Neural Correlates of Auditory Attention in an Exogenous Orienting Task

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Abstract

In an exogenous orienting task, attention is increased to the target stimulus if the cue validly predicts the target's location and the cue and target occur in quick succession. With a longer interval between the cue and target, the opposite effect occurs: attention is inhibited for validly cued targets. These attentional phenomena are known as facilitation, and inhibition of return (IOR), respectively. Both effects have been extensively explored in vision but less so in the auditory domain. The visual N2pc, an attention-related event-related potential (ERP) component has been used to examine the neural correlates of IOR (McDonald et al., 2009; Yang et al., 2012), but recently, an auditory analog of the N2pc was discovered, known as the N2ac (Gamble & Luck, 2011). To our knowledge, no previous study has explored the neural basis of exogenous attentional facilitation and IOR in the auditory modality. The present study sought to fill this gap using the N2ac as a neural marker of auditory spatial attention. Brain activity was recorded from nineteen participants while they performed a Posner exogenous auditory orienting task. We compared the ERPs elicited by the target stimulus for short (200 ms) cue-to-target intervals (facilitation), and long (700 ms) cue-to-target intervals (IOR). We observed behavioral and electrophysiological evidence of attentional facilitation, and a behavioral trend of IOR, but no apparent electrophysiological evidence of IOR. This study demonstrates that the N2ac is enhanced by exogenous attention during the facilitation phase of the cue-to-target interval, but remains unaffected during the later IOR phase. These findings suggest some similarities as well as some differences between this newly discovered ERP component (N2ac) and its visual analog, the N2pc.

To my mom and dad, and to all the infinite cosmic luck that brought me to you

Chapter 1: Introduction

1.1 Auditory orienting and spatial attention

Relevant sensory signals exist always in the presence of concurrent irrelevant signals. For humans and most organisms, processing complex incoming sensory information and orienting attention to different locations in the environment is fundamental to successful adaptive behavior. Spatial attention can be oriented by intentionally allocating attention to a specific location, known as endogenous orienting. Conversely, attentional orienting can occur automatically and reflexively, known as exogenous orienting, based on the salience of a stimulus (Mondor & Breau 1999).

A good way to illustrate the different types of attentional orienting is with relatable examples. If you were walking through a dark forest and heard a noise coming from behind a tree, your attention would automatically focus on the location of that noise. This response occurs instinctively, and you don't need to actively make the decision to pay attention to the noise you hear. Because of your current location (the dark forest), it is very advantageous that you respond quickly and reflexively. This is an example of exogenous orienting, and the noise is an example of an exogenous cue. While the noise heard in a dark forest is a particularly salient stimulus, exogenous orienting of attention occurs from many different types of cues in the external environment, such as the brightening of a light or the sound of a door slamming. However, our attention is also controlled volitionally, when we take the time to interpret a sound cue and then internally generate a decision for how we want to respond. This type of attention, brought under the control of our goals and decisions, is called endogenous orienting. The most frequently used example of an endogenous cue is an arrow pointing towards a specific direction. Unlike the noise in the dark forest, an arrow doesn't cause an instinctive response, but instead requires you to make a decision about how you will direct your attention. Similarly, attentional orienting in the auditory sensory modality occurs both, reflexively and in a goal-oriented fashion, that is, under the control of exogenous cues from the external environment, and endogenous cues from the internal environment.

1.2 Inhibition of return and the Posner cueing paradigm

Because we are constantly bombarded with many different competing exogenous and endogenous cues, it can be disadvantageous to orient our attention to locations that we have recently attended. In other words, if our attention could only focus on the specific location of a recent auditory cue, we would be unable to attend to other incoming salient cues in the auditory scene. Therefore, attention may actually shift to other areas in the peripheral environment, reducing the amount of attention directed at the initial location of a given cue. Successful auditory orienting relies on various spatial attentional mechanisms that may either, inhibit or facilitate our response to auditory cues.

In order to assess attentional shifts in the visual modality, Michael Posner created a neuropsychological test known as the Posner cueing task (Posner & Cohen 1984). The task is designed to assess either exogenous or endogenous orienting of attention (see Fig. 1.1). For the exogenous cueing paradigm, participants fixate at a central point on the computer screen, which is flanked on the left and right by two peripheral boxes. The exogenous cue is presented by brightening the outline of one of the peripheral boxes, causing the viewer to reflexively shift their attention to the illuminated box. Importantly, this is a shift of attention, and not a shift of gaze. Then after a brief interval from the onset of the exogenous cue, the target stimulus (usually a shape such as a triangle, square, etc.) appears in the center of one of the two boxes. The interval between the onset of the cue and the onset of the target is called the stimulus onset asynchrony or SOA, and is sometimes more intuitively referred to as the cue-target interval (CTI)[1]. In the endogenous cueing paradigm, the experiment also starts with a central fixation on the computer screen flanked by right and left peripheral boxes. The endogenous cue, however, is presented on the center of the screen, in the same location as the fixation point (as opposed to in the periphery). The endogenous cue is a directional cue, such as an arrow, that points to either the left or the right peripheral boxes. This causes the viewer to make a volitional shift in attention (i.e. not reflexive) to the cued box. In the exogenous cueing version, for valid trials, cue and target stimuli appear in the same box (i.e. both

[1] In the present study, we refer to the interval between cue and target as the cue-target interval (CTI) as opposed to SOA.

appearing in the left box), while for invalid trials, the target stimulus appears in the box opposite the cued box. Similarly, in the endogenous cueing version, the target appears in the same box that the arrow pointed to in valid trials, but in the opposite box in invalid trials. In both versions, participants respond to the target stimulus indicating which side it appeared on immediately after they detect it, and their reaction time is recorded (Posner & Cohen 1984).

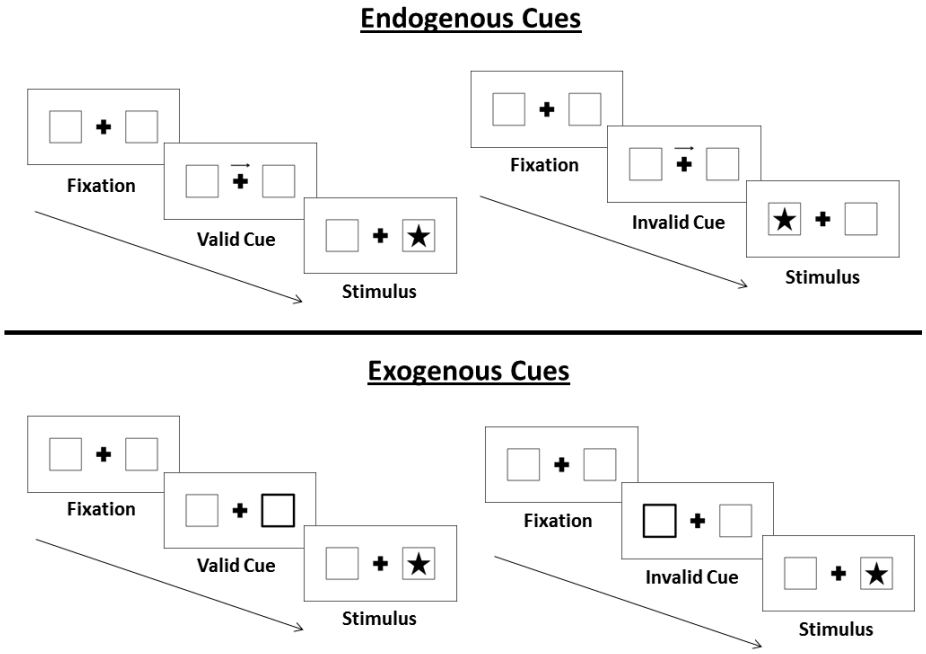


Figure 1.1 The Posner cueing paradigm with endogenous and exogenous cues. The endogenous cue is an arrow pointing to one of the boxes, the exogenous cue is the highlighting of the cued box.

The Posner exogenous cueing paradigm evokes automatic shifts of attention that are characterized by a biphasic response time (RT) pattern (Posner & Cohen 1984. See fig. 1.2). When target stimuli appear at the cued location following a short CTI, RT is faster for valid compared to invalid trials; in other words, participants respond faster when the cue and target appear in the same location as compared to when they appear in opposite locations (See Fig. 1.2a). This effect, known as facilitation, has been found to occur for CTIs of 100 to 250 ms. In contrast, at longer CTIs, RTs are actually faster for invalidly cued trials (See Fig. 1.2b); this is true for all CTIs that are longer than 200 ms,

but generally the chosen interval is between 400 to 3000 ms in order to best induce this effect (Mondor, 1999; Spence and Driver, 1998; Tassinari et al., 2002; Mondor & Breau, 1999). That is, after a long CTI, participants respond faster to a target appearing on the opposite side of the cued location. This phenomenon of valid cues producing longer reaction times than invalid cues, as well as enhanced accuracy for detecting invalidly cued targets, is known as inhibition of return (IOR) (Mondor & Breau 1999, Mondor et al. 1998).

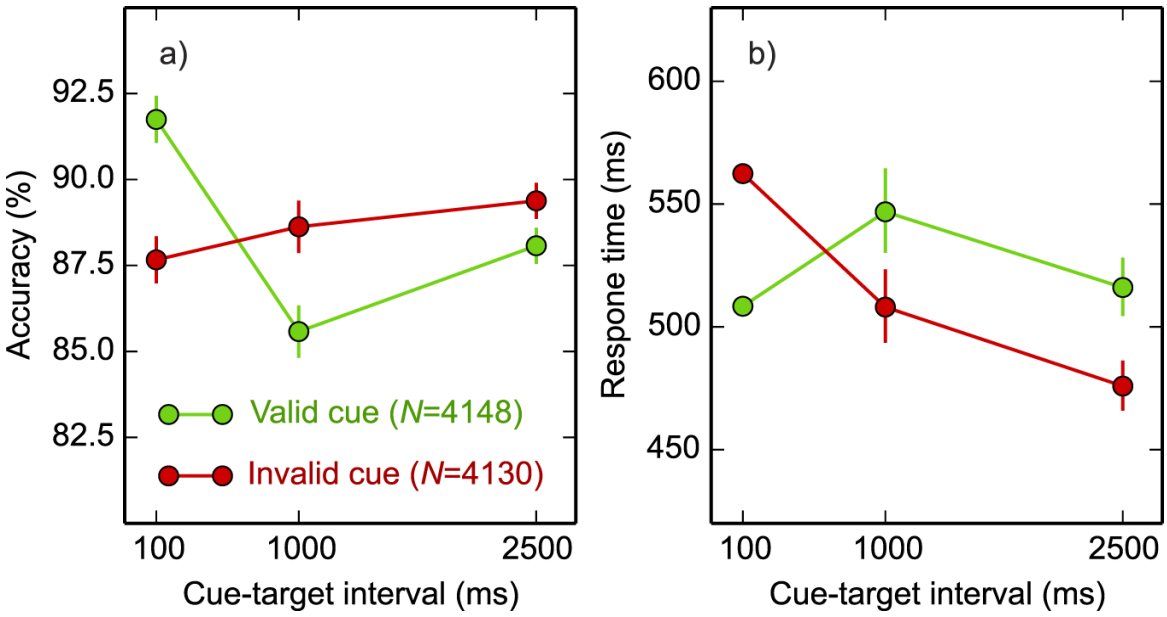


Figure 1.2 Percent accuracy and RTs in the Posner cueing paradigm
Biphasic RT pattern and percent accuracy pattern as induced by facilitation and IOR. At longer cue-target intervals, RTs to the invalid cue are shorter than to the valid cue (IOR). Figure adapted from Mathôt et al. 2014.

IOR and facilitation have been observed in both the visual and auditory modalities, but is much less documented in the latter. It has been proposed that IOR may be a mechanism for adaptive human behavior, because it favors novelty in visual or auditory searches by inhibiting attention from returning to recently attended areas (Wang & Klein 2010; Berdica et al. 2014). The IOR phenomenon indicates that inhibitory processes, as well as facilitative processes, may play a critical role in attentional search. While facilitative processes are necessary for effective attention towards stimuli that occur from the same location in rapid succession, our complex sensory world presents us

with stimuli occurring in many different locations in space and time. Therefore, inhibitory processes are necessary in order to conserve our attention and not be overwhelmed by constant input of visual and auditory stimuli.

1.3 Spatial attention in the visual domain: The N2pc

Researchers of spatial attention in both the auditory and visual domain have sought to address the question of what processes drive the way we attend to our environment using a brain recording method with high temporal resolution. Electroencephalography (EEG) is a measure of brain activity acquired from the passive recording of electrical potentials at the scalp. These recordings are then time-locked to a particular event (e.g. stimulus presentation), and averaged over numerous trials in order to explore the modulations of neural activity that correspond specifically to that event. The waveforms produced by this procedure are known as event-related potentials (ERPs). Averaging together several individual ERP waveforms, averages out any electrical noise or activity representing neuronal events unrelated to that event. Researchers compare the average of hundreds of ERPs elicited by one stimulus with the average of hundreds of ERPs elicited by another stimulus, which allows us to determine if/when brain activity differed between these two different stimuli at a millisecond by millisecond level of analysis (Luck 2014). The millisecond level analysis of ERPs can be very informative for addressing which specific attentional processes underlie a phenomenon such as IOR. For IOR and other similar attentional effects, small differences in timing can produce significantly different results; in the case of IOR, all intervals above approximately 200 ms are likely to produce an inhibitory effect in a valid trial as opposed to a facilitation effect. Therefore, the high temporal resolution of the ERP method is essential for studying processes that are highly sensitive to small time differences.

The allocation of attentional resources in order to process complex and simultaneous sensory information has been extensively studied in the visual attention literature. This type of selective spatial attention has been explored in vision using the N2-posterior contralateral, event-related potential component, known as the N2pc, that appears over the visual cortex contralateral to the spatial location that the subjects attend

to. The N2pc component is useful for investigating attentional orienting in vision with excellent temporal resolution. First described by Luck & Hillyard (1994), the N2pc is a consistently greater contralateral negative deflection of the ERP waveform over the visual cortex, appearing at approximately 200 ms after the onset of the attended stimulus.

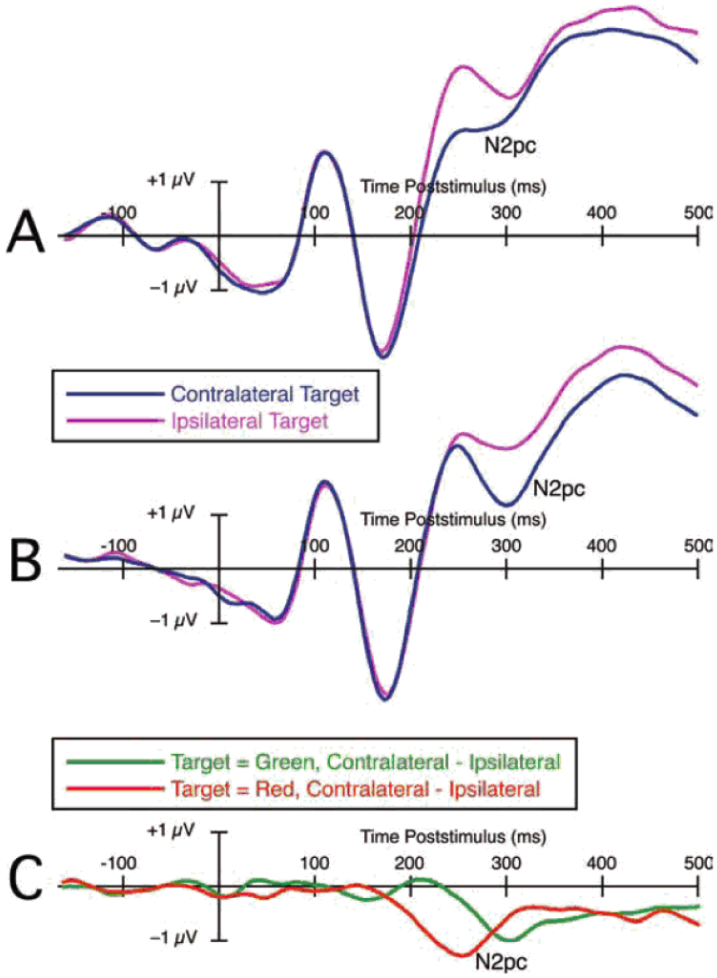


Figure 1.3 Grand average ERP waveforms from an N2pc study
Grand averages of contralateral and ipsilateral waveforms for red targets (A), green targets (B), and contralateral-minus-ipsilateral difference waveforms for the red and green targets (C). In this example, the red targets elicited an earlier N2pc compared to the green targets. Figure adapted from Luck et al. 2006.

The N2pc is a larger negativity appearing from approximately 200–300 ms when the target appears in the contralateral visual field compared to when it appears in the ipsilateral visual field. That is, larger over the left hemisphere (LH) for targets presented

in the right visual field (RVF), and larger over the right hemisphere (RH) for targets presented in the left visual field (LVF). In order to control for any overall differences between RH and LH, the N2pc is usually collapsed across right and left hemispheres into averaged contralateral and ipsilateral waveforms. Because the visual system is highly lateralized, the N2pc component can be isolated from other overlapping ERP components by calculating a contralateral-minus-ipsilateral difference wave. Collapsing across the left and right hemispheres to form a difference wave, allows us to isolate brain activity that reflects specifically the focusing of attention, independent of any overall differences between left and right hemispheres or between left and right targets, with the ending result being a larger negativity contralateral to the attended stimulus (See Fig. 1.3). The contralateral nature of the N2pc makes it possible to isolate attention-related activity from various other components elicited by simultaneously presented attended and unattended objects in the visual field (Gamble & Luck 2011).

1.4 IOR in visual exogenous cue tasks with the N2pc

Electrophysiological studies have been instrumental in examining the role of different attentional processes involved in IOR. Posner's initial evaluation of the attentional processes underlying IOR was that it reflected an inhibition of motor processes, by exerting an inhibitory bias in overt eye movements (Taylor & Klein 2000, Posner et al. 1985). Other research has proposed that IOR reflects the inhibition of perceptual processes (Spalek & Di Lollo, 2007) or the covert deployment of attention (Reuter-Lorenz et al. 1996). Currently, the most well accepted hypothesis is that IOR improves search of the visual environment by inhibiting inspection of recently attended objects and locations (McDonald et al. 2009, Chica & Lupiáñez 2009). When performing the Posner task with a long CTI, the individual's attention is initially directed toward the cued location but then the long CTI allows for an inhibitory process to develop, which biases attention away from the cued location. Thus, more time is required to shift attention back to the cued location than is required to shift attention to a new location. In other words, IOR may be explained by the disengagement of attention from an initially cued location, which facilitates visual and auditory search by encouraging attentional

shifts to novel locations (Yang et al. 2012, Klein 2000). The current research on attentional mechanisms underlying IOR have indicated not only that orienting attention away from the cued location may produce IOR, but also that any subsequent attentional processes may be inhibited by IOR (Mcdonald et al. 2009).

Mcdonald et al. (2009) created a paradigm to study visual IOR and how subsequent attentional processes may be inhibited by IOR, namely via a delay in the covert deployment of attention. Covert deployment of attention requires subjects to mentally shift their focus of attention without moving their eyes. Their endogenous visual paradigm combined elements of the standard target– target task (successive targets, re-orienting events at fixation) with elements of standard visual-search tasks (multiple-element arrays). This paradigm differed slightly from the valid and invalid cueing types of the Posner paradigm. There were three trial types: change, neutral, and repeat. Over successive trials, a target would appear either at the location of a preceding target (repeat) or at the location of a preceding nontarget (change). The change condition is somewhat analogous to invalid trials, because the target appears in a recently unattended location, while the repeat condition is analogous to valid trials. In the neutral condition, the target display was preceded by a nontarget display. Both targets and non-targets were colored discs, randomly selected from three different colors. A target-indicator display at the beginning of a trial contained a colored disc presented below the fixation point, which acted as the endogenous cue to indicate which of the three discs was the target for that trial. After a CTI of 1200 ms, target stimuli were presented either on the left or the right of fixation, with non-targets presented *simultaneously* on the opposite side. Stimulus displays contained either a target and nontarget disc, or two non-targets; thus IOR was induced by presenting target stimuli in the presence of other non-target competing stimuli.

The results indicated that the amplitude of the N2pc was smaller for targets appearing at recently attended locations compared to recently unattended locations, but that the covert deployment of attention was not delayed (i.e. there were no latency differences between valid and invalid trials). These results indicate that inhibitory processes reduced the probability of shifting attention to recently attended locations, but did not delay the deployment of spatial attention.

McDonald et al. also analyzed their results to determine the duration of the IOR or, in other words, how long the inhibitory effects lasted. N2pc amplitudes and mean RTs for target displays were analyzed when they were preceded by one same-location target (first repeat) or two same-location targets (second repeat). They found both, behaviorally and electrophysiologically, that the magnitude of IOR decreased after successive repetitions of targets appearing in the same location, i.e. the second repeat trials. That is, there was behavioral inhibition for the first repeat target but not for the second repeat target, and the N2pc amplitude was reduced for the first repeat target but not the second. Thus, they concluded that the duration of IOR is *at most* 2,400 ms long (the duration of two repeat trials).

A recent study by Yang et al. (2012) also used the N2pc component to further isolate the attentional processes involved in IOR, but with an important difference. This study elicited an N2pc using a non-predictive exogenous cuing paradigm to determine the role of attentional processes in the IOR effect. They presented targets on a 2-stimulus search display and, in contrast with much of previous N2pc research (such as McDonald et al. that have used endogenous cueing paradigms), attention was oriented by exogenous cues. In their experiment, two gray placeholder boxes were presented at the center of the screen, with a target indicator display at the beginning of each block, informing participants which color would be the target for that block. This study also used three trial types: valid, invalid and neutral. For valid and invalid trials, the exogenous cue was a color change of one of the placeholder boxes, either right or left, for a 100 ms interval. For the neutral trial, both placeholder boxes changed color, so that neither side of the visual field was exogenously cued. After an interval of 900 ms (CTI = 1000 ms), both placeholder boxes changed color, either to the target color (indicated at the beginning of the block) or to the nontarget color.

Yang et al. found that the N2pc amplitudes were similar across valid, invalid, and neutral cue types, in contrast to the results of McDonald et al. However, this study found that the N2pc was *delayed* for valid cues compared to invalid cues. This latency finding suggests that the IOR effect (in exogenous orienting) is closely associated with spatial attentional processes that delay the deployment of attention to targets appearing at recently cued locations. These results are in contrast to McDonald et al., who suggest that

the probability of shifting attention is reduced, but that the deployment of attention itself is *not* delayed.

1.5 The N2ac: an auditory analog of the N2pc

While the N2pc and other methods have been used to investigate exogenous and endogenous orienting in vision, mapping of spatial attention with electrophysiological methods is less common in the auditory modality. Recently, Gamble & Luck (2011) found the N2ac, an auditory ERP component analog to the visual N2pc component. That is, the N2ac is elicited by selective attention in an auditory task. This was the first study to find an auditory analogue of the N2pc component, as it was previously unclear whether the auditory system was sufficiently lateralized to be isolated from the rest of ERP activity by collapsing the signals from the right and left hemispheres.

In order to further investigate a possible auditory N2pc analogue, Gamble & Luck used simultaneous presentation of two stimuli randomly selected from four different natural sounds, presented concurrently on separate speakers (right or left). One sound was designated as the target for an entire experimental block. While all four stimuli could be randomly selected for a given trial, the target was present in 50% of the trials for every block, and each of the four sounds was chosen as a target for two experimental blocks. Participants indicated whether the target was present or absent in each trial. In this experiment, the location of the target (right or left speaker) was not explicitly task-relevant because the design did not utilize valid or invalid trials. However, subjects were required to orient their attention to the location of the target in order to discriminate it from the simultaneously presented stimulus.

Gamble & Luck found that the auditory targets elicited a contralateral-minus-ipsilateral difference over an anterior electrode cluster, which was named the N2ac (N2-anterior contralateral) component by the authors (See Fig. 1.4). The anterior electrode cluster showed greater negativity over the hemisphere contralateral to the target, compared to the hemisphere ipsilateral to the target, from approximately 200 to 500 ms after stimulus onset. The effect of contralaterality in the anterior electrode cluster was significantly different from zero, which demonstrated that discriminating the target sound

from the bilateral pair caused a significantly more negative potential over the contralateral hemisphere compared to the ipsilateral hemisphere.

In a second experiment, Gamble & Luck presented unilateral stimuli in order to assess whether the contralateral responses obtained for bilateral stimuli used in exp. 1 reflected additional attentional processes necessary to discriminate between the simultaneously presented sounds. Importantly, in contrast with the bilateral stimuli of exp. 1, there was no negativity in the N2 latency range at the anterior contralateral cluster elicited by unilateral stimuli. Thus it appears that the N2ac component may only be elicited by the attentional processes required to discriminate a target stimulus that is in competition with a simultaneously presented distractor stimulus.

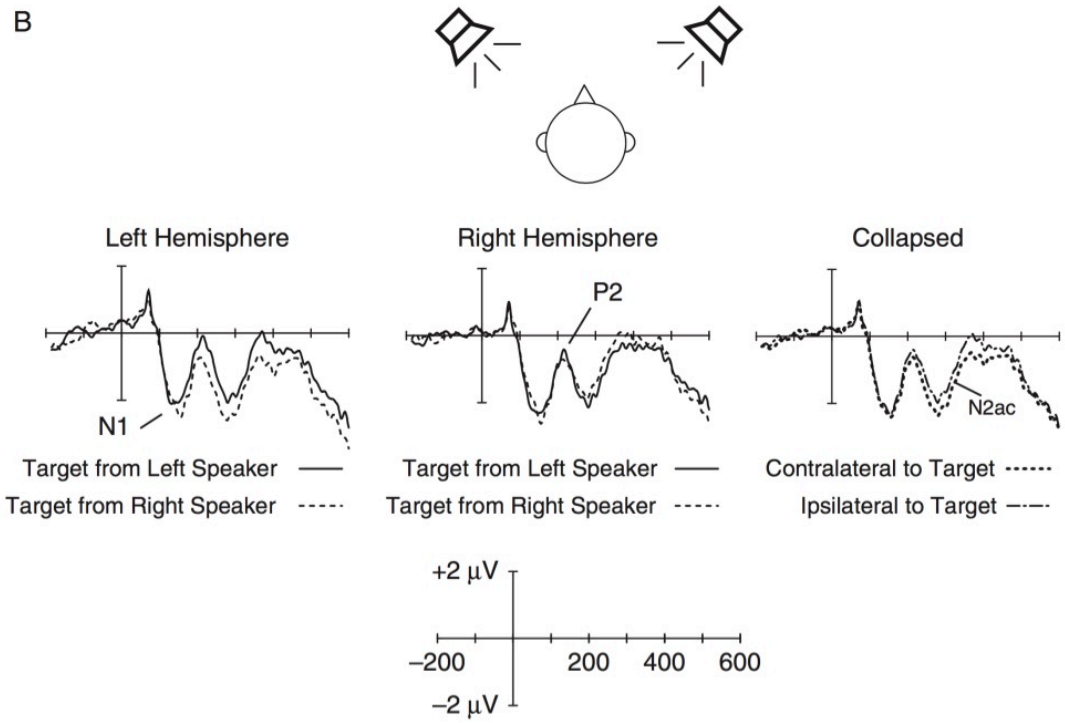


Figure 1.4 Translating the visual N2pc paradigm into an analogous auditory paradigm Pairs of stimuli were presented simultaneously and participants subjects responded to a specific target sound that could occur in either the left or the right speaker, while the non-target stimulus occurred in the opposite speaker. These waveforms are grand averages over an anterior cluster of electrode sites (F3, F7, C3, T7, F4, F8, C4, T8). Figure adapted from Gamble & Luck 2011.

In sum, Gamble & Luck provided the first description of the N2ac, an ERP component that may potentially share many attributes with the more extensively

researched N2pc component. However, this study described the N2ac as a component elicited by the selective attentional processes involved in discriminating two simultaneously presented stimuli, as opposed to the exogenous and endogenous cueing paradigms employed by many N2pc experiments. As of yet, since the N2ac is a relatively recently discovered ERP component, further research has yet to examine whether this auditory ERP component can be used in an exogenous auditory spatial orienting task to examine the neural activity associated with IOR and facilitation. If the N2ac is elicited for both these attentional phenomena, this would provide evidence that the auditory N2ac component is indeed analogous to the visual N2pc.

1.6 Neuroimaging studies of auditory orienting and IOR

The limited neuroimaging research conducted on the neural networks underlying auditory exogenous orienting has included a few studies using functional magnetic resonance imaging (fMRI) (Mayer et al., 2007; Mayer et al., 2009; Teshiba et al., 2013). fMRI is highly useful for investigating anatomically and functionally specific areas of activation, e.g. the auditory cortex (AC), during an auditory orienting task. This method can also be used to examine functional connectivity (fcMRI) of intrinsic neural activity during resting state. Thus fMRI has been essential for studying the activation of the AC and supplementary neural networks during exogenous auditory orienting and IOR. In particular, fMRI has allowed Mayer and colleagues to develop a model of the neural mechanisms underlying auditory spatial localization and auditory attention in general. In particular, this involves investigating how information is processed differentially in the right versus the left AC. Hemispheric asymmetries within the AC may depend on different attentional states during auditory processing (Teshiba et al. 2013).

In a recent study, Teshiba et al. (2013) investigated how neural activity is allocated in auditory spatial attention and the role of hemispheric asymmetries in the AC. One current theory of auditory orienting was proposed by Spierer et al. (2009), suggesting that right tempo-parietal areas create global auditory spatial representations, while precise computation of spatial coordinates occurs contralaterally within the left AC, and both contra- and ipsilaterally within the right AC (Spierer et al. 2009). Building off

of this research, Teshiba et al. investigated two different models of auditory spatial attention. The contralateral model predicts that the AC of both hemispheres show equally strong response to contralateral, relative to ipsilateral stimuli. The neglect model, in contrast, predicts a strong contralateral response in the left AC, while the right AC responds equally strongly to both contra- and ipsilateral stimuli.

In order to further investigate the activation of the primary and secondary AC in support of either of these models, fMRI data were collected during an exogenous auditory orienting task, and during a resting state task in order to measure intrinsic AC connectivity. The orienting task included both, a short and a long CTI in order to induce both facilitation (i.e. faster reaction times to valid trials) and IOR (i.e. longer reaction times to valid trials) respectively. The fMRI analysis then addressed which model, contralateral or neglect, was supported during these different attentional states. Finally, the resting state data were analyzed using a functional connectivity analysis (fcMRI), in order to examine whether intrinsic neural activity of the AC was consistent with either the contralateral or the neglect models.

The fMRl results revealed a laterality by validity interaction at the 200 ms CTI, with greater bilateral neural activity in the ACs for contralateral compared to ipsilateral valid trials. This result demonstrates that, for validly cued targets appearing after a short CTI, both auditory cortices show an increased neural activation to contralateral stimuli. Importantly, a laterality by validity interaction was also observed at the longer 700 ms CTI (IOR). However, in this case, valid trials produced increased contralateral bias only on the left AC, but no increase of contralateral activation on the right AC. Therefore, this result shows that when validly cued targets appeared after the 700 ms CTI, only the left AC showed an increase in neural activity to contralateral stimuli, but no greater activation of the right AC. No difference in activation between right and left invalid trials was observed for either the short or the long CTIs.

A contralaterality index was computed in order to determine whether the contralateral and neglect models were supported during either facilitated attention or in IOR. The index was calculated by subtracting ipsilateral from contralateral stimulus activation, in order to further quantify differences in contralateral bias between left and right AC. Results indicated a similar degree of contralateral bias for the left and right AC

at 200 ms CTI. In contrast, the 700 ms CTI elicited greater contralateral bias for the left AC compared with the right AC, and overall indicated greater contralateral bias in the left AC itself, relative to the 200 ms CTI.

These results indicate that the contralateral model is supported during facilitated attentional orienting, but the neural activation during IOR is consistent with the neglect model. This finding may potentially be explained by increased attentional modulation by fronto-parietal networks in the right hemisphere during IOR. In addition, the fcMRI results indicated that hemispheric asymmetries in the AC can also be observed during a resting state. The analysis found greater functional connectivity for the left, compared to the right primary AC, and also greater activation for the right secondary AC compared to the left secondary AC. Teshiba et al. suggest that these results are further evidence of functional differences in the right and left AC, for both attentional orienting and intrinsic neural activity. The model of auditory attention proposed by Spierer et al. (2009) also supports a model of differential activation in the left and right AC, which suggests that the auditory cortices are functionally different in their processing of auditory stimuli. The fcMRI results of Teshiba et al.'s study support Spierer et al.'s theory that the right AC is modulated by frontoparietal attentional networks to create a global representation of auditory space, while specifics of spatial orienting are processed within the left AC.

1.7 The Present Study

The N2ac is a recently discovered ERP component, and as of yet, has not been used to study the phenomenon of IOR using an exogenous orienting task in the auditory modality. Additionally, further investigation of the contralateral and neglect models described in the Teshiba et al. (2013) fMRI study will benefit greatly from complementary ERP research. While the spatial resolution of fMRI is its greatest advantage, this method only represents the average activity of an indirect measure (blood-oxygenation level, or hemodynamic response) over the course of a few seconds, which is a relatively long period of time considering that neurons fire over the course of one millisecond. Therefore, ERPs have a significant temporal advantage over fMRI, and allow us to study attentional processes involved in a phenomenon like IOR, with fine-

grain temporal resolution. Due to their unique spatial and temporal advantages and disadvantages, it is highly useful to employ both techniques whenever possible.

The present study used the N2ac ERP component to investigate auditory spatial attention via an exogenous orienting task, focusing on IOR. Auditory orienting has been studied using various imaging and behavioral methods, but research has yet to investigate the N2ac component during different attentional states of auditory processing. This study used the auditory orienting task employed by Teshiba et al. (2013) to elicit the N2ac component discovered by Gamble & Luck (2011). In contrast to previous ERP research on auditory orienting and selective attention, a short and long CTI were utilized in order to induce both facilitation and IOR.

The design of this study adapted the IOR paradigm of the Teshiba et al. fMRI study, in combination with the ERP technique in order to elicit the N2ac component. We used a short and a long CTI between cue and target, as described in Teshiba et al.'s experiment, in order to investigate the facilitation and inhibitory processes reported above and additionally studied the effects of validity and laterality. However, the fMRI paradigm is not completely transferable to an electrophysiological experiment. Most importantly, the fMRI study utilized a unilateral target, i.e. a single target sound (without a simultaneous competing sound). However, as discussed above, the second experiment of Gamble & Luck found that the N2ac was not elicited by a single lateralized tone in isolation. Therefore, the task was modified to include a distractor stimulus, presented concurrently with the target stimulus following the exogenous cue.

Furthermore, the task used in Teshiba et al. simply required participants to indicate which side the target had appeared on, and the target was the same across the entire experiment (i.e. a detection task). The present experiment used instead a discrimination task, similar to that used by Gamble & Luck to obtain the N2ac. Our task then used two possible target sounds, presented an equal number of trials, and required the participants to identify which of the two targets they heard in each trial.

In sum, the present experiment combines various aspects of previous studies to examine the auditory IOR and facilitation phenomena in a novel exogenous cueing paradigm. The ERP component being examined here is the N2ac, which has not yet been used in a Posner cueing paradigm. Previous research has investigated IOR in Posner

paradigms or Posner-like paradigms, but only in the visual domain and specifically focusing on the N2pc. However, a number of prior N2pc studies with IOR have used endogenous cueing paradigms (McDonald et al. 2009), while fewer have used an exogenous cueing paradigm (Yang et al. 2012). We wanted to examine an exogenous cueing task similar to the one used in Yang et al., but in the auditory domain. Furthermore, we wished to use two CTIs (short and long), to induce both facilitation and IOR as was done in Teshiba et al., while Yang et al. only used a long CTI. With this previous research in mind, we designed an experiment that would elicit the N2ac per the requirements found by Gamble & Luck, with two CTIs as used by Teshiba et al., and with an exogenous orienting task similar to Yang et al.

1.8 Hypotheses

Question 1: Will the IOR or facilitation phenomenon elicit the N2ac?

The N2ac has been found with simultaneously presented stimuli when subjects were required to endogenously attend to the target sound in the presence of a distractor sound (Gamble & Luck 2011). However, the N2ac has not yet been studied with the exogenous Posner cueing paradigm, and it is not yet clear whether the different attentional states produced by this paradigm will elicit the N2ac.

We predict that the facilitation effect will elicit N2ac. While we expect to observe the N2ac in anterior contralateral electrode sites for both the Valid 200 and Invalid 200 conditions, we also predict that the N2ac for Valid targets in the short CTI will either have an earlier latency or larger amplitude than Invalid targets.

In addition, we expect that IOR will elicit the N2ac. If the N2ac is consistent with its visual analogue, we expect to observe the N2ac over anterior contralateral electrode sites when IOR is induced by targets following a long CTI on the opposite side of the cued location.

Question 2: Will the N2ac with long CTI show a difference in amplitude to valid vs. invalid trials in line with McDonald et al.'s findings? If the N2ac is observed as an increased negativity for recently uncued locations compared to recently cued locations,

then this would indicate that IOR reduces the probability of shifting attention to cued locations, but does not delay the covert deployment of attention.

Question 3: Will the N2ac with a long CTI show a difference in latency to valid vs. invalid trials in line with Yang et al.'s findings? If the N2ac shows a delayed latency for recently cued locations, in comparison to uncued locations, this would indicate that IOR reflects *delayed* allocation of spatial attention to targets appearing at recently cued locations, as opposed to a reduction in the probability of shifting attention to those locations.

Chapter 2: Methods

2.1 Participants

A total of 22 Reed College students (15 female, mean age = 21.45 years old) participated in the study. All participants reported normal audition and were required to have normal, or corrected-to-normal visual acuity in order to participate in the study. Participants were screened to ensure that they had no history of neurological trauma which might interfere with electrophysiological activity. No participants were excluded due to failure to perform above chance on the task, but 3 participants were excluded due to excessive EEG artifacts. Participants were compensated with one Psychology department lottery ticket for every 30 minutes of participation, for a chance to win $50. Informed written consent was collected from all participants, and all experimental procedures were approved by the Reed College Institutional Review Board.

2.2 Stimuli

The stimuli were primarily modeled after the Teshiba et al. (2013) auditory orienting task and the Gamble & Luck (2011) N2ac experiment. The stimuli were constructed such that the distractor and target stimuli were equated for loudness but could be easily distinguished from one another. Two speakers were placed at equal distance, (70 cm) one to each side of participant's' ears. The cue stimulus was a 100 ms monaural tone pip (1000 Hz) presented to either the right or left speaker. The monaural target tone pips were either a 1550 Hz sound (Target 1), or 2100 Hz sound (Target 2), and were each presented for one-third of the total number of trials (37.5% of trials each). All tones started and ended with a 10 ms rise/fall, in order to reduce the perception of a "click" noise that occurs in pure sine wave noises. Each target tone was presented simultaneously with a 100 ms distractor white noise burst in the opposite speaker (i.e. the distractor was presented on the left side for target tones appearing in the right side, and on the right side

for target tones appearing in the left side). Loudness and intensity of targets and distractor stimuli were all equated.

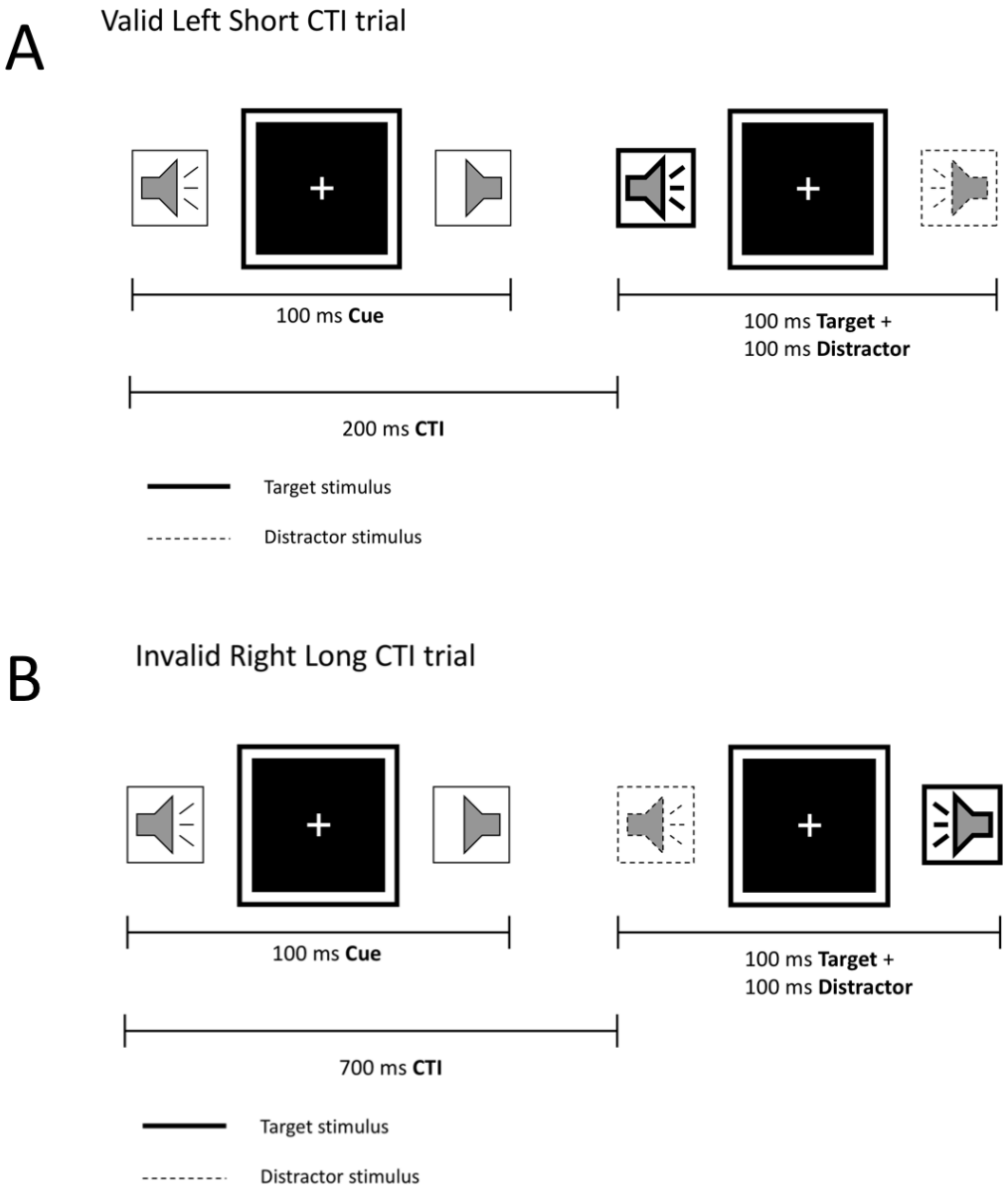


Figure 2.1 Example Stimuli

Sequence of events for Valid Left Short CTI trials and Invalid Right Long CTI trials. Cue stimuli are presented on the left side in both trials. The target stimuli (presented on the left side in Valid Left Short CTI, and on the right side in Invalid Right Long CTI) are symbolized by a bold line, with the distractor stimulus (white noise) symbolized by a dotted line. Left and right targets, and short and long CTIs, were equally probable.

Half (50%) of trials were valid and half were invalid (see below). In valid trials, the cue appeared in the same location as the target. That is, the target was played (after a time interval) on the same side as the previously presented cue. For invalid trials, the cue appeared on the opposite side of the target location, such that if a cue appeared on the right speaker, the target would be heard in the left speaker. (see Fig. 2.1). Laterality of the target was varied so that 50% of trials had the target presented in the left speaker, and the other 50% in the right speaker. Finally, we tested two different intervals between the onset of the cue and the onset of the target (CTI). Trials with short (200 ms) CTI and trials with long (700 ms) CTIs were each used in 50% of trials. Thus, the crossing of our three variables; Validity (2), laterality (2) and CTI (2) produced eight different conditions.

The same eight conditions were used for each of the two possible target tones, and therefore each experimental block had sixteen conditions. A single experimental block consisted of 224 trials, with 14 trials per each of the 16 conditions. The block of 224 trials was presented 7 times during the experimental session for a total of 98 trials per condition for each target. In the ERP analysis, target conditions were collapsed such that each of the 8 trial types contained 196 trials.

All stimuli were presented using Presentation (Neurobehavioral Systems, San Francisco CA).

2.3 Procedure

Participants were seated in an electrically shielded recording chamber, 70 cm away from the computer monitor and 70 cm away from each of two laterally placed speakers, in order to maintain a consistent auditory space. Prior to any recordings, the stimuli were presented in isolation, first the cue, followed by Target 1 and Target 2, so that participants were familiar with the time interval between stimuli and to make sure they could easily identify and discriminate between them. Subsequently, participants were given two practice blocks consisting of 10-20 trials each, depending on the subject's performance, until they demonstrated understanding of the procedure and ability to do the

task. Subjects were instructed to keep their eyes on a fixation cross for the entire block in order to minimize eye movement artifacts.

Once the experiment proper started, a given trial consisted of the presentation of a white fixation cross on the center of a black screen, that remained there for the entire block. After a 1000 ms delay, the cue tone of 100 ms duration was presented. Following the onset of the cue tone, and after a time interval of 200 or 700 ms, the 100 ms target and distractor tones were presented simultaneously, each coming from a different speaker. Participants were given 1000 ms to press one of two buttons to indicate which of the two targets was presented. If the participant failed to respond, or responded with the incorrect button, the next trial initiated automatically after the 1000 ms interval. In addition, trials were separated by an inter-trial interval of 1000 ms +- 500 ms randomly varied to prevent the participant from anticipating the next stimulus. Participants were instructed to press the left button of a response box with their right index finger whenever they detected the lower-pitched target stimulus (Target 1), and the right button with their right middle finger for the higher-pitched target (Target 2). RTs for both valid and invalid trials were recorded. A short break was given to the participants at the end of each block or whenever they requested additional breaks.

2.4 EEG Recording

Participants' brain activity was continuously recorded throughout the discrimination task. The whole session lasted approximately 2.5 hours, including preparation and intermittent breaks. Participants were fitted with a 64-channel electrode cap. Electrodes were placed on the left and right mastoids, on the outer side of the left and right eye, and below the left eye, as well as a ground electrode on the CP6 position. Impedance levels were kept below 25kΩ. This was achieved with the use of a saline-based gel and some gentle rubbing of the scalp with a blunt-tip needle, in order to abrade away a thin layer of dead skin cells. Immediately after the session finished, the cap was removed and participants had the option to wash their hair in the lab.

2.5 Data Analysis

EEG data were processed using BrainVision Analyzer software (Brain Products, Germany). EEG was recorded using FCz as a reference, and the re-referenced off-line to the average of the mastoid electrodes. Trials were discarded semi-automatically from analysis if they contained an eye blink (VEOG > 150μV) or eye movement artifact (HEOG > 70 μV), or if any electrodes exceeded predefined signal amplitudes. Participants with fewer than one third (33%) of trials in any given condition after artifact rejection were excluded from analyses to ensure reasonable signal/noise ratio in the averaged ERP waveforms (n = 3). A total of 19 participants were included in the final dataset. ERPs were time-locked to target stimulus onset and baseline corrected at -100 to 0 ms, and low-pass filtered at 30 Hz.

For our ERP analysis, we first collapsed the waveforms across target type (low-pitched target and high-pitched target) to avoid physical stimulus confounds. Furthermore, visual inspection of the waveforms for the two target types indicated that the ERPs were similar across targets.

Our main comparisons were within subjects between conditions, collapsing across the laterality of the target stimulus (whether the target appeared on the right or the left side). The final four Conditions, collapsing across laterality, were as follows: Valid 200 CTI, Valid 700 CTI, Invalid 200 CTI, and Invalid 700 CTI. Grand averages were computed for all contralateral targets and all ipsilateral targets across the four Conditions. We then examined the mean amplitudes for the contralateral-minus-ipsilateral difference waves, time locked to the presentation of the target stimulus.

Because there is only one published study concerning the N2ac (Gamble & Luck 2011), and none published using a cueing paradigm, we did not have an existing study on which to base our time window for analysis. Therefore, we based the time window selection on an initial visual analysis of the grand averaged waveforms elicited by the target stimulus in all electrodes. Based on this analysis, we decided on a time window of 100 – 200 ms post-stimulus to measure the mean amplitude of the N2ac.

All data were analyzed using Stata: Data Analysis and Statistical Software.

Chapter 3: Results

3.1 Behavioral Results

A 2 x 2 x 2 (Laterality x Validity x CTI) repeated measures ANOVA was performed to examine RT differences. The ANOVA revealed a main effect of Validity ($F(2,18) = 5.05$, $p = 0.04$), and a main effect of CTI ($F(2,18) = 5.81$, $p = 0.03$), but no effect of laterality ($F(2,18) = 0.23$, ns). The analysis also found a trending interaction between CTI and Validity ($F(2,18) = 3.11$, $p = 0.08$), but this effect did not reach significance (See Fig. 3.1).

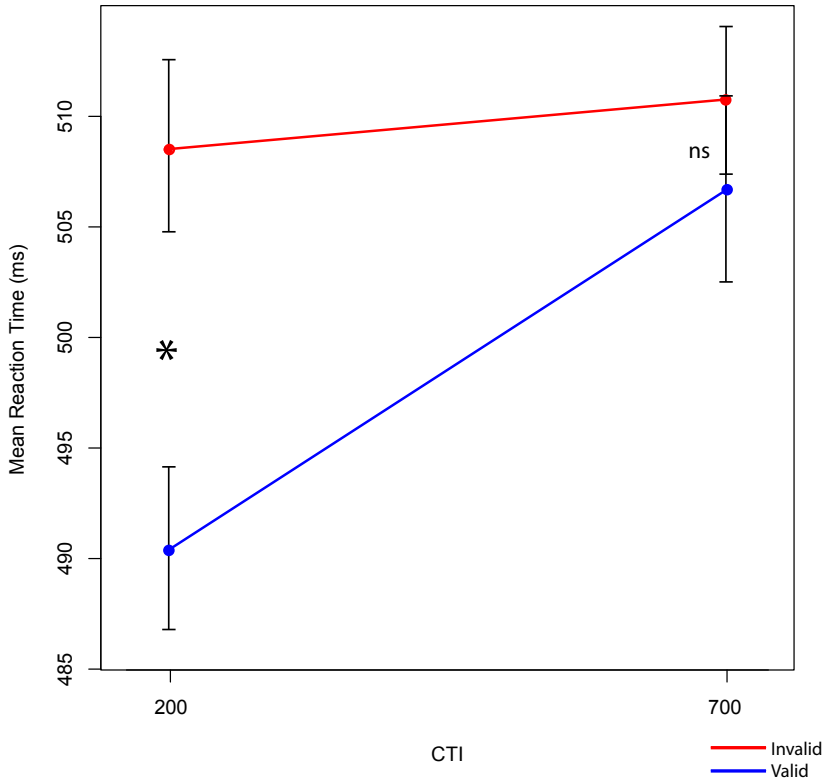


Figure 3.1 Behavioral results for facilitation and IOR

Mean RTs for Valid 200, Invalid 200, Valid 700, and Invalid 700 conditions, collapsing across laterality and excluding all incorrect responses. The significant difference between Valid 200 and Invalid 200 is evidence for facilitation.

Paired t-tests showed that RTs for Valid 200 (M = 489.17 SD = 76.73) trials were significantly faster than RTs for Invalid 200(M = 508.35 SD = 76.42; t(18) = -2.32, p = 0.03) trials, while RTs for Valid 700 (M = 507.92 SD = 74.68) trials were not significantly different from RTs for Invalid 700 (M= 510.93 SD = 77.41; t(18) = -0.58, ns) trials (see Fig. 3.1).

Overall, participants showed the typical pattern of behavior for facilitation (faster RTs for Valid 200 trials compared with Invalid 200 trials). While RTs for Valid 700 trials were not statistically different from Invalid 700 trials, the interaction between CTI and validity neared significance, indicating that our behavioral results were trending towards IOR.

Behavioral results revealed an overall accuracy rate of 96.68% ± 3.64 for Target 1 and 96.59% ± 5.75 for Target 2, demonstrating that participants had relatively little difficulty performing the task and that the two targets had similar rates of accuracy, confirmed by a paired t-test (t(18) = 0.12, ns). Analysis of RTs for the two targets found a mean RT of 480.64 ms ± 83.67 for Target 1, and a mean RT of 466.40 ms ± 76.59 for Target 2. A paired t-test revealed this difference to be significant, showing that participants responded faster to Target 2 (t(18) = 2.10, p = 0.049).

3.2 Electrophysiological Results

Figure 3.2 shows waveforms averaged across laterality in two representative electrodes in the left (C5) and the right hemisphere (C6), and for each of the four conditions. Typical auditory ERP components, such as the N1 and N2 can be observed as negative-going waveforms with maximum amplitude over anterior or central electrode cites (Luck 2014). The N2ac is calculated by first creating the average of the contralateral waveforms (right hemisphere electrodes for targets on the left, and left hemisphere electrodes for targets on the right) and the average of the ipsilateral waveforms (right hemisphere electrodes for targets on the right, left hemisphere electrodes for targets on the left). It is the difference between these waveforms what reveals the N2ac (see shaded area).

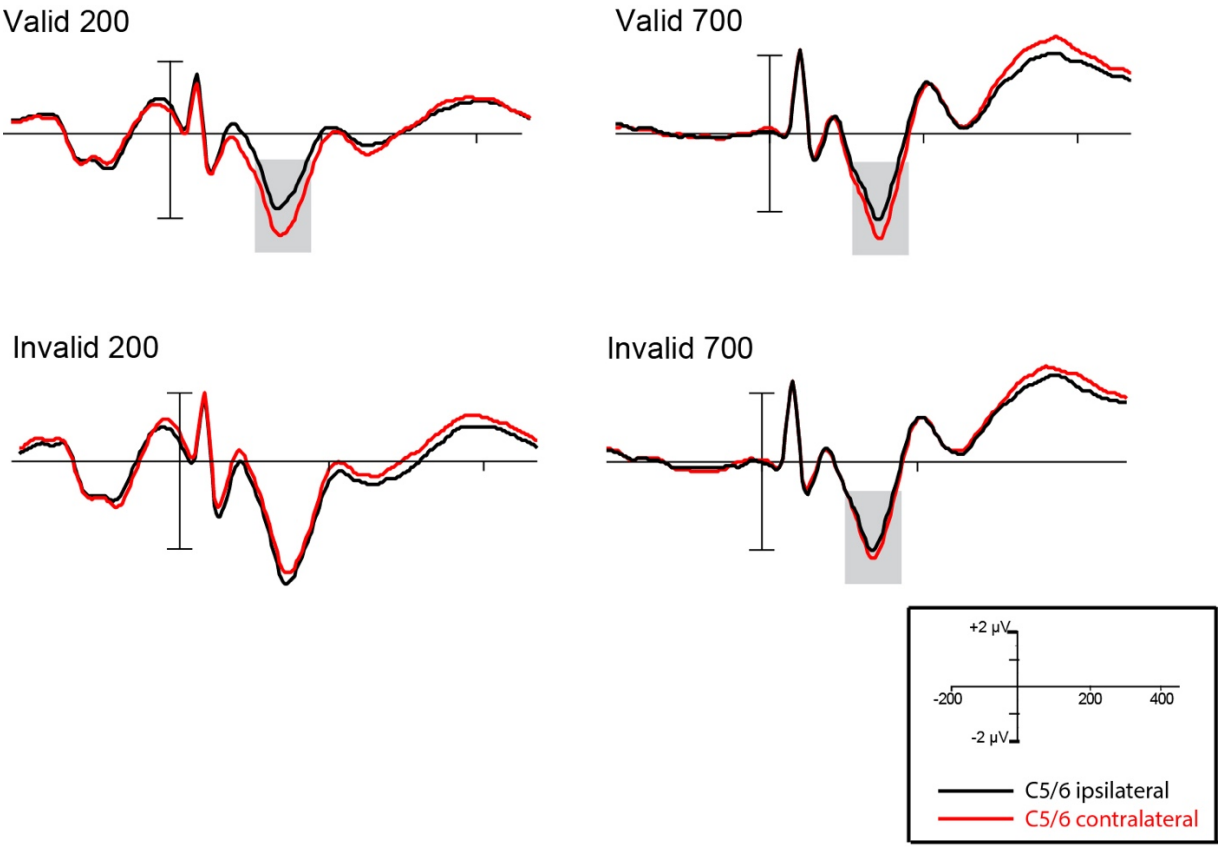


Figure 3.3A N2ac contralateral and ipsilateral ERP waveforms
The N2ac effect is shown here with grand averages of contralateral waveforms overlaid onto ipsilateral waveforms for all four conditions. Waveforms recorded from C5 and C6 electrode sites were selected to best visualize the N2ac effect.

3.2.1 The N2ac component

In line with Gamble and Luck (2011), we created a pooled average of 20 anterior electrodes (F3/4, F5/6, F7/8, FC3/4, FC5/6, FC7/8, C1/2, C3/4, C5/6, T7/8). However, we included additional sites because having used 64 instead of 32 electrodes, we had additional electrodes that covered a similar scalp area. Fig. 3.2 shows these pooled average waveforms for the left hemisphere (first column) and right hemisphere (middle column) for targets appearing on the left speaker overlaid with targets appearing on the right speaker. The right column shows contralateral waveforms overlaid with ipsilateral waveforms (collapsing across hemisphere and speaker side). The small difference between them is the N2ac.

In order to isolate the N2ac, we computed contralateral-minus-ipsilateral difference waves for each individual participant. Mean amplitudes measured within a 100-200 ms window in the difference waves were submitted to a one-way ANOVA with Condition (Valid 200, Valid 700, Invalid 200, and Invalid 700) as our within-Ss variable. This analysis revealed a highly significant effect of Condition ($F(3,18) = 39.96$, $p < 0.0001$). Fig. 3.3A shows collapsed contralateral and ipsilateral grand averages for each of the four experimental conditions. Again, to isolate the N2ac, we calculated the difference between contra- and ipsilateral waveforms to create difference waves (see Fig. 3.3B).

A visual analysis made evident an N2ac effect for three out of the four conditions, which was largest for the Valid 200 CTI. We confirmed this with a series of paired t-tests examining mean amplitude differences between the four Conditions. This analysis revealed a larger negativity for Valid 200 ($M = -0.70\mu V$ $SD = 0.40$) trials compared to Invalid 200 ($M = 0.42\mu V$ $SD = 0.27$; $t(18) = 8.38$, $p < 0.0001$) trials, to Valid 700 ($M = -0.33\mu V$ $SD = 0.31$; $t(18) = -4.87$, $p = 0.0002$) trials, and to Invalid 700 ($M = -0.14\mu V$ $SD = 0.32$; $t(18) = -5.53$, $p < 0.0001$) trials. In addition, although it did not reach significance, there was a trend for a larger negativity for the Valid 700 trials compared to Invalid 700 trials ($t(18) = 1.83$) $p = 0.08$).

In addition, single sample t-tests were used to determine if the mean amplitude difference for all four Conditions was significantly difference from zero. These t-tests found that the mean amplitude difference was significantly different from zero for the Valid 200 condition ($t(18) = -7.51$, $p < 0.0001$), Valid 700 condition ($t(18) = -4.65$, $p = 0.0002$), and Invalid 200 condition ($t(18) = 6.72$, $p < 0.0001$), and nearing significance for Invalid 700 condition ($t(18) = -1.96$, $p = 0.069$). Importantly, the effects in the Valid 200, Valid 700, and Invalid 700 conditions, resulted in negative-going difference waveforms, while the Invalid 200 condition resulted in a positive-going difference waveform. We address this latter positivity in the discussion.

Based on a visual analysis of ERP waveforms and difference waves from all four Conditions, (See Figure 3.4A) suggests an earlier onset for the Valid 200 condition compared with the other three conditions.

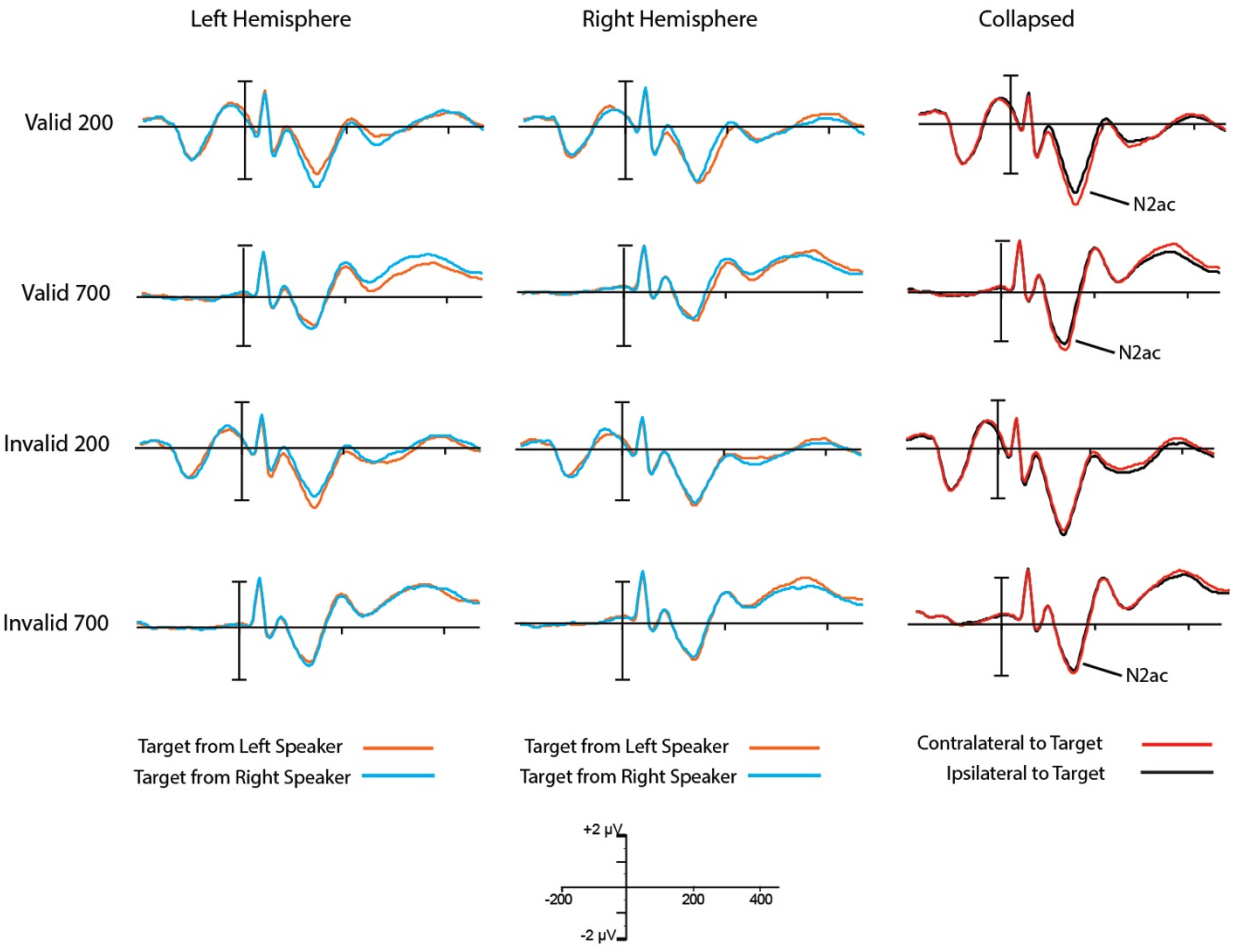
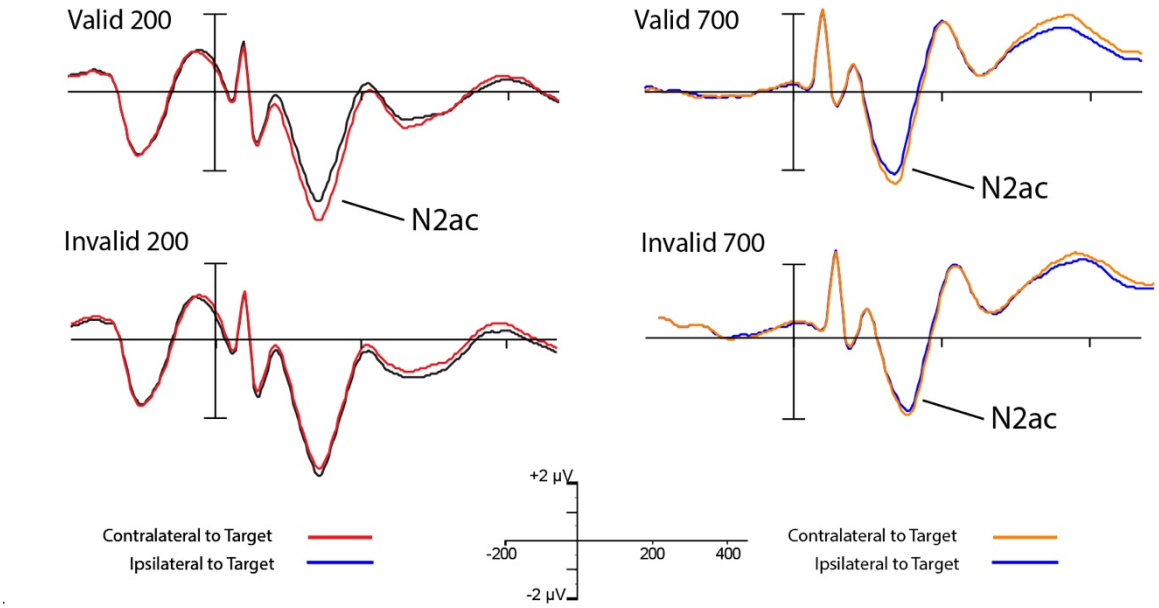


Figure 3.2 N2ac results for the anterior electrode cluster

Grand averages across an anterior cluster of electrode sites (F3/4, F5/6, F7/8, FC3/4, FC5/6, FC7/8, C1/2, C3/4, C5/6, T7/8). Targets appearing in the left and right speaker are shown for both left hemisphere and right hemisphere electrode sites. The right column shows contralateral waveforms are shown overlaid on top of ipsilateral waveforms to visualize the effect of the N2ac effect.

A



B

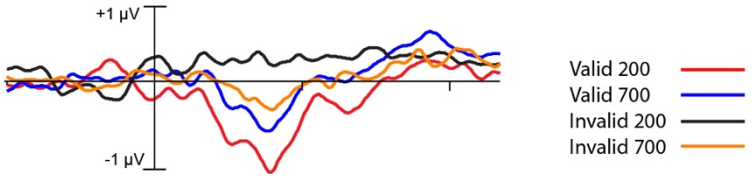


Figure 3.3A N2ac effect.

Contralateral waveforms overlaid onto ipsilateral waveforms for pooled anterior electrodes.

Figure 3.3B N2ac effect difference waves

Contralateral-minus-ipsilateral difference waves (averaged across an anterior electrode cluster) for each condition.

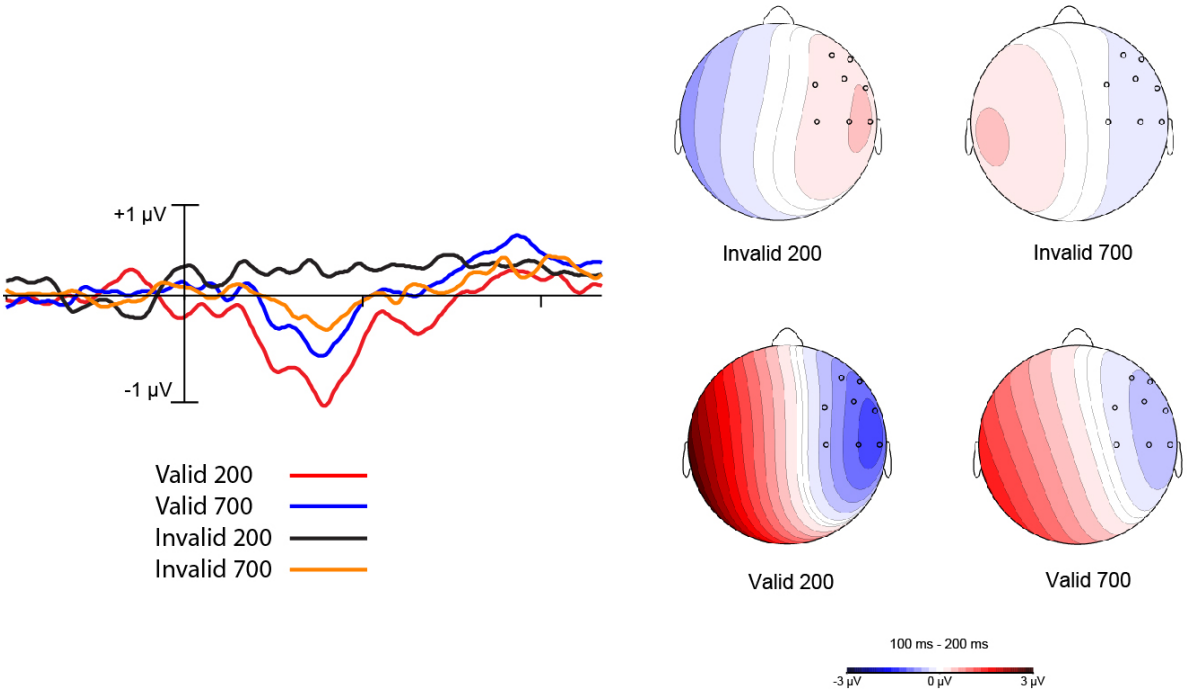


Figure 3.4 N2ac difference waves and difference maps

On the left, contralateral-minus-ipsilateral difference waves (averaged across an anterior electrode cluster) for each experimental condition. On the right, difference maps showing mean amplitude differences averaged across the 100ms – 200ms time window for each of the four conditions. Electrodes used in data analysis are indicated with small circles. The left hand side of each 'head' should be ignored in this figure.

Chapter 4: Discussion

Previous EEG research on inhibition of return (IOR) has mainly focused on visual stimuli, using the Posner cueing paradigm (Yang et al. 2012) or similar paradigms (McDonald et al. 2009). In the current study, we used an auditory paradigm similar to one previously employed in an fMRI study (Teshiba et al. 2013) investigating the differential activation of the left and right auditory cortex during facilitation and IOR. We adapted this paradigm to be used in an event-related potential (ERP) study. In particular, we needed to make changes to be able to use a recently discovered ERP component, the N2ac, found to be elicited during a simple auditory discrimination task with no manipulation of cue validity. Because the N2pc has been successfully used to study attentional processes involving IOR in the visual modality, we hypothesized that an analogous auditory component, the N2ac, would also be elicited by IOR in the auditory modality. Furthermore, the research in the visual modality has indicated either, a change in mean amplitude (McDonald et al. 2009), or a change in latency (Yang et al. 2012) of the N2pc associated with IOR. The current study aimed to determine whether the N2ac would also be elicited during an auditory orienting task (analogous to the N2pc in the visual modality), and if so, whether an auditory IOR would be reflected in a change in amplitude or a change in latency of the N2ac.

4.1 Behavioral Findings

Our behavioral findings showed a typical pattern of facilitation for the short CTI condition; Responses to the target in Valid 200 trials were faster than responses to targets in Invalid 200 trials. In contrast, we failed to find an immediately apparent behavioral pattern of IOR since, contrary to our predictions, RTs for Invalid 700 trials were not significantly faster than Valid 700 trials. However, in line with our predictions for IOR, we found a trend for a significant Validity x CTI interaction effect.

In short, these behavioral results indicate that, while our paradigm was effective in producing the facilitation effect, we were not completely successful in inducing IOR. This could possibly be explained by the changes we made to the Teshiba et al. (2013) methods in order to elicit an N2ac. First, we used a discrimination task instead of a detection task. That is, our participants were required to identify a particular target, instead of simply detecting the location of the target. Additionally, we introduced a distractor noise (in the opposite speaker) presented concurrently with the target. This change was done because Gamble and Luck (2011), found that the N2ac was not elicited by unilateral stimuli, and required instead competition between concurrent bilateral stimuli. Therefore, it could be that the discrimination task we used did not require participants to attend to the location of the target, which may be helpful or even necessary for inducing IOR in the auditory modality. Furthermore, the use of the distractor noise may have affected participant's ability to accurately perceive the location of the target. For the facilitation effect, these factors may have been irrelevant since it improved attention towards same-location cues and targets. However, it may be that the auditory IOR effect is more sensitive to the location of the cue and target; requiring the participant to perceive the cue and the target as coming distinctly from a different location.

In addition, we found that the higher-pitched target (Target 2) produced significantly faster reaction times than the lower-pitched target (Target 1). Although we equated the two targets for loudness, it appears that the higher-pitched sound was still somehow more salient to participants. This is possibly because both the cue and Target 1 were lower-pitched, thus making the highest-pitched target the easiest for participants to perceive due to its contrast. While the presentation of all targets was randomized and the two targets were equally distributed amongst all the possible conditions, it is possible that the increased salience of Target 1 decreased the behavioral effect of IOR. For future research, the two target noises could be closer in pitch (to each other) such that they are equally salient and equally distinguishable from the cue.

It should also be noted that IOR in general may be more difficult to obtain in the auditory modality compared to the visual modality, due to the functional neuroanatomy of the auditory system. The visual system is lateralized such that sensory information from both the right visual field and left visual field is processed in the left and right

hemisphere of the brain and of the visual cortex respectively. In contrast with the visual system, the projections of the auditory system provide both ipsilateral and contralateral inputs to the cortex. Therefore, there is bilateral representation of each cochlear nucleus in both hemispheres (Kolb & Wishaw, 2009). Meanwhile, it is well known from neuroimaging and lesion data that there are significant hemispheric asymmetries between the left and right auditory cortices (Zatorre et al. 1999; Brunetti et al. 2008; Bellmann et al. 2001; Tanaka et al. 1999). Due to these structural and functional asymmetries, auditory stimuli presented on the left side may be processed differently from stimuli presented on the right side (as was investigated by Teshiba et al. 2013). Therefore, attentional effects that rely on the lateralized presentation of stimuli, such as IOR, may not be as easily observed with auditory stimuli as with visual stimuli. Similarly, the choice of a specific paradigm may have an impact on our chances to observe a possibly elusive IOR effect in audition.

In order to further investigate the effectiveness of the paradigm we used here, a purely behavioral study should be conducted first using this task. With more participants, we may decrease variability, making it more likely that IOR would eventually emerge from our paradigm. However, if the task is in fact ineffective at inducing IOR, it would be necessary to investigate how to effectively elicit the N2ac without erasing the IOR effect.

4.2 Facilitation elicits the N2ac

ERPs were recorded to target stimuli in an auditory Posner cueing paradigm in valid and invalid trials, with either a short or long cue-target interval (CTIs), in order to investigate attentional processes related to auditory IOR.

ERP analysis was carried out for four conditions (collapsing across laterality): Valid 200, Valid 700, Invalid 200, and Invalid 700. A visual analyses indicated that there was no latency difference between the Valid 700 and Invalid 700 conditions. Therefore, we failed to find results analogous to the N2pc findings from Yang et al. (2012). However, our visual analysis of the N2ac difference waveforms indicates that the Valid 200 condition has an earlier onset latency than the Invalid 200 condition (and earlier than

both 700 CTI conditions). This result suggests that the facilitation effect may be in line with the findings of Yang et al. (2012), as we observed a delayed latency for recently uncued compared to recently cued locations at the short CTI (although Yang et. al. tested only a long CTI).

4.3 N2ac Mean Amplitude Differences

We analyzed contralateral-minus-ipsilateral difference waveforms averaged across an anterior electrode cluster. In this cluster, we found that in Valid 200, Valid 700, and Invalid 700 trials, the voltage contralateral to the target was more negative than the voltage ipsilateral to the target, with the main effect occurring approximately 100-200 ms after target stimulus onset. Interestingly, the timing of this effect is much earlier than the one reported by Gamble and Luck (2011) who found a 200 msec onset for their N2ac effect. We address this discrepancy later in this discussion.

The N2ac was largest in the Valid 200 condition, followed by the Valid and Invalid 700 conditions. While the N2c for Valid 200 trials was significantly larger than the one observed in Valid 700 and both Invalid conditions, the Valid 700 and Invalid 700 conditions were only trending towards being significantly different from each other. In addition, the direction of the latter effect was opposite to our expectation, with the Valid 700 condition trending towards a more negative amplitude than the Invalid 700. Finally, the Invalid 200 condition was significantly different from the other conditions, eliciting a larger *positivity*. This result shows that for the Invalid 200 condition, the *ipsilateral* waveform was actually more negative than the contralateral waveform, clearly opposite to the normal N2ac effect.

In short, consistent with our predictions, we observed an N2ac effect reflecting facilitation in the Valid 200 condition. However, although we also expected to observe an N2ac for the Invalid 200 condition (albeit probably smaller or delayed), we found instead an effect opposite of the N2ac for this condition. Finally, as hypothesized, we did observe an N2ac effect for the both Valid 700 and Invalid 700 conditions. However, these conditions were statistically identical.

Our results with regards to mean amplitude differences do not conform to McDonald et al. (2009)'s previous IOR study utilizing the N2pc. However, the present study and McDonald et al. differed experimentally in several key ways. As discussed in the introduction, McDonald et al. employed a paradigm different from the typical Posner cueing paradigm to elicit IOR. In addition, McDonald et. al. utilized an endogenous cue instead of the exogenous cue as the one we used in this experiment. Importantly, McDonald et al. used only a long CTI condition because their experiment was designed to elicit only IOR, not facilitation. In fact, our study differs from most previous IOR studies in the ERP literature because we used *both* a short and a long CTI. We found that the N2ac was most pronounced in the Valid 200 condition, indicating that the effect of facilitation is to increase attention to recently cued locations while reducing the probability of shifting attention to uncued locations. No previous ERP research has indicated how the N2pc responds to a short CTI in an exogenous Posner cueing paradigm. Our behavioral and electrophysiological results provide new evidence that the N2ac is elicited by facilitation in an exogenous cueing paradigm in the auditory modality.

However, we also expected to find that the N2ac would have a larger amplitude for the Invalid 700 compared to the Valid 700, providing evidence that the N2ac can be used as evidence of auditory IOR. Our results did not yield statistically significant differences between these two conditions, contrary to our expectations derived from the mean amplitude differences found by McDonald et al. (2009). However, our behavioral results were trending towards the IOR effect. It is possible that with more participants, we may observe mean amplitude differences that are more in line with the findings of McDonald et al.

4.4 Timing of the N2ac

We found a mean amplitude difference between contralateral and ipsilateral waveforms in three of our four conditions. We identified this effect as the N2ac, which occurred approximately 100 – 200 ms after target stimulus onset. The effect we observed here was significantly earlier than the original N2ac study, where Gamble & Luck (2011) found an amplitude difference from 200 – 500 ms after stimulus onset. Our effect is also

significantly earlier than the typical N2pc. For example, the peak negative voltage of the Npc found by McDonald et al. (2009) appeared approximately 210 ms post stimulus.

We suggest several explanations for why we observed such an early peak of the N2ac in comparison with previous N2ac and N2pc research. First, we should expect an earlier ERP component in an auditory study compared to a visual study. Auditory stimuli have significantly faster processing time than visual stimuli due to the signal transduction of the auditory system occurring much faster than for the visual system. In line with this fact, RTs for auditory stimuli occur up to 70 ms faster than RTs for visual stimuli (Shelton & Kumar 2010). However, this still leaves the question of why our N2ac was much earlier than the N2ac discovered by Gamble & Luck (2011).

One main factor to consider is the timing and design of our experiment versus the timing and design of theirs. Gamble & Luck conducted an experiment where two different auditory stimuli (i.e. a pure tone and white noise) were presented simultaneously in a separate speaker, and the participant had to indicate which sound was the target. The stimuli were all 750 ms in duration, and the interval between the onset of each stimuli was 1500 ms ± 500 ms. However, no cueing was involved in their paradigm, meaning that the participant's attention was never intentionally cued towards one side over the other. In contrast, our experiment did use an exogenous cueing paradigm, the duration of our stimuli was significantly faster (100 ms), and we used either a 200 ms or a 700 ms CTI. Consequently, the pacing of our experiment was much faster, and especially with the shorter duration between trials, our participants were required to shift their attention at a much quicker rate. Therefore, the timing of the observed ERP components would also be much faster than in the N2ac experiment designed by Gamble & Luck.

4.5 Positive effect of the Invalid 200 condition

We found that the Invalid 200 condition failed to elicit the N2ac, and in fact that the pattern of results for this condition was the opposite. Instead of the typical effect of contralateral attention eliciting an N2pc and an N2ac, for Invalid 200 trials we observed that the voltage ipsilateral to the target was in fact more negative than the voltage contralateral to the target. This resulted in a positive difference wave that was

significantly different from zero. In short, we can conclude that the effect of the Invalid 200 condition was not null, but rather opposite of what we expected.

These ERP results seem to suggest that auditory attention was not effectively oriented to the target stimuli in the Invalid 200 condition, and therefore the contralateral effect of attention was not observed. Let's recall the structure of the Invalid 200 condition: the cue sound is presented in either the left or the right speaker, then, at the end of a 200 ms interval beginning at the onset of the cue, the target sound is presented in the *opposite* side, concurrent with a distractor noise presented in the speaker where the cue was presented. Because the CTI is so short in this condition, it may be possible that participants' attention is still oriented to the location of the cue, even when the target is being presented on the opposite side. Thus, if attention is still directed at the location of the cue even when the target is being presented, we may have observed a contralateral effect of attention to the *cue* as opposed to the target. In other words, we may have found that in the Invalid 200 condition, voltages contralateral to the cue were more negative than ipsilateral voltages to the cue. This would mean that we would observe the effect of the N2ac at the presentation of the cue as opposed to the presentation of the target, because attention is not effectively oriented to the target noise in this condition. In this case, it would make sense that the target sound would elicit a larger ipsilateral waveform than contralateral waveform, since the contralateral effect of the N2ac would have already occurred at the cue, and we may be observing the last part of such effect.

Further analysis of our data will be able to answer this question more conclusively. One possibility is to time-lock the EEG to the cue instead of the target, which will allow us to examine if the N2ac effect is in fact occurring at the cue in the Invalid 200 trial. Another possibility for a future modification of this experiment is to include a "cue-only" trial, in which the cue sound is presented either from the left or the right speaker, but no target or distractor sound is presented, and the participant is required to withhold a response. This would allow us to observe the electrophysiological effect of the cue in isolation, which we would then be able to use to "subtract" out its effect from a cue-target trial. The cue-only trial could be used to cancel out the effect of the cue in the Invalid 200 condition, so that we might observe the effect of the target in isolation in

order to determine if the neural activity produced by the cue is causing the effect we observed in the Invalid 200 condition.

4.6 Future Directions

As stated above, further behavioral studies should be conducted in order to fully determine how to elicit both the N2ac and IOR in the same paradigm. Another direction for future research on this topic is to include cue-only trials in every experimental block, in which the cue was presented but not the target or distractor noise, as described above. The cue-only trials can not only be used to isolate the effect of the cue for the Invalid 200 condition, but can also be used to test the contralateral and neglect models of auditory attention, as was done in the fcMRI analysis of Teshiba et al. (2013).

The cue-only trials can be used in the ERP analysis to examine separately the activation of the right and left hemispheres in response to contra- and ipsilateral stimuli, once again by subtracting out the effect of the cue from cue-target trials, such that the effect of the target is isolated. Since the question of the lateralization of the auditory system is essential for research on components such as the N2ac, it will be very useful to have ERP evidence of differential activation of the right and left hemispheres in response to auditory stimuli.

4.7 Conclusions

Our results confirmed that the N2ac is elicited by facilitation in an auditory orienting task. With only one currently published study on the N2ac, our experiment is possibly the first to employ an exogenous Posner-cueing paradigm in order to elicit the N2ac and further investigate its similarity to the N2pc. The main finding of facilitation, both behaviorally and electrophysiologically, indicates that the N2ac, like the N2pc, also involves processes of selective attention and discrimination of stimuli. Furthermore, our results also indicate that the auditory system is sufficiently lateralized to produce an N2pc-like effect for facilitation, which is encouraging to the success of future research using lateralized auditory stimuli. In their initial study, Gamble & Luck wondered

whether the auditory system was sufficiently lateralized, (in comparison to the clear lateralization of the visual system), to elicit a component analogous to the N2pc. Our results for facilitation confirm that the auditory system also shows an effect of contralateral attention.

We found a behavioral trend towards IOR, but this effect was only trending towards significance; likewise, we failed to find electrophysiological evidence for IOR as a mean amplitude or latency difference in N2ac, as predicted based on previous research. However, we are confident that future research will clarify whether the lack of the IOR effect was due to the particular task, so that further experiments can determine if the N2ac is in fact sensitive to the IOR phenomenon.

References

Bellmann, A., Meuli, R., and Clarke, S. "Two Types of Auditory Neglect." *Brain: A Journal of Neurology* 124, no. Pt 4 (April 2001): 676–87.

Berdica, E., Gerdes, A.B.M., Pittig, A., and Alpers, G. "Inhibition of Return in Fear of Spiders: Discrepant Eye Movement and Reaction Time Data." *Journal of Ophthalmology* 2014 (2014): 1–8. doi:10.1155/2014/183924.

Bowers, G.N., and McComb, R.B. "Measurement of Total Alkaline Phosphatase Activity in Human Serum." *Clinical Chemistry* 21, no. 13 (December 1975): 1988–95.

Brunetti, M., Della Penna, S., Ferretti, A., Del Gratta, C., Cianflone, F., Belardinelli, P., Caulo, M., Pizzella, V., Olivetti Belardinelli, M., and Romani, G.L. "A Frontoparietal Network for Spatial Attention Reorienting in the Auditory Domain: A Human fMRI/MEG Study of Functional and Temporal Dynamics." *Cerebral Cortex (New York, N.Y.: 1991)* 18, no. 5 (May 2008): 1139–47. doi:10.1093/cercor/bhm145.

Chica, A.B., and Lupiáñez, J. "Effects of Endogenous and Exogenous Attention on Visual Processing: An Inhibition of Return Study." *Brain Research* 1278 (June 2009): 75–85. doi:10.1016/j.brainres.2009.04.011.

Gamble, M.L., and Luck, S.J. "N2ac: An ERP Component Associated with the Focusing of Attention within an Auditory Scene: The N2ac Component." *Psychophysiology* 48, no. 8 (August 2011): 1057–68. doi:10.1111/j.1469-8986.2010.01172.x.

Hendrickson, W.A., and Ward, K.B. "Atomic Models for the Polypeptide Backbones of Myohemerythrin and Hemerythrin." *Biochemical and Biophysical Research Communications* 66, no. 4 (October 27, 1975): 1349–56.

Hultberg, B., and Masson, P.K. "Activation of Residual Acidic Alpha-Mannosidase Activity in Mannosidosis Tissues by Metal Ions." *Biochemical and Biophysical Research Communications* 67, no. 4 (December 15, 1975): 1473–79.

Kolb, B., & Whishaw, I.Q. (2009). *Fundamentals of human neuropsychology*. Macmillan.

Luck, S.J. *An Introduction to the Event-Related Potential Technique*. Second edition. Cambridge, Massachusetts: The MIT Press, 2014.

Luck, S.J., Fuller, R.L., Braun, E.L., Robinson, B., Summerfelt, A., and Gold, J.M. "The Speed of Visual Attention in Schizophrenia: Electrophysiological and Behavioral Evidence." *Schizophrenia Research* 85, no. 1–3 (July 2006): 174–95. doi:10.1016/j.schres.2006.03.040.

Luck, S.J., and Hillyard, S.A. "Spatial Filtering during Visual Search: Evidence from Human Electrophysiology." *Journal of Experimental Psychology: Human Perception and Performance* 20, no. 5 (1994): 1000–1014. doi:10.1037/0096-1523.20.5.1000.

Mayer, A.R., Franco, A.R., and Harrington, D.L. "Neuronal Modulation of Auditory Attention by Informative and Uninformative Spatial Cues." *Human Brain Mapping* 30, no. 5 (May 2009): 1652–66. doi:10.1002/hbm.20631.

Mayer, A.R., Harrington, D.L., Stephen, J., Adair, J.C., and Lee, R.R. "An Event-Related fMRI Study of Exogenous Facilitation and Inhibition of Return in the Auditory Modality." *Journal of Cognitive Neuroscience* 19, no. 3 (March 2007): 455–67. doi:10.1162/jocn.2007.19.3.455.

McDonald, J.J., Hickey, C., Green, J.J., and Whitman, J.C. "Inhibition of Return in the Covert Deployment of Attention: Evidence from Human Electrophysiology." *Journal of Cognitive Neuroscience* 21, no. 4 (April 2009): 725–33. doi:10.1162/jocn.2009.21042.

Mondor, T.A. "Predictability of the Cue-Target Relation and the Time-Course of Auditory Inhibition of Return." *Perception & Psychophysics* 61, no. 8 (November 1999): 1501–9.

Mondor, T.A., and Breau, L.M. "Facilitative and Inhibitory Effects of Location and Frequency Cues: Evidence of a Modulation in Perceptual Sensitivity." *Perception & Psychophysics* 61, no. 3 (April 1999): 438–44.

Mondor, T.A., Breau, L.M., and Milliken, B. "Inhibitory Processes in Auditory Selective Attention: Evidence of Location-Based and Frequency-Based Inhibition of Return." *Perception & Psychophysics* 60, no. 2 (February 1998): 296–302.

Posner, M.I., and Cohen, Y. "Components of Visual Orienting." In *Attention and Performance X: Control of Language Processes*, 531–56, 1984.

Posner, M.I., Rafal, R.D., Choate, L.S., and Vaughan, J. "Inhibition of Return: Neural Basis and Function." *Cognitive Neuropsychology* 2, no. 3 (August 1985): 211–28. doi:10.1080/02643298508252866.

Priess, H.W., Heise, N., Fischmeister, F., Born, S., Bauer, H., and Ansorge U. "Attentional Capture and Inhibition of Saccades after Irrelevant and Relevant Cues." *Journal of Ophthalmology* 2014 (2014): 1–12. doi:10.1155/2014/585921.

Prime, D.J., Tata, M.S., and Ward, L.M. "Event-Related Potential Evidence for Attentional Inhibition of Return in Audition." *Neuroreport* 14, no. 3 (March 3, 2003): 393–97. doi:10.1097/01.wnr.0000058779.36017.b9.

Prime, D.J., and Ward, L.M.. "Auditory Frequency-Based Inhibition Differs from Spatial IOR." *Perception & Psychophysics* 64, no. 5 (July 2002): 771–84.

Reuter-Lorenz, P.A., Jha, A.P., and Rosenquist, J.N. "What Is Inhibited in Inhibition of Return?" *Journal of Experimental Psychology. Human Perception and Performance* 22, no. 2 (April 1996): 367–78.

Shelton, J., and Kumar, G.P. "Comparison between Auditory and Visual Simple Reaction Times." *Neuroscience & Medicine* 01, no. 01 (2010): 30–32. doi:10.4236/nm.2010.11004.

Spalek, T.M., and Di Lollo, V. "The Time Required for Perceptual (nonmotoric) Processing in IOR." *Psychonomic Bulletin & Review* 14, no. 2 (April 2007): 327–31.

Spence, C., and Driver, J. "Auditory and Audiovisual Inhibition of Return." *Perception & Psychophysics* 60, no. 1 (January 1998): 125–39.

Spierer, L., Bellmann-Thiran, A., Maeder, P., Murray, M.M., and Clarke S. "Hemispheric Competence for Auditory Spatial Representation." *Brain* 132, no. 7 (July 1, 2009): 1953–66. doi:10.1093/brain/awp127.

Tanaka, H., Hachisuka, K., and Ogata, H. "Sound Lateralisation in Patients with Left or Right Cerebral Hemispheric Lesions: Relation with Unilateral Visuospatial Neglect." *Journal of Neurology, Neurosurgery, and Psychiatry* 67, no. 4 (October 1999): 481–86.

Tassinari, G., Campara, D., Benedetti, C., and Berlucchi, G. "The Contribution of General and Specific Motor Inhibitory Sets to the so-Called Auditory Inhibition of Return." *Experimental Brain Research* 146, no. 4 (October 2002): 523–30. doi:10.1007/s00221-002-1192-8.

Tata, M.S., and Ward, L.M. "Spatial Attention Modulates Activity in a Posterior 'where' Auditory Pathway." *Neuropsychologia* 43, no. 4 (January 2005): 509–16. doi:10.1016/j.neuropsychologia.2004.07.019.

Taylor, T.L., and Klein, R.M. "Visual and Motor Effects in Inhibition of Return." *Journal of Experimental Psychology. Human Perception and Performance* 26, no. 5 (October 2000): 1639–56.

Teshiba, T. M., Ling, J., Ruhl, D.A., Bedrick, B.S., Pena, A., and Mayer, A.R.. "Evoked and Intrinsic Asymmetries during Auditory Attention: Implications for the Contralateral and Neglect Models of Functioning." *Cerebral Cortex* 23, no. 3 (March 1, 2013): 560–69. doi:10.1093/cercor/bhs039.

Wang, Z., and Klein, R.M. "Searching for Inhibition of Return in Visual Search: A Review." *Vision Research* 50, no. 2 (January 2010): 220–28. doi:10.1016/j.visres.2009.11.013.

Yang, D., Yao, S., Ding, C., Qi S., and Lei, Y. "Electrophysiological Evidence for Inhibition of Return Effect in Exogenous Orienting." *Experimental Brain Research* 221, no. 3 (September 2012): 279–85. doi:10.1007/s00221-012-3170-0.

Zatorre, R.J., Mondor T.A., and Evans, A.C.. "Auditory Attention to Space and Frequency Activates Similar Cerebral Systems." *NeuroImage* 10, no. 5 (November 1999): 544–54. doi:10.1006/nimg.1999.0491.