activation may be necessary to execute the task (van Dijk et al., 2003; Pugh et al., 1996). Activity of the PCC has been associated with memory function (Duzel et al., 1999), whereas the ACC has been associated with cognitive conflict, decision-making, and perceived error-likelihood during highly demanding cognitive tasks (Braver et al., 2001; Brown & Braver, 2005). The executive influence of these regions may be directly related to ABRM task performance.

The relationship between speed of processing and cognition

The speed of information processing is important because it may control the quantity and quality of information that reach post-perceptual cognitive processes. Consolidation of the spectral characteristics of an auditory stimulus in the appropriate temporal order is critical to develop an accurate representation of the stimulus. This representation is used for cognitive mechanisms when the stimulus is no longer physically present. If the perceptual consolidation process is cut short, stimulus representations may be inaccurate in consciousness, which may adversely affect behavior.

The importance of the speed of auditory information processing can be seen in human behavior. Excessive backward masking has been observed in the elderly and in people with language impairments causing an inability for auditory information to guide behavior. Recent work has attempted to identify a fundamental perceptual limitation in the auditory domain that is critical to oral and written language processing (Griffiths et al., 2003; Tallal et al., 1997). This limitation may be perceptual consolidation. For example, children and adults with Dyslexia demonstrate significantly longer auditory processing time requirements (threshold) for perceptual recognition of auditory tones (Tallal, 1980; Heath et al., 1999). Using an ABRM design, some dyslexic children and adults require a longer MOD between test tones and a mask than normal controls in order to identify the tone, suggesting a deficit in rapid auditory perceptual processing (Griffiths et al., 2003; McArthur & Hogben, 2001). Similarly, elderly individuals show deficits in rapid auditory perceptual processing as demonstrated by larger thresholds on ABRM tasks when compared to younger adults. The mask onset delay was much larger (360 ms) for the elderly than for the young adults (248 ms), suggesting that the elderly were significantly slower in auditory processing time (Newman & Spitzer, 1983).

The speed of processing may be especially important to populations such as the Blind in which the accuracy of short-term auditory memory is heavily relied upon. In particular, LB individuals who acquire blindness after visual maturity become increasingly dependent on auditory information for processes such as detection and recognition and also navigation through their environment. Similar to the deficits in rapid auditory processing of the elderly and dyslexic individuals compared to controls, LB individuals show inferior performance on a variety of auditory perceptual tasks compared to EB. The EB demonstrate superior performance on higher-level auditory perceptual tasks, such as memory and attention tasks, when compared to LB or SC

(Lessard et al., 1998; Amedi et al., 2003; Röder & Rösler, 2003; Collignon et al., 2006). However, EB and LB do not differ on tasks that measure pre-perceptual sensory thresholds of auditory amplitude and frequency detection (Yates et al., 1972) or gap detection tasks (Weaver & Stevens, 2006; However, see Muchnick et al., 1991). EB individuals are also able to form perceptual representations of complex auditory stimuli significantly faster than LB or SC individuals as measured on an ABRM task (Stevens & Weaver, unpublished results; Stevens & Weaver, 2005). This suggests that the enhancements in the EB likely occur at a post-sensory, perceptual stage in the information-processing stream, and that faster speed of information processing is associated with superior cognitive performance.

CMP and auditory perception in the Blind

Superior behavioral performance in the EB has been associated with cross-modal activity of visual cortices during non-visual tasks (Amedi et al., 2003; Theoret et al., 2004; Gougoux et al., 2005;). However, the activation of visual cortices in LB individuals during non-visual tasks is a matter of debate (Burton, 2003). Some studies demonstrate primary visual (V1) cortex activity during non-visual tasks in LB subjects (Büchel et al., 1998 a, b; Burton 2002a,b, 2004), whereas others do not (Sadato et al., 2002; Cohen et al., 1999). Many factors may influence the location and degree to which this activation may occur in the visual cortex including age of onset of blindness, degree of blindness (e.g. no light or motion perception), and the duration of the blindness. Additionally, it has been argued that the task stimuli and/ or design may influence CMP in the LB. For example, visual CMP in response to tactile stimulation of Braille may be caused by the analysis of the spatial arrangement of the dots in a Braille cell.

Alternatively, auditory tasks showing visual CMP in response to heard nouns may be a result of induced visual imagery of when the LB individual was once able to read print (Burton, 2003). The use of non-verbal auditory stimuli in an ABRM design may limit the amount of visual influence in order to examine the degree of CMP in the LB brain.

The point at which the perceptual consolidation process is situated in the information-processing hierarchy is at the stage where advantages in the EB are detected (Stevens & Weaver, 2005). Increasing the speed of perceptual consolidation through training might reduce the instances of competition between stimuli for perceptual resources, increase the number of representations that make it into cognition, and reduce the number of stimuli lost to competition. Thus the detail of the auditory environment may be enhanced. Such training has been examined using ABRM tasks to show that practice can improve the ability to detect backward-masked tones (Wright et al., 1996; Roth et al., 2001). An important aspect of these tasks was to determine if training on one aspect of the ABRM would generalize to improve performance of untrained masking tasks. Although ABRM thresholds could be reduced, generalization to untrained tasks were not evident, suggesting that learning was specific to the condition being trained (Wright et al., 1996; Roth et al., 2001). Similar results were demonstrated on a different task of rapid auditory temporal-interval discrimination training (Wright et al., 1997). Although these tasks examined the degree of generalization to untrained masking tasks, they did not examine generalization to untrained non-masking tasks. Additionally, there are no studies that have examined the influence of training on behavior or functional brain activity in the LB. Training may induce CMP in the LB that may lead to superior performance on an ABRM task compared to SC and be similar to that of the EB. If the

LB were to exhibit superior ABRM performance and CMP after training, then CMP may underlie the behavioral improvement. If the LB show superior behavioral performance but no CMP, than functional changes in auditory cortex might underlie the superior behavioral performance after training. If the LB do not demonstrate superior performance from the SC after training, than similar functional activity should be observed between groups.

Training-related changes in brain activity

The effect of training has demonstrated plastic changes at both local and global levels in the brain (Buonomano & Merzenich, 1998) and seems to depend on the function that is being trained. For example, cognitive tasks requiring attention, decision-making or memory often engage multiple parts of the brain including frontoparietal networks, whereas motor or sensory tasks may only display changes in the primary cortices being used. Imaging studies using positron emission tomography (PET), which measures the metabolism of a substance (usually glucose) with a radioactive tag, and fMRI have reported three unique patterns of training-related changes in neural activity previously reviewed (Kelly and Garavan, 2005; Chein et al., 2005). An *increase* in brain activity is associated with an enlargement of the volume of active voxels overlaying a particular neuroanatomical area and/ or an increase in peak signal from an area after training (Karni et al., 1995; Honda et al, 1998; Nyberg et al., 2003; Olesen et al., 2004). This pattern of activity may indicate an increase in the number of active neurons or an increase in gain of existing neurons to enhance processing (Furmanski et al., 2004). A *decrease* in activity is the pattern of activity cited most often after training, and has been described as a reduction in the spatial extent of activation overlaying a particular neuroanatomical area and/ or a decrease in peak signal of that area (Garavan et al., 2000; Jancke et al., 2001; Erickson et al., 2006; Landau et al., 2004). This pattern of activity has been explained as an increase in the efficiency of a subset of neurons or neuronal networks that was active during acquisition and performance of the task (Petersen et al., 1998). Neurons or networks that are not required for practiced performance may no longer be active. Finally, a *reorganization* of functional brain activity is characterized by distinct changes in the location of activity, disappearance of activity, or an addition of new activity following training (Fletcher et al., 1999; Bernstein et al, 2002; Staines et al., 2002; Glabus et al, 2003). Reorganization of activity has been associated with "process switching" in which different tasks are being performed both neurobiologically and cognitively (i.e. different strategic processes) before and after training (Poldrack, 1998, 2000) that may reflect a top-down strategy shift rather than a change in neural function.

Training or practice on a task results in alterations in the underlying neural mechanisms responsible for the processing of that task. The characterization of brain activity before and after intensive training on an ABRM task has not been reported. The importance of using an ABRM task is that it measures perceptual consolidation, which may be a fundamental limitation on information processing in cognition. Ultimately one goal is to elucidate a modality-independent neural mechanism from which a training method could be devised and applied to any cognitive or behavioral dysfunction. Such a mechanism remains elusive as a result of complex study designs, the modality that is trained, and poor controls for task difficulty between pre- and post-training sessions. ABRM training could increase the speed of perceptual consolidation and improve auditory perception for people with declining or dysfunctional auditory processing during normal aging or in populations affected with dyslexia, respectively. Additionally, ABRM training could be utilized to enhance learning and perception in populations that are overly dependent on the auditory environment such as the LB. The current study has integrated previous research, across modalities, in an attempt to uncover such a mechanism.

Overview

Chapter two examines the hypothesis that perceptual consolidation rate is an important determinant of STM capacity. Multiple regression analyses were used to show that perceptual consolidation threshold, as measured by the ABRM task, was significantly correlated with STM memory capacity, as measured by a novel auditory tone span task (TST). Chapter three examines the hypothesis of whether training can improve perceptual consolidation rate in SC, and used fMRI to characterize the changes in functional brain activity associated with auditory training. Five days of training was found to significantly improve ABRM thresholds. General linear model analyses revealed decreased functional activity at the whole brain and ROI levels of the brain that were consistent with previous imaging studies of ABRM and training. Chapter four examines the hypothesis that LB individuals would show an advantage in the acquisition or overall performance of ABRM training compared to SC who performed the same task, and that training would improve performance to be similar to that of EB. A repeated measures analysis of variance (ANOVA) revealed that five days of ABRM training improved behavioral performance, but the LB did not show an advantage in acquisition or overall performance of the ABRM task than SC. A between group ANOVA also revealed that training did improve LB performance on the ABRM task to be similar to that of non-trained EB individuals. This chapter also examined the pattern of neural activity in the LB brain before and after ABRM training using fMRI. General linear model analyses revealed a similar pattern of a decrease in brain activity in the LB as in the SC. No CMP was observed in the LB before or after training. The Discussion explores the relationship between perceptual consolidation and STM, and examines unpublished results about how ABRM training affects STM capacity. Imaging results are discussed in light of the similar patterns of functional activity between the LB and SC, and how the LB brain does not exhibit CMP before or after ABRM training. Conclusions are drawn about how visual maturation limits the degree of enhancement in audition in the LB, and how CMP underlies supranormal abilities of the EB.

Chapter 2: Auditory perceptual consolidation and short-term memory

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Abstract

Sensory information from the environment is first transduced into pre-perceptual sensory traces before being represented in cognition. Perceptual consolidation is the integration of sensory traces of a stimulus into a durable perceptual representation. The representation is used for cognitive functions such as memory when the stimulus is no longer physically present. This experiment investigated whether a relationship exists between the speed of the perceptual consolidation process and auditory short-term memory (STM) capacity. Complex tone-pair stimuli were created for an auditory backward mask (ABRM) task that measured perceptual consolidation rate based on individuals' temporal sensitivity threshold. This eliminated confounds related to inter-individual discrimination differences. Individual backward mask thresholds determined that an auditory mask had to be delayed an average of 99 milliseconds (ms) in order for subjects to accurately perform the task. In a separate session, subjects performed a tone-span task (TST) with short (10 ms) and long (200 ms) inter-stimulus intervals (ISI) to determine the maximum tone span that could be held in STM. Tone span was greater for the 200 ms ISI condition than for the 10 ms ISI condition. Multiple regression analyses demonstrated that individual backward masking thresholds were associated with individual tone span performance. This suggests that the speed of perceptual consolidation is significantly associated with auditory STM capacity. These findings indicate that perceptual consolidation plays an important role in the initial encoding of a stimulus and may predict the capacity of auditory STM.

Introduction

The transient nature of auditory stimuli requires an efficient system for rapid memory formation of a stimulus stream so the encoding of one stimulus is not disrupted by subsequent stimuli. At the same time, temporal-spectral organization must be preserved in order to retain the identity of the stimulus (Winkler & Näätänen, 1992, Näätänen & Winkler, 1999). This consolidation of stimulus elements into a perceptual whole occurs over time and the speed with which it is accomplished varies between individuals (Efron 1963; Kallman & Morris, 1984; Stevens & Weaver, 2005). Auditory backward recognition mask (ABRM) tasks have been utilized to measure the duration of the perceptual consolidation process (Stevens & Weaver, 2005). ABRM tasks demonstrate the delay required for the formation of a stable auditory percept that is no longer susceptible to a mask stimulus (Massaro, 1972, a; Massaro, 1975). Results from ABRM tasks suggest that the formation of an auditory stimulus representation requires up to 200 ms to consistently support discrimination of two tones (Kallman & Massaro, 1983; Stevens & Weaver, 2005).

Consolidation of the spectral characteristics of an auditory stimulus in appropriate temporal order is critical in order to develop an accurate representation of the stimulus for cognitive mechanisms when the stimulus is no longer physically present. If the perceptual consolidation process is cut short, incomplete stimulus representations may reach consciousness and adversely affect behavior. Using a pre-determined level of performance accuracy on the ABRM task (e.g., 75% correct), one can test individuals at several different mask onset delays (MOD) and estimate the minimum amount of time necessary to produce that level of performance in each individual. This MOD threshold may reflect efficiency of the consolidation process such that an individual with a relatively short MOD threshold may be more efficient at perceptually consolidating stimulus characteristics than an individual who requires a longer MOD threshold. When measuring the minimum amount of time required to accurately form a representation of an auditory stimulus, it is critical to avoid confounding the perceptual consolidation process with sensory discrimination ability. Therefore, we created ABRM stimuli with spectral-temporal changes based on individual subject performance on a two-tone temporal order judgment (TOJ) task (Hirsch, 1959). This had the advantage of controlling for individual differences in temporal sensitivity and at the same time allowing the use of complex auditory stimuli rather than pure tones.

Memory span tasks such as reading span (Daneman & Carpenter, 1980), and digit span (Case et al., 1982) have been used to index the capacity of memory. The maximum span is an indication of each subject's STM capacity. These tasks make use of language or number stimuli that carry semantic meaning. The semantics may invoke cognitive processes that are used on a daily basis and may over predict the capacity of auditory STM. Stimuli that carry less semantic meaning, such as pure tones, would provide a better estimate of the auditory STM capacity. While we refer to this as STM, it is possible that these auditory abilities may also reflect encoding mechanisms of working memory. Other conceptualizations of working memory (e.g., Cowan, 1988; 1999) have offered models that are agnostic to a large degree about the sensory domain in which the stimuli are presented. It is not known what perceptual processes set a limit on auditory STM. It is possible that a fast rate of perceptual consolidation allows for more stimuli to be consolidated in a short period of time. Thus, more stimuli may reach STM.

We investigated whether the time necessary to form a stable representation of a brief auditory stimulus, as measured with the ABRM task, predicted the capacity of auditory STM, as measured with a novel TST task. We hypothesized that subjects who showed a fast rate of perceptual consolidation would also have a large auditory STM capacity. Furthermore, this conception of auditory encoding and short-term memory suggests that increasing the inter-stimulus interval in the TST should improve performance by permitting greater perceptual consolidation and reducing inter-tone interference. We report that an individual's speed of perceptual consolidation measured with an ABRM task is associated with STM as measured by the TST task. In addition, a longer ISI increases auditory STM capacity in the TST.

Method

Subjects

Thirty subjects were initially recruited from the Portland, OR area and were screened for hearing deficiencies and neurological illness. Three subjects had incomplete data sets and were not used in the analysis. Twenty-seven subjects (13 male, 14 female) were used. Mean age was 26.8 years with a range from 23-31 years. All subjects provided informed consent in accordance with NIH and Oregon Health & Science University IRB requirements. Initial analysis revealed one subject that was a bivariate outlier in the regression. Inclusion of this data point significantly affected the correlation between ABRM and TST performance (at both ISI conditions). Therefore the subject was removed, leaving 26 subjects in the regression. Removal of any additional subject from the data did not affect the regression analyses.

------------------------------Insert Figure 1 about here -------------------------

TOJ

All subjects participated in two 1.5-hour testing sessions on separate days. Day 1 included the TOJ and ABRM tasks and Day 2 consisted of the TST. The stimulus presentation, timing and data acquisition was managed by Presentation software (Neurobehavioral Systems, www.neurobs.com). Subjects listened to digitally generated, binaurally presented, auditory stimuli through Sennheiser HD265 headphones. Each tone was 10 ms in length with 2 ms rise and fall times, sampled at 44kHz (Figure 1A). Subjects were familiarized with a "low" tone (2 kHz) and a "high" tone (4 kHz). Each trial of the TOJ task consisted of a high and a low tone presented in a random order, initially with a stimulus onset asynchrony (SOA) of 100 ms (onset-to-onset). Subjects indicated the order of two tones played as either Low-High or High-Low by pressing the appropriate response key on a keyboard. The task utilized a three-down, one-up rule in which the SOA between tones decreased after three correct responses, and increased after one incorrect response. This provided a response accuracy of 75% (Levitt, 1971). The initial step-size was 10 ms and was reduced to 5 ms when the subject reached an SOA of 30 ms. When the SOA reached 15 ms the step decreased from 5 ms to 1 ms. A "reversal" was calculated when the SOA direction switched (i.e. from increasing to decreasing, or vice versa). Subjects performed the task until they committed eight reversals. The SOA threshold was calculated as the mean SOA value over the last four reversals. The TOJ task was repeated twice and the SOA was calculated as the average threshold of the two runs. The 2 kHz and 4kHz frequencies and 10 ms stimulation duration were used to create tone-pair stimuli (High-Low, Low–High) for the ABRM task. Each individual's SOA separated the tones within each pair (Figure 1).

ABRM

On each ABRM trial subjects heard two auditory tone-pair stimuli and performed a two alternative forced choice discrimination of whether the two tone-pairs were played in the "same" or "different" order (Figure 1B). On Mask trials, the mask was presented following the offset of the second tone-pair at MODs of 20, 40, 80, 160, and 320 ms from the offset of the second tone-pair. All stimulus intensities were set to 65dB, sound-pressure-level, in both ears. The mask was presented at 72 dB. Stimulus timing and waveforms were monitored with an oscilloscope (Tektronix, Beaverton, OR). In addition to the mask trials, non-mask trials were also presented to ensure that discrimination of the stimulus pairs was maintained throughout the task. Subjects indicated whether the two tone-pair stimuli were the same or different by pressing the appropriate key on a keyboard. In order to adjust the discrimination difficulty to individual performance, the SOA threshold obtained in the TOJ task was used to separate the tones within each pair. The two stimuli were separated by a one second ISI and then followed by a masking stimulus. The mask consisted of 100 ms of combined 2 kHz and 4 kHz frequencies. The non-mask and mask trials were presented pseudo-randomly such that all MODs were sampled without replacement before the list was re-initiated. Each delay was presented on 40 trials.

TST

In order to measure short-term auditory memory capacity, a tone span task was created. Subjects listened to two lists of tones and determined whether the order of the second list of tones was the same or different from the first list (Figure 1C). The initial list length was three tones. The number of tones in a list was adjusted based on the subject's response accuracy. Following three correct responses at a given list length, an additional tone was added. Following an incorrect response, the list length was reduced by one tone. A reversal was calculated when the list length direction switched (i.e. from increasing to decreasing, or vice versa). The task terminated after the eighth reversal. The maximum number of tones that could be remembered was calculated as the mean list length over the last four reversals. Tones were 200 ms in duration and all tones within a list differed by a maximum frequency ratio of 0.85 (smaller ratios are easier to discriminate) in order to avoid within-list discrimination problems. Each list was created *de novo* on each trial by randomly selecting a single frequency, generating the set of tones spaced at 0.85 frequency ratio, and then randomizing their order of presentation. On trials in which the series were the same, the series was presented again in the same order. On trials in which the two lists differed, the same set of tones was randomized a second time to create the second list. Therefore, the lists contained the same tones but in a different order. In addition, on trials where the lists differed and the list length was greater than three, the first and last tones in the first and second lists were kept the same so they would not be used to discriminate between the lists. Two presentation rates were created to vary the time available for perceptual consolidation of each tone in a list: in one condition the ISI between tones was 10 ms and in a second condition the ISI was 200 ms.. The delay between the tone lists was always 1000 ms.. Subjects performed three blocks of each ISI condition for a total of 6 blocks.

Data Analysis

The average SOA threshold for each individual was calculated from two blocks of the TOJ task. An estimate of the MOD that produced 75% response accuracy in the ABRM task was calculated for each subject. Fitting a line between the MOD values that straddled the 75% accuracy point and then solving the linear equation for the MOD value calculated the estimate. On the TST, the average list length was calculated separately for the 10 ms ISI and 200 ms ISI conditions. This was calculated by taking the average tone span for the final reversal from each of the three blocks. The effect of ISI on memory span was determined with a paired t-test. Finally, a standard multiple regression analysis using SPSS 11.02 (SPSS Inc, Chicago, IL) was used to calculate the unique variance in TST performance accounted for by ABRM thresholds with TOJ thresholds. TST performance during the 10 ms and 200 ms ISI conditions was used as the dependent variable. ABRM threshold and TOJ threshold were used as independent variables. An outlier was found in the TST 200 ms ISI condition and was removed from the analysis.

Results

The average individual TOJ threshold across blocks was 6.52 ± 2.02 ms (standard error), with a range of 1-54 ms.. The average response accuracy on the ABRM task depended on the MOD (Figure 2A). The average MOD needed to reach 75% accuracy on the ABRM task was 99.10 ± 13.86 ms, with a range from 0 – 320 ms.

------------------------------Insert Figure 2 about here --------------------------

An effect of ISI was revealed on the TST such that tone span in the 10ms condition (5.38± 0.48) was shorter than in the 200 ms condition (6.64 ± 0.36) (Figure

2B). A paired t-test confirmed that the 200 ms ISI significantly improved tone span compared to the 10 ms ISI: (t (27) = -3.629, $p = 0.001$).

The relationship between the ABRM and TST was carried out with a standard regression model separately for the 10 ms and 200 ms TST conditions (Figure 3). TOJ and ABRM thresholds were used as independent variables. The significance value for entry into the model was set at $P < 0.05$. When the 10 ms ISI condition was examined, neither TOJ nor ABRM thresholds accounted for a significant amount of variance in TST performance (adjusted $R^2 = 0.076$): F (2,24) = 2.068, $p = 0.148$. Regression analysis with the 200 ms ISI condition demonstrated that ABRM threshold accounted for significant variance (adjusted $R^2 = 0.339$): F (2,24) = 7.665, $p = 0.003$. ABRM threshold accounted for significant variance in the TST 200 condition, whereas the TOJ did not (Table 1).

Discussion

The results from this study demonstrated a close relationship between ABRM and TST performance. This supported our hypothesis that faster perceptual consolidation rate was related to greater STM capacity. An individual's threshold on the ABRM task provided an estimate of the time needed to form a percept of the second stimulus in a two-stimulus discrimination. The ABRM threshold accounted for a significant portion of the variance in individual performance on the auditory TST. Recognition judgment between lists during the TST is dependent on complete and accurate encoding of each individual tone within a list. Faster perceptual consolidation may lead to a more stable memory representation by decreasing interference from subsequent stimuli, and by increasing the time available for further stimulus encoding. Thus, a representation of each tone is formed before the perceptual consolidation process can be disrupted by a subsequent tone. The same principle is true in the ABRM task. The tone-pair stimuli must quickly be consolidated into a perceptual representation to avoid being disrupted by the mask. The TOJ task did not account for a significant source of variability in TST performance because it does not place a restraint on perceptual consolidation of the stimuli, but rather measures an individual's sensitivity to spectro-temporal changes in auditory stimuli.

The strong association between perceptual consolidation and auditory tone span contrasts with the weak association between TOJ thresholds and auditory tone span. The importance of this finding lies in the fact that rapid spectral-temporal processing is primarily dependent on discrimination of rapid changes in auditory stimulation. The TOJ threshold reflects mechanisms involved in determining the sequence of auditory events at a fine temporal resolution when there is no constraint placed on the time available to perform the discrimination. The combined use of the TOJ and ABRM tasks allowed us to control the contribution of spectral-temporal sensitivity in the context of speed of processing in order to examine the contributions of discrimination ability on the rate of stimulus representation formation. Although the discrimination made in the ABRM probably relies on similar spectral-temporal analysis as the TOJ, the duration of the perceptual consolidation phase is only revealed when it is constrained by a masking stimulus. The possible confound of potential differences in long-term memory formation and recall of the two-tone stimuli was eliminated. By presenting the tone-pairs in a discrimination paradigm (judge whether the two stimuli are the same or different) we eliminated the possibility of differences in subject retention of accurate representation of each of the High-Low and Low-High stimulus combinations (Efron, 1963). Therefore, the influence of the MOD on the recognition of the second tone-pair stimulus was isolated from long-term memory effects and suggests that the masking effect is related to speed of processing.

While it is not possible to specify the direction of the relationship between perceptual consolidation and STM, one logical interpretation is that the perceptual consolidation process precedes the creation of a representation of the stimuli in STM. A study of visual working memory reported that consolidation and working memory are independent processes (Woodman & Vogel, 2005). A baseline visual consolidation condition was compared with a second condition in which previously viewed information from a visual stimulus was maintained during visual consolidation. The authors hypothesized that if consolidation and working memory were performed by the same mechanisms then consolidation should be less efficient in the condition where maintenance of previously viewed information was required. However, the results indicated that consolidation was not affected by maintained information in working memory, suggesting that the two processes were independent (Woodman & Vogel, 2005). This result suggests the existence of two stages in the encoding of information in memory; a consolidation stage in which representations are created for previously presented stimuli, and a memory stage where items are used in cognition. In the non-verbal auditory domain where strategies such as verbal recoding and rehearsal are limited, perceptual consolidation is an important determinant of auditory memory capacity and may be the limiting step in auditory cognition and memory. By this account, faster perceptual consolidation makes auditory events more rapidly available to other representational systems, and may improve the quality of auditory memory and increase the rate at which behaviors can be accomplished

-----------------Insert Figure 3 about here ----------------------------

The longer tone span memory in the 200 ms ISI condition demonstrates the influence of speed of processing on the TST. It suggests that inter-item interference was reduced by the longer ISI, which allowed for a full perceptual consolidation process of durable representations in memory. When presented too quickly, as in the 10 ms ISI condition, a tone may interfere with perceptual consolidation of the preceding tone thereby causing a partial or incomplete representation of the first tone to reach memory. Other theories might predict a correlation between the 10 ms ISI condition and TST performance. The retention interval in the 200 ms is approximately 101 ms longer than the perceptual consolidation process (99 ms). A decay model would predict better TST performance in the 10 ms ISI condition because of the shorter ISI and therefore the stimulus representations would decay less. This is not the case. Rather, the longer 200 ms ISI improved performance despite the fact that it added additional time to the retention interval. Therefore our data demonstrate the importance of a fast speed of processing of auditory stimuli so they can be protected from being overwritten by subsequent auditory stimuli. The 10 ms ISI did not allow enough time for each tone to be perceptually consolidated. Thus, essential discriminative spectro-temporal information may have been lost.

However, STM capacity is still limited even when stimulus presentation-rates are longer than the time necessary for perceptual consolidation to be completed. This indicates that while perceptual consolidation contributes to memory capacity, there are multiple other mechanisms influencing memory representations. While it seems logical that perceptual consolidation would necessarily precede STM, the relationship between perceptual consolidation and STM may be strongly influenced by top-down effects of selective attention. Selective attention may produce increased sensitivity to the frequency domains present in the tone-pairs that served as stimuli, and as a result, speed their consolidation. Selective attention also appears to enhance perception within a critical frequency band and may also attenuate interference from neighboring frequencies. Studies of signal detection have demonstrated that subjects are able to detect sounds at an expected frequency in a noisy background at much lower signal to noise ratios than sounds presented at unattended frequencies (Scharf et al., 1987; Dai et al., 1991; Oxenham & Plack, 2000). Although perceptual consolidation precedes STM in a sequential model of sensory to cognitive events, selective attention may provide a top-down influence that produces either enhancement in the particular frequency range and/or event timing of the task, or suppression of the effects of the mask on the stimulus that precedes it. It is possible in the context of the ABRM task that greater maintenance of the tone representations in STM may be permitted by selective attention. This might allow for retrospective analysis of the tone pairs *after* the mask is presented. Retrospective analysis might allow for possible resolution of the spectro-temporal elements with greater accuracy than what could be achieved by analysis of the tone information before the mask was played.

Perceptual consolidation may be a common mechanism underlying perceptual processing of sensory information. The speed of processing has been show to be important across modalities and tasks. Backward masking and attentional blink experiments in the visual domain indicate that an uninterrupted consolidation period is vital to forming a stable representation of a visual image. If the consolidation period is cut short, the formation of a perceptual representation is not completed. Several visual rapid stimulus presentation studies suggest the perceptual representation of the first stimulus needs to be consolidated quickly to avoid being overwritten by subsequent stimuli (Chun & Potter, 1995; Vogel & Luck, 2002; Jiang, 2004). This is particularly important when the mask shares spatial characteristics with the target stimulus. Likewise, Jiang (2004) proposed that a representation of a visual array of dots is susceptible to disruption within a temporal window of 0- 200 ms. Auditory rapid serial presentation tasks demonstrate that varying the temporal separation between two targets allowed for the measure of auditory information processing time (Duncan et al., 1997). Subjects significantly missed detection of a target when it was presented up to 375 milliseconds following a previous stimulus. The ABRM thresholds in this study suggested that perceptual consolidation of the complex tones occurred on average in 99 ms. The shorter window of time in the ABRM task is likely due to controlling for sensory discrimination ability of each individual subject. The TOJ measured this time to be about 6.5 ms, which may be very small due to the pure auditory tones. The discrimination in visual tasks may take longer.

This temporal window may reflect the interaction of echoic memory with longer-term representational systems that are necessary for the conscious representation of stimulus events, and may be a mechanism that supports a domain-general limit on information processing. Therefore it would be of great interest to determine whether increasing the speed of processing (perceptual consolidation) through training would generalize to increase STM capacity. If training the perceptual consolidation process does not improve STM capacity, it may be the case, as mentioned above, that STM capacity exerts a top down influence and mediates speed of processing.

Notes: There was one exception to the pattern of better performance on the TST200 versus the TST10. Although this subject's average TST 10 span was 18 and TST 200 span was 11, the subject had the second longest tone span on the TST 200 condition. The subject reported that the tones in the TST10 could be strung together into a melody while in the TST200 condition the tones had to be remembered distinctly. This suggests that there is a trade off between the perceptual encoding of the stimuli and the memory requirement.

Tables and Figures

Table 1. Standard regression model coefficients, t-test, zero-order correlation, and partial correlation for 200 ms ISI tone span task serving as dependent variable.

Variables	Beta	t	P	Zero-order	Partial	Part
(Constant)		12.256	0			
ABRM	-0.489	-2.914	0.008	-0.571	-0.511	-0.465
TOJ	-0.265	-1.582	0.127	-0.417	-0.307	-0.252

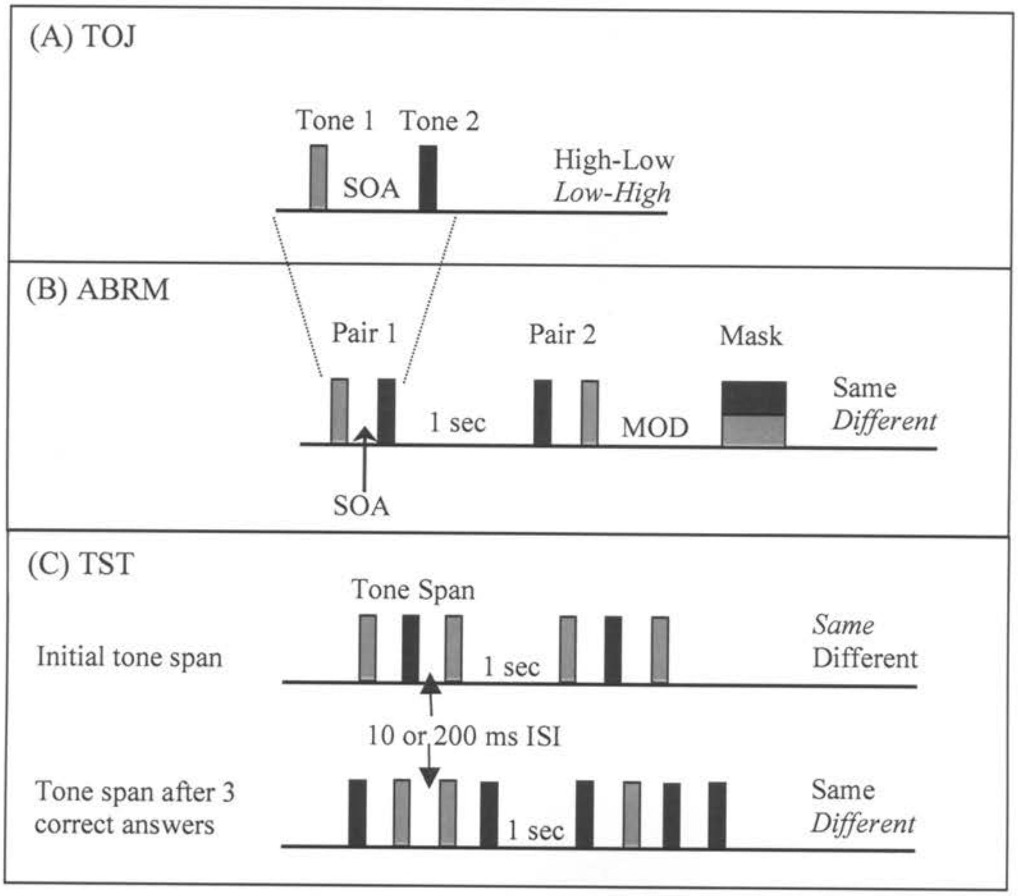

Figure 1. Illustration of the TOJ, ABRM, and TST tasks. (A) TOJ task utilizing 2 kHz and 4 kHz tones that were10 ms in duration with 2 ms rise and fall times. The SOA was calculated as the minimum ISI to make a correct order judgment. (B) The ABRM task utilizing the tone-pairs and SOA from the TOJ task. Mask stimulus is a combination of the tone-pair frequencies. MOD threshold was calculated 75% accuracy. (C) The TST started with three tones (Top) and a single tone was progressively added (Bottom) according to a 3-up/ 1-down rule (see methods) to determine each individual's maximum tone span. Tones were 200 ms in duration and all tones within a list differed by a maximum frequency ratio of 0.85. The TST was performed in three blocks with a 10 ms ISI between tones and three blocks with a 200 ms ISI between tones for a total of six blocks. Each person's tone span for the 10 and 200 ms ISI conditions was calculated as the average tone span of the three blocks.

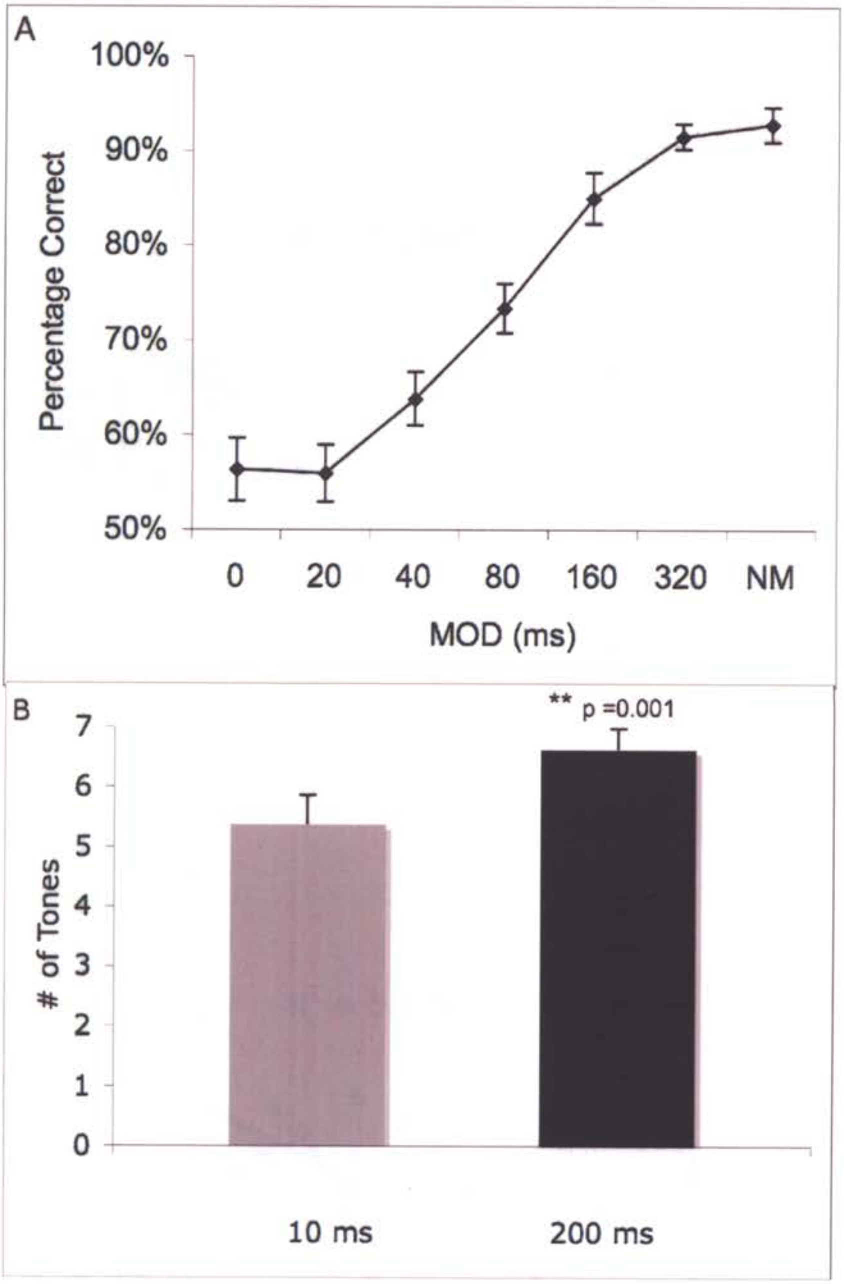

Figure 2. Results of the ABRM and TST tasks. A) Performance response accuracy as a function of the mask onset delay in the ABRM task. Error bars represent one standard error. B) Tone Span Task data for the 10ms and 200 ms ISI conditions showing group average tone spans. Tone span was significantly longer in the 200 ms ISI condition (p = 0.001, paired T-test).

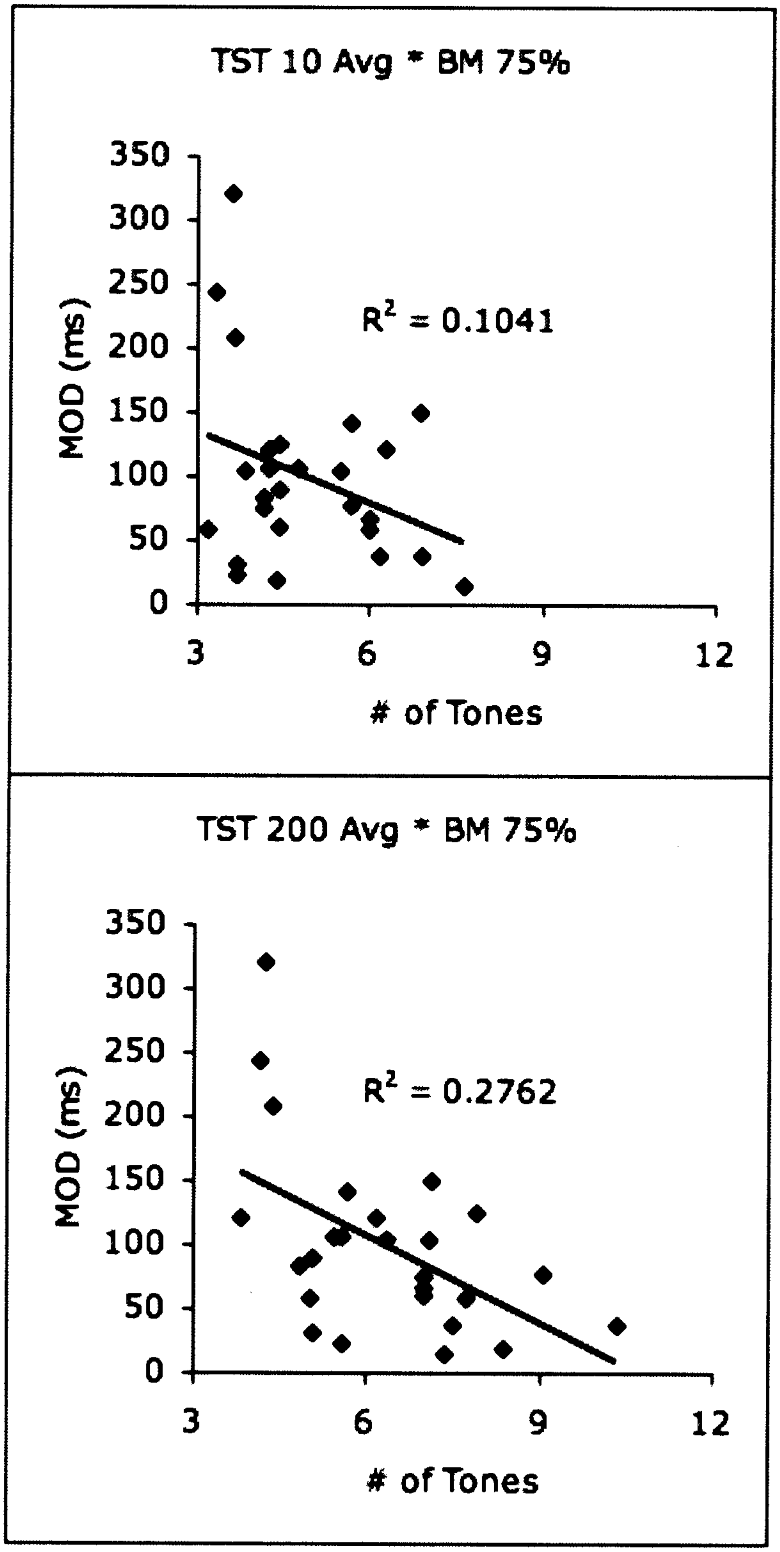

Figure 3. Scatter plots of estimated mask onset delay necessary to produce 75% accuracy on the ABRM task and performance on the TST for the A) 10 ms ISI condition and (p = 0.148) B) the 200 ms ISI condition (p = 0.003).

Chapter 3: Changes in functional brain activity following auditory training

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Abstract

Our understanding of the stages of information processing from initial perception to a stable memory representation continues to evolve. Increasingly, these functions have been shown to be sensitive to training. In the auditory domain, the time necessary to effectively consolidate a stimulus representation has been assessed previously using backward recognition masking (ABRM). The current study describes how behavioral performance and functional brain activity change after training perceptual consolidation on an ABRM task. Subjects showed a significant decrease in the mask onset delay threshold required to make an order judgment of two complex auditory stimuli. Using functional magnetic resonance imaging (fMRI), we examined the changes in functional brain activity associated with perceptual stimulation and task difficulty. Consistent with results from other training studies, our analysis revealed a trend for the volume of neural activity to decrease at the whole-brain and region-of-interest levels. Even-related analysis revealed significant decreases in blood oxygen level dependent (BOLD) signal in intraparietal sulcus (IPS), dorsolateral prefrontal cortex (DLPFC), and anterior cingulate cortex (ACC), which are core components of memory and attention systems. Although activity decreased after training, there was a precise overlap with pre- and post-training activity. This suggests that training-related improvements in ABRM performance resulted from the improved efficiency of the same neuronal networks required to learn the task. Attention-related brain regions help cope with novel demands during acquisition of a task, but decrease in activity as information and associations become stored in task-specific brain areas.

Training can improve the performance of human cognitive skills ranging from sensory discrimination to attention and memory (Ball et al., 2002). Identifying the neural mechanisms of training-induced changes in brain activity is important in order to develop techniques to facilitate behavioral performance in healthy persons, populations with neurological disease, and during healthy or unhealthy aging. Training has demonstrated changes in task-related fMRI signal at both local and global levels in the brain (Buonomano & Merzenich, 1998); the pattern of change is dependent on the novelty and type of learning required in the task. These changes have been categorized as an increase, decrease, or reorganization of activity, (Kelly & Garavan, 2005). For example, *increased* activity is observed as an enlargement of the volume of active voxels or increase in peak signal of a particular anatomical area. Increased activity has been reported in sensory, motor, and working memory tasks (Honda et al., 1998; Iacoboni et al., 1996; Nyberg et al, 2003; Oleson et al., 2004). This pattern of activity may indicate recruitment of more neurons or an increase in gain of existing neurons to enhance processing (Furmanski et al., 2004). Similarly, *decreased* activity has been indexed by a reduction in the spatial extent of activation or a decrease in peak signal in a region of interest (Erickson et al., 2006; Garavan et al., 2000; Jancke et al., 2001; Landau et al., 2004). This pattern of activity could be explained as an increase in the efficiency of a particular area, or a decrease in the amount of attention or effort required to perform the task due to over-learning (Petersen et al., 1998). Finally, *reorganization* is characterized by distinct changes in location of activity, disappearance of activity, or an addition of new activity following training (Bernstein et al., 2002; Fletcher et al., 1999; Glabus et al., 2003; Staines et al., 2002). Reorganization has been associated with changes in strategy, or "process switching" in which different tasks are being performed both neurobiologically and cognitively before and after training (Poldrack et al., 1998; Poldrack, 2000). The literature suggests that changes in brain activity after training seem to be task-specific, such that increases, decreases, or reorganization of activity occur in those brain regions most relevant to the task.

Agreement on the pattern of change in neural activity following training has been hampered by task designs that do not differentiate between learning- and performance-related changes in functional activity. For example, training can increase capacity limits on a working memory task (Oleson et al., 2004), which is thought of as an improvement in performance. However, this also increases the amount of perceptual stimulation as well as the memory load. Thus, it is difficult to determine what changes in functional brain activity are due to increased memory load or perceptual stimulation, or which changes in activity are specific to learning. Likewise, learning- and performance-related changes in brain activity are confounded in study designs in which the perceptual stimulation remains the same from pre- to post-training and the task difficulty becomes easier. In order to distinguish training-related changes due to perceptual difficulty from those due to learning, separate conditions must be contrived to permit assessment of similar stimulus parameters as well as similar performance levels. The current study utilized such conditions in an ABRM task that provides a measure of the speed of auditory perception (Stevens & Weaver, 2005).

The ABRM presents two sound stimuli (tone pairs) followed by a masking sound at various delays following the second stimulus. An uninterrupted amount of time is required for perceptual consolidation of the tone-pair stimuli into durable perceptual representations available to cognitive mechanisms. These representations are used to determine whether the tone-pairs were played in the same or different order. The delay at which the mask stimulus no longer disrupts the ability to make a discriminative judgment between the two stimuli is considered the time required for perceptual consolidation to occur. The ABRM task was chosen for this study because previous reports have demonstrated that congenitally blind individuals show a faster rate of perceptual consolidation than sighted counterparts, and in turn show better auditory memory abilities. The perceptual consolidation phase might be the essential encoding phase of auditory memory (Stevens & Weaver, 2005), and a recent study has demonstrated a positive relationship between perceptual consolidation and auditory short-term memory (Stevens & Kohout, in preparation). The degree to which training can improve the speed of perceptual consolidation is unknown.

We examined if perceptual consolidation rate could be increased after extensive ABRM training. Functional MRI was used to characterize how brain activity in ABRM-activated areas change after training. We created conditions to distinguish between training-related changes due to task difficulty from those due to changes in perceptual stimulation. We controlled for task difficulty by calculating a mask onset delay (MOD) that maintained subject performance at a constant level (65%) before and after ABRM training (but perceptual stimulation increased). We controlled for perceptual stimulation by including two conditions with mask onset delays (0 ms and 160 ms) that remained constant before and after training (where task difficulty decreased). We also included a fourth condition in which no stimuli were presented that allowed us to examine preparatory activity to an alert cue that signaling the onset of each trial. An event-related design permitted visualization of significantly active regions of interest (ROI) at pre- and post-training scans, and to analyze how the time course of BOLD activity in particular ROIs was correlated with behavior.

---------------------------------- Insert Figure 1 about here ----------------------------------

Six individuals with normal hearing and no neurological illness participated in this study. The group consisted of three males and three females (one left-handed) with a mean age of 32 (range 24-41). All subjects provided informed written consent in accordance with the Declaration of Helsinki and approved by the Oregon Health and Science institutional review board before participation in the study. Behavioral training was carried out in a quiet testing room. Stimulus presentation, timing and data acquisition was managed by Presentation™ software (Neurobehavioral Systems, www.neurobs.com). Stimulus timing and waveforms were monitored with an oscilloscope (Tektronix, Beaverton, OR). Subjects listened to digitally generated stimuli through Sennheiser™ HD265 headphones.

Each subject participated in 5 days of training over an 11-day period in which the pre-test began on a Friday, training was carried out Monday through Friday of the next week, and the post-test was completed on the following Monday. The testing procedure involved three steps. First, to control for individual temporal discrimination differences that could affect the ABRM task, subjects performed a temporal order judgment (TOJ) task. This was used to adjust the tone stimuli that were then used on the ABRM task. This TOJ task presented two consecutive 10 ms tones (2 ms rise/ fall time): one "low" tone (2.0 kHz) and one "high" tone (4.0 kHz) sampled at 44kHz and presented binaurally. The tone order was generated randomly on each trial, with an initial stimulus onset asynchrony (SOA) of 100 ms (onset-to-onset). Subjects indicated the order of the two tones presented on each trial by pressing the appropriate response key on the keyboard. We determined individual thresholds by utilizing a three-down, one-up adjustment, where the SOA between tones decreased by 10% after three consecutive correct responses and increased by 10% after one incorrect response. This produces a response accuracy of 79% (Levitt, 1971). A reversal was calculated when the SOA direction switched (i.e. from increasing to decreasing, or vice versa). Subjects performed the task until they committed eight reversals. The threshold SOA was calculated using the mean SOA value over the last four reversals from two runs of the TOJ task. Calculating each individual's discrimination threshold eliminated any confound in which spectral-temporal discrimination influenced perceptual consolidation rate.

---------------------------------- Insert Table 1 about here ----------------------------------

Next, subjects performed the ABRM task (Fig. 1) with two tone-pair stimuli (High-Low, Low-High) that were created based on their TOJ performance. The High-Low and Low–High stimulus pairs had an adjusted SOA threshold obtained from each subject's TOJ. Tone-pairs were separated by a 500 ms ISI. Subjects were required to demonstrate 90% accuracy on 40 non-mask trials before beginning the ABRM. If subjects failed to reach 90%, 10 ms was added to the tone-pair SOA, and they were re-tested (Stevens & Weaver, 2005). Upon reaching 90% accuracy, subjects started the ABRM task (Figure 1). On mask trials, the mask was 100 ms of combined 2 kHz and 4 kHz frequencies with 10 ms rise and fall times, and was presented following of the second tone-pair at MODs of 0, 10, 20, 40, 80, 160, and 320 ms (offset to onset). In addition to the mask trials, non-mask trials were also presented to ensure that discrimination of the stimulus pairs was maintained throughout the task. The non-mask and mask trials were presented pseudo-randomly such that all MODs were sampled without replacement before the list was re-initiated. Each MOD and non-mask condition was presented 50 times for a total of 400 trials. The MOD at which each subject made the correct order judgment at 65% accuracy was recorded and then used in the subsequent scanning session, along with MODs of 0 milliseconds (ms), 160 ms, and a "no-trial" (NT) condition. The 65% threshold was chosen to allow ample room for improvement so that a threshold could be calculated after training.

For training (Appendix Fig. 1), subjects were randomly assigned to one of two procedures and completed 660 trials per day of the ABRM task during the week between pre and post-tests. Three blocks of 200 trials were completed each day, with 20 non-mask practice trials before each block. One version (progression), used the same adjustment of MOD as described above, with a starting MOD of 320 ms and reduced the delay by 10% (i.e. 32 ms) after three correct answers or increased 10% after one incorrect answer. The second variation of the ABRM training (intensity) manipulated the intensity of the mask at a set MOD. The 65% MOD calculation from the pre-test ABRM was set as the delay at which the mask was played. The backward mask intensity (BMI) started at an inaudible level (30 db SPL) and increased after 3 successive correct answers by a factor of 1.2 (BMI = BMI x 1.2). Our subjects were not given explicit feedback after each trial, which is not required to improve behavioral performance after training (Gaab et al., 2006), but changes in MOD and BMI in our tasks provided intrinsic cues to changes in performance. The ABRM task was repeated three days after completion of the training procedure to obtain the post-training65% MOD.

MOD thresholds for the pre-training and post-training ABRM tasks are shown in Figure 2. Five days of training reduced the average 65% MOD threshold in all subjects but one (who was already at a MOD of 10 ms): pre-training average = 90 ms to a post-training average = 21 ms. One subject had an extreme pre-training ABRM 65% calculation (320 ms) which, after training, improved to a post-training65% calculation of 52 ms.. Due to the variability and relatively small sample, we used non-parametric Wilcoxon tests to confirm that training consistently decreased MOD threshold (p = .043). Two control subjects that did not participate in the training did not show improvements in ABRM threshold (data not shown). This suggests that perceptual consolidation, as measured by the ABRM task, can be improved with five days of training, and is consistent with previous auditory training studies that have demonstrated significant performance gains after five days of training on tasks of auditory attention and memory (Gaab et al., 2006; Jancke et al., 2001; Menning et al., 2000; Tremblay et al., 1998), and specifically in auditory backward masking (Wright et al., 1996).

To test how training affected brain activity, subjects were scanned before and after training. Functional images were acquired with an EPI-BOLD pulse sequence on a whole-body 3T Siemens Trio (Munich, Germany) scanner using a standard two-channel head coil. The functional data was acquired with a navigator echo-guided, BOLD sequence clustered acquisition technique with the following parameters: repetition time (TR) = 2330 ms, delay in TR = 900 ms, echo time (TE) = 50 ms, flip angle (FA) = 90°, field-of-view (FOV) = 240 mm^2, imaging matrix = 64 x 64, and 17 slices with a 5 mm slice thickness in axial orientation for maximal coverage of the brain. The slice volume was acquired during the initial 1430 ms of each TR leaving a 900 ms interval between

TRs for trial presentation. To reduce expectation and habituation effects on the time course functional activity, a jitter of 5,6, or 7 TRs (11.6- 16.3 sec) was used between each trial onset (Dale & Buckner, 1997). A high-resolution, heavily T1-weighted anatomical scan (3D MPRAGE), was acquired for anatomical co-registration with the functional data, using the following parameters: 144 axial slices, slice thickness 1 mm, TR = 2300 ms, TE = 4.38 ms, FA = 12°, FOV = 256 mm^2, imaging matrix = 256 x 256. To prevent significant head movement, the subject's head was stabilized with padded clamps attached to the head coil.

---------------------------------- Insert Figure 2 about here ----------------------------------

Auditory stimuli were presented via Koss (Milwaukee, WI) electrostatic headphones inside the scanner. A button box was used to record responses both in the testing room and inside the scanner. During scanning, subjects heard an alert sound (three 600 Hz 50 ms tones with 50 ms ISI) during the silent period of the TR preceding an ABRM trial. The alert cue had two advantages: first, due to the random intervals between trials, the alert sound made subjects less likely to commit errors due to inattention. Second, it allowed us to observe the effect of the alert cue on fMRI response following training (described below). Three mask onset delays were used: two were fixed (0 ms and 160 ms) and a third that was the 65% MOD calculated in the pre and post-training ABRM tasks. This condition was set to each subject's 65% accuracy level, measured immediately before scanning, in order to determine the change in functional activity when difficulty level was matched. The 10 and 160 ms conditions allowed for comparison of changes in functional activity when task difficulty changed (presumably less difficult after training). The NT condition was used as a baseline during which the subject heard the alert sound but no ABRM trial was presented. This condition allowed for detection of brain areas showing preparatory response to the alert sound alone. Each condition was presented 20 times for a total of 80 trials.

Functional data were analyzed using Brain Voyager QX software (Brain Innovation, Maastricht, The Netherlands). The functional data were preprocessed using slice-time correction, linear trend removal, and a high-pass filter at 5 cycles per time course to remove low-frequency oscillations in the fMRI signal. All functional data were interpolated into 1x1x1 mm^3 voxels, z-normalized, and transformed to standard Talairach stereotaxic space (Talairach & Tournoux, 1988) to allow for pooling across subjects. A general linear model was applied with separate beta weights calculated for each condition of the ABRM (0, 65%, 160) as well as for the NT condition.

We found a precise overlap of activity before and after training in frontal and parietal areas (Table 1) that is consistent with areas identified in previous ABRM studies (Stevens & Snodgrass, in preparation; van Dijk & Backes, 2003). These areas showed a reduction in the volume of activity from pre- to post-training, which suggests that similar neural networks were active during initial acquisition and after extensive training [Fig 2). We analyzed ROIs within posterior parietal lobe, prefrontal cortex, insula, and anterior cingulate cortex by extracting the peak BOLD signal values for each subject using event-related averaging. The peak signal was chosen as the highest BOLD signal value from the five acquisitions following an alert cue. Non-parametric Wilcoxon signed rank tests were used to assess the change in peak signal intensity change for all subjects from before to after training. While nearly all ROIs showed decreases with training, only two reached significance. A region in the left DLPFC showed a significant decrease in peak

BOLD signal in the 160 ms condition in all subjects (p = .028) (Figure 3). A second region in the left IPS significantly decreased in activity in the 65% condition after training (p = 0.043) (Figure 3).

A separate, area under the curve (AUC) analysis was used to measure training-related changes in the overall duration and amplitude of the event-related BOLD activity. Three ROIs showed significant decreases of activity from pre- to post-training across subjects: the same left-lateralized DLPFC and IPS regions and the ACC. The ACC and left DLPFC significantly decreased in AUC in the 160 ms condition after training (p = 0.028 for both), whereas activity in the left IPS decreased in the NT condition (p = 0.046) (Figure 4). None of the ROIs revealed consistent increases in BOLD signal.

---------------------------------- Insert Figure 3 about here ----------------------------------

---------------------------------- Insert Figure 4 about here ----------------------------------

The current task made use of a condition (65%) in which perceptual load was held constant before and after training to determine the relationship between perceptual load and brain activity. We observed a decrease in peak BOLD signal in the 65% condition after training, which demonstrates that brain activity decreases even when perceptual difficulty is held constant. Our observed decreases in signal contradict previous work that has demonstrated an increase in signal after training (Oleson et al., 2004). In that study, increases in brain activity were observed in prefrontal and parietal cortices after five weeks of working memory training. However, the increased signal could be attributed to increased perceptual load as subjects were trained to increase working memory capacity after training. Similarly, increases in activity have been observed after training of a dual-task when compared to single-task processing (Erickson et al., 2006). The dual-task requires the processing of multiple tasks at the same time whereas the single task requires the processing of just one task. Therefore, an increased perceptual load during dual-task processing could underlie the increased activity after training.

The current study focused on perceptual learning of an auditory task, while previous studies have focused on working memory, motor skill learning or language. While training tasks may activate modality-specific cortex that differ among studies, there seems to be a set of anterior brain regions, particularly the ACC and DLPFC, which are active across all training tasks (Chein & Schneider, 2005). These observations partially support a "scaffolding-storage" framework that distinguishes among brain regions that are involved in the instantiation of task demands during initial learning (scaffold) and those that are utilized for task-specific memories during practiced performance (storage) (Petersen et al., 1998). Since storage regions are likely to depend on the modality of the stimuli involved, sites may differ among studies (Kelly & Garavan, 2005). Therefore, areas common to training studies that use different stimuli likely reflect processes common to training or task acquisition. Similar to previous studies that utilized verbal or motor paradigms, we also observed anterior activation in lateral and medial frontal cortex. Therefore, we suggest that scaffolding regions such as IPS, DLPFC, and ACC reflect modality independent areas that assist task-specific storage areas during initial acquisition of a task. Unlike studies that employed different tasks that activate mostly frontal lobe areas, our experiment utilized pure auditory tones that invoked brain activity from posterior sensory and perceptual regions. After ABRM training, spectro-temporal characteristics of stimuli, as well as the mechanisms specific to improved ABRM performance, may be stored in brain regions such as the superior temporal gyrus that are closely linked to auditory perception. We did not observe a significant change in the activity of any possible auditory storage areas, including the superior temporal gyrus STG (Figure 5). This suggests that regions associated with scaffolding help storage regions acquire the task. When the storage regions can effectively perform the task, less activity is required from the scaffolding regions. The decrease in activity observed in our study is consistent with a positron emission topography (PET) study (Raichle et al., 1994) that examined brain activity during naïve and practiced performance of a verb generation task. Activity was found to be greater in anterior cingulate, left prefrontal, and posterior temporal cortex during naïve performance of the task and decreased after practice. Our results also fit well with a recent fMRI and meta-analytic study suggesting a domain-general control network for learning that acts to support novel but not practiced task performance (Chein & Schneider, 2005).

Highly demanding tasks typically activate frontal lobe areas including the ACC and DLPFC as well as parietal areas such as the IPS (Brown & Braver, 2005; Corbetta & Shulman, 2002; Fan et al., 2002). These fronto-parietal regions may improve perception by selectively attending to stimuli and/or suppressing distracting information, and are more active in conditions when stimuli are attended to than conditions when the stimuli are ignored (Kastner & Pinsk, 2004; Kastner & Ungerleider, 2000; Pinsk et al., 2004). The degree to which fronto-parietal regions are active is positively coupled to attention demand, and activity within these regions should also correlate with task difficulty. Task difficulty may be interpreted in one of two ways: the relative difficulty between conditions (e.g. 0 ms vs. 160 ms MOD), or the difference in difficulty within a condition before and after training. Our results suggest that task difficulty within a condition modulates neural signal, but difficulty between conditions does not. We did not observe a significant difference in event-related BOLD activity between 0 ms, 65%, and 160 ms conditions in attention-related ROIs before or after training (see Figures 2, 3, & 4). Rather, we observed a significant decrease in brain activity within a condition as subjects improved performance of that condition after training. The decrease in activity within a condition may reflect a decrease in attentional resources required to accomplish equal or improved performance in that condition as before training. The excess of attentional resources may then be utilized for other cognitive processes.

During acquisition of the task, subjects may have been tuning their hearing to the specific characteristics of the auditory stimuli that provided the greatest discriminative information. We assume that subjects used top-down attentional modulation to employ one of two strategies in order to obtain discriminative stimulus information. One method that may have been used was an attempt to suppress the backward mask to reduce interference. A second method that could be employed was to selectively attend to the stimuli by closing the temporal window after a distinguishing characteristic of the trial was heard (e.g. trying to listen for the first tone of the second tone pair). With extensive training, the subjects may have settled on a particular strategy that thereby reduced brain activity attributed to initial acquisition of the task. We did not observe any reorganization of brain activity after training, which has previously been associated with strategy or process switching (Poldrack et al., 1998). Because we didn't observe significant reorganization of brain activity, it is likely that our subjects improved the efficiency of the strategy that was used during initial acquisition. Since identical stimuli (2 kHz/ 4 kHz tones, and the mask) were used for every trial, the only characteristic that differed between conditions was the MOD. Therefore, we can attribute differences in brain activity between brain regions to only the MOD.

While the decrease in peak signal change from pre to post training only reached significance in the 65% condition in the IPS, a similar trend to decrease was present in the other three conditions. Furthermore, signal change did not vary across levels of task difficulty within each scanning session; therefore it is unlikely that IPS activity in our study reflects the subject's perception of task difficulty. For the same reason, it is also unlikely that this region was involved in suppression of distracting information (Donner et al., 2003; Wojciulik & Kanwisher, 1999) since signal change would have varied across conditions depending on MOD. Rather, the IPS may be involved in the maintenance of attentional focus to improve stimulus perception during information processing (Chein & Schneider, 2005; Corbetta & Shulman, 2002). Perception of a stimulus during auditory stream analysis in the ABRM task could be enhanced by selective attention to a particular part of the trial (for example, listening to the first tone of the second tone pair for comparison with the first tone in the first tone pair). As the perceptual consolidation process became more efficient with training and the auditory system became more attuned to discriminating the stimuli, a decrease in IPS signal may have reflected a decrease in the amount of attention required to make the order judgment with the same 65% accuracy as before training.

The prefrontal cortex is involved in executive functions such as goal-directed planning. In a perceptual task, the prefrontal cortex may apply task instructions to coordinate the activity of task-specific regions during initial task performance. Top-down attention, in which knowledge is used from past experience or expectations rather than sensory stimulation, may be a mechanism that improves performance in the ABRM task by priming pre- and post-perceptual systems to process task stimuli. Frontal projections to posterior attention regions such as the IPS apply selective, goal-directed attention, which enhances perception of a stimulus when specific information is known ahead of time (Corbetta & Shulman, 2002). During initial performance of the ABRM task, top-down attentional resources are spread among the entire tonotopic auditory cortex. Repeated presentation of ABRM trials may cause certain neural networks between the temporal and parietal lobes to fire together consistently (such as the 2k and 4k Hz areas of cortex) in a Hebbian fashion, whereas unstimulated auditory regions no longer receive attentional resources. Training may focus the attentional resources to establish the circuitry required to improve the receptiveness of these specific tonotopic areas. Less executive influence is needed once the auditory processing regions become efficient at processing the stimuli on their own, therefore resulting in a decrease in activity of executive regions (Petersson et al., 1999; Sakai et al., 1998).

-------------------------------- Insert Figure 5 about here --------------------------------

The ACC has been implicated in cognitive control of behavior and decision-making. Many studies have shown ACC activity during response conflict (Braver et al., 2001) and more recently in error prediction such that ACC activity increases proportionally with error likelihood (Brown & Braver, 2005). Our results demonstrated that AUC decreased for all conditions in the ACC, with the only significant decrease in the 160 ms condition. The 160 ms condition was relatively easier than the others since it had the longest MOD and was therefore the condition with the lowest probability of making a response selection error. Training further reduced the likelihood of making an error judgment, which resulted in a significant decrease of AUC in the ACC in this condition. Therefore our results support previous accounts of ACC activity related to processing error likelihood. However, our results cannot rule out the possibility of the ACC as an "activity monitor" that tracks and records activity from task-relevant areas (Chein & Schneider, 2005) for visual (Mesulam, 1990) and auditory (Benedict et al., 2002; Sevostianov et al., 2002) attention in the posterior parietal lobe and dorsolateral prefrontal cortex (Goldman-Rakic, 1988; Koski & Paus, 2000). Acting as a monitor, ACC activity changes proportionally with the relative activity of the other regions. Our data demonstrates decreases in peak BOLD signal and AUC in the IPS and DLPFC after training. If acting as a monitor, the reduction in activity of the IPS and DLPFC may decrease the monitoring that is required of the ACC.

In summary, five days of training significantly decreased perceptual consolidation rate in the ABRM task. Event-related fMRI analysis revealed significantly decreased peak BOLD signal in attention-serving areas after training. Statistical maps display a concise overlap of ROI activity from both pre-training and post-training fMRI scans in which no new ROIs were seen after training, and no ROIs showed a shift in location. The fact that our data does not show reorganized activity suggests our subjects learned to increase the efficiency of their initial strategy resulting in a reduction of the cognitive and neural resources needed to perform the ABRM task. The effect of training to decrease activity of executive brain regions is biologically relevant as it might free up attentional resources to be reallocated for use in other cognitive processes. Together the data support a scaffolding-storage hypothesis where increased brain activity is seen while coping with novel task demands until appropriate information and associations are stored in task-specific brain areas, which are task-dependent.

Table and Figures

Table 1. Activation clusters detected using the full general linear model with a minimum cluster threshold of 100 voxels (p = 0.0005).

Pre					**Post**				
x	**Y**	**Z**	**mm3**	**Structure**	**X**	**Y**	**Z**	**mm3**	**Structure**
Frontal					**Frontal**				
5	50	18	148	R Cingulate Gyrus	-29	19	1	525	L Insula
31	46	24	295	R Middle Frontal Sulcus	41	13	7	2034	R Insula
40	36	19	1941	R Inferior Frontal Sulcus	45	0	41	1670	R Precentral Gyrus
43	24	34	503	R Middle Frontal Gyrus	-44	3	22	242	L Precentral Sulcus
-29	39	21	612	L Sub-gyral	-30	-21	50	830	L Precentral Sulcus
-2	13	40	8779	Anterior Cingulate Cortex	-2	13	40	991	Anterior Cingulate Cortex
23	22	51	163	R Superior Frontal Sulcus					
41	14	3	4603	R Insula					
-38	10	7	3066	L Insula					
48	4	31	2809	R Precentral Gyrus					
-34	-16	53	539	L Precentral Gyrus					
Parietal					**Parietal**				
-50	-26	26	2920	L Postcentral Gyrus	39	-45	42	1610	R Posterior Parietal
57	-20	27	265	R Postcentral Gyrus	-30	-51	41	1570	L Posterior Parietal
-41	-36	45	4335	L Posterior Parietal					
39	-46	42	4526	R Posterior Parietal					
1	-51	28	169	R Posterior Cingulate Gyrus					
Occipital									
-50	-62	24	1249	L MT					
-7	-59	17	249	L Precuneus					
Cerebellum									
3	-52	-9	169	R Cerebellum					
Sub-cortical									
-11	-14	13	3103	L Thalamus					
9	-16	11	1616	R Thalamus					
29	-6	16	151	R Putamen					
-23	-21	7	144	L Putamen					
-10	-23	11	157	L Mesencephalon					
-2	-31	4	371	L Fornix					
-1	-38	-11	229	L Colliculi					

X, Y, and Z are coordinates in a standard stereotactic space in which positive values refer to regions right of (X), anterior to (Y), and superior (Z) to the anterior commisure.

Figure 1: ABRM design and results. A) Schematic of TOJ task used to create stimuli for the ABRM task. The TOJ task utilized 2 kHz and 4 kHz tones that were 10 ms in duration with 2 ms rise and fall times. The SOA was calculated as the minimum ISI to make a correct order judgment. (B) The ABRM task utilized the tone-pairs and SOA from the TOJ task. Mask stimulus is a combination of the tone-pair frequencies. MOD threshold was calculated at 65% accuracy before and after training. Solid lines represent individual subject performance, and the dotted line represents the group average. Inset column graph shows significant decrease in post-training group-averaged 65% MOD threshold (p = 0.043; Wilcoxon test).

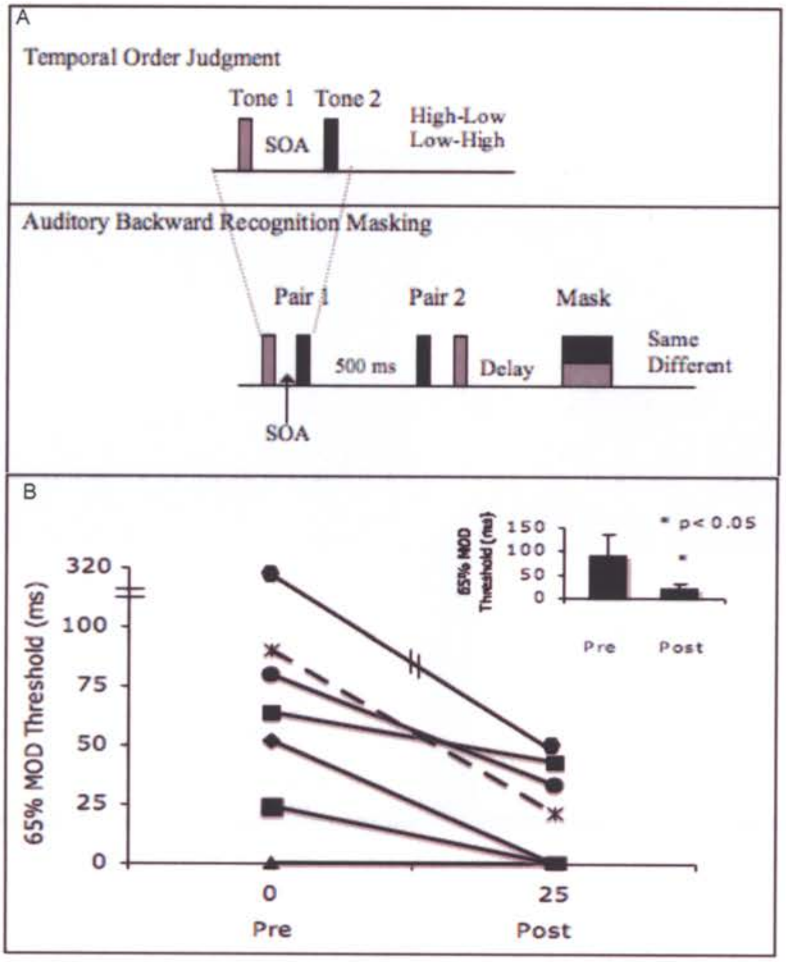


Figure 2: Overlay of pre- and post-training functional activity during the ABRM task. A full general linear model was first used to obtain separate maps of significant group-averaged pre- (yellow) and post-training (red) activity using a statistical threshold of p = 0.005. The individual maps were then overlaid to display overlapping activity (orange) and visualize how the volume of activity changed after training. Green arrows link ROIs with the event-related time course of activity of the voxels within that ROI.

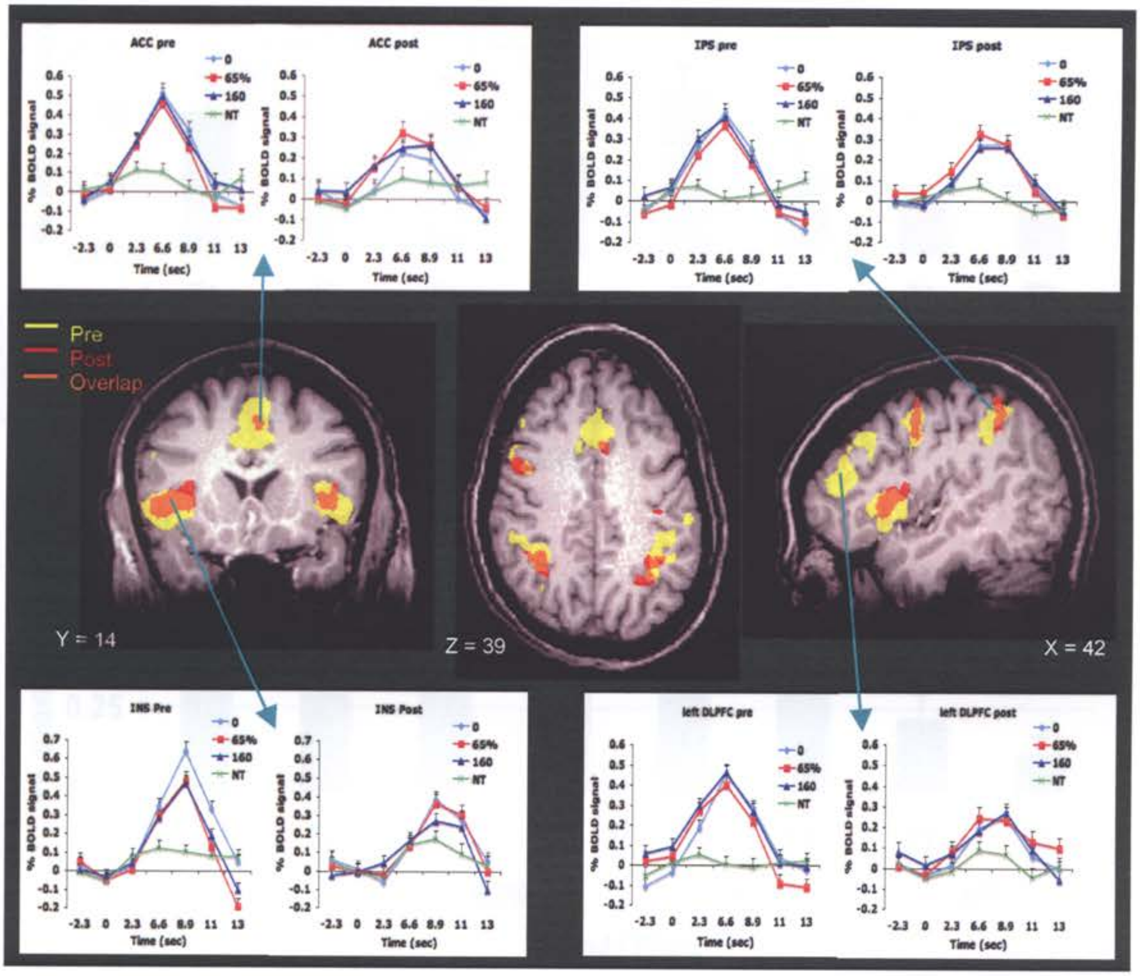


Figure 3: Change in peak BOLD signal after training. Peak BOLD signal values were taken from fMRI scans before (T1) and after (T2) training. A significant effect of training was found in (*a*) left-lateralized DLPFC in the 160 ms condition (p = 0.028), and (*b*) in the IPS in the 65% condition (p = 0.043) (Wilcoxon test).

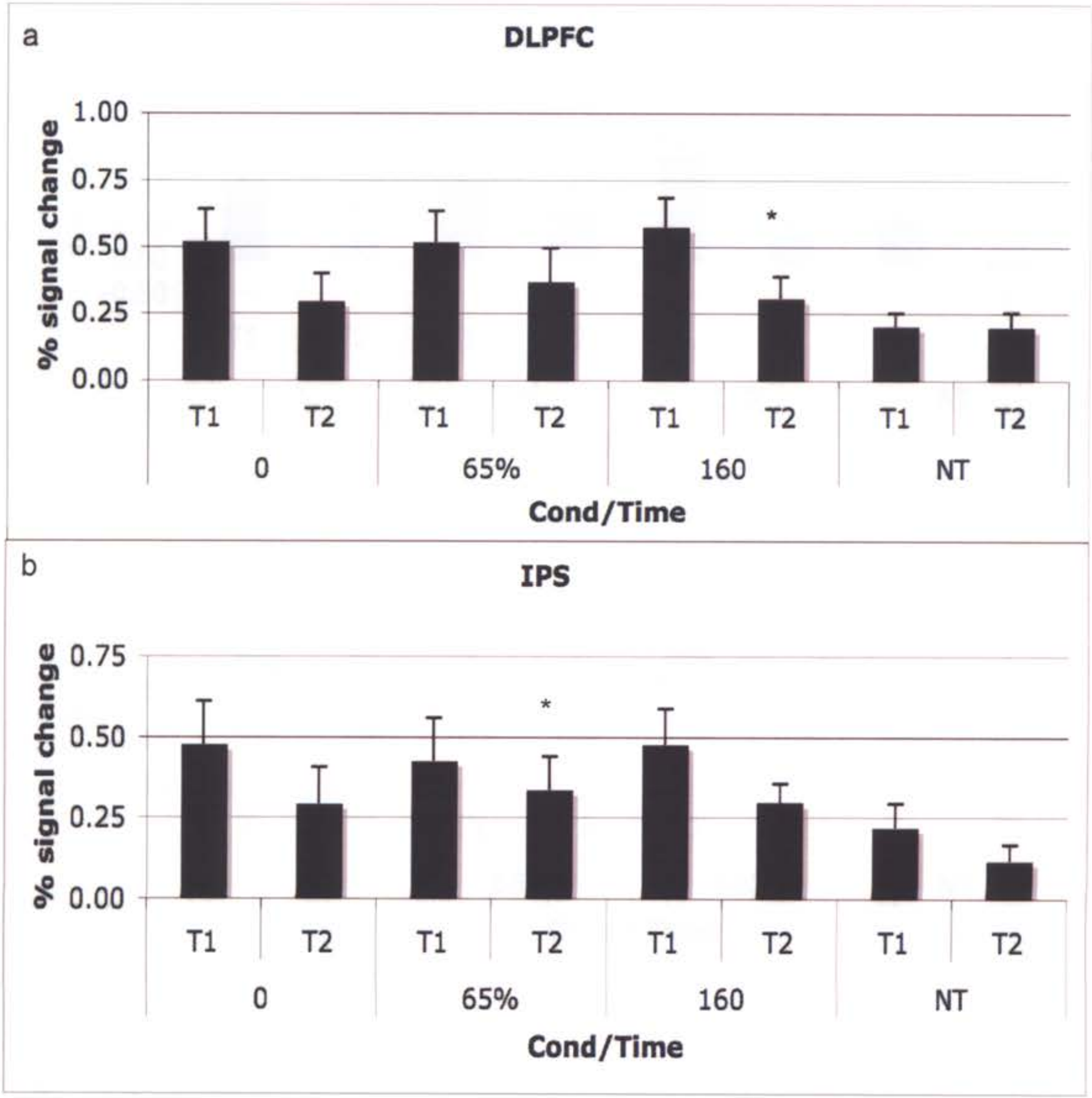


Figure 4: Change in area under the curve (AUC) after training. Values were calculated as the sum of percent signal values taken from fMRI scans before (T1) and after (T2) training. A significant effect of training was found in (*a*) left-lateralized DLPFC in the 160 ms condition (p = 0.028), (*b*) in the IPS NT condition (p = 0.046), and (c) in the ACC in the 160 ms condition (p = 0.028) (Wilcoxon test).

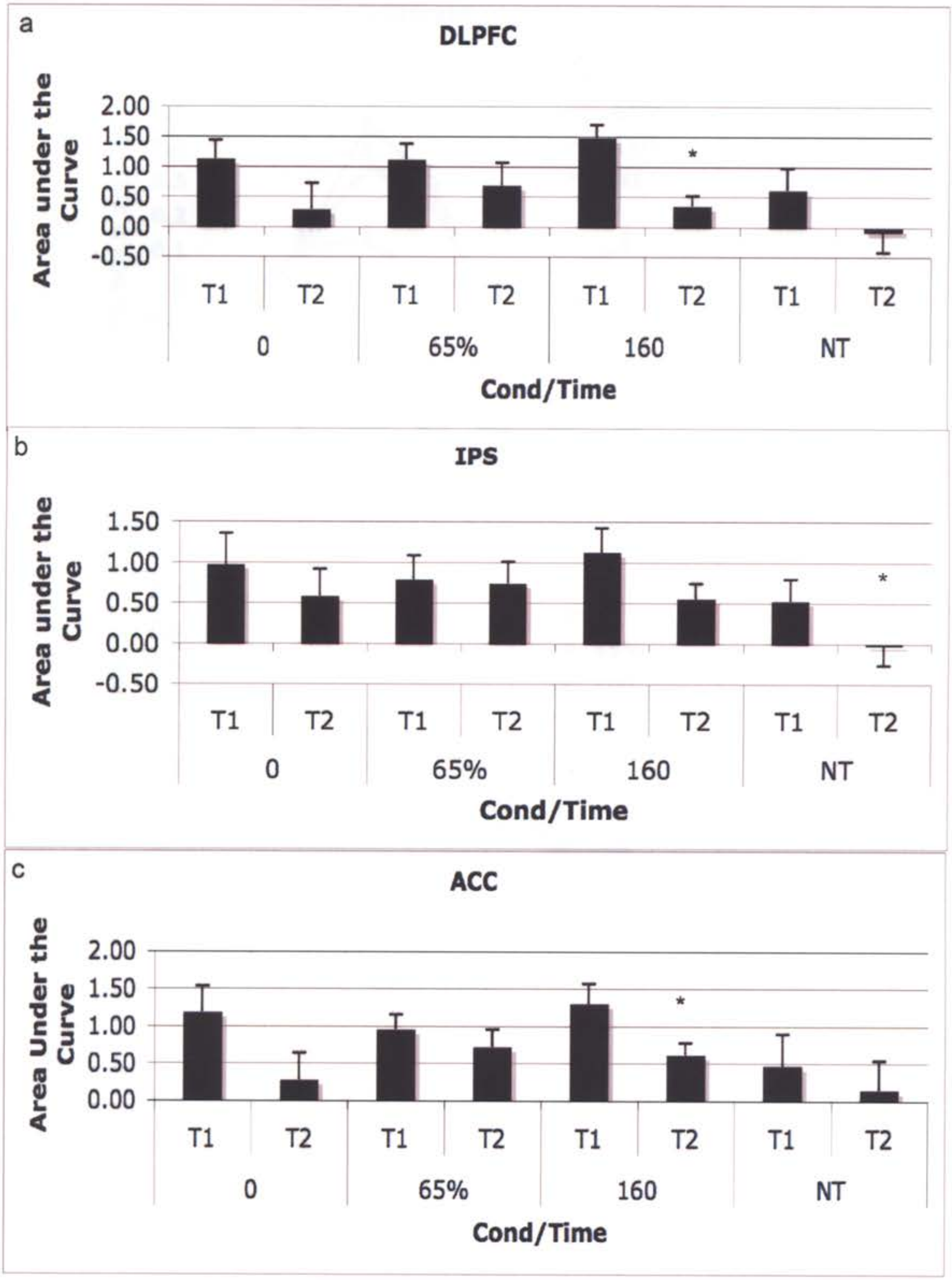
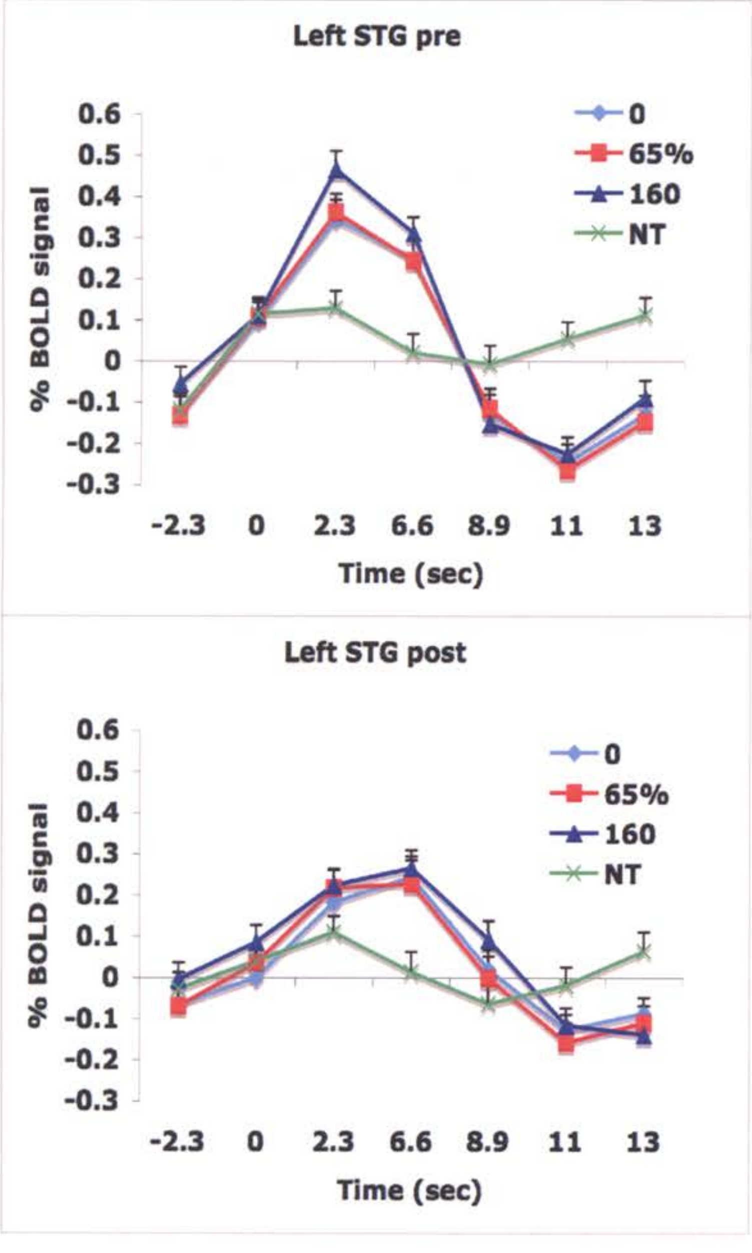


Figure 5: Event-related time course of left superior temporal gyrus activity before (pre) and after (post) training. There was not a significant effect of training on either peak signal change or AUC.



Chapter 4: Changes in behavior and functional brain activity in late blind individuals following auditory training

Keith M. Kohout and Alexander A. Stevens

This manuscript will be submitted to *Brain Research*

Abstract

Individuals who become blind after visual maturity (late blind or LB) demonstrate inferior performance on auditory perceptual tasks when compared to early blind (EB) individuals. It is unknown whether training can improve auditory perceptual abilities in the LB. Functional brain-imaging studies have revealed that superior behavioral performance of the EB on auditory tasks is correlated with cross-modal plasticity (CMP) of the visual cortex. The current study examined whether training could improve LB performance on an auditory backward recognition mask (ABRM) task to a performance level similar to EB. Functional magnetic resonance imaging (fMRI) was used to determine whether CMP was evident before or after training. ABRM performance of the LB significantly improved after training, which is consistent with results from a previous training study using the same experimental design in sighted counterparts (SC). However, performance of the LB was still inferior to the level previously reported in EB individuals. Functional MRI revealed a decrease of activity in fronto-parietal brain regions but no evidence of CMP before or after training. The existence of CMP in the LB brain is a matter of debate in the literature. Our study allowed for observation of CMP during acquisition of an auditory task or the possible induction of CMP after learning an auditory task through intensive training. We did not observe CMP at either point, which is consistent with the body of literature that suggests the LB do not show CMP during auditory tasks. Additionally, the results suggest that the LB brain is governed by the same neural plasticity principles as the normal sighted brain.

Introduction

Blind individuals rely on memory and the accurate processing of information in the spared modalities to guide them without sight. Several studies have demonstrated that blindness results in enhanced auditory perceptual and cognitive abilities (Amedi et al., 2003; Liotti et al., 1998; Röder et al., 2000). For example, early blind (EB) individuals, who lost their sight very early during visual development (often < 2 years of age), have demonstrated superior performance on auditory tasks when compared to late blind (LB) individuals who lost their sight after visual maturation, and sighted counterparts (SC) (Gougoux et al., 2004). This demonstrates that compensatory advantages are only available to individuals who became blind during development. Therefore, individuals who become blind after full visual maturity are not afforded the compensatory abilities in the remaining modalities. To our knowledge, no study has examined whether auditory perceptual abilities of LB individuals can be improved with training.

Particular performance enhancements of the EB are observed on auditory tasks such as sound localization, backward recognition masking, and memory that require perceptual processing of auditory stimuli (Lessard et al., 1998; Stevens & Weaver, 2005; Amedi et al., 2003; Röder & Rösler, 2003). However, EB perform similarly to the SC and LB on tasks that measure low-level sensory thresholds of auditory amplitude (Yates et al., 1972) or gap detection (Weaver & Stevens, 2006). Thus, the enhancements in the EB likely occur at a post-sensory, perceptual stage in the information-processing stream. We previously hypothesized that the speed of consolidating sensory traces of an auditory stimulus into a durable perceptual representation available to cognitive mechanisms, termed perceptual consolidation, might be the mechanism underlying auditory perceptual enhancements in the EB (Stevens & Weaver, 2005). EB individuals were able to form perceptual representations of complex auditory stimuli significantly faster than LB individuals (unpublished results) or SC (Stevens & Weaver, 2005) on an auditory backward recognition mask (ABRM) task. ABRM tasks estimate the time necessary for auditory stimulation to give rise to a stable representation of the stimulus when the stimulus is no longer physically present (Massaro, 1972, a). ABRM tasks require the discrimination between two stimuli that are followed by a backward mask at various mask onset delays (MOD). The delay in time at which the mask no longer disrupts performance indicates the time necessary to perceptually consolidate stimulus elements into a stable representation.

Recent studies have indicated that training on the ABRM task can significantly improve perceptual consolidation rate in SC individuals (Kohout & Stevens, 2006). In addition, functional magnetic resonance imaging (fMRI) demonstrated that the behavioral improvement after ABRM training was accompanied by a decrease in the degree of activity in frontoparietal regions of the brain. The effect of training on functional brain activation in SC has demonstrated plastic changes at both local and global levels in the brain (Buonomano & Merzenich, 1998), and neuroimaging studies have reported three unique patterns of training-related changes in brain activity (reviewed by Kelly & Garavan, 2005). An *increase* in brain activity has been reported from separate sensory, motor, and working memory tasks as an enlargement of the volume of voxels overlaying a particular neuroanatomical area and/ or an increase in peak signal after training (Karni et al., 1995; Honda et al, 1998; Nyberg et al., 2003; Olesen et al., 2004). This pattern of activity may indicate an increase in the number of active neurons or an increase in gain of existing neurons to enhance processing (Furmanski et al., 2004). A *decrease* in activity is the most abundantly reported change in brain activity following training throughout the literature and has been shown in a variety of tasks as a reduction in the spatial extent of activation overlaying a particular neuroanatomical area, a decrease in peak signal, or a decrease in area under the curve (Garavan et al., 2000; Jancke et al., 2001; Erickson et al., 2006; Landau et al., 2004). This pattern of activity has been explained as an increase in the efficiency of a subset of neurons or neuronal networks that was active during acquisition and performance of the task (Petersen et al., 1998). Neurons or networks that are not required for practiced performance are no longer active. Finally, a *reorganization* of functional brain activity is characterized by distinct changes in the location of activity, disappearance of activity, or an addition of new activity following training (Fletcher et al., 1999; Bernstein et al, 2002; Staines et al., 2002; Glabus et al, 2003). Reorganization of activity has been associated with "process switching" in which different tasks are being performed both neurobiologically and cognitively (i.e. different strategic processes) before and after training (Poldrack, 1998, 2000). Although the functional brain activity of auditory backward masking in SC has been observed both with (Kohout & Stevens, 2006) and without training (van Dijk et al., 2003), the pattern of activity in blind individuals before or after training of the ABRM is unclear.

Neuroimaging of the blind brain during non-visual tasks has illuminated different patterns of activation when compared to SC. For example, performance of non-visual tasks by the EB has revealed cross-modal plasticity (CMP) of visual cortical regions commonly associated with the processing of visual information (Amedi et al., 2003;

Gougoux et al., 2005; Theoret et al., 2004). However, the activation of visual cortices in LB individuals during non-visual tasks is a matter of debate (Burton, 2003). Some studies demonstrate V1 activity in LB subjects during non-visual tasks (Büchel et al., 1998 a, b; Burton 2002a,b, 2004), whereas others do not (Sadato et al., 2002; Cohen et al., 1999). It is unclear why the EB, but not LB, consistently show CMP during non-visual tasks. Many factors may influence the location and degree to which CMP may occur in the LB, such as the age of onset of blindness, degree of blindness (e.g. no light or motion perception), and the duration of the blindness.

To our knowledge, this is the first study to investigate training-related changes in behavior and neural activity in an auditory perceptual task using a LB population. We sought to determine if visual deprivation in the LB would lead to greater acquisition and/or performance of the ABRM task compared to previously reported SC (Kohout & Stevens, 2006). We also examined whether five days of training on the ABRM task could improve LB performance to be similar to that of superior, non-trained performance of the EB (Stevens & Snodgrass, in preparation). In addition, fMRI was used to examine and compare patterns of brain activity before and after training of the ABRM task with previously reported SC. We were interested if fMRI would reveal CMP in the LB brain during acquisition of the ABRM task, after intensive training on the ABRM task, or not at all.

Methods

Subjects

Seven late-blind individuals participated in this study. Each subject was evaluated for hearing deficits, cognitive or neurological illness, and cause of blindness. The group consisted of 5 males and 2 females (one left-handed) with a mean age of 52 (range (36-62). Table 1 shows each subject's age, cause of blindness, age of blindness onset, and relative Braille experience. All subjects provided informed written consent approved by the Oregon Health and Science institutional review board. One subject (AS) did not participate in fMRI scanning due to recent surgery.

--------- Insert Table 1 Here ---------

TOJ

Behavioral tests were conducted in a quiet testing room. The TOJ task was designed to measure the minimum amount of time needed to discriminate the order of presentation of two 10 ms tones (2 ms rise/fall time): one "low" tone (2 kHz) and one "high" tone (4 kHz) sampled at 44kHz and presented binaurally (Figure 1). On each trial the tone order was determined randomly, with an initial stimulus onset asynchrony (SOA) of 100 ms (onset-to-onset). Subjects indicated the order of two tones played by pressing the appropriate response key on the keyboard. Utilizing a three-down, one-up rule, the SOA between tones decreased by 10% after three correct responses and increased by 10% after one incorrect response. This procedure provides a response accuracy of 79% (Levitt, 1971). A reversal was calculated when the SOA direction switched (i.e. from increasing to decreasing, or vice versa). Subjects performed the task until they committed eight reversals. The threshold SOA was calculated using the mean SOA value over the last four reversals from two runs of the TOJ task. Stimulus presentation, timing and data acquisition was managed by Presentation™ software (Neurobehavioral Systems, www.neurobs.com). Stimulus timing and waveforms were monitored with an oscilloscope (Tektronix, Beaverton, OR). Subjects listened to digitally generated stimuli through Sennheiser™ HD265 headphones.

ABRM

Two tone-pair stimuli were created for the ABRM task. The 2 kHz and 4kHz frequencies (20 ms duration; five ms rise and fall time) were used to create tone-pair stimuli (High-Low, Low–High), with the SOA threshold obtained from the TOJ used to separate the tones within a pair (Figure 1). Subjects were required to demonstrate 90% accuracy on 40 non-mask trials before beginning the ABRM. If subjects failed to reach 90%, 10 ms was added to the tone-pair SOA, and they were re-tested. Upon reaching 90% accuracy, subjects performed a two-alternative forced-choice discrimination with and without a backward mask. Tone-pairs were separated by a 500 ms ISI. On mask trials, the mask was 100 ms of combined 2 kHz and 4 kHz frequencies with 10 ms rise and fall times, and was presented following the offset of the second tone-pair at mask onset delays (MOD) of 0, 10, 20, 40, 80, 160, and 320 ms. In addition to the mask trials, non-mask trials were also presented to ensure that discrimination of the stimulus pairs was maintained throughout the task. The non-mask and mask trials were presented pseudo-randomly such that all MODs were sampled without replacement before the list was re-initiated. Each MOD and non-mask condition was presented 50 times for a total of 400 trials.

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Training

Each subject participated in 7 days of training over an 11-day period in which the pre-test began on a Friday, training was carried out Monday through Friday of the next week, and the post-test was completed on the following Monday. The first and last sessions lasted for about 2.5 hours and each of the five training days lasted one hour. Subjects completed 660 trials per day of the ABRM task during the week between pre and post-tests. Three blocks of 200 trials were completed each day, with 20 non-mask practice trials before each block. One version (progression), used the same adjustment of MOD as described above, with a starting MOD of 320 ms and reduced the delay by 10% (i.e. 32 ms) after three correct answers or increased 10% after one incorrect answer. The second variation of the ABRM training (intensity) manipulated the intensity of the mask at a set MOD. The 65% MOD calculation from the pre-test ABRM was the initial delay at which the mask was played. The backward mask intensity (BMI) started at an inaudible level (30 db SPL) and increased after 3 successive correct answers by a factor of 1.2 (BMI = BMI * 1.2). After one incorrect answer the intensity of the mask was attenuated by a factor of 1.2.

fMRI scanning

Functional images were acquired with an EPI-BOLD pulse sequence on a whole-body 3T Siemens Trio (Munich, Germany) scanner using a standard two-channel head coil. Using an event-related design, the functional data was acquired with a navigator echo-guided, prospective motion correction clustered acquisition technique with the following parameters: repetition time (TR) = 2330 ms, delay in TR = 900 ms, echo time (TE) = 50 ms, flip angle (FA) = 90°, field-of-view (FOV) = 240 mm^2, imaging matrix =

64 x 64, and 17 slices with a 5 mm slice thickness in axial orientation for maximal coverage of the brain. The slice volume was acquired during the initial 1430 ms of each TR leaving a 900 ms interval between TRs for trial presentation. To reduce expectation and habituation effects on the time course functional activity, a jitter of 5,6, or 7 TRs was used. A high-resolution, heavily T1-weighted anatomical scan (3D MPRAGE), was acquired for anatomical co-registration with the functional data, using the following parameters: 144 axial slices, slice thickness 1 mm, TR = 2300 ms, TE = 4.38 ms, FA = 12°, FOV = 256 mm^2, imaging matrix = 256 x 256. The subject's head was stabilized with padded clamps attached to the head coil.

Auditory stimuli were presented via Koss (Milwaukee, WI) electrostatic headphones inside the scanner. A button box was used to record responses both in the testing room and inside the scanner. The pre and post-test scans consisted of an event-related version of the ABRM task. Practice trials were played for the subject before the scanning session began in order to adjust them to the scanning environment. Subjects were instructed that they would hear an alert sound (three 600 Hz 50 ms tones with 50 ms ISI) followed by a scanner acquisition and then a trial that consisted of the two tone-pairs and a mask. Three mask onset delays were used: two were fixed (0 ms and 160 ms) and a third that was calculated at the MOD needed to perform the task at 65% accuracy. This condition was set to each subject's 65% accuracy level in order to determine the change in functional activity when difficulty level was matched. The 10 and 160 ms conditions allowed for comparison of changes in functional activity when task difficulty changed (presumably easier in the post-test). The fourth, no-trial (NT) condition was used as a baseline during which the subject heard the alert sound followed by a scanner acquisition but no trial stimuli. In this instance, the subject waited for the next alert sound. This condition allowed for detection of brain areas showing preparatory response to the alert sound alone. Each condition was presented 20 times for a total of 80 trials.

Data Analysis

Behavior

To evaluate the effect of training on the 65% MOD threshold performance change in the ABRM task, a repeated measure analysis of variance (ANOVA) was completed using SPSS statistical software (Chicago, Il). We were also interested if five days of intensive ABRM training could increase LB behavioral performance to be similar to that of non-trained EB performance on the same task (Stevens & Snodgrass, in preparation). To do this, a percent correct score was calculated at each MOD (7) for each subject (7). To establish that the LB performed significantly lower during initial performance of the ABRM task, pre- training LB data was compared to that of non-trained scores from EB subjects who performed the same task using repeated measures ANOVA. To assess how training affected LB performance on the ABRM task, post-training ABRM performance in the LB was compared to the non-trained performance of the EB using a repeated measures ANOVA.

------- Insert Figure 2 Here ------

Imaging

Functional data were analyzed using Brain Voyager QX software (Brain Innovation, Maastricht, The Netherlands). The functional data were preprocessed using slice-time correction, linear trend removal, and a high-pass filter at 5-cycles/ time course to remove low-frequency oscillations in the fMRI signal. All functional data were interpolated into 1x1x1 mm^3 voxels, z-normalized, and transformed to standard Talairach stereotaxic space (Talairach & Tournoux, 1988) to allow for pooling across subjects.

Volume maps of significant functional activity for pre and post-training scans were created using a random effects general linear model (GLM) in order to visualize ROIs that were responsive during the task. The random effects analysis allowed for a stringent criteria and greater generalization to the population level. All maps used a minimum cluster-size of 100 contiguous voxels and a p-value of .005 to control for false discoveries and restrict the analysis to display only groups of highly active voxels. Two contrast analyses were then completed for pre and post-scans. First, a 160 ms > NT contrast was completed to examine the effect of not controlling for task difficulty on brain activity after training. The NT condition was subtracted from the 160 ms condition because both contained an alert cue but the NT condition never contained an ABRM trial. The second contrast that was completed subtracted the NT condition from the 65% condition (65% > NT). This contrast allowed for observation of brain activity before and after training when task difficulty was held constant in the 65% condition.

The resulting pre and post-training z-maps for each contrast were then overlaid in order to characterize the location of active ROIs. Brain Voyager software was used to manually define and quantify the volume (in voxels) of overlapping pre- and post-training ROIs to determine the degree to which activity changed after training (Table 2).

Pre- and post-training BOLD time course comparison

To determine how the blood oxygen level dependent (BOLD) signal within a ROI changed after training, BOLD signal values for each ROI were extracted and were averaged by trial type. The average percent BOLD signal change from baseline for each scanner acquisition (time in seconds) from each individual subject was then averaged across the group. Pre- and post-training group averages were then compared to assess the degree of signal change within an ROI after training.

--------- Insert Table 2 Here ---------

Results

Auditory Backward Recognition Mask Performance

The LB group had a pre-training average 65% MOD calculation of 73 ms and a post-training average of 37 ms (Figure 2A). At the alpha level = 0.05, a one-factor repeated measures ANOVA revealed a significant effect of time (F (1, 5) = 7.095, p = .045) using the Greenhouse-Geisser correction for violations of sphericity. Figure 2B shows the change in ABRM performance for each individual subject. The type of training had no effect on performance. LB subjects did not show an advantage in acquisition or overall performance in the ABRM task when compared to a group of SC subjects (F < 1; data not shown) who participated in the same training task previously reported (Kohout & Stevens, (2006).

ABRM performance of the LB before and after training was compared to that of EB subjects who performed the ABRM task without practice (Stevens & Snodgrass, in preparation). Before training, LB performance on the ABRM task was inferior to that of EB subjects (Figure 3). A repeated measures ANOVA revealed a main effect of group (F(1, 10) = 17.22; p = 0.002), a main effect of MOD (F(1.82, 18.23) = 24.04; p = 0.000). There was not a group by MOD interaction (p = 0.295). We also examined whether training improved ABRM performance of the LB at each MOD to be similar to the non-trained EB. A repeated measures ANOVA revealed a main effect of MOD (F(1.78, 17.76) = 17.46; p = 0.000), but importantly, not a main effect of group (F(1,10) = 0.973; p = 0.347. This means that training improved LB performance to be not significantly lower than that of the EB. There was not a group by MOD interaction (p = 0.187).

ROI Volume and Time Course Analysis

Event-related fMRI revealed extensive activity throughout the brain from the pre-training scan under the 160 ms > NT contrast (Figure 4). In stark contrast, there was no significant activity observed after training when using the same contrast. Thus, when pre- and post-training scans were overlaid, there were no overlapping regions of activity when task difficulty was not controlled for in the 160 ms condition. It is possible that lack of post-training activity could result from a combination of a decrease in the 160 ms BOLD response and increase in the NT BOLD response. However, the BOLD signal from the 160 ms and NT conditions both seemed to decrease after training (e.g. Fig. 6, right).

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Extensive pre-training activity was also observed in the 65% > NT contrast. However, unlike the 160 ms >NT contrast, significant post-training activity was observed in the 65% > NT contrast (Figure 5) although to a far less extent than in the pre-training scan. Ten distinct ROIs were significantly active in the post-training contrast maps that overlapped precisely with pre-training activity (Table 2). The difference in observed activity between these two contrasts is a lack of any significant post-training activity when task difficulty became easier with training (i.e. 160 ms > NT condition), versus the small but significant activity observed in 10 ROIs when task difficulty remained constant (i.e. 65% > NT contrast).

Upon further examination, the BOLD signal within the 160 ms condition consistently decreased after training across the brain when task difficulty was not held constant. Event-related activity from the inferior parietal lobule (IPL) demonstrates how the 160 ms curve decreases after training, but the NT condition remains relatively unchanged (Figure 6). Conversely, when pre- and post-training scans were overlaid, there was overlapping activity in the IPL in the 65% > NT contrast. Event-related time course of the BOLD signal of the 65% condition only showed a slight trend to decrease in various ROIs when task difficulty was held constant (Figure 6). Thus, significant post-training activity was still observed in the z-map of the 65% > NT contrast.

We examined the group-averaged pre and post-training activity in the occipital lobe of the LB for CMP in response to the ABRM trial. To ensure that any observed activity was in response to the ABRM stimuli and not the alert cue, the 65% > NT and 160 ms > NT contrasts were used. Neither the 65% > NT contrast or the 160 ms >NT contrast revealed a significant volume of CMP in any part of the occipital lobe before or after auditory training (Figure 7).

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Discussion

The results from our novel training study reveal several notable conclusions regarding auditory perception in the LB. First, five days of training significantly improved behavioral ABRM performance. Second, late onset blindness does not confer an advantage in acquisition or overall performance of the ABRM task when compared to

SC subjects who participated in the same training regimen. Third, training significantly improved ABRM thresholds in the LB. Further analysis of ABRM performance at each MOD indicated that, after training, the LB were performing at similar levels as non-trained EB individuals. Fourth, fMRI maps reveal a decrease in the volume of brain activity at whole-brain and ROI levels after training. The BOLD signal intensity decreased within all ROIs when the task difficulty became easier (160 ms) from pre- to post-training, but remained relatively unchanged when task difficulty was held constant (65%). Finally, significant CMP was not observed either during acquisition or after extensive training on the ABRM task.

Training induced changes in behavioral performance

Five days of training significantly improved the average 65% MOD threshold in the ABRM task for our LB subjects. Training also increased the percentage of correct responses at each MOD. Other training studies have improved cognitive measures such as memory, reasoning, and speed of processing with long-lasting effects up to two years after training (Ball et al., 2002). Previous auditory training studies have demonstrated significant performance gains after five days of training (Kohout & Stevens, 2006; Tremblay et al., 1998; Menning et al., 2000; Jancke et al., 2001; Gaab et al., 2006), but none have utilized a sensory-deprived population. Using the exact same experimental design as described in this study, Kohout and Stevens (2006) trained SC subjects on the ABRM task. Comparison across studies reveals that initial performance on the ABRM task was similar between LB and SC groups, as was the degree of improvement in 65% MOD threshold after training. The results demonstrate that late onset blindness did not enhance the acquisition or skilled performance of the ABRM task compared to SC.

Initial performance of the LB was inferior to that of non-trained EB who performed the same task (Stevens & Snodgrass, in preparation). However, training was able to improve the initial inferior performance of the LB to a similar level of performance of the EB. One factor that may explain why EB demonstrate superior performance during initial performance on a task is the age of onset of blindness. EB have been reported to outperform the LB in other tasks such as non-spatial auditory tasks (Gougoux et al., 2004). Changes in the neural mechanisms that underlie compensatory abilities of the spared modalities may prosper during the beginning years of life. Consequently, the compensatory changes in neural connectivity may be restricted for individuals who lose their sight after visual maturity.

------- Insert Figure 5 Here ------

Training induced changes in neural activity

Studies examining the time course of auditory perceptual learning have demonstrated that significant changes in neurophysiological measures occur on the same day or before behavioral improvements (Tremblay et al., 1998). Thus, we hypothesized that neurophysiological changes would have occurred in the LB before changes in behavioral performance. Indeed we observed notable decreases in the volume of active voxels from pre- to post-training produced from both general linear model contrasts. This result is consistent with the results from our previous training task with SC using the same experimental design (Kohout & Stevens, 2006). In that study, our analysis revealed a trend for the volume of neural activity to decrease at the whole-brain and ROI levels. Even-related analyses revealed significant decreases in BOLD signal in intraparietal sulcus (IPS), DLPFC, and anterior cingulate cortex (ACC); core components of the human working memory and attention systems. Pre- and post-training activity showed precise anatomical overlap suggesting that training-related enhancement of performance resulted from the improved efficiency within these frontoparietal networks. When task difficulty was held constant (65% > NT) in the current experiment, significant overlap of pre- and post-training activity was observed in similar networks underlying executive function such as the ACC, IPL, and SPL. Since we did not observe a reorganization of activity in either study, which is associated with strategy-switching, it is likely that the observed decrease in the volume of activity represents an improved efficiency of the neuronal networks that were active during acquisition and initial performance of the task (Petersen et al., 1998). In other words, only a subset of neurons active before practice were required to maintain the same level of performance (i.e. 65%) after practice.

However, when task difficulty was not held constant (160 ms > NT), there was not a significant volume of post-training activity and thus no overlap of pre- and post-training activity. BOLD signal within active pre-training ROIs decreased after training. This may be explained by the fact that since the MOD was held constant in the 160 ms condition, subjects became familiar with the condition and the task became easier. Because the MOD was more than long enough for the perceptual consolidation process to occur, the subject easily able to make a correct order judgment. As the perceptual consolidation rate improved with training, the 160 ms MOD became easier resulting in a decrease in the BOLD signal.

------- Insert Figure 6 Here ------

Recent studies have discussed the involvement of frontal lobe and posterior parietal regions in the voluntary control (top-down) influence of attention during cognitive tasks (Yantis & Serences, 2003; Serences et al., 2005; Kincade et al., 2005). Activation of these areas may improve performance on highly demanding cognitive tasks by anticipating trial presentations. Corbetta and others (2000) demonstrated that the IPS was activated during the direction and maintenance of attention to a location in space. They suggested that the IPS is involved in top-down, voluntary control of attention since the area was active during a cue period before a stimulus was presented. Although largely studied for its role in control of visual attention, parietal activation has been shown in auditory tasks requiring top down attention (Shomstein and Yantis, 2006). These areas may have been more active before training by detecting discriminative information to perform the task. However, activity from these areas may decrease after repeated presentation of the trials during training. Additionally, the ACC has been implicated in a large number of executive processes, but most recently has been related to cognitive conflict and perceived error-likelihood during highly demanding cognitive tasks (Brown & Braver, 2005). As more correct answers are made with practice, error-likelihood decreases. The effect of training to decrease activity of attention serving brain regions has been shown before (Raichle et al., 1994; Erickson et al., 2006), and is biologically relevant as it might free up attentional resources to be reallocated for use in other cognitive processes. This does not necessarily mean that other brain areas would increase in activity, because new stimuli are not presented in a trial and no new cognitive processes are required. However, if an additional stimulus was to be presented that required cognitive processing, the extra resources may be used to attend and aid in the processing of the new stimulus.

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The effect of late onset blindness on neural activity

Many studies have demonstrated that early blind (EB) individuals display enhancements when compared to LB or SC on tasks of auditory sound localization (Lessard et al., 1998), auditory memory (Amedi et al., 2003; Röder & Rösler, 2003,) auditory attention (Collignon et al., 2006) and in auditory backward recognition mask tasks (Stevens & Weaver, 2005). A critical element that may account for the enhanced behavioral performance of the EB may be CMP. Many studies have observed CMP of visual cortical areas that normally process visual information during non-visual cognitive tasks (Kujala et al., 1995; Röder et al., 1996; Sadato et al., 1996, 1998; Weeks et al., 2000), and have even correlated superior performance on these tasks with the degree of CMP (Amedi et al., 2003; Gougoux et al., 2005).

However, the ability of the LB brain to display CMP during non-visual tasks is controversial (Burton, 2003). For example, Sadato et al., (2002) reported that area V1 was activated during a tactile discrimination task in blind subjects who lost their sight before 16 years of age (EB), but was suppressed in blind subjects who lost their sight after 16 years of age (LB). Conversely, Burton and others (2002a,b) demonstrated that both EB and LB subjects displayed visual cortical activity during verb generation in response to Braille-read or heard nouns. Our task design did not reveal any CMP in the group-averaged LB data before or after training. Two contrasts were used (65% > NT; 160 ms > NT) to guarantee that any observed activity was related to the processing of ABRM stimuli and not the presentation of the alert cue. A contrast of the 65% or 160 ms conditions to baseline would only provide a measure of V1 response to auditory stimulation and not ABRM stimulus processing.

Given the importance of the auditory modality for blind individuals, it is unfortunate that LB individuals cannot utilize the compensatory behavioral advantages typical of the EB. Therefore, training-induced improvements on auditory tasks may allow for enhanced learning and adaptation of LB individuals to their new environment at a faster rate than normal. Understanding the changes in functional brain activity is important in order to understand which types of training can maximize improvement in learning. We did observe decreases in BOLD signal from frontoparietal brain regions in the LB both when task difficulty was held constant and when it became easier. Therefore, in order to increase brain activity in these areas, and presumably behavioral abilities as well, the level of difficulty of a task must be increased with training. It is not surprising then that studies of high cognitive demand which require processing of two tasks at once (Erickson, 2006) or the increase in working memory capacity (Nyberg, 2003; Olesen, 2004) show increases in functional brain activity after training. Therefore, in the case of the LB, training tasks should be devised which target specific functions important to perception of the auditory environment. These include sound localization, the speed of auditory information processing, and auditory memory. The difficulty of the task should be increased over time in an attempt to increase brain activity, and hopefully auditory perception.

Table 1. Subject data

SUBJECT	AGE	CAUSE	AGE OF ONSET	BRAILLE (yrs)
AS	45	Diabetes	29	Yes (13)
CK	62	Diabetes; Glaucoma	32	Yes (20)
DC	36	Glaucoma	22	Yes (11)
FS	61	Retinitis Pigmentosa	32	Yes (16)
PK	41	Retinal Detachment	8	Yes (24)
RH	52	Rigors; Glaucoma	7	Sparse (0)
TC	58	Cong. Cataracts	12	Yes (35)

Table 1. Description of age, cause of blindness, age of onset, and Braille experience of late blind participants. All diabetic subjects checked insulin levels at home prior to training. Subject AS was excluded from scanning due to additional medications.

Table 2. Overlapping ROIs in the 65% > NT contrast

	Radiologic Conv.		Pre	Post		
ROI	**Hem**	**Tal**	**Voxels (mm^3)**		**Voxel Change**	**% Change**
ACC	R	5, 8, 50	9,987	356	-9,631	2,706
ACC	L	-8, 4, 45	10,986	1,063	-9,923	934
FEF	L	-24, -11, 55	1,168	134	-1,034	773
INS	R	33, 16, -1	5,715	179	-5,536	3,094
IPL	R	33, -54, 40	7,008	615	-6,393	1,041
MTG	L	-44, -58, -4	641	773	132	-16
PreCG	L	-40, -3, 39	4,840	599	-4,241	709
PreCG	R	51, -3, 37	687	116	-571	493
Precun	L	-21, -76, 27	4,299	132	-4,167	3,158
SPL	L	-22, -63, 46	4,275	258	-4,017	1,558

Table 2. Description of hemisphere (hem) and talairach coordinates (X, Y, Z) for the overlapping pre and post-training ROIs using the 65% > NT contrast.

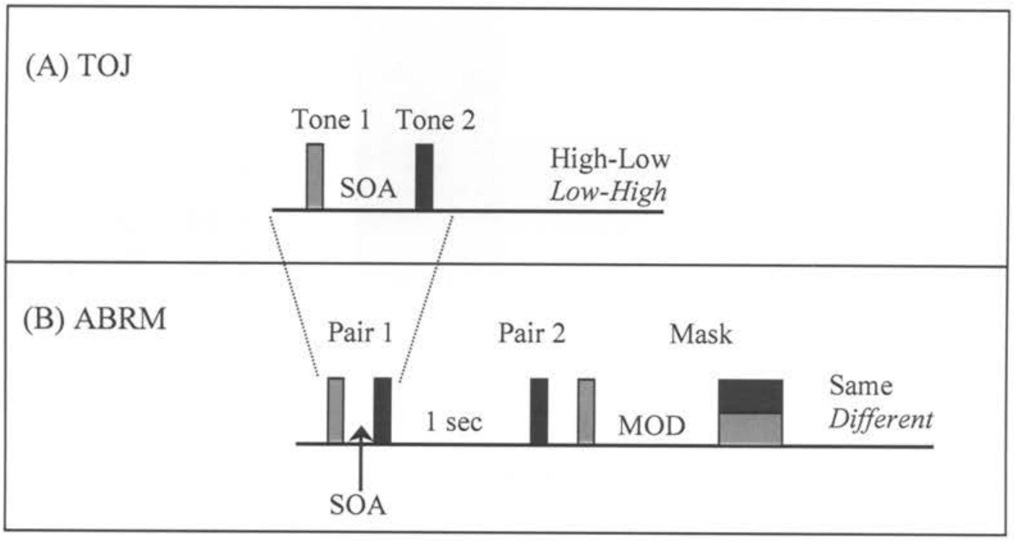

Figure 1. TOJ and ABRM. A) The TOJ task presented two tones (2 and 4 kHz) on each trial in random order. The stimulus onset asynchrony (SOA) was progressively decreased according to a 3-down/ 1-up rule to determine each subject's minimum threshold for accurately perceiving the order of two tones. B) The ABRM task presented two tone-pair stimuli (pair 1 & 2) followed by a masking sound at various delays (mask onset delay, MOD) ranging from 0 – 320 ms. The mask consisted of the 2 and 4 kHz tones presented together for 100 ms.

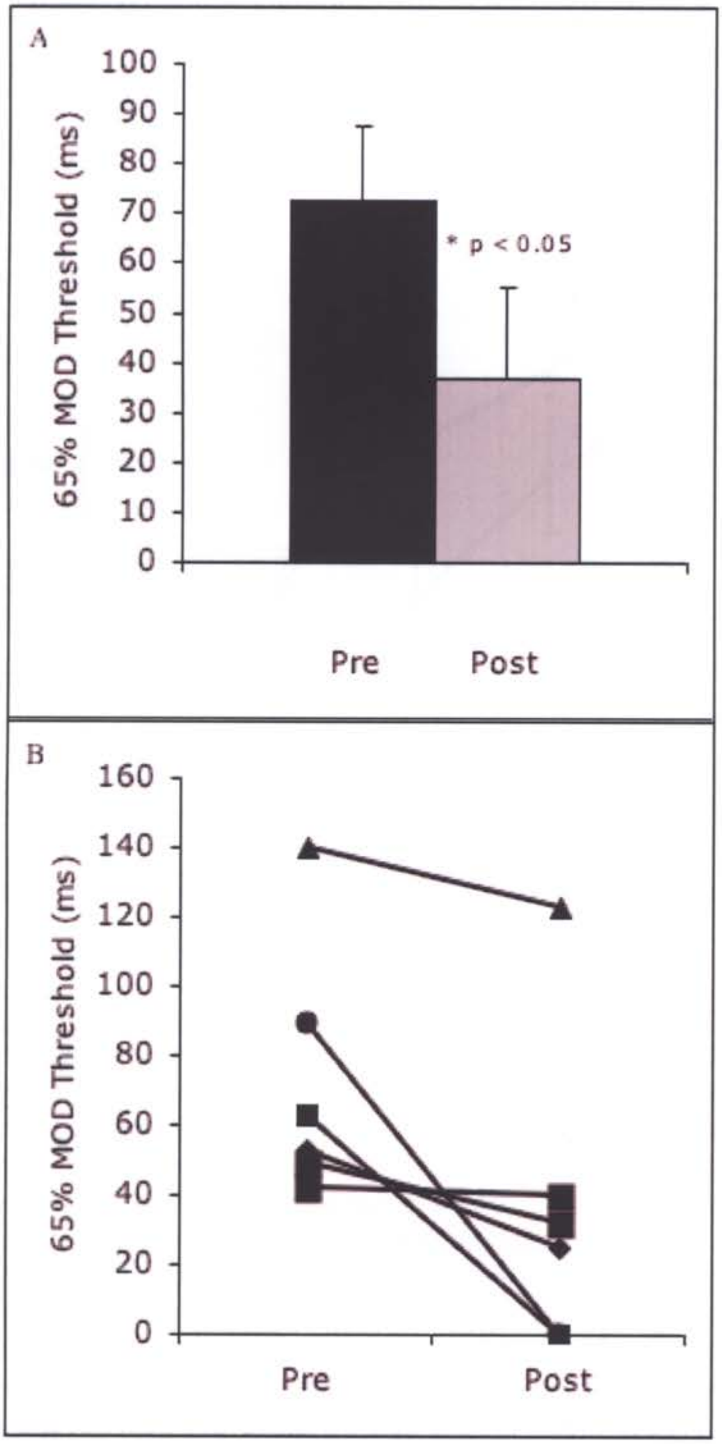

Figure 2. A) Group averaged pre- and post-training65% ABRM calculation. Error bars represent standard error. Reductions in average 65% ABRM calculation were significant at the alpha = 0.05 level using a repeated measures ANOVA. B) Individual pre- and post-training65% ABRM performance.

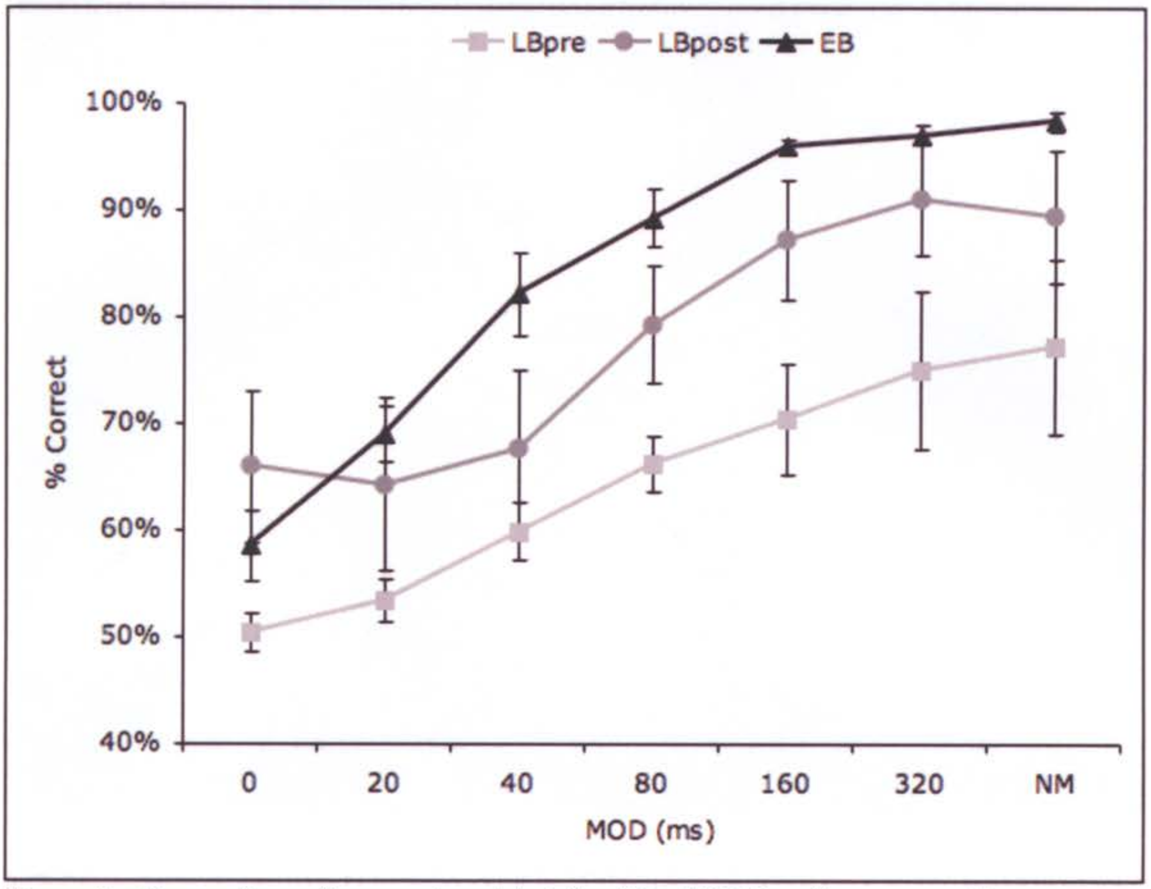

Figure 3. Comparison of pre- and post-training LB ABRM performance with non-trained EB ABRM performance (unpublished results). A multivariate general linear model revealed significant differences in the percentage of correct responses during all MODS between pre-training LB and non-trained EB (all p's < 0.049). A repeated-measures ANOVA (time) revealed that at all MODs improved from pre- to post-training in the LB, but the effect of time was not significant (p = 0.072). Pairwise comparisons of all MODs revealed only trends for improvement (all p's > 0.054). A comparison of post-training LB and non-trained EB performance using a multivariate general linear model revealed that there was not an effect of group (p = 0.153). The percent correct performance did not differ between post-training LB and non-trained EB at any MOD (all p's > 0.162).

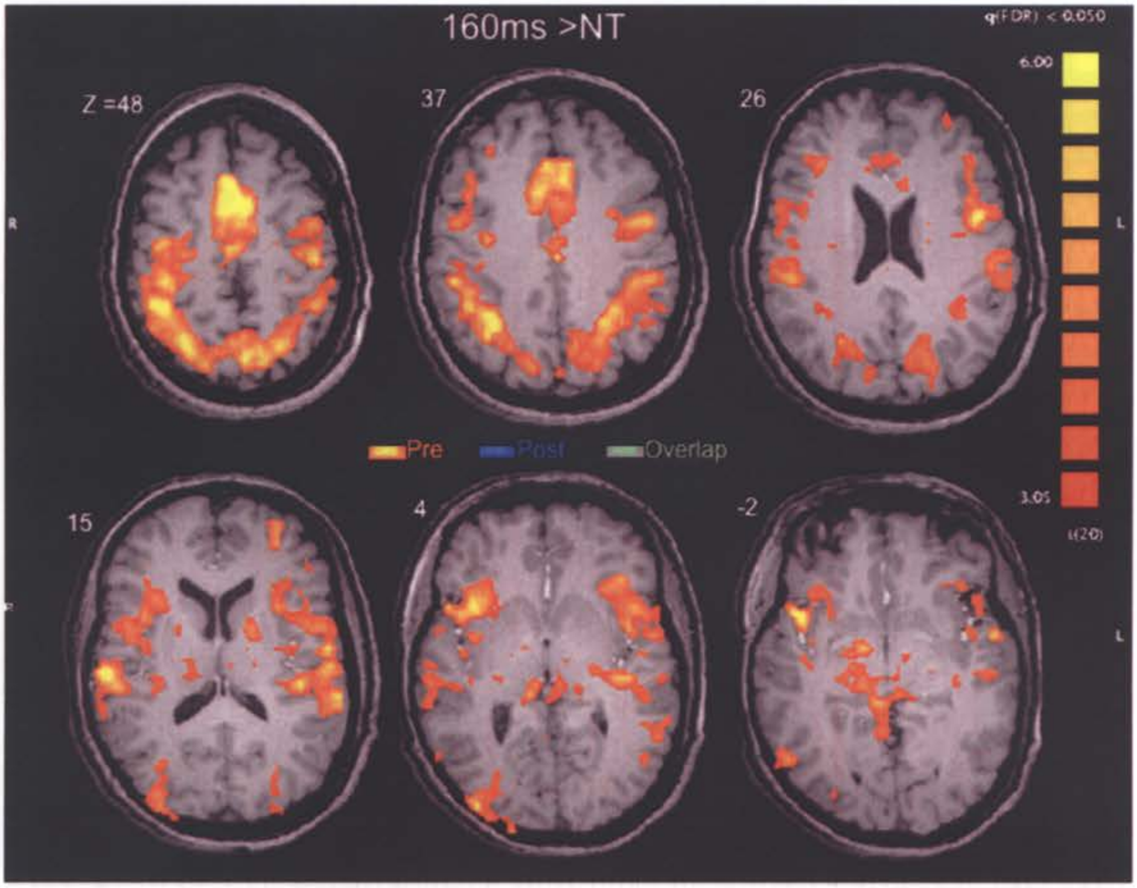

Figure 4. Standard talairach brain with co-registered functional BOLD activity using the 160 ms > NT contrast. Functional activity from pre and post scans was analyzed using a random-effects general linear model and then pre (yellow/orange) and post (blue/purple) were overlaid on a standardized brain. A false discovery rate threshold of 0.05 and a cluster minimum of 100 contiguous voxels were used to remove small bands of activity and display only highly active voxels. Using the 160 ms > NT contrast, significant post-training activity was not observed, resulting in an overall decrease in the volume of functional activity following training.

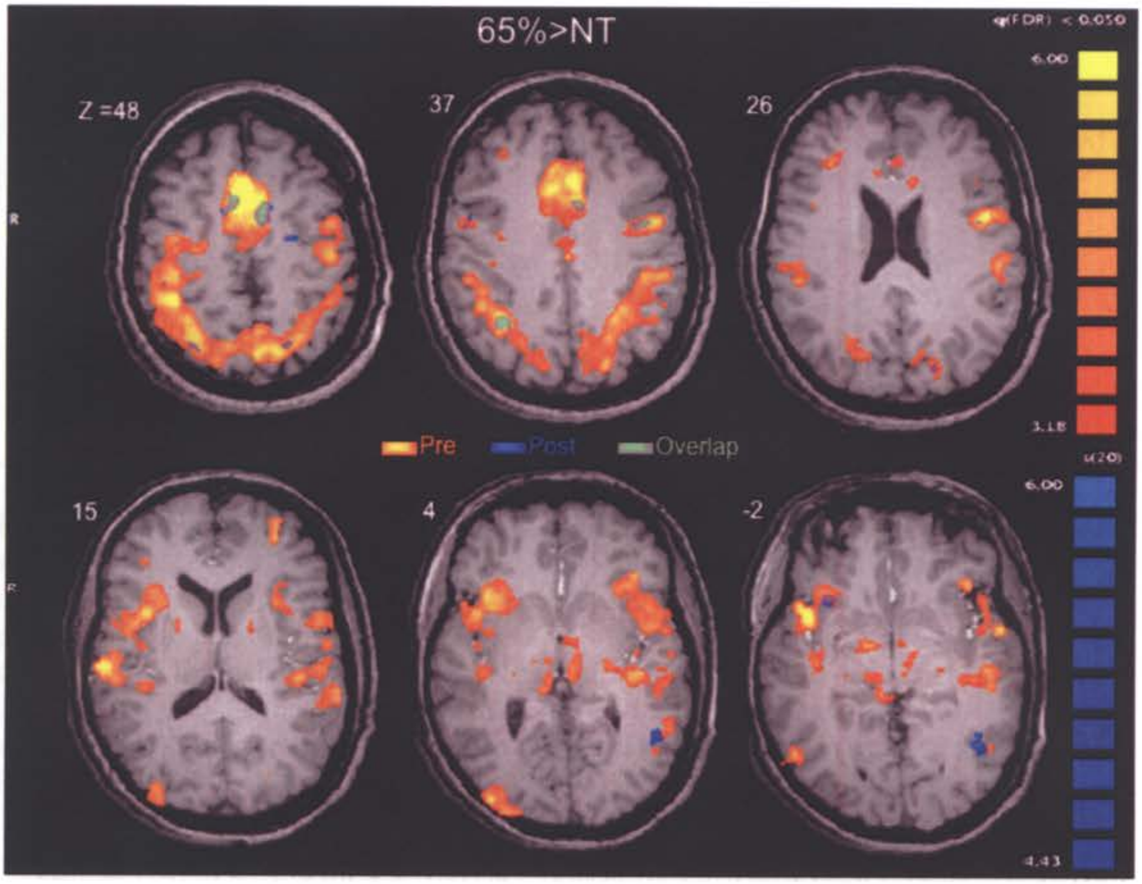

Figure 5. Standard talairach brain with co-registered functional and event-related BOLD activity using the 65% > NT contrast. Functional activity from pre and post scans was analyzed the same as in Figure 4. Using the 65% > NT contrast, significant activity was observed both before and after training. Overlapping regions of pre and post-training activity (table 2) were found in the left and right cingulate cortex, left frontal eye field, left and right posterior parietal lobe, left motor cortex, left precuneus, left middle temporal gyrus, and right insula.

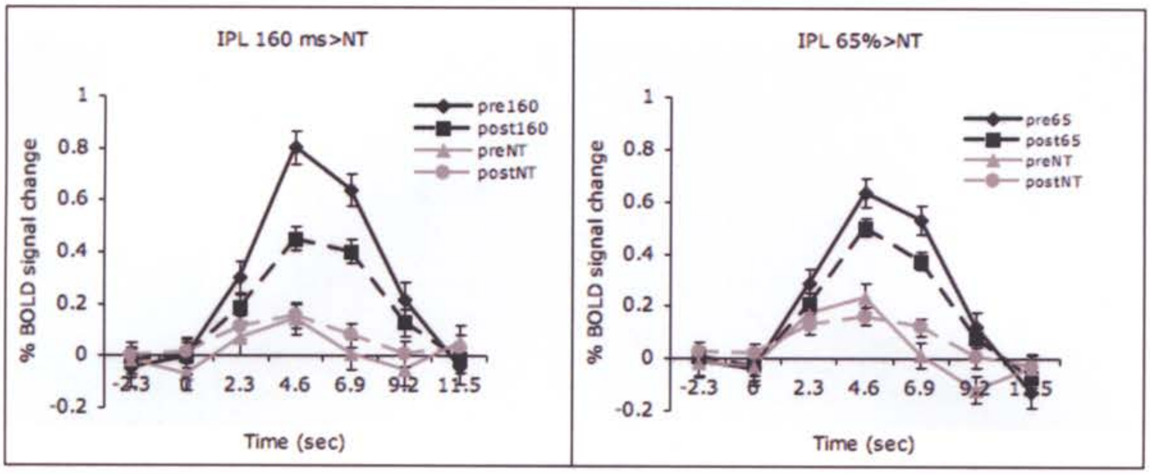

Figure 6. Event-related time course of BOLD activity in the right IPL. *Left:* The graph shows the decrease in event-related BOLD activity from pre (solid line) to post- (dashed line) training in the IPL from the 160 ms condition. The vertical axis represents the percent change in BOLD signal from baseline. The horizontal axis represents the sequence of a trial where the cue is presented at zero seconds and the ABRM stimuli at 2.3 seconds. *Right:* The graph shows how the time course of event-related BOLD activity does not decrease as much when using the 65% condition from the same IPL ROI.

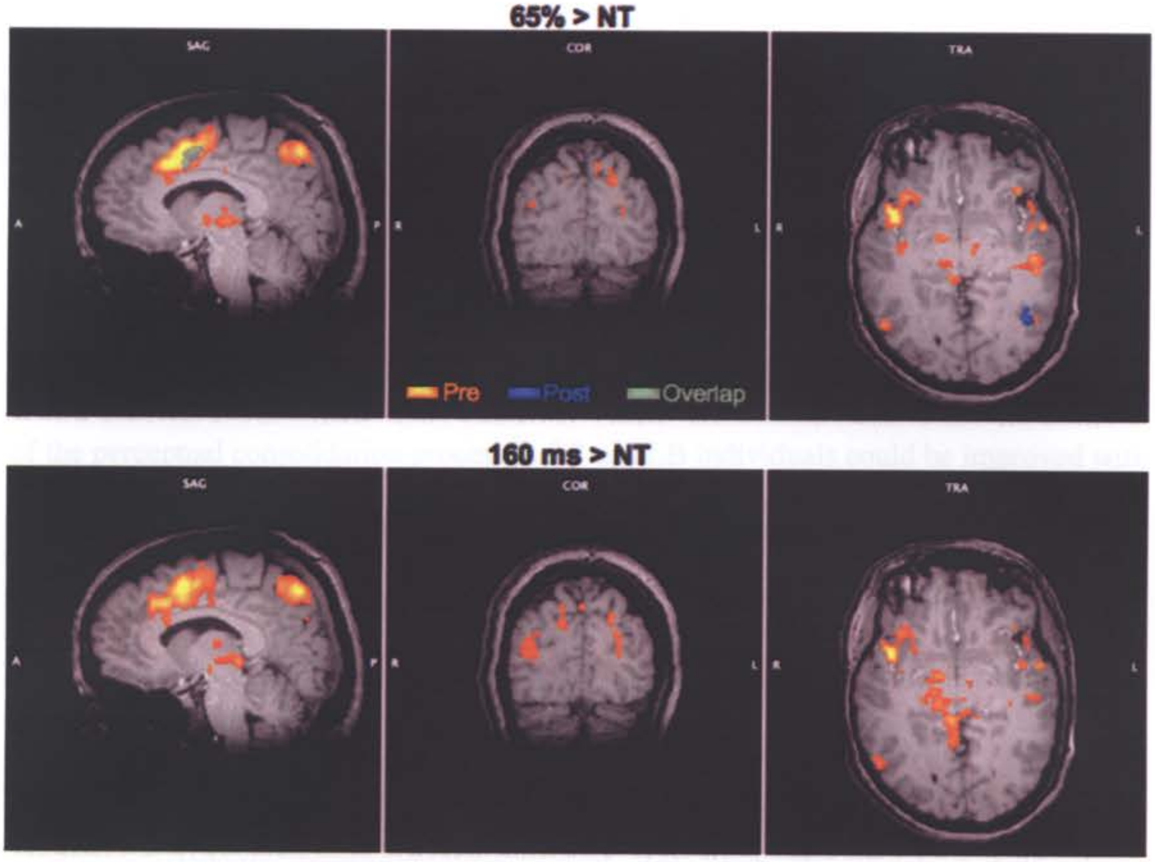

Figure 7. Overlay of z-maps before (yellow/orange) after (blue/purple) training using the 65% > NT contrast (top) and 160 ms > NT contrast (bottom). Gray/ green areas represent areas of overlapping pre- and post-training activity. No cortical activity was observed in the occipital lobe before or after seven days of auditory training. Data were analyzed using a general linear model with a false discovery rate threshold of 0.05 and a cluster minimum of 100 contiguous voxels (see methods).

Chapter 5: General Discussion

The results presented in this thesis support our hypothesis that a positive relationship exists between the speed of auditory information processing and auditory STM capacity. Individuals with a fast rate of perceptual consolidation in the ABRM task also had a larger STM memory capacity in the TST task. We hypothesized that the speed of the perceptual consolidation process in SC and LB individuals could be improved with five days of training. Our hypothesis was supported by significant improvements in both LB and SC ABRM thresholds after training. Performance gains in the LB were no different than in the SC, and reached an asymptote similar to performance of non-trained EB (unpublished results). This suggests that blindness alone does not confer enhanced auditory perceptual abilities. Rather, enhanced ability seems reserved for individuals blinded early in life during development. However, it does seem that the speed of auditory information processing can be improved with training.

This thesis also demonstrated through the use of fMRI that improvements in ABRM performance were accompanied by changes in functional brain activity. Functional MRI was an ideal technique to employ because it allowed for examination of the hemodynamic response of a brain region to an ABRM trial over time. Conditions devised here enabled the examination of brain activity related to both task difficulty and sensory stimulation. In both conditions, a reduction in the overall volume of activity was observed in the same ROIs in SC and LB groups. Overlapping fronto-parietal brain regions were active before and after training when task difficulty was held constant. In contrast, there was no overlap of pre- and post-training activity when task difficulty was not held constant because post-training activity decreased below significance. This suggests that fronto-parietal areas such as the IPL, DLPFC, and ACC are related to the degree of concentration required to perform a task at a certain level (e.g. 65%) in both LB and SC. Fronto-parietal regions are often cited as being areas of the brain related to attention and memory (Mesulam, 1990). Since activity in these regions decreased both when task difficulty was held constant and when it decreased, future training studies should increase the difficulty of the task over time in an attempt to increase brain activity, and presumably auditory perception.

This thesis also addressed a controversial issue of whether the LB exhibit CMP during non-visual tasks (Burton, 2003). LB individuals were trained on an auditory perceptual task to examine if CMP would be observed before or after training. Here, group-averaged fMRI results demonstrated that CMP was not observed in the LB occipital cortex before or after auditory training. This result is similar to some studies that have demonstrated a lack of CMP in the LB during non-visual tasks (Sadato, 2002), but is in contrast to other studies that have demonstrated CMP in the LB (Burton, 2004). CMP has been associated with superior sensory perceptual processing and memory abilities in the EB (Gougoux et al., 2005). Since CMP was not observed in the brain of our LB subjects, and their initial behavioral performance was inferior to the level of the EB (unpublished results), our results indirectly support a functional role for CMP in the EB. The changes in neural activity that accompanied improvements in performance after training arose from general-purpose attention areas in frontal and parietal cortices. The combined behavioral and imaging results suggest that improvements in the auditory perceptual abilities in the LB are similar to what can be achieved in the SC, and are limited to what can be achieved through the training of auditory attention.

Perceptual consolidation as a fundamental limit to sensory perceptual processing

Tasks across modalities that have demonstrated an effect of the speed of stimulus consolidation on behavior have fueled the question of whether a fundamental limitation exists on sensory perceptual processing. This limitation could be the perceptual consolidation process. Similar to the ABRM, RSVP tasks have found that a certain amount of uninterrupted time is needed for perceptual processing of a stimulus. In the RSVP, two target stimuli (T1, T2) are embedded within a list of up to 20 distractor stimuli. At the end of a trial, the subject must recall the presence of T2 after correctly identifying T1. The subject is often unable to report the presence of T2 when it follows 200-600 milliseconds after T1. This refractory period has been termed the attentional blink (AB) because it reflects the amount of time in which attentional processes are dedicated to the perceptual processing of T1 (Raymond et al., 1992; Vogel et al., 1998; Vogel & Luck, 2002). This blink in attention renders the person temporarily unable to perceive subsequent stimuli. The AB has also been demonstrated in the auditory system (Duncan et al.1997; Goddard & Slawinski, 1999; Tremblay et al., 2005; Vachon, 2005). In the auditory RSP task, varying the temporal separation between two targets allows for the measurement of auditory information processing time (Duncan et al., 1997). Subjects significantly missed detection of T2 when it was presented up to 375 milliseconds following T1.

Similar perceptual processing durations are observed in the ABRM task. In its most simple form, the ABRM task presents two auditory stimuli followed by a third masking sound at varying MODs (Stevens & Weaver, 2005; Stevens & Kohout, in preparation; Kohout & Stevens, 2006). The ABRM task measures the time required for auditory perceptual processing by demonstrating that at a short MOD, subjects are unable to consolidate stimulus information to make an order judgment. Participants report being able to hear that the tones were presented, but are not able to perceptually consolidate the characteristics that identify one tone from the other. However, at a long MOD, the stimuli are not masked and are therefore consolidated into perceptual representations used to make an order judgment. Backward recognition masking has also been observed in the visual domain (Enns & Di Lollo, 2000). The results across visual and auditory ABRM studies suggest that a range of 99-250 ms is required to perceptually consolidate task stimuli (Stevens & Weaver, 2005; Stevens & Kohout, in preparation; Kohout & Stevens, 2006; Enns & Di Lollo, 2000). Even with varying durations, it is possible that the MOD threshold in the ABRM design and the AB in the RSVP design both describe the perceptual consolidation process. Further research is required to clarify whether perceptual consolidation and the AB describe the same process. Since the speed of perceptual consolidation has been demonstrated as a critical precursor to accurate sensory perception in both auditory and visual domains, it is an ideal candidate as the general limiting factor in information processing.

Perceptual consolidation training and generalization

ABRM tasks demonstrate that the speed of perceptual consolidation of auditory stimuli is critical to making a correct recognition judgment between stimuli. The importance of quickly processing an auditory stimulus is so that a perceptual representation can be formed before being disrupted by the mask stimulus. Therefore, if the perceptual consolidation process is the limiting factor in perceptual processing of sensory information, and the speed of this process can be increased with training, accurate information might more readily reach cognition to better guide behavior.

Increasing the perceptual consolidation rate may also generalize to improve non-trained cognitive functions. Improvements in performance on ABRM tasks have been reported after 10 sessions of training (Wright et al., 1996; Roth et al., 2001). Testing for generalization after ABRM training has not demonstrated significant performance improvements in untrained masking tasks (e.g. simultaneous and forward masking) or conditions (to untrained ear) (Wright et al., 1996, 1997; Roth et al., 2001). However, generalization has been seen in an untrained ABRM task that used the same MOD interval but different tone frequencies, but not in the same experiment when the same frequencies but different MOD intervals were used (Wright et al., 1997). This suggests that training-related improvements were specific to the temporal aspects of the ABRM. However, no study to date has examined the generalization of ABRM training to non mask-related cognitive tasks such as STM capacity.

Both of the ABRM training experiments discussed in this thesis tested for generalization to improvements in STM capacity. TST tasks were given before and after ABRM training to determine if increasing perceptual consolidation rate would increase STM capacity. We hypothesized that increasing the rate of perceptual consolidation would allow for more tones to be perceptually processed within the TST lists. This hypothesis was based on the positive relationship between perceptual consolidation and STM capacity presented in Chapter 2. The tones might be better represented in STM and lead to greater recall of the number of tones presented in a list. Five days of training significantly improved ABRM performance in both SC and LB groups, but generalization to increased TST performance was not observed. Although we did not observe an increase in STM capacity in SC or LB subjects after ABRM training, a correlation was observed between pre-training TST performance and post-training ABRM performance. This result may suggest that STM capacity is a predictor of the ability to improve ABRM threshold, rather than ABRM threshold as a predictor of STM capacity.

One possible explanation for this result is that greater STM allows for efficient retrospective analysis of the tone pairs in memory. When relating to the two-stage model of information processing (Chun & Potter, 1995), it is possible that the two tone-pair stimuli and the mask from an ABRM trial were represented in a large-capacity STM store. However, only the tone-pair representations received further analysis in the small-capacity system, whereas the mask did not. This may have allowed for accurate analysis of the tone-pairs, leading to greater recognition performance. It would be useful for future studies to examine the effect of STM training on non-trained tasks, such as the ABRM or RSVP, that measure speed of information processing. A related study reported that five weeks of training improved working memory and generalized to improve non-trained tasks related to working memory (Klingberg et al., 2002). However, this result still does not demonstrate full generalization to improve a fundamentally different task. The fact that working memory training improved performance on a untrained working memory-related task points to the same specificity demonstrated in ABRM tasks; training of these processes only improves related tasks but does not seem to show generalization.

Because our experiment did not utilize a control group that participated in pre- and post-training tests without training in-between, caution must be observed when suggesting that training was responsible for the improvement in perceptual consolidation rate. It is possible that improvements in behavior may arise from familiarity with the stimuli or the testing environment. Ball and others (2002) observed improvements in behavioral performance from a subset of control subjects who did not participate in the training procedure. However, sighted control subjects who performed the same ABRM task did not show behavioral improvements from pre- to post-tests without training, whereas subjects who participated in training did (Kohout & Stevens, 2006). Additionally, Gaab and others (2006) demonstrated that single trial feedback was not required to improve behavioral performance after training. Therefore, subjects were not given feedback after each individual trial in our experiment.

Functional brain activity during the ABRM task

To date, only one neuroimaging study has investigated brain activity during the ABRM task. Using fMRI, van Dijk and Backes (2003) demonstrated that although the ABRM task is auditory in nature, multiple brain regions are active in response to the ABRM stimuli. Regions such as the inferior frontal gyrus, Broca's area, anterior temporal gyrus, and bilateral IPL showed significant activity during the ABRM task in addition to primary and secondary auditory cortex (van Dijk & Backes, 2003). These areas are related to auditory and language functions. Additionally, regions typically associated with cognition and attention such as the ACC, PCC, posterior parietal, middle frontal gyrus, and putamen were also active when ABRM trials were compared to silence (van Dijk & Backes, 2003).

The fMRI results from this thesis are congruent with those reported by van Dijk and Backes (2003). Our ABRM task revealed multiple brain regions outside of auditory cortex to be significantly more active than silence, particularly in frontal and parietal cortices like the ACC and IPL, respectively. However, our data did not reveal significant activity in primary auditory cortex. This may have occurred because scanner noise washed out any significant differences between trial-related and scanner-related activity in the auditory cortex (Scarff et al., 2004). To avoid this possible confound, van Dijk and Backes (2003) used a sparse imaging block design to minimize the effect of scanner noise. We attempted to do the same by utilizing an event-related design where trials are presented during silent inter-scan intervals. Since the primary auditory cortex is responsible for processing sound frequency, it is also possible that activity was not observed in this area because the ABRM task required more than just frequency processing. The ABRM task required auditory perceptual judgments that may have activated auditory association areas outside of the temporal lobe. Lastly, it is also possible that our design did not allow for the temporal resolution to observe primary auditory activity.

The advantage of using an event-related design is that the hemodynamic time course in response to neural activity within a brain region can be examined in response to a specific stimulus. Even if an area of the brain does not show significantly active voxels, the hemodynamic response can be extrapolated. Hemodynamic responses in this thesis demonstrated reductions in BOLD signal, and by association neural activity, in fronto-parietal brain regions, but no significant changes in primary auditory areas. The disadvantage of an event-related design is that many more trials are needed to observe significant stimulus-related activity. Therefore, more scans may have been needed to view significant active voxels over auditory cortex. Adding trials increases the amount of time that the subject is inside the scanner and may lead to fatigue. Because our subjects were already inside the scanner for an hour, we did not want to add more trials. Reducing the number of conditions (e.g. removing the 0 ms condition) may eliminate a possible effect of fatigue while increasing the number of trials for the remaining conditions.

Certain studies have explored which brain regions may be critical for the temporal processing required in the ABRM task. Language-impaired children and adults demonstrate deficits in ABRM tasks but not auditory simultaneous recognition mask (ASRM) tasks. The ABRM deficit is thought to occur because the relevant information is coded in the temporal pattern of active input fibers (Wright et al., 1997). The ASRM task, however, requires pre-perceptual frequency discrimination (determining whether a tone was played during the mask) that activates different spatial groups of hair cells. To understand which brain regions are important for the temporal aspect of auditory processing, van Dijk and Backes (2003) contrasted activity from ABRM trials with activity from ASRM trials. The authors hypothesized that if ABRM and ASRM tasks require different auditory functions, but identical cognitive functions, then differences in auditory-related brain regions would be seen. Alternatively, frontal and parietal differences would be observed if the ABRM and ASRM require different cognitive functions. The contrast analysis revealed differences in brain activity outside of the auditory cortex. Specifically, the anterior temporal gyrus and the ACC were active to a greater degree during high performance of the ABRM task compared to the ASRM task.

The activity of these regions was therefore related to the cognitive differences between the tasks. As time was the only variable that differed between the tasks, activity in the ACC and anterior temporal gyrus was related to the temporal aspect of the ABRM (van Dijk & Backes, 2003). Since language-impaired individuals show performance deficits on the ABRM task, the combined results indirectly suggest that brain regions outside of the auditory cortex may be important targets when training auditory perceptual processing.

Training-related changes in functional brain activity

An fMRI study with normal and dyslexic children demonstrated that regions such as the ACC, frontal cortex, and posterior parietal cortex were less active in the dyslexic children (Temple et al., 2003). However, as sensory stimulation increased with auditory training, a higher performance of perceptual processing was required. The exact same frontoparietal regions that showed a deficit before now showed an increase in activity to a level similar to that of normal children (Temple et al., 2003). Just as greater activity was seen in brain areas outside of the auditory cortex in the current ABRM task, greater changes in activity were observed in brain regions outside of the auditory cortex after ABRM training. Frontal regions such as the DLPFC and ACC, and parietal regions such as the IPS and IPL, demonstrated significant training-related decreases in activity when sensory stimulation was held constant and task difficulty became easier. This occurred most often in the 160 ms condition. Interestingly, when task difficulty was held constant, but sensory stimulation increased, similar frontoparietal regions remained active before and after training. Thus, dysfunction of these regions may underlie auditory processing deficits such as in language where sensory stimulation remains constant.

The imaging results from this thesis demonstrated that the volume of active voxels decreased after training, especially when task difficulty was not controlled for and sensory stimulation remained constant. The decreased activity occurred in frontoparietal regions often associated with attention and memory (Mesulam, 1990), including IPS, DLPFC, and ACC. This is consistent with a myriad of other training studies that have shown similar results (for reviews, see Chein & Schneider, 2005; Kelly & Garavan, 2005). The decrease in activity is likely a result of attenuated demand on the executive or supervisory functions that these regions are associated with. For example, less attention may be required for stimuli whose parameters never change and task difficulty gets easier (e.g. 160 ms condition), whereas the same amount of attention is required when parameters change but task difficulty remains the same (65%). Our results show that the frontoparietal regions were equally active in volume and BOLD signal before and after training when task difficulty remained constant. This supports the idea that these regions mediate the performance level of task-processing regions. Unfortunately, attempts to correlate behavioral performance with neural activity resulted only in non-significant trends. This was most likely due to a small sample size. Nevertheless, the data supports the idea that frontoparietal regions perform a supervisory role during task performance and influence auditory perceptual processing.

Functional relevance of CMP in the Blind

Our fMRI results did not show CMP in the LB before or after ABRM training. Although some studies support this finding (Cohen et al., 1999; Sadato, 2002), others contradict this finding by showing CMP in the LB (Burton 2002, a, b; Burton 2004). CMP in the LB is not as extensive as in the EB, and does not seem to correlate with behavior (Burton, 2003). Thus, questions arise as to how CMP is manifested in the blind, and whether CMP is functionally relevant to enhanced cognitive abilities.

Two anatomical theories could explain CMP observed in the blind (Bavelier & Neville, 2002). The first is that during normal brain development subcortical auditory inputs make synaptic connections within the visual cortex in addition to the normal connections in auditory cortex. Observed activity of this auditory input in the visual cortex would be suppressed by dominant visual input in normal sighted subjects. The absence of visual input (as in the blind) might release the auditory inputs from inhibition and allow their activity to be observed in response to auditory stimulation. Alternatively, CMP may arise from a shift in synaptic balance and expression of cortico-cortical feedback connections from auditory cortex which normally only modulate the processing of visual information (Shimony et al., 2005). Synaptic competition would occur outside of the auditory cortex in the blind based on over-reliance on auditory stimulation, and significant CMP would be observed during auditory tasks. If a lack of visual stimulation releases normal cross-modal auditory input, then CMP should be observed in the LB prior to training. If CMP expression was dependent upon overuse of the auditory modality, it is possible that CMP could be observed in LB subjects after auditory training.

Although changes in functional brain activity were evident in the LB brain when comparing pre- and post-training scans, results were similar to SC reported previously (Kohout & Stevens, 2006), and there was no evidence of CMP before or after training. This suggests that neither cross-modal input from normal development was unmasked, nor that cortico-cortical feedback connections were expressed during training. A recent diffusion tensor imaging (DTI) study using a LB population showed that relative anisotropy values of the visual fiber tract were not different from sighted controls, and that axonal degeneration of the optic radiation did not occur in LB subjects (Schoth et al., 2006). Thus, even after years of blindness, the LB brain shows similar white matter tractography as sighted individuals. It is not known whether this white matter connectivity is dormant or still responsive to stimulation. If subcortical auditory connections were present in the occipital lobe in our LB subjects, they may still be masked by the mere presence of geniculocalcarine fiber tracts to the primary visual cortex. In the same fashion, auditory cortical feedback connections to the visual cortex may not be able to be expressed. It is possible that in tasks that have demonstrated LB CMP in response to Braille (Buchel et al., 1998, Burton 2002 a, 2004), visual imagery is used to analyze Braille shape and orientation (Millar, 1987). This visual imagery may recruit the activity of the present geniculocalcarine or auditory feedback connections in the visual cortex. We hoped to minimize the use of visual imagery by using non-verbal, pure tone auditory stimuli. Although it cannot be said for sure that the ABRM task did not elicit some sort of visual imagery, it may be a possible explanation of why we did not observe CMP before or after training.

Alternatively, our training design might not have allowed enough time for synapses to be unmasked or for cortico-cortical feedback connections to be expressed (i.e. it may take more than five days). However, an interesting study demonstrated that CMP could be induced in normal sighted subjects during five days of blindfolding in response to tactile and auditory processing (Pascual-Leone & Hamilton, 2001). The authors suggested that the time course of these functional changes are too fast for cortico-cortical connections to be established and therefore cross-modal input must have been present from development was and masked by dominant visual input. However, the use of normal SC subjects suggests intact geniculocalcarine connections were present as in the LB (Schoth et al., 2006) and may have invoked visual imagery during task performance. The LB subjects used in our study reported not having random visual imagery but were able to visualize certain objects when asked. Post-training debriefing suggested that the subjects did not use visual imagery as a method to perform the ABRM task.

The results suggest that age of onset of blindness governs the potential of compensatory auditory perceptual functions of LB individuals to be similar to sighted individuals. Individuals blinded before or early during visual development express compensatory advantages in the remaining modalities, whereas individuals blinded after visual development do not. Thus, similar to SC, enhancements in the efficiency of the neural substrates that subserve executive functions such as selective attention are what underlie behavioral improvements in the LB. CMP may be what underlies the supranormal performance in the EB. This indirectly supports the theory that CMP in the EB is functionally relevant to superior behavioral performance on non-visual cognitive tasks (Amedi et al., 2003; Theoret et al., 2004; Gougoux et al., 2005).

Conclusions

The speed of auditory information processing, as measured by our ABRM task, is correlated with auditory STM, as measured by the TST task. Training improved perceptual consolidation thresholds on the ABRM task in both SC and LB groups. Changes in functional brain activity were observed in fronto-parietal brain regions, which suggest that improvements in perceptual consolidation rate may be related to improved auditory attention. ABRM training did not generalize to improve performance of untrained cognitive measures, such as STM capacity, that does not rely on rapid temporal processing. Thus, the speed of information processing, or perceptual consolidation, is not likely to be the common mechanism that determines performance in all aspects of cognition. Rather, the common mechanism may be the efficiency of short-term or working memory. Thus, perceptual consolidation training should only be applied to specific cognitive dysfunctions in which the speed of information processing is impaired, including Dyslexia or language processing.

References

Amedi, A., Raz, N., Pianka, P., Malach, R., & Zohary, E. (2003). Early 'visual' cortex activation correlates with superior verbal memory performance in the blind. *Nat Neurosci*, 6(7), 758-66.

Ball, K., Berch, D., Helmers, K., Jobe, J., Leveck, M., Marsiske, M., Morris, J., Rebok, G., Smith, D., Tennstedt, S., Unverzagt, F., Willis, S. (2002) Effects of cognitive training interventions with older adults. *JAMA,* 288 (18), 2271-2281.

Bavelier, D., & Neville, H. J. (2002). Cross-modal plasticity: where and how? *Nat Rev Neurosci*, 3(6), 443-52.

Benedict, R. H., Shucard, D. W., Santa Maria, M. P., Shucard, J. L., Abara, J. P., Coad, M. L., et al. (2002). Covert auditory attention generates activation in the rostral/dorsal anterior cingulate cortex. *J Cogn Neurosci*, 14(4), 637-45.

Bernstein, L. J., Beig, S., Siegenthaler, A. L., & Grady, C. L. (2002). The effect of encoding strategy on the neural correlates of memory for faces. *Neuropsychologia*, 40(1), 86-98.

Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L., & Snyder, A. (2001). Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. *Cereb Cortex*, 11(9), 825-36.

Broadbent, D. E. (1958). *Perception and Communication*,

Brosch, M., & Schreiner, C. E. (1997). Time course of forward masking tuning curves in cat primary auditory cortex. *J Neurophysiol*, 77(2), 923-43.

Brosch, M., Schulz, A., & Scheich, H. (1998). Neuronal mechanisms of auditory backward recognition masking in macaque auditory cortex. *Neuroreport*, 9(11), 2551-55.

Brown, J. W., & Braver, T. S. (2005). Learned predictions of error likelihood in the anterior cingulate cortex. *Science*, 307(5712), 1118-21.

Buchel, C., Price, C., Frackowiak, R. S., & Friston, K. (1998). Different activation patterns in the visual cortex of late and congenitally blind subjects. *Brain*, 121 (Pt 3), 409-19.

Buonomano, D. V., & Merzenich, M. M. (1998). Cortical plasticity: from synapses to maps. *Annu Rev Neurosci*, 21, 149-86.

Burton, H. (2003). Visual cortex activity in early and late blind people. *J Neurosci*, 23(10), 4005-11.

Burton, H., Sinclair, R. J., & McLaren, D. G. (2004). Cortical activity to vibrotactile stimulation: an fMRI study in blind and sighted individuals. *Hum Brain Mapp*, 23(4), 210-28.

Burton, H., Snyder, A. Z., Conturo, T. E., Akbudak, E., Ollinger, J. M., & Raichle, M. E. (2002, a). Adaptive changes in early and late blind: a fMRI study of Braille reading. *J Neurophysiol*, 87(1), 589-607.

Burton, H., Snyder, A. Z., Diamond, J. B., & Raichle, M. E. (2002, b). Adaptive changes in early and late blind: a FMRI study of verb generation to heard nouns. *J*

Neurophysiol, 88(6), 3359-71.

Case, R. (1982). Operational efficiency and the growth of short-term memory span. *Journal of Experimental Child Psychology*, 33 (3), 386.

Chein, J. M., & Schneider, W. (2005). Neuroimaging studies of practice-related change: fMRI and meta-analytic evidence of a domain-general control network for learning. *Brain Res Cogn Brain Res*, 25(3), 607-23.

Chun, M. M., & Potter, M. C. (1995). A two-stage model for multiple target detection in rapid serial visual presentation. *J Exp Psychol Hum Percept Perform*, 21(1), 109-27.

Cohen, L. G., Weeks, R. A., Sadato, N., Celnik, P., Ishii, K., & Hallett, M. (1999). Period of susceptibility for cross-modal plasticity in the blind. *Ann Neurol*, 45(4), 451-60.

Collignon, O., Renier, L., Bruyer, R., Tranduy, D., & Veraart, C. (2006). Improved selective and divided spatial attention in early blind subjects. *Brain Res*, 1075(1), 175-82.

Corbetta, M., Kincade, J. M., Ollinger, J. M., McAvoy, M. P., & Shulman, G. L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nat Neurosci*, 3(3), 292-97.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci*, 3(3), 201-15.

Cowan, N. (1988). Evolving conceptions of memory storage, selective attention, and their mutual constraints within the human information-processing system. *Psychol Bull*, 104(2), 163-91.

Cowan, N., Nugent, L. D., Elliott, E. M., Ponomarev, I., & Saults, J. S. (1999). The role of attention in the development of short-term memory: age differences in the verbal span of apprehension. *Child Dev*, 70(5), 1082-97.

Dai, H. P., Scharf, B., & Buus, S. (1991). Effective attenuation of signals in noise under focused attention. *J Acoust Soc Am*, 89(6), 2837-42.

Dale, A. M., & Buckner, R. L. (1997). Selective Averaging of Rapidly Presented Individual Trials using fMRI. *Hum Brain Mapp*, 5, 329-40.

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior*, 19 (4), 450-66.

Donner, T. H., Kettermann, A., Diesch, E., Villringer, A., & Brandt, S. A. (2003). Parietal activation during visual search in the absence of multiple distractors. *Neuroreport*, 14(17), 2257-61.

Duncan, J., Martens, S., & Ward, R. (1997). Restricted attentional capacity within but not between sensory modalities. *Nature*, 387(6635), 808-10.

Duzel, E., Cabeza, R., Picton, T. W., Yonelinas, A. P., Scheich, H., Heinze, H. J., et al. (1999). Task-related and item-related brain processes of memory retrieval. *Proc Natl Acad Sci U S A*, 96(4), 1794-99.

Efron, R. (1963). Temporal perception, aphasia and de'ej'a vu. *Brain*, 86, 403-24.

Enns, J. T., & Di Lollo, V. (2000). What's new in visual masking? *Trends Cogn Sci*, 4(9), 345-52.

Erickson, K. I., Colcombe, S. J., Wadhwa, R., Bherer, L., Peterson, M. S., Scalf, P. E., et al. (2006). Training-Induced Functional Activation Changes in Dual-Task

Processing: An fMRI Study. *Cereb Cortex*,

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. *J Cogn Neurosci*, 14(3), 340-47.

Fletcher, P., Buchel, C., Josephs, O., Friston, K., & Dolan, R. (1999). Learning-related neuronal responses in prefrontal cortex studied with functional neuroimaging. *Cereb Cortex*, 9(2), 168-78.

Furmanski, C. S., Schluppeck, D., & Engel, S. A. (2004). Learning strengthens the response of primary visual cortex to simple patterns. *Curr Biol*, 14(7), 573-78.

Gaab, N., Gaser, C., & Schlaug, G. (2006). Improvement-related functional plasticity following pitch memory training. *Neuroimage*, 31(1), 255-63.

Garavan, H., Kelley, D., Rosen, A., Rao, S. M., & Stein, E. A. (2000). Practice-related functional activation changes in a working memory task. *Microsc Res Tech*, 51(1), 54-63.

Glabus, M. F., Horwitz, B., Holt, J. L., Kohn, P. D., Gerton, B. K., Callicott, J. H., et al. (2003). Interindividual differences in functional interactions among prefrontal, parietal and parahippocampal regions during working memory. *Cereb Cortex*, 13(12), 1352-61.

Goddard, K. M., & Slawinski, E. B. (1999). Modality specific attentionl mechanisms can govern the attentional blink. *Canadian Acoustics*, 27, 98-99.

Goldman-Rakic, P. S. (1988). Topography of cognition: parallel distributed networks in primate association cortex. *Annu Rev Neurosci*, 11, 137-56.

Gougoux, F., Zatorre, R. J., Lassonde, M., Voss, P., & Lepore, F. (2005). A functional neuroimaging study of sound localization: visual cortex activity predicts performance in early-blind individuals. *PLoS Biol*, 3(2), e27.

Griffiths, Y. M., Hill, N. I., Bailey, P. J., & Snowling, M. J. (2003). Auditory temporal order discrimination and backward recognition masking in adults with dyslexia. *J Speech Lang Hear Res*, 46(6), 1352-66.

Hall, D. A., Johnsrude, I. S., Haggard, M. P., Palmer, A. R., Akeroyd, M. A., & Summerfield, A. Q. (2002). Spectral and temporal processing in human auditory cortex. *Cereb Cortex*, 12(2), 140-49.

Heath, S. M., Hogben, J. H., & Clark, C. D. (1999). Auditory temporal processing in disabled readers with and without oral language delay. *J Child Psychol Psychiatry*, 40(4), 637-47.

Hirsch, I. J. (1959). Auditory Perception of Temporal Order. *The Journal of the Acoustical Society of America*, 31, 759-67.

Honda, M., Deiber, M. P., Ibanez, V., Pascual-Leone, A., Zhuang, P., & Hallett, M. (1998). Dynamic cortical involvement in implicit and explicit motor sequence learning. A PET study. *Brain*, 121 (Pt 11), 2159-73.

Iacoboni, M., Woods, R. P., & Mazziotta, J. C. (1996). Brain-behavior relationships: evidence from practice effects in spatial stimulus-response compatibility. *J Neurophysiol*, 76(1), 321-31.

Jancke, L., Gaab, N., Wustenberg, T., Scheich, H., & Heinze, H. J. (2001). Short-term functional plasticity in the human auditory cortex: an fMRI study. *Brain Res Cogn Brain Res*, 12(3), 479-85.

Jiang, Y., & Kumar, A. (2004). Visual short-term memory for two sequential arrays: one integrated representation or two separate representations? *Psychon Bull Rev*, 11(3), 495-500.

Kahn, B. J. (1971). Backward recognition masking: Interference of shift of attention. *Unpublished manuscript (cited in Massaro, 1972, a)*,

Kallman, H. J., & Massaro, D. W. (1983). Backward masking, the suffix effect, and preperceptual storage. *J Exp Psychol Learn Mem Cogn*, 9(2), 312-27.

Kallman, H. J., & Morris, M. D. (1984). Backward recognition masking as a function of ear of mask presentation. *Percept Psychophys*, 35(4), 379-84.

Karni, A., Meyer, G., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1995). Functional MRI evidence for adult motor cortex plasticity during motor skill learning. *Nature*, 377(6545), 155-58.

Kastner, S., & Pinsk, M. A. (2004). Visual attention as a multilevel selection process. *Cogn Affect Behav Neurosci*, 4(4), 483-500.

Kastner, S., & Ungerleider, L. G. (2000). Mechanisms of visual attention in the human cortex. *Annu Rev Neurosci*, 23, 315-41.

Kelly, A. M., & Garavan, H. (2005). Human functional neuroimaging of brain changes associated with practice. *Cereb Cortex*, 15(8), 1089-102.

Keysers, C., & Perrett, D. I. (2002). Visual masking and RSVP reveal neural competition. *Trends Cogn Sci*, 6(3), 120-25.

Kincade, J. M., Abrams, R. A., Astafiev, S. V., Shulman, G. L., & Corbetta, M. (2005). An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention. *J Neurosci*, 25(18), 4593-604.

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *J Clin Exp Neuropsychol*, 24(6), 781-91.

Kohout, K. M., & Stevens, A. A. (Submitted). Changes in functional brain activity following auditory training.*Neuroscience Letters*

Kohout, K. M., & Stevens, A. A. (In preparation). Changes in behavior and functional brain activity in late blind individuals following auditory training.

Koski, L., & Paus, T. (2000). Functional connectivity of the anterior cingulate cortex within the human frontal lobe: a brain-mapping meta-analysis. *Exp Brain Res*, 133(1), 55-65.

Kujala, T., Huotilainen, M., Sinkkonen, J., Ahonen, A. I., Alho, K., Hamalainen, M. S., et al. (1995). Visual cortex activation in blind humans during sound discrimination. *Neurosci Lett*, 183(1-2), 143-46.

Landau, S. M., Schumacher, E. H., Garavan, H., Druzgal, T. J., & D'Esposito, M. (2004). A functional MRI study of the influence of practice on component processes of working memory. *Neuroimage*, 22(1), 211-21.

Lessard, N., Pare, M., Lepore, F., & Lassonde, M. (1998). Early-blind human subjects localize sound sources better than sighted subjects. *Nature*, 395(6699), 278-80.

Levitt, H. (1971). Transformed up-down methods in psychoacoustics. *J Acoust Soc Am*, 49(2), Suppl 2:467+.

Massaro, D. W. (1970). Preperceptual auditory images. *J Exp Psychol*, 85(3), 411-17.

Massaro, D. W. (1972). Preperceptual images, processing time, and perceptual units in auditory perception. *Psychol Rev*, 79(2), 124-45.

Massaro, D. W. (1975). Backward recognition masking. *J Acoust Soc Am*, 58(5), 1059-65.

Massaro, D. W. (1972). Stimulus information vs. processing time in auditory pattern recognition. *Perception and Psychophysics*, 12, 50-56.

McArthur, G. M., & Hogben, J. H. (2001). Auditory backward recognition masking in children with a specific language impairment and children with a specific reading disability. *J Acoust Soc Am*, 109(3), 1092-100.

Menning, H., Roberts, L. E., & Pantev, C. (2000). Plastic changes in the auditory cortex induced by intensive frequency discrimination training. *Neuroreport*, 11(4), 817-22.

Mesulam, M. M. (1990). Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Ann Neurol*, 28(5), 597-613.

Millar, S. (1987). Perceptual and task factors in fluent braille. *Perception*, 16(4), 521-36.

Näätänen, R. (1988). Implications of ERP data for psychological theories of attention. *Biol Psychol*, 26(1-3), 117-63.

Näätänen, R., & Winkler, I. (1999). The concept of auditory stimulus representation in cognitive neuroscience. *Psychol Bull*, 125(6), 826-59.

Newman, C. W., & Spitzer, J. B. (1983). Prolonged auditory processing time in the elderly: evidence from a backward recognition-masking paradigm. *Audiology*, 22(3), 241-52.

Nyberg, L., Sandblom, J., Jones, S., Neely, A. S., Petersson, K. M., Ingvar, M., et al. (2003). Neural correlates of training-related memory improvement in adulthood and aging. *Proc Natl Acad Sci U S A*, 100(23), 13728-33.

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nat Neurosci*, 7(1), 75-79.

Oxenham, A. J., & Plack, C. J. (2000). Effects of masker frequency and duration in forward masking: further evidence for the influence of peripheral nonlinearity. *Hear Res*, 150(1-2), 258-66.

Pascual-Leone, A., & Hamilton, R. (2001). The metamodal organization of the brain. *Prog Brain Res*, 134, 427-45.

Petersen, S. E., van Mier, H., Fiez, J. A., & Raichle, M. E. (1998). The effects of practice on the functional anatomy of task performance. *Proc Natl Acad Sci U S A*, 95(3), 853-60.

Petersson, K. M., Elfgren, C., & Ingvar, M. (1999). Dynamic changes in the functional anatomy of the human brain during recall of abstract designs related to practice. *Neuropsychologia*, 37(5), 567-87.

Pinsk, M. A., Doniger, G. M., & Kastner, S. (2004). Push-pull mechanism of selective attention in human extrastriate cortex. *J Neurophysiol*, 92(1), 622-29.

Poldrack, R. A. (2000). Imaging brain plasticity: conceptual and methodological issues--a theoretical review. *Neuroimage*, 12(1), 1-13.

Poldrack, R. A., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. (1998). The neural basis of visual skill learning: an fMRI study of mirror reading. *Cereb Cortex*, 8(1), 1-10.

Pugh, K. R., offywitz, B. A., Shaywitz, S. E., Fulbright, R. K., Byrd, D., Skudlarski, P., et al. (1996). Auditory selective attention: an fMRI investigation. *Neuroimage*, 4(3 Pt 1), 159-73.

Raichle, M. E., Fiez, J. A., Videen, T. O., MacLeod, A. M., Pardo, J. V., Fox, P. T., et al. (1994). Practice-related changes in human brain functional anatomy during nonmotor learning. *Cereb Cortex*, 4(1), 8-26.

Raymond, J. E., Shapiro, K. L., & Arnell, K. M. (1992). Temporary suppression of visual processing in an RSVP task: an attentional blink?. *J Exp Psychol Hum Percept Perform*, 18(3), 849-60.

Röder , B., & Rösler , F. (2003). Memory for environmental sounds in sighted, congenitally blind and late blind adults: evidence for cross-modal compensation. *Int J Psychophysiol*, 50(1-2), 27-39.

Röder , B., Rösler , F., Hennighausen, E., & Nacker, F. (1996). Event-related potentials during auditory and somatosensory discrimination in sighted and blind human subjects. *Brain Res Cogn Brain Res*, 4(2), 77-93.

Röder , B., Rösler , F., & Neville, H. J. (2001). Auditory memory in congenitally blind adults: a behavioral-electrophysiological investigation. *Brain Res Cogn Brain Res*, 11(2), 289-303.

Roth, D. A., Kishon-Rabin, L., & Hildesheimer, M. (2001). Auditory backward masking and the effect of training in normal hearing adults. *J Basic Clin Physiol Pharmacol*, 12(2 Suppl), 145-59.

Sadato, N., Okada, T., Honda, M., & Yonekura, Y. (2002). Critical period for cross-modal plasticity in blind humans: a functional MRI study. *Neuroimage*, 16(2), 389-400.

Sadato, N., Pascual-Leone, A., Grafman, J., Deiber, M. P., Ibanez, V., & Hallett, M. (1998). Neural networks for Braille reading by the blind. *Brain*, 121 (Pt 7), 1213-29.

Sadato, N., Pascual-Leone, A., Grafman, J., Ibanez, V., Deiber, M. P., Dold, G., et al. (1996). Activation of the primary visual cortex by Braille reading in blind subjects. *Nature*, 380(6574), 526-28.

Sakai, K., Hikosaka, O., Miyauchi, S., Takino, R., Sasaki, Y., & Putz, B. (1998). Transition of brain activation from frontal to parietal areas in visuomotor sequence learning. *J Neurosci*, 18(5), 1827-40.

Scarff, C. J., Dort, J. C., Eggermont, J. J., & Goodyear, B. G. (2004). The effect of MR scanner noise on auditory cortex activity using fMRI. *Hum Brain Mapp*, 22(4), 341-49.

Scharf, B., Quigley, S., Aoki, C., Peachey, N., & Reeves, A. (1987). Focused auditory attention and frequency selectivity. *Percept Psychophys*, 42(3), 215-23.

Schoth, F., Burgel, U., Dorsch, R., Reinges, M. H., & Krings, T. (2006). Diffusion tensor imaging in acquired blind humans. *Neurosci Lett*, 398(3), 178-82.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. *Psychol Sci*, 16(2), 114-22.

Sevostianov, A., Fromm, S., Nechaev, V., Horwitz, B., & Braun, A. (2002). Effect of attention on central auditory processing: an fMRI study. *Int J Neurosci*, 112(5), 587-606.

Shimony, J. S., Burton, H., Epstein, A. A., McLaren, D. G., Sun, S. W., & Snyder, A. Z. (2005). Diffusion Tensor Imaging Reveals White Matter Reorganization in Early Blind Humans. *Cereb Cortex*,

Shomstein, S., & Yantis, S. (2006). Parietal cortex mediates voluntary control of spatial and nonspatial auditory attention. *J Neurosci*, 26(2), 435-39.

Staines, W. R., Padilla, M., & Knight, R. T. (2002). Frontal-parietal event-related potential changes associated with practising a novel visuomotor task. *Brain Res Cogn Brain Res*, 13(2), 195-202.

Stevens, A. A., & Snodgrass, M. T. (In preparation). Visual and Auditory Cortical Response during Rapid Auditory Discrimination in the Congenitally Blind. *Cereb Cortex*,

Stevens, A. A., & Weaver, K. (2005). Auditory perceptual consolidation in early-onset blindness. *Neuropsychologia*,

Stevens, A. A., Kohout, KM. (In preparation). Auditory Perceptual Consolidation and Short-Term Memory. *Journal of Experimental Psychology*,

Talairach, J., & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain.

Tallal, P. (1980). Auditory temporal perception, phonics, and reading disabilities in children. *Brain Lang*, 9(2), 182-98.

Tallal, P., & Rice, M. L. (1997). Evaluating new training programs for language impairment. *ASHA*, 39(3), 12-13.

Temple, E., Deutsch, G. K., Poldrack, R. A., Miller, S. L., Tallal, P., Merzenich, M. M., et al. (2003). Neural deficits in children with dyslexia ameliorated by behavioral remediation: evidence from functional MRI. *Proc Natl Acad Sci U S A*, 100(5), 2860-65.

Theoret, H., Merabet, L., & Pascual-Leone, A. (2004). Behavioral and neuroplastic changes in the blind: evidence for functionally relevant cross-modal interactions. *J Physiol Paris*, 98(1-3), 221-33.

Tremblay, K., Kraus, N., & McGee, T. (1998). The time course of auditory perceptual learning: neurophysiological changes during speech-sound training. *Neuroreport*, 9(16), 3557-60.

Tremblay, S., Vachon, F., & Jones, D. M. (2005). Attentional and perceptual sources of the auditory attentional blink. *Percept Psychophys*, 67(2), 195-208.

Vachon, F., & Tremblay, S. (2005). Auditory attentional blink: masking the second target is necessary, delayed masking is sufficient. *Can J Exp Psychol*, 59(4), 279-86.

van Dijk, P., & Backes, W. H. (2003). Brain activity during auditory backward and simultaneous masking tasks. *Hear Res*, 181(1-2), 8-14.

Vogel, E. K., & Luck, S. J. (2002). Delayed working memory consolidation during the attentional blink. *Psychon Bull Rev*, 9(4), 739-43.

Vogel, E. K., Luck, S. J., & Shapiro, K. L. (1998). Electrophysiological evidence for a postperceptual locus of suppression during the attentional blink. *J Exp Psychol*

Hum Percept Perform, 24(6), 1656-74.

Weaver, K. E., & Stevens, A. A. (2006). Auditory gap detection in the early blind. *Hear Res*, 211(1-2), 1-6.

Weeks, R., Horwitz, B., Aziz-Sultan, A., Tian, B., Wessinger, C. M., Cohen, L. G., et al. (2000). A positron emission tomographic study of auditory localization in the congenitally blind. *J Neurosci*, 20(7), 2664-72.

Wessinger, C. M., VanMeter, J., Tian, B., Van Lare, J., Pekar, J., & Rauschecker, J. P. (2001). Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging. *J Cogn Neurosci*, 13(1), 1-7.

Winkler, I., Paavilainen, P., & Naatanen, R. (1992). Can echoic memory store two traces simultaneously? A study of event-related brain potentials. *Psychophysiology*, 29(3), 337-49.

Wojciulik, E., & Kanwisher, N. (1999). The generality of parietal involvement in visual attention. *Neuron*, 23(4), 747-64.

Woodman, G. F., & Vogel, E. K. (2005). Fractionating working memory: consolidation and maintenance are independent processes. *Psychol Sci*, 16(2), 106-13.

Wright, B. A., Buonomano, D. V., Mahncke, H. W., & Merzenich, M. M. (1997). Learning and generalization of auditory temporal-interval discrimination in humans. *J Neurosci*, 17(10), 3956-63.

Wright, B. A., Johnston, P. A., & Reid, M. D. (1996). Learning and Generalization in Auditory Backward Masking. *The Journal of the Acoustical Society of America*, 100, 2818.

Yantis, S., & Serences, J. T. (2003). Cortical mechanisms of space-based and object-based attentional control. *Curr Opin Neurobiol*, 13(2), 187-93.

Yates, J. T., Johnson, R. M., & Starz, W. J. (1972). Loudness perception of the blind. *Audiology*, 11(5), 368-76.

Appendix

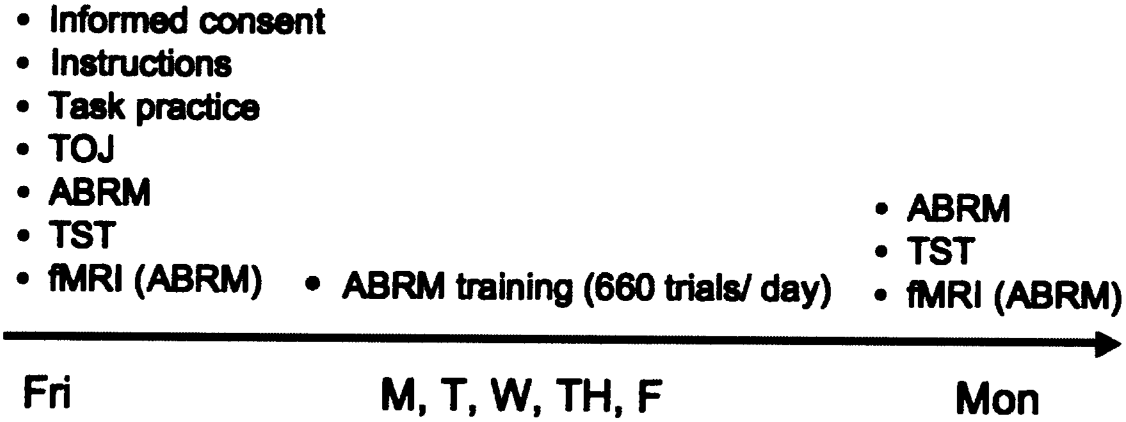

Figure 1: General task design.