DISSERTATION

THREE TYPES OF SENSORY GATING: EXPLORING INTERRELATIONSHIPS,

INDIVIDUAL DIFFERENCES, AND IMPLICATIONS

Submitted by

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WE HEREBY RECOMMEND THAT THE DISSERTATION PREPARED UNDER OUR SUPERVISION BY CARLY YADON ENTITLED THREE TYPES OF SENSORY GATING: EXPLORING INTERRELATIONSHIPS, INDIVIDUAL DIFFERENCES AND IMPLICATIONS BE ACCEPTED AS FULFILLING IN PART REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY.

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ABSTRACT OF DISSERTATION

THREE TYPES OF SENSORY GATING: EXPLORING INTERRELATIONSHIPS,
INDIVIDUAL DIFFERENCES, AND IMPLICATIONS

The primary purpose of this dissertation was to determine how information is selectively processed in the brain through sensory gating mechanisms. Filtering, habituation, and orienting are three types of sensory gating that have never been investigated together in the same study. Although it has been well established that sensory gating is abnormal in many clinical groups, there remains a fundamental lack of understanding regarding the mechanisms of gating. For example, the functional significance of sensory gating, as well as how different types of sensory gating are related to basic brain processes and to each other, is poorly understood. Using an event-related potential (ERP) paradigm, I measured P50, N100, and P200 filtering, habituation, and orienting and administered a sequence of neuropsychological measures of attention to forty-two healthy adults. I found that filtering, orienting, and habituation and the three ERP components had different patterns of results, suggesting that the three paradigms measured distinct types of sensory gating and that gating is a multistage process. For all three types of sensory gating, higher-level attention tasks tended to predict gating responses better than lower-level attention tasks. This dissertation demonstrated that

sensory gating has functional importance and these three gating paradigms seem to reflect different types of gating that should be explored in their own right.

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Chapter 1: General Introduction

"I just can't focus. I hear all of the sounds and I can't shut them out… I hear everything. I hear the computer, I hear the air conditioning, I hear your pen writing, I see people in the other room, and it all distracts me."

~ Schizophrenia patient (Light & Braff, 2003)

A student is sitting in a classroom. She is writing down notes from the PowerPoint presentation and listening to her instructor's voice. The students in front of her are whispering. Every few minutes, someone comes into the room late and brushes past her to find a seat. The heating unit's fan intermittently runs throughout the class. Every several seconds someone coughs or sneezes. People in the classroom are wearing bright clothing in a variety of colors and textures; they are wearing perfume and cologne. They are tapping their pens, wiggling in their chairs, and sighing from time to time. In this cacophony of sensory information, how does this student pay attention to the speaker?

To more efficiently process the wide range of sensory information that is present in the environment, the brain has evolved a system of checks and balances that allows for a *selective* processing of sensory information.   Sensory gating is a neurological process that ensures that more resources are devoted to important sensory information and fewer resources are devoted to unimportant information.

Sensory gating overview

One can think of the process of sensory gating as a gate that can swing open to "gate-in" relevant sensory information as well as swing closed to "gate-out" irrelevant sensory information (Boutros & Belger, 1999). Gating-in is a response reflecting preferential treatment to novel stimuli in the environment, with one characterization being an orienting response. Gating-out is characterized by filtering or habituating to

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repetitive stimuli in the environment. Sensory gating is considered an adaptive,

protective mechanism (Lijffijt, Lane, et al., 2009) because it is important to be able to

quickly respond to novel information and also to ignore (not continue to devote resources

to) repetitive stimuli. Most of the research on sensory gating has been conducted in the

auditory modality. Therefore, the work presented in this report will be limited to the

auditory modality as well.

Event-related potentials

Event-related potential techniques allow investigators to measure the brain's

response to specific events or stimuli. In a simple event-related potential (ERP)

paradigm, stimuli are presented to a participant during an electroencephalogram (EEG)

recording; the electrical activity of the brain is time-locked to the stimuli. A waveform is

produced from the raw EEG using various data processing procedures. ERP waveforms

elicited by specific sensory stimuli are predictable and produce a set of expected peaks

and valleys, called ERP components. Luck (2005) defined a component as "scalp-

recorded neural activity that is generated in a given neuroanatomical module when a

specific computational operation is performed" (p. 59). In other words, the components

are thought to reflect specific processes or responses. Because of this, an ERP for a

given stimulus is highly reproducible for a given set of stimulus parameters. ERPs across

individuals are similar and they usually have an expected morphology (i.e., the overall

shape and order of the peaks and valleys), but they also reveal individual differences.

These individual differences may correspond to the nuances in the way each individual's

brain responds to a stimulus or to differences in brain structure or neurophysiological

function. Healthy adults have variability in their responses, but children and individuals

with neurological disabilities will show even greater variability within a sample (e.g., Patterson et al., 2008; Segalowitz & Davies, 2004).

An auditory ERP has a characteristic morphology for a typical sound stimulus. These peaks and valleys (i.e., the components) allow for neural processing to be tracked starting just after a stimulus is presented, with millisecond precision. Components are named for their polarity (either positive or negative) and latency (when the component's amplitude is the largest); for example, P50 is a positive-going peak that peaks in amplitude about 50 ms after a sound has been presented.

Activity in the auditory cortex is present by about 30 ms after the onset of a sound. Typically a positive peak is observed around 30 ms that is thought to reflect basic auditory cortex processing originating from the primary auditory cortex (Simons & Perlstein, 1997). This is followed by a positive peak around 50 ms, called the "P50" component. The P50 component is thought to reflect more complex auditory cortical processing and is possibly mediated by the frontal cortex (Korzyukov et al., 2007). A negative peak around 100 ms, the "N100" component, is thought to reflect the early attentional processing of sounds (Kisley, Noecker, & Guinther, 2004). The N100 is followed by another positive peak around 200 ms, the "P200" component, thought to reflect selective attention, or the conscious attention switching to sounds (Picton & Hillyard, 1974).

Historically, sensory gating has been indexed using the P50 component. This component was originally chosen because it was thought to be outside the influence of attention (i.e., "preattentive"; Adler et al., 1982). Recently, the N100 and P200 components have been investigated in addition to the P50 component. All three of these

are considered middle-latency components (Boutros, Korzyukov, Jansen, Feingold, & Bell, 2004), because they occur later than the early sensory components such as the brainstem evoked responses, yet earlier than the later cognitive components such as the P300 component (Boutros & Belger, 1999). Some work has correlated sensory gating responses for different components and found no relationship – such as between the P50 and N100 components (e.g., Kisley et al., 2004; Moura, Triñanes-Pego, & Carrillo-de-la-Peña 2010). Thus, these three components are thought to represent different stages of sensory gating. Because these components represent different stages of auditory processing, unique information is obtained from each.

The functional differences among the P50, N100, and P200 components likely reflect the degree to which these components are susceptible to attentional modulation. Wan, Crawford, and Boutros (2007) proposed that the P50, N100, and P200 components reflect three stages of auditory sensory gating: preattentive, early attentive, and late attentive, respectively. More and more evidence is accumulating that all three of these components could play an important role in sensory gating as a multistage process (Boutros et al., 2004). That these three components are differentially modified by attention allows investigators to better track how sensory gating may relate to attention or to tasks that require attention.

Types of sensory gating

 Gating-in

 Orienting is characterized by an increase in the brain's response to novel sounds. Orienting can be measured in a variety of ways. One way is to use a paradigm that contains a series of identical tone sounds (often called "standard" sounds) where a novel

or "deviant" sound is inserted in the series of those standard sounds. The increase in

amplitude for the deviant sound compared to the standard sound(s) (across all middle-

latency components) is a type of orienting response. The greater the amplitude

discrepancy for these two types of stimuli, the stronger the orienting response. Orienting

can be measured as a difference score – subtracting the response to the standard sound

preceding the deviant from the amplitude of the response to the deviant sound (as was

done in the present report).

Gating-out

Filtering, as it is conceptualized in the present report, is a single-trial phenomenon

where the brain's response to the second of two identical sounds is reduced (across all

middle-latency components). Typical stimuli in a filtering task are briefly-presented

clicks, although filtering has also been obtained with tone stimuli (e.g., Ninomiya, Sato,

Onitsuka, Hayashida, & Tashiro, 2000). Filtering is usually quantified by an amplitude

ratio of the brain's response to two auditory stimuli presented as a pair. For example, the

brain's response to the second sound is divided by the brain's response to the first sound.

In most neurologically typical adults, the amplitude for the middle-latency components to

the second sound is lower or suppressed compared to the averaged amplitude to the first

sound. This suppression is thought to represent the filtering of the redundant information

(i.e., the identical stimulus). Of the types of sensory gating discussed in this dissertation,

filtering is by far the most well understood and the most studied.

Habituation is a multiple-trial phenomenon characterized by a gradual reduction

in response due to repeated presentations of a stimulus. Although habituation has been

studied in depth using behavioral and peripheral nervous system measures (e.g.,

Venables, 1977), there has not been much work that has examined habituation using scalp-recorded ERPs. Long-term habituation is the reduction in brain response to stimuli over an extended period of time, such as several minutes. This type of habituation can be assessed by comparing the brain responses at the beginning of an experimental session compared to the brain responses at the end of an experimental session (e.g., Naber, Kathmann, & Engel, 1992). Some work suggests that later-occurring ERPs have been found to habituate in a long-term paradigm more than the early evoked potentials, yet there is evidence that the middle-latency components, such as the P50 and N100, also habituate (Johnson & Yonovitz, 2007). Short-term habituation has also been investigated. Stimuli in a short-term habituation task are typically tones presented in a repeated series over a period of several seconds (e.g., Rosburg et al., 2004). Like long-term habituation, one way to quantify short-term habituation is by directly comparing the amplitude of the brain response to the first stimulus in a series to the amplitude of the brain response to the last stimulus in a series. The greater the discrepancy between these two values, the greater the habituation. Intermediate values may also be investigated to probe the gradual nature of habituation. Short-term habituation will be investigated in the present report in an effort to better understand the habituation mechanism.

Habituation is conceptually similar to filtering and it is not yet clear whether they are distinct neurological phenomena or whether one is a special case of the other. There are only a handful of studies that have examined the relationship among these three types of sensory gating and no single study had investigated all three. The terms filtering and habituation are sometimes used interchangeably in the literature. Specifically, many articles that report data from a filtering paradigm use the terms filtering and habituation

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as if they were synonymous. At this point it is not clear if "habituation" as it is currently measured in the literature (i.e., a series of sounds recorded in an ERP paradigm) is a unique phenomenon. One of the purposes of this dissertation is to investigate the relationship between filtering and habituation and determine whether they are distinct phenomena.

Perturbations in sensory gating: Clinical groups

Sensory gating has likely received such experimental interest because several clinical populations are reliably impaired on this measure. For example, it is well documented that individuals with schizophrenia fail to filter auditory information properly. When measured in a classic P50 filtering paradigm (paired click design), evoked amplitude is much greater to the second (redundant) click in individuals with schizophrenia compared to controls (Olincy et al., 2000). Because of the highly replicable results across studies and the findings that filtering deficits occur in unaffected family members (Clementz, Geyer, & Braff, 1998), P50 filtering has been investigated as a potential endophenotype for schizophrenia (Freedman et al., 1997; Gottesman & Gould, 2003).

Although schizophrenia is the clinical group that has received the most interest, numerous other populations have been found to have filtering deficits, such as individuals with migraine (Ambrosini, De Pasqua, Afra, Sandor, & Schoenen, 2001), panic disorder (Ghisolfi et al., 2006), Alzheimer's disease (Jessen et al., 2001), alcoholism (Marco, Fuentemilla, & Grau, 2005), post traumatic stress disorder (Neylan et al., 1999), Huntington's disease (Uc, Skinner, Rodnitzky, & Garcia-Rill, 2003), and bipolar disorder (Schluze et al., 2007). It is not yet fully understood how the mechanisms underlying

sensory gating contribute to the pathology of disorders, or whether similar mechanisms are involved in different clinical populations.

Components other than the P50 are also beginning to be investigated in clinical disorders. For example, individuals with schizophrenia are impaired on filtering for the N100 component (Boutros et al., 2009) and on detection of a deviant stimulus (similar to what I define as orienting in this paper) using the mismatch negativity component (Wynn, Sugar, Horan, Kern, & Green, in press). The N100 and P200 components have also been found to be abnormal for individuals with bipolar disorder (Lijffijt, Moeller, et al., 2009). Because more and more studies are demonstrating deficits for P50, N100, *and* P200 components in clinical groups, it is important to better understand these components in healthy adults. For example, do these components differentially relate to higher level cognitive processes? Does one's neurophysiological response for one component dictate the response for another component? Further motivation for studying N100 and P200 sensory gating is that these components produce far more reliable results (e.g., test-retest reliability) than the P50 component – something that is critical for clinical investigators and interventions (Fuerst, Gallinat, & Boutros, 2007).

Perturbations in sensory gating: Control groups

Among typical adults, there is variability for sensory gating responses, meaning that some adults have very good sensory gating and some adults have very poor sensory gating. In studies of healthy adult participants, this variability is advantageous if we hope to correlate sensory gating responses to a host of other measures, such as other neurophysiological processes or cognitive processes. Sufficient variability is important

in correlation measurement because a restriction of variability can reduce the ability to predict responses of one variable as a function of another (Bobko, 2001).

An interesting phenomenon that remains to be understood is that a percentage of (otherwise healthy) adults have abnormal filtering. Abnormal filtering has been suggested to be an amplitude ratio (second stimulus divided by first stimulus) that is greater than .50 (i.e., less than 50% of the amplitude is reduced) (Potter, Summerfelt, Gold, & Buchanan, 2006). Patterson et al. (2008) reported that 40% of control participants (from data that was collected in a subset of institutions in their meta-analysis) had P50 filtering scores within one standard deviation of the scores of schizophrenia patients (i.e., suppression between 79.9% and 55.6%) (but, see Waldo et al., 1994).

An interesting question that remains to be elucidated is to what behavioral outcomes poor sensory gating might be related. In other words, what are the functional consequences for a healthy young adult who exhibits reduced P50, N100, or P200 sensory gating? Although these individuals likely use compensatory strategies to cope with any "deficits," it is an intriguing question considering that some of these participants' filtering scores are similar to those of a schizophrenia patient. One purpose of this dissertation is to evaluate the functional significance of sensory gating, which includes how gating may relate to higher level processes.

Theoretical implications

It has been well established at the behavioral level that exposing organisms to sounds under certain conditions produces characteristic effects. For example, a novel, or unexpected sound presented in the environment should trigger an orienting response. This orienting response is an allocation of attention toward the novel stimulus. There are

muscular adaptations that facilitate orienting such as head turning and eye movement toward the stimulus (Leslie, 1996). On the other hand, a sound that is repeatedly presented should trigger a reduction in attention to a stimulus over time. For example, if a refrigerator is humming, one usually does not pay any attention to it after a short while, yet if one consciously directs his or her attention toward the sound, it can be heard again. These behavioral reactions to sensory stimuli are thought to be mostly hard-wired and occur without conscious effort (Leslie, 1996), yet the neurophysiological underpinnings have not been thoroughly investigated.

Sensory gating has been suggested to be a protective process that allows us to attend to important things and ignore unimportant things (Lijffijt, Lane, et al., 2009). Therefore, it is possible that the observed behaviors (attentional orienting to novelty and attentional reduction to repetition) are the functional manifestations of the neurophysiological responses that are observed in sensory gating paradigms. If this were the case, our conceptualization of habituation could be thought of as a gradual waning of attention over time due to repeated presentations of a stimulus; orienting could be thought of as directing attention towards novel stimuli; and filtering could be thought of as a more rapid attentional reduction. However, the brain-behavior relationship for how attention is allocated to sensory stimuli and what controls that allocation is not well understood.

An important starting point to understanding the functional purposes of the different types of sensory gating is to demonstrate that sensory gating has a functional purpose in the first place. We know that sensory gating is reliably impaired in some clinical groups and we understand a little about its mechanism and what attenuates or enhances it. However, we do not yet understand what the very purpose of sensory gating

is or what specific functions are related to sensory gating (Lijffijt, Lane, et al., 2009).

Very few empirical studies have demonstrated that gating relates to higher level functions

(Potter et al., 2006). An important question is what, if any, are the behavioral

consequences of poor sensory gating? For example, neurophysiological responses on

sensory gating tasks might be related to performance on behavioral measures, such as

cognitive measures of attention. By selectively processing sounds from the environment,

sensory gating may make our cognitive processing more efficient. However, if this were

true, then different types of sounds should produce different degrees of sensory gating.

For example, the brain might gate more salient stimuli differently compared to less

salient stimuli.

It is also important to distinguish different types of sensory gating at the

neurological level, if we hope to match these to particular behaviors. For instance, are

there distinct neurological mechanisms for different types of sensory gating, or do the

different types of gating belong to the same, underlying gating mechanism? If

neurophysiological responses were not correlated and were also related to different

outcome measures, it would suggest that filtering, habituation, and orienting are unique

mechanisms.

P50 filtering has been found to be mostly outside the influence of voluntary

attention (Jerger, Biggins, & Fein, 1992; Kho, et al., 2003, but see Guterman, Josiassen,

& Bashore, 1992 who demonstrate that filtering was worse when participants attend to

stimuli) whereas N100 filtering is strongly affected by direction of attention toward

stimuli (Jerger, et al., 1992). As previously stated, the P50 component and N100

component are thought to index different aspects of sensory gating. Because N100

filtering is a later-occurring phenomenon that is thought to represent a more complex

process than P50 filtering, Kisley et al. (2004) suggested that N100 filtering deficits

relate more to attentional problems whereas P50 filtering deficits relate more to

perceptual problems. Exploring different ERP components allows us to better understand

the relationship between attention, perception, and sensory gating.

Understanding how sensory gating relates to behavior has implications for clinical

groups. At this point, if a patient from a clinical group has an abnormal observable

reaction to a sensory stimulus, it is not understood if that is because one or more sensory

gating mechanisms are abnormal or if the behavior is a manifestation of some other

process. As we go to develop treatments for individuals who report being sensitive to

sensory stimuli, it will be important to better understand the neurophysiological

underpinnings of sensory gating and how sensory gating relates to behavior.

In addition to the relationship between sensory gating and behavior, it is also

poorly understood how sensory gating relates to basic auditory processes. Discrimination

can be described as how well the brain can distinguish different types of stimuli, such as

high intensity and low intensity stimuli. Better discrimination ability suggests that the

brain is better at assessing qualities of stimuli, which may relate to better sensory gating.

Therefore, the brain would be gathering more information about a sound and might more

effectively engage in other neural processes, such as gating. Organization can be

described as how systematic the brain's response is to different stimuli. In addition to

discrimination, a more organized auditory response pattern may relate to better gating.

Understanding the relationship between gating and more basic processes such as

discrimination and organization would be useful clinically because we could categorize

individuals with certain basic auditory processing deficits as being high risk for sensory gating difficulties. One advantage to measuring more basic electrophysiological processes versus more complex processes is that more basic processes are generally easier to measure and more reliable (Rentzsch, Jockers-Scherübl, Boutros, & Gallinat, 2008).

Methodological implications

This dissertation advances our understanding of methodological effects on sensory gating in several ways. First, there has not yet been a published study that includes filtering, habituation, and orienting together in one study. We studied all three paradigms and used the same two tones across all three paradigms, which allowed for the direct comparison of the brain's response among these paradigms. We are also reporting data from three components: P50, N100, and P200. Many sensory gating studies only report data from the P50 component. The N100 and P200 are middle-latency components that are thought to provide unique information from P50 and reflect different stages of attentional processing (Boutros et al., 2004). Whereas the P50 component has been demonstrated to play an important role in the pathology of certain clinical conditions, we might be losing valuable data by excluding N100 and P200. Finally, we used brief tones for stimuli in all three gating paradigms; most sensory gating studies (particularly filtering) have used clicks for stimuli. The orienting measure we used requires that tones are used (because the "deviant" stimulus is a higher frequency than the other tones, thus making it different sounding). Because we used tones for the paradigm that contained our habituation and orienting measures, we also used tones for the filtering paradigm. Although filtering has been reported using tones (e.g., Ninomiya et al, 2000),

there have been relatively few studies that used stimuli other than clicks. It is important to establish that we can achieve gating under a variety of methodological circumstances, in order for results to be robust and generalizable. In other words, we should ensure that gating is not an effect that only works when click stimuli are employed, but rather works when other auditory stimuli are used as well.

The present study

Although sensory gating (particularly filtering) has been studied using ERPs for over 30 years now, many questions remain unanswered. This dissertation aimed to examine broad, big-picture questions about sensory gating and draw connections between paradigms in an effort to better understand sensory gating as a unified construct.

In chapter three, I tested the relationship between auditory discrimination and sensory gating and the relationship between organization and sensory gating. In chapter four, I compared filtering, habituation, and orienting, both as a mechanistic process and for participants' responses across these three measures.   Finally, in chapter five, I examined the functional significance of sensory gating by comparing filtering for salient and less salient stimuli and by comparing gating to neuropsychological measures of attention.

Chapter 2: Methodology

Participants

Forty two adults (19 male, 23 female) aged 18-24 (M = 19.12, SD = 1.49) participated in this study. These volunteers were undergraduate university students who received course credit for participating. This experiment required participants to complete two experimental sessions on separate days; three participants did not complete the second session[1]. Therefore, thirty nine participants (17 male, 22 female) contributed data for all paradigms.

Participants were given a list of exclusion criteria in the study advertisement online, and were discouraged from signing up for the study if they met any of criteria. Participants completed informed consent and a demographic screening questionnaire upon arriving to the Brainwaves Research Laboratory. Exclusion criteria were any history of a traumatic brain injury with loss of consciousness (Kisley, et al., 2004), any history of a serious neurological disease/disorder, psychotic disorders, bipolar disorder (Lijffijt, Moeller, et al., 2009), smoking within one hour of the study (Adler, Hoffer, Griffith, Waldo, & Freedman, 1992), or taking medications that have been known to affect sensory gating, such as antipsychotic medications (Nagamoto et al., 1996)[2]. No participants were excluded based on these criteria, although we do not know how many participants self-excluded based on the advertisement. All procedures adhered to federal regulations and were approved by the Colorado State University Institutional Review Board.

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[1] One participant was not feeling well and could not continue and the other two participants did not show up.

[2] Five participants were currently taking birth control, one participant was currently taking acne medication, one participant was currently taking allergy medicine, and one participant was currently taking Effexor.

Procedure

    Study design and experiment outline

    Each participant completed two research sessions. The two sessions were completed on two separate days, within two weeks of each other (although a few were conducted more than two weeks apart due to scheduling issues[3]). On both visits, participants completed an EEG portion first, followed by a behavioral testing portion. For the first session, participants completed auditory threshold testing, three EEG paradigms (sensory registration, high-frequency filtering, and low-frequency filtering), and a set of standard neuropsychological diagnostics (vocabulary and matrix reasoning from the Wechsler Abbreviated Scale of Intelligence (WASI), crossing off A's simple motor speed task, and selective A's selective attention task). For the EEG portion, the sensory registration paradigm was always conducted first, but the filtering paradigms were counterbalanced; for the behavioral portion, the WASI was always conducted first, but the "A" tasks were counterbalanced. For the second session, participants completed one EEG paradigm (habituation and orienting paradigm), and neuropsychological tasks (digit span forward and backward tasks, Trail Making Tests A and B, and a Stroop task). The behavioral tasks for the second session were counterbalanced.

    For the electroencephalogram (EEG) testing, participants were seated upright in a high-backed chair for the duration of the experiment. Before the EEG recording, participants were given instructions for how to produce artifact-free EEG data in the experiment, which included a brief artifact reduction tutorial where participants were shown their online EEG so that they could see the effects of eye blinks and muscle

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[3] Two participants' visits were three weeks apart, one participant's visits were two months apart, and one participant's visits were almost three months apart.

tension on the recording. The entire EEG portion of the study took about 3 hours (1.5

hours each session). For the behavioral testing, participants sat at a table across from the

experimenter and completed the tasks either verbally or using paper and a pencil. The

entire behavioral portion took about 2 hours (1 hour each session).

Auditory threshold testing

Auditory threshold testing was used to screen for potential hearing deficits. To

test their hearing thresholds, participants were fitted with ear-insert earphones (ER-3A,

Etymotic Research)[4] and instructed to press a button on a mouse every time they heard a

click. After the first click was presented (3 ms), a stepping procedure was employed to

determine auditory threshold whereby the intensity was decreased a step if the mouse

button was pressed and increased two steps if no response was made (Levitt, 1971). The

step size was 5 dB for the first four successive responses and then became 2.5 dB. The

threshold procedure ended after there were 13 successive responses. The value obtained

by averaging the lowest intensities during the last nine responses was used as the

threshold for that participant. The program was constrained so that it would never

present a hearing level greater than or equivalent to 110 dB SPL (auditory startle

threshold). No participants had abnormal hearing for the threshold measurement and no

participant reported having hearing deficits on the demographic questionnaire.

Sensory registration paradigm

Using a paradigm that was adapted from Lincoln, Courchesne, Harms, & Allen

(1995), participants were presented with four tone types (E-Prime software;

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[4] All the auditory tasks employed these earphones.

Psychological Software Tools, Pittsburgh, PA)[5]: low-frequency, low-intensity tones (1000 Hz, 50 dB SPL), low-frequency, high-intensity tones (1000 Hz, 70 dB SPL), high-frequency, low intensity tones (3000 Hz, 53 dB SPL)[6], and high-frequency, high-intensity tones (3000 Hz, 73 dB SPL). All the tones were 50 ms in duration with 10 ms of rise and fall ramping. The interstimulus interval (ISI) was two seconds; tones were randomly presented 100 times each. Tones were presented in four blocks of 100 stimulus presentations with a several second break in between blocks for participants to rest. Participants watched a muted claymation cartoon during this task[7].

Filtering paradigm: low-frequency tones

Participants were presented with 100 pairs of tones (1000 Hz, 70 dB SPL, 50 ms in duration with 10 ms of rise and fall ramping). The ISI was 500 ms and the intertrial interval (ITI) was eight seconds. Before the experiment began, participants were presented with a sample pair of tones to ensure that no startle response was present. None of the participants exhibited a startle response.

Filtering paradigm: high-frequency tones

This paradigm was identical to the low-frequency tone filtering paradigm, except the tones were 3000 Hz and 73 dB SPL.

Habituation and orienting paradigm

Participants were presented with eight tones in a series. There were three different series types: The "no deviant" series contained eight identical "standard" tones

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[5] All EEG stimuli were presented using this software.

[6] The high-frequency tones were increased by 3 dB to make the energy from stimuli physically equivalent (American National Standards Institute, 2004).

[7] Participants watched muted Wallace and Gromit claymation cartoons during all of the EEG tasks.

(1000 Hz, 70 dB SPL, and 50 ms in duration with 10 ms of rise and fall ramping). The "4th position deviant" series contained eight tones – seven standard tones described above with the fourth tone replaced with the "deviant" tone (3000 Hz, 73 dB SPL, and 50 ms in duration with 10 ms of rise and fall ramping). The "5th position deviant" series contained eight tones – seven standard tones described above with the fifth tone replaced with the deviant tone. The ISI between each tone sound in a series was 500 ms and the ITI between the different tone series was 8-10 s with an average of 9 s. There were 80 random presentations of each tone series, and each participant received the same random order. Stimuli were presented in four separate blocks with a several second break in between so participants could rest.

Electrophysiology

Electrophysiological system and recording parameters

Electrophysiological data were recorded with a BioSemi ActiveTwo system (BioSemi B.V., Amsterdam, Netherlands). After a conductive gel was applied, thirty-two Ag/AgCl electrodes were inserted into the plastic electrode holders in an elastic cap. Eight additional electrodes were applied to monitor eye artifacts and for offline referencing. Specifically, a pair of electrodes was placed: above and below the left eye, just lateral to the outer canthus of each eye, on the earlobes, and mastoid bones. For the ActiveTwo system, a traditional ground and reference electrode arrangement is replaced with the active Common Mode Sense (CMS) and passive Driven Right Leg (DRL) electrodes, with the CMS serving as the online reference and the DRL as ground. Data were online low pass filtered at 268 Hz with a sampling rate of 1024 Hz.

Waveform analysis and component identification

Data were analyzed offline with BrainVision Analyzer software (Brain Products, Munich, Germany). ERPs were extracted for all tone types in each of the tasks in order to measure the P50, N100, and P200 components. For the P50 component, data were referenced to the left ear lobe, bandpass filtered from 10-75 Hz (rolloff 24 dB/octave), segmented from 100 ms before click onset to 500 ms after onset, baseline corrected to a 100 ms prestimulus baseline, artifact rejected (+/- 100 µV), and averaged. The N100 and P200 components were processed exactly as the P50 component except data were bandpass filtered from .23-30 Hz to best reveal the component's primary oscillatory features. The N100 and P200 data were also submitted to a program that removed the effects of eye blinks (Segalowitz & Desjardins, 2004)[8]. The P50, N100, and P200 components were identified separately by analyzing the ERPs at electrode Cz[9] (Nagamoto, Adler, Waldo, Griffith, & Freedman et al., 1991). All peaks were selected using a semi-automatic peak-picking program that was custom built in the Brainwaves Research Laboratory using MATLAB software (Mathworks).

The P50 component was identified as the highest positive peak between 35-90 ms (Pratt, Starr, Michalewski, Bleich, & Mittleman, 2008) after click onset. Amplitude was measured from the P50 peak to the zero baseline because this method has been found to be more reliable than the peak-to-peak measurement (Rentzsch, Gomez-Carrillo de Castro, Neuhaus, Jockers-Scherübl, & Gallinat, 2008). The N100 component was

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[8] Eye blinks were not an issue for the P50 component because the filter's lower bound (10 Hz) was high enough to remove the effects of the lower-frequency eye blinks. However, for the N100 and P200 components, the lower bound of the filter (.23 Hz) did allow eye blinks in the data.

[9] All ERP data throughout this report were reported from electrode Cz unless otherwise stated.

defined as the lowest negativity between 75-150 ms (Boutros et al., 2006). Amplitude was measured from the N100 peak to the zero baseline (Kisley et al., 2004)[10]. The P200 component was defined as the highest positive peak between 130-270 ms[11] (Davies, Gavin & Chang, 2010). Amplitude was measured from the P200 peak to the zero baseline.

For each participant, data were considered missing if a component was not present. If a participant had a missing component for a given paradigm, his or her data were excluded for that component in that paradigm – data for other components and other paradigms were still included in the overall analyses. More specific details regarding component identification and sensory gating quantification are outlined as they are relevant in the chapters that follow.

Behavioral testing

Wechsler Abbreviated Scale of Intelligence (WASI) [12]

The WASI has four subtests and is an abbreviated version of a Wechsler intelligence test. For this study, we administered two of the four tests: one verbal IQ test (vocabulary) and one performance IQ test (matrix reasoning).

For the vocabulary task, participants were asked to define words. The experimenter said the word aloud then pointed to the word in the test booklet. The participant gave his or her responses verbally. Per the criteria in the WASI manual, a participant's responses were scored based on the quality of his or her answer.

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[10] For all reported data, the absolute value of the N100 component was used (Lijffijt, Lane, et al., 2009).

[11] In a few instances, the N100 and P200 components were +/- 5 ms outside of their ranges.

[12] We verified that all participants had normal IQ scores measured by the WASI Vocabulary and Matrix Reasoning tasks (mean IQ = 109.69, SD = 11.52), to ensure that they could competently complete the remaining cognitive and neuropsychological tasks.

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Specifically, if a participant did not define the word correctly they were given a score of 0, if he or she got part of the definition correct they were given a score of 1 and if he or she got the entire definition correct he or she was given a score of 2. The participant was "queried" if his or her answer was ambiguous and given a second chance to get the full 2 points possible. The test was discontinued if a participant received five consecutive scores of 0. The maximum number of items that could be completed was 42 and the maximum raw score a participant could get was 80.

For the matrix reasoning task, participants were asked to solve puzzles. Each puzzle contained a grid of four squares – three contained images and the fourth square was empty. A participant had to choose what image belonged in the empty square, among five image choices at the bottom of the page. There was always a pattern among the three images in the grid; therefore, the task is thought to measure how good a participant is at discovering that pattern and using it to solve each puzzle. A participant received 1 point for the correct response and 0 points for the incorrect response. The task was discontinued if a participant received four consecutive scores of 0, or four scores of 0 on five consecutive items. The maximum number of items (i.e., puzzles) that could be administered was 35 and the maximum raw score a participant could get was 35.

Crossing off A's: simple motor speed

This task was created to measure simple motor speed. A participant was given an 8.5" x 11" piece of paper that contained 418 repetitions of the capital letter "A". The A's were organized in rows. A participant was given a pencil and told to cross off (put a single slash through) as many A's as they could (working one row at a time from left to right) before the experimenter said "stop". The experimenter timed the participant for

one minute.   Performance on this task was measured as the number of A's that the participant crossed off in one minute.

Selecting A's: selective attention

This task was created to measure selective attention. A participant was given an 8.5" x 11" piece of paper that contained 60 capital letter A's that were scattered among distracter letters. A participant was given a pencil and told to cross off (put a single slash through) as many A's as he or she could before the experimenter said "stop".   The experimenter timed the participant for one minute using a stopwatch.   Performance on this task was measured as the number of A's that the participant crossed off in one minute.

Digit span forward

This task was based on the digit span forward task from the WAIS. The digit span forward task is thought to measure focused attention and short-term memory (Cohen, Salloway, & Sweet, 2008). In this task, the experimenter read series of digits out loud at a rate of one digit per second. After each series, a participant had to verbally recall the entire series. There were two unique versions of each series length; series ranged from two to twelve and were presented in ascending order. If a participant got at least one of the two series correct, that set size was passed and they were given the next set size. The task was discontinued after the participant failed both items in a given series set size.

Digit span backwards

This task was also based on the WASI. The digit span backwards task is thought to measure working memory in addition to attention and short-term memory (Kessels,

van den Berg, Ruis, & Brands, 2008). The procedure for this task was identical to the digit span forward task, except a participant was instructed to verbally recall the digit series backwards. This task was always administered after the Digit Span Forward task.

Trail Making Task - Part A

This task is part of the Halstead-Reitan Neurological test battery.   Along with the Trail Making Task – Part B, it is thought to measure visual attention and cognitive flexibility, although Part B is more cognitively taxing and more difficult (Corrigan & Hinkeldey, 1987). This task has been found to be a good discriminator of overall cognitive ability, particular for individuals who have sustained a traumatic brain injury (Corrigan & Hinkeldey, 1987). A participant was presented with an 8.5” x 11” piece of paper that contains small circles housing the numbers 1-25, which were randomly distributed across the page. The experimenter told a participant to draw a line from number one to two, two to three, and so on until he or she reached a circle marked “end”. The participant was instructed to work as quickly as he or she could. Errors were pointed out and a participant had to correct their mistake before they could move on.   The score was recorded as the total time it took to complete the task.

Trail Making Task - Part B

This task was identical to the Trail Making Task – Part A, except some circles contained numbers (from 1-13) and some circles contained letters (from A-M). The numbers and letters were distributed randomly. A participant was told to draw a line from 1 to A, A to 2, 2 to B and so on (always alternating numbers and letters) until he or she reached the circle marked end. This task was always administered after the Trail Making Task – Part A.

Stroop task

This task was the Golden Stroop Color and Word Task (Golden, 1978). A participant was first presented with an 8.5" x 11" sheet of paper that contained color words (i.e., RED, BLUE, GREEN) printed in black and white ink arranged in five columns. A participant was asked to read the words out loud. For the second part, a participant was given X's (i.e., XXXX) printed in red, green, or blue ink. The participant was asked to name the color of the ink the words were printed in. For the third part, the participant was given words (i.e., RED, BLUE, GREEN) printed in red, green and blue ink. The words were all printed in ink color that was incongruent with the printed work (e.g., the word RED printed in green ink). Like in part two, the participant was asked to name the color of the ink the words were printed in. For all three parts, the participant was told to complete the task as fast as he or she could. If a mistake was made the experimenter asked the participant to correct himself or herself and keep reading. All three parts were scored as how many items the participant could complete in 45 seconds.

Chapter 3: The study of the relationship between auditory detection and auditory sensory gating

Rationale

In order for perception of auditory information to occur, the brain must take in information from discrete auditory stimuli in the environment and process the stimuli in a sequence of steps in the central nervous system. The ERP technique is ideal to measure the brain's detection of auditory stimuli. A paradigm that contains simple, discrete tones provides a means to measure the brain's ability to process sounds. In what we refer to as an auditory registration paradigm, simple tone sounds are presented to participants; these tones vary on the dimension of frequency as well as intensity (Davies & Gavin, 2007; Davies et al., 2010). Previous ERP work suggests that the brain should respond to particular types of sounds in a characteristic manner. For example, ERP amplitude in the registration paradigm is typically greater for higher-intensity sounds compared to lower-intensity sounds (Davies et al., 2010; Lincoln et al., 1995). Although expected "signatures" or patterns of data are present for most ERP measures, there are usually individual differences among participants. Therefore, the strength of auditory "registration" (how the brain responds to simple auditory stimuli) for one individual is different from the registration of a different individual. An assumption of the present report is that these types of individual differences are meaningful and tell us something useful about the way a participant processes auditory information. Individual differences can be understood by relating participants brain responses across different ERP measures.

To quantify auditory sensory registration, both the brain's ability to discriminate between stimuli (e.g., the magnitude of the brain's response to high-intensity versus low-

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intensity tones) and how organized the brain's response is to the tones can be examined. Organization in timing can be observed by identifying how consistent the brain's responses are in time for different tone types. In other words, if the brain's response to all four tones in the registration paradigm occurred at exactly the same time, then the organization would be perfect. The distance between the tones' latencies (the times in ms associated with the highest or lowest amplitudes for each component) is one measure of the degree of organization, with greater latency discrepancies representing greater disorganization.

There is some evidence that a more robust and more organized pattern of auditory registration is better than a less robust and less organized pattern. For example, children's auditory registration has been found to be weaker, with a more disorganized response pattern compared to adults (Davies et al., 2010). This suggests that the mature brain has a more discriminating, more organized auditory detection system. Moreover, children with sensory processing disorders have a weaker, less organized auditory registration response compared to typically developing children (Davies et al., 2010).

In order to selectively process a sound stimulus (e.g., gate), the brain must evaluate that stimulus in the context of previously presented auditory information; this is why sensory gating paradigms contain a minimum of two sounds. In other words, the brain must process the initial sound and then make a comparison between the new sound and the initial sound. If the new sound is identical or very similar to the initial sound then we would expect filtering or habituation. On the other hand, if the new sound is sufficiently different from the initial sound then we would expect orienting. It is likely, then, that the more information the brain can gather about an initial sound and the better

the brain can discriminate between two different types of sounds, the more appropriate

the gating response will be. Because we do not yet understand how sensory gating relates

to more basic auditory processing, we related auditory registration responses to filtering,

orienting, and habituation. Specifically, we examined how discrimination in the

registration paradigm (measured by amplitude differences for high-intensity versus low-

intensity tones) and organization (measured by the difference in latency between the high

and low frequency sounds) related to filtering (the reduction in amplitude for a repeated

sound), orienting (the increase in amplitude for a novel sound), and habituation (the

reduction in amplitude for several repeated sounds). Discrimination in the registration

paradigm for the high-frequency tones was compared to filtering for high-frequency

tones and discrimination for low-frequency tones in the registration paradigm was

compared to filtering for low-frequency tones. It is predicted that more discriminating

and more organized auditory registration will predict more robust sensory gating, because

sensory gating is dependent up on the initial processing of sounds.

Data analysis

Specific ERPs of interest

For the auditory registration paradigm, the brain's *discrimination* of sounds was

measured as the N100 and P200 amplitude for the low intensity low-frequency (1000 Hz)

tones subtracted from the high intensity low-frequency tones and the low intensity high-

frequency (3000 Hz) tones subtracted from the high intensity high-frequency tones.

Organization was measured as the peak latency for the N100 and P200 components (time

in ms associated with the lowest N100 amplitude and highest P200 amplitude) for the

high intensity low-frequency (1000 Hz) tones compared to the peak latency for the high intensity high-frequency (3000 Hz) tones.

For the filtering paradigm (both low and high-frequency paradigms), filtering was measured in the way that is most frequently used in the literature – by computing an amplitude ratio[13] (de Wilde, Bour, Dingemans, Koelman, & Linszen, 2007). Specifically, the amplitude of the brain's response to the second tone was divided by the amplitude of the brain's response to the first tone, producing a ratio measurement. The ratio of amplitudes produces a number from approximately 0-1, with smaller numbers representing better filtering[14].

For the orienting measure, orienting was derived by subtracting the amplitude for the tone preceding the deviant tone from the amplitude of the deviant tone, which created a difference score[15]. For this and subsequent analyses, the series that contained a deviant tone in the fourth position was used to measure orienting versus the series that contained a deviant tone in the fifth position. This is because the series with the deviant tone in the fourth position is a more pure measure of orienting because it avoids some of the anticipation effects that may be present in the series with the deviant tone in the fifth position[16].

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[13] In subsequent chapters, filtering was quantified this way as well.

[14] In a couple of instances, the P50 and P200 peaks for the second tones were just below the baseline, resulting in a negative amplitude value. To prevent the amplitude ratio from being negative, these cases were scored as zero (Kisley et al., 2004). For the lower-frequency tones, this occurred one time for the P50 component, and six times for the P200 component. For the higher-frequency tones, this occurred one time for the P50 component.

[15] In subsequent chapters, orienting was quantified this way as well.

[16] Participants can expect that the tone in the fourth position has a 1/3 chance of being deviant, whereas participants can expect that a tone in the fifth position has a 1/2 chance of being deviant.

Effects of the experimental manipulations

For these analyses, we describe if we achieved statistically significant gating for our filtering, habituation, and orienting paradigms, and if we achieved the expected pattern of results for the registration paradigm, based on previous literature.

For the registration paradigm, four dependent samples *t* tests were performed that compared: N100 amplitude for the high-frequency low-intensity tone compared to the high-frequency high-intensity tone, N100 amplitude for the low-frequency low-intensity tone compared to the low-frequency high-intensity tone, P200 amplitude for the high-frequency low-intensity tone compared to the high-frequency high-intensity tone, and P200 amplitude for the low-frequency low-intensity tone compared to the low-frequency high-intensity tone. For all four tests, significantly higher amplitude for high intensity tones compared to low intensity tones are expected based on previous literature (Lincoln et al., 1995).

For the filtering paradigm, a dependent samples *t* test was performed that compared the amplitude for the first tone compared to the amplitude for the second tone (for both the low and high-frequency paradigms). A significant difference in amplitude is indicative of a filtering effect.

For the orienting response, a dependent samples *t* test was performed that compared the amplitude for the deviant tone compared to the amplitude for the tone preceding the deviant tone. A significant difference in amplitude is indicative of an orienting effect.

For the habituation effect, the amplitude of the eighth click was compared to the amplitude of the first click using a dependent samples *t* test. Significantly smaller

amplitude for the eighth click is indicative of the typical habituation effect. The amplitudes of every other tone were also compared to the eighth tone.

Additional research questions

The overarching research question presented above was whether auditory registration related to sensory gating. A number of comparisons were made for these two paradigms (all using the N100 and P200 components): Using the Pearson product-moment correlation (*r*), discrimination in the registration paradigm for low-frequency tones was correlated with filtering for low-frequency tones and discrimination for high-frequency tones was correlated with filtering for high-frequency tones; organization in the registration paradigm (for high intensity tones) was correlated with filtering; discrimination and organization (for high intensity tones) in the registration paradigm were correlated with orienting and habituation.

Results and Discussion

Alpha was set at .05 for all inferential tests in this report.

Effects of the experimental manipulations

Sensory registration – higher amplitude for high-intensity versus low-intensity tones

For the registration paradigm, N100 amplitude for high-frequency high-intensity tones ($M = 8.35$, $SD = 3.25$) was significantly higher than for high-frequency low-intensity tones ($M = 5.25$, $SD = 1.85$), $t (41) = 8.15$, $p < .001$; P200 amplitude for high-frequency high-intensity tones ($M = 5.97$, $SD = 3.77$) was significantly higher than for high-frequency low-intensity tones ($M = 2.20$, $SD = 1.96$), $t (41) = 7.02$, $p < .001$; N100 amplitude for low-frequency high-intensity tones ($M = 8.99$, $SD = 3.33$) was significantly

higher than for low-frequency low-intensity tones ($M = 5.71$, $SD = 2.37$), t (41) = 7.72, p

< .001; and P200 amplitude for low-frequency high-intensity tones ($M = 5.43$, $SD = 3.37$)

was significantly higher than for low-frequency low-intensity tones ($M = 2.72$, $SD =$

2.04), t (41) = 5.12, $p < .001$ (see figure 1). These findings are as predicted and

consistent with previous research.
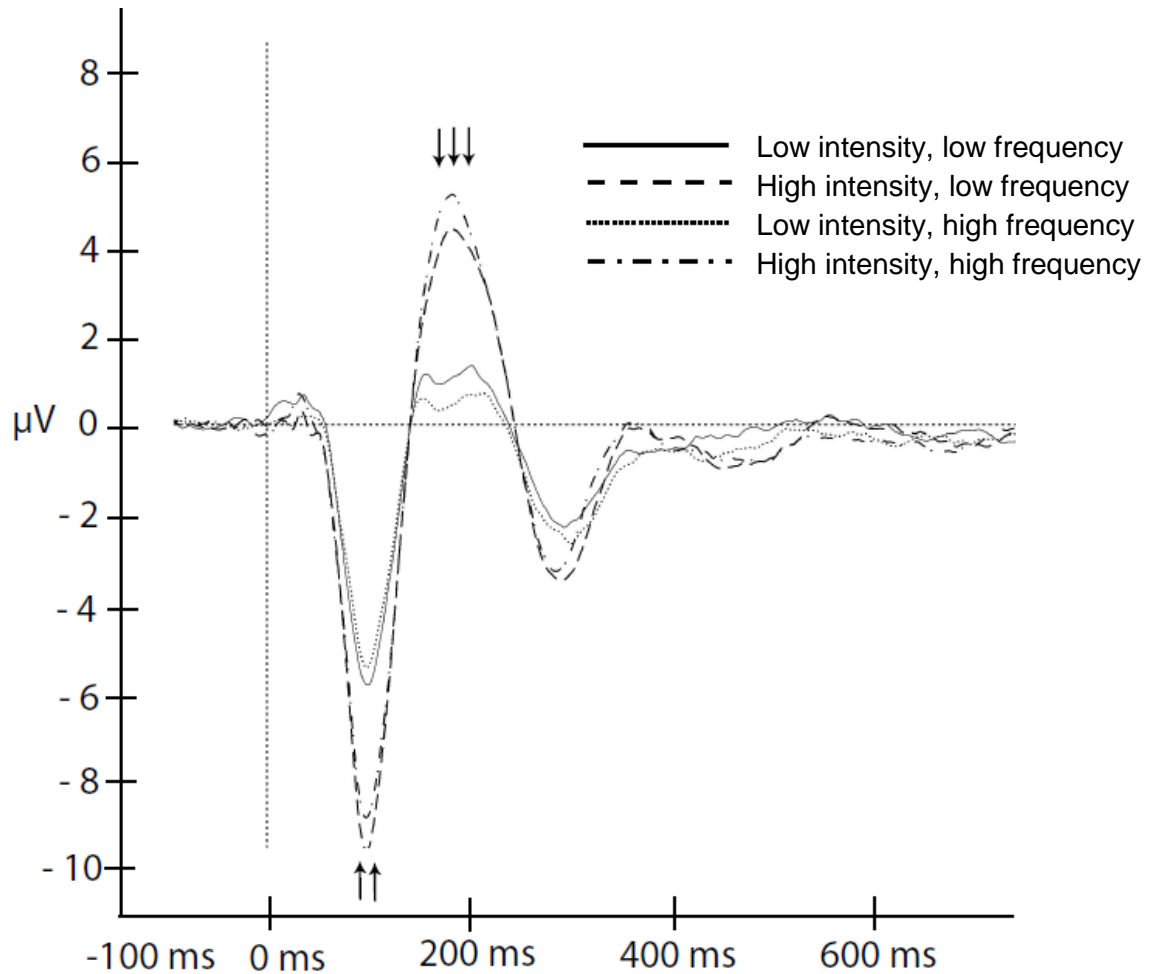
Figure 1: Grand average ERP waveforms for the sensory registration paradigm (filtered
.23-30 Hz), presented as amplitude (in µV) of the four tones as a function of time (in ms).
Higher-intensity tones had significantly higher amplitude compared to lower-intensity
tones, which represents the typical auditory registration effect. Vertical dotted line
indicates stimulus onset. Double arrows point to the N100 component and triple arrows
point to the P200 component. All data reported from electrode Cz, n=42.

Filtering – amplitude reduction for second tone

For the lower frequency tones[17], the amplitude for the second tone was significantly lower than the amplitude of the first tone for the P50 component (see figure 2), $t (40) = 7.16$, $p < .001$, the N100 component, $t (40) = 7.18$, $p < .001$, and the P200 component (see figures 3,4), $t (40) = 10.35$, $p < .001$. For amplitude means and standard deviations, see table 1.

Table 1

Means and (SD) for P50, N100 and P200 amplitudes and amplitude ratios for the filtering paradigm

	High-frequency tones			Low-frequency tones		
Components	Tone 1 amp.	Tone 2 amp.	Amp. ratio	Tone 1 amp.	Tone 2 amp.	Amp. ratio
P50	2.55	1.38	.56	2.72	1.61	.64
	(.97)	(.76)	(.30)	(1.10)	(.86)	(34)
N100	9.02	5.40	.64	9.01	6.04	.71
	(3.86)	(2.57)	(.31)	(3.45)	(2.80)	(.31)
P200	7.97	2.42	.29	7.96	2.57	.33
	(4.21)	(2.18)	(.25)	(3.60)	(2.28)	(.29)

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[17] Except when responses for high versus low-frequency filtering was directly compared, low-frequency tones were used in our quantification of filtering because the lower-frequency tones are more representative of what has been reported in the literature (e.g., Lijffijt, Lane, et al., 2009).

Figure 2: Grand average ERP waveforms for the P50 component of the filtering paradigm (filtered 10-75 Hz), presented as amplitude (in μV) of the two lower frequency tones as a function of time (in ms). The second tone had significantly reduced amplitude compared to the first tone, which represents the typical filtering effect. Vertical dotted line indicates stimulus onset. Single arrow points to the P50 component. All data reported from electrode Cz, n=41.
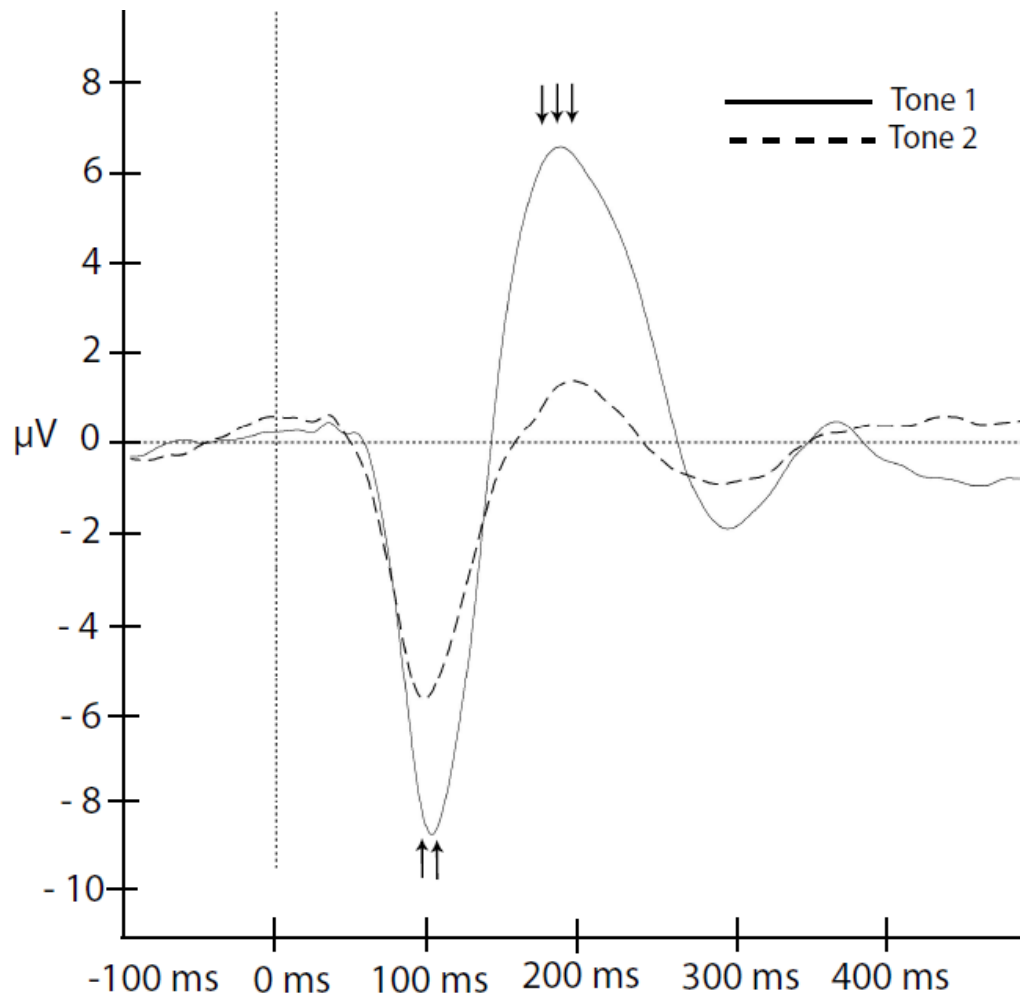
Figure 3: Grand average ERP waveforms for the N100 and P200 components of the filtering paradigm (this is the same as figure 2 except is filtered .23-30 Hz), presented as amplitude (in µV) of the two lower frequency tones as a function of time (in ms). The second tone had significantly reduced amplitude compared to the first tone, which represents the typical filtering effect. Vertical dotted line indicates stimulus onset. Double arrows point to the N100 component and triple arrows point to the P200 component. All data reported from electrode Cz, n=41.
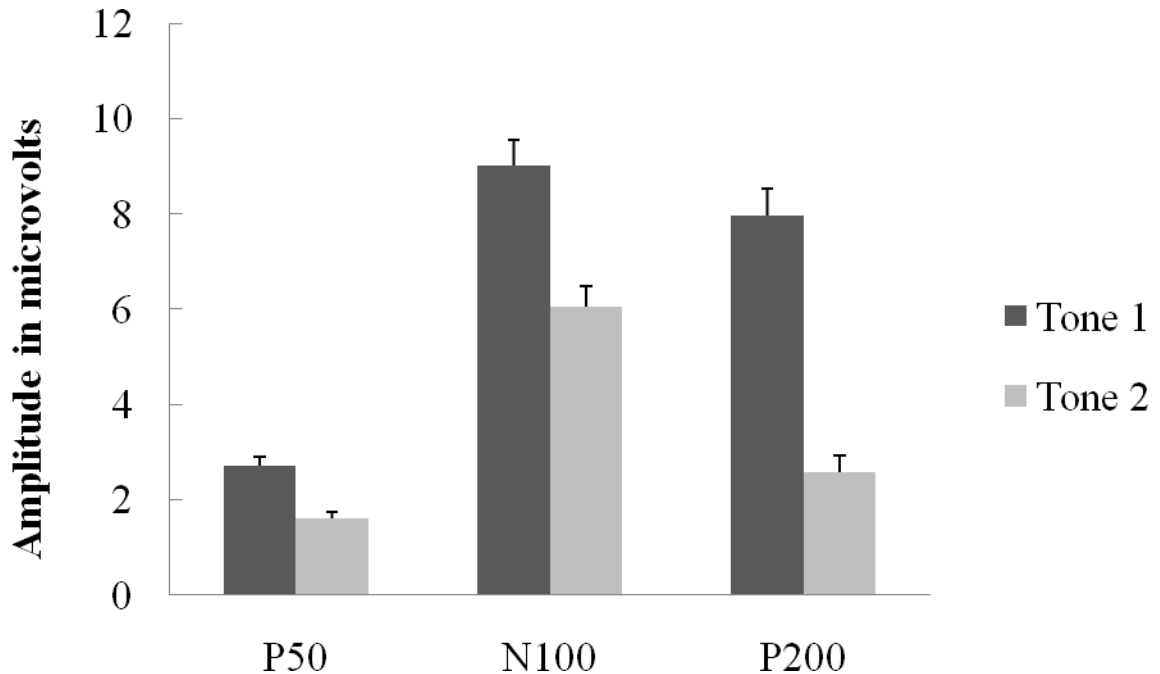
Figure 4: Amplitude for low frequency first and second tones for P50, N100 and P200 components. As was expected, there was a significant reduction in amplitude for the second tone compared to the first tone across all three components. Error bars represent standard error.
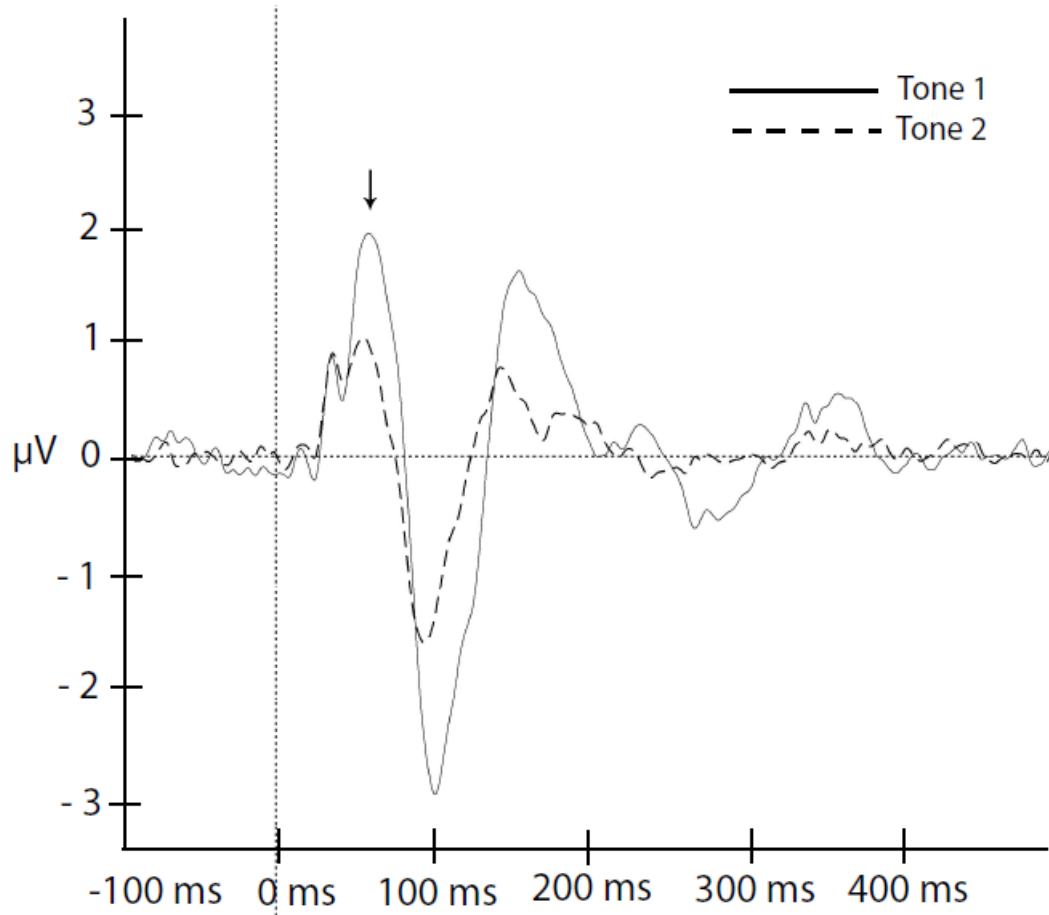
For the higher frequency tones, the amplitude for the second tone was significantly lower than the amplitude of the first tone for the P50 component (see figure 5), $t(41) = 8.38$, $p < .001$, the N100 component, $t(41) = 7.50$, $p < .001$, and the P200 component (see figures 6,7), $t(41) = 10.54$, $p < .001$ (see table 1). These results suggest that for both high and low-frequency tones across all three components, we achieved significant gating (amplitude reduction for the second click). Therefore, this demonstrates that 1000 and 3000 Hz tones are appropriate for use in filtering studies.

Figure 5: Grand average ERP waveforms for the P50 component of the filtering paradigm (filtered 10-75 Hz), presented as amplitude (in µV) of the two higher frequency tones as a function of time (in ms). The second tone had significantly reduced amplitude compared to the first tone, which represents the typical filtering effect. Vertical dotted line indicates stimulus onset. Single arrow points to the P50 component. All data reported from electrode Cz, n=42.
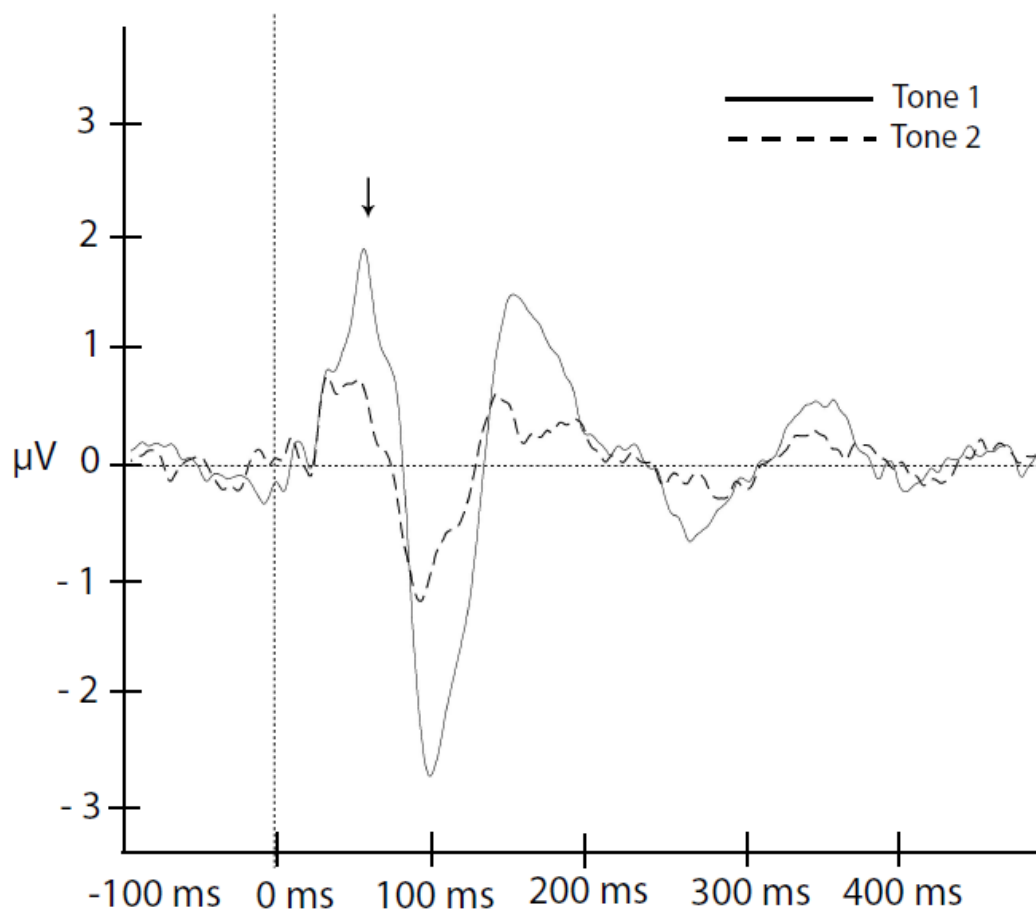
Figure 6: Grand average ERP waveforms for the N100 and P200 components of the filtering paradigm (filtered .23-30 Hz), presented as amplitude (in µV) of the two higher frequency tones as a function of time (in ms). The second tone had significantly reduced amplitude compared to the first tone, which represents the typical filtering effect. Dotted line indicates stimulus onset. Double arrows point to the N100 component and triple arrows point to the P200 component. All data reported from electrode Cz, n=42.
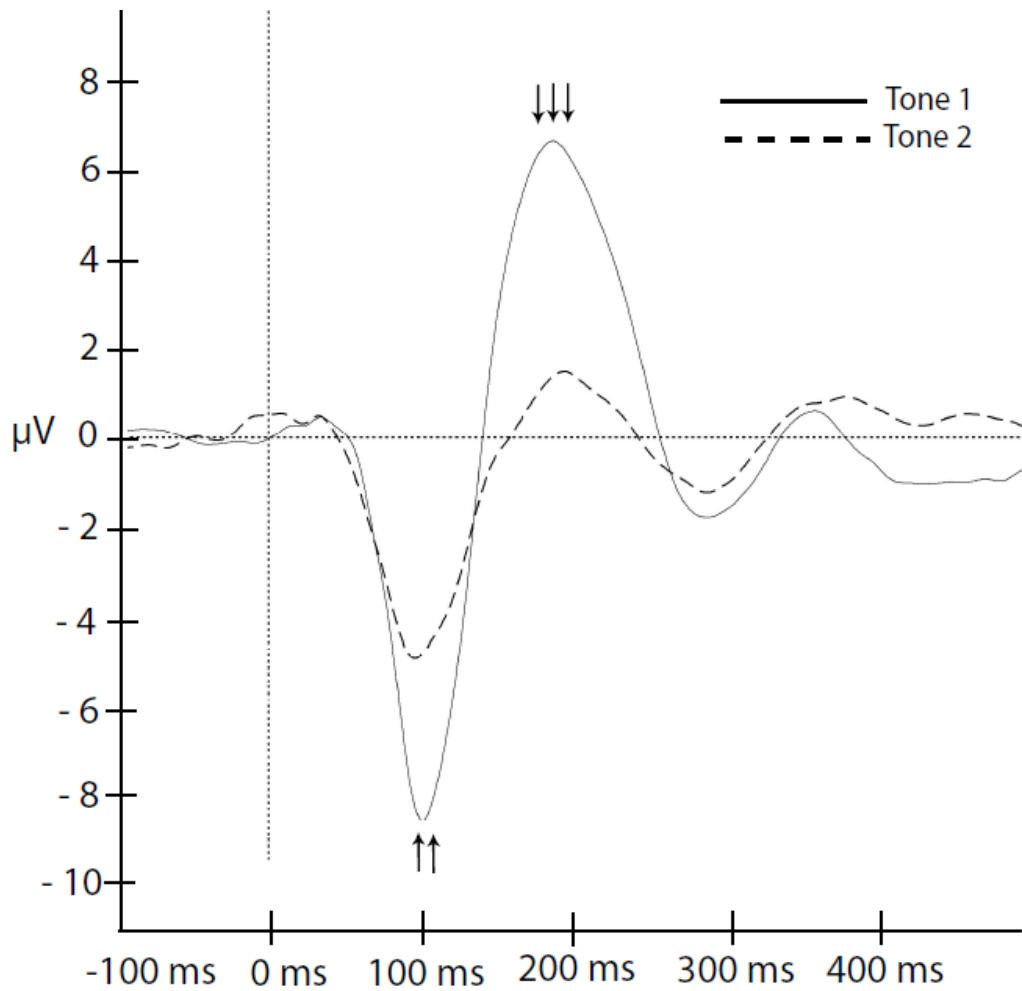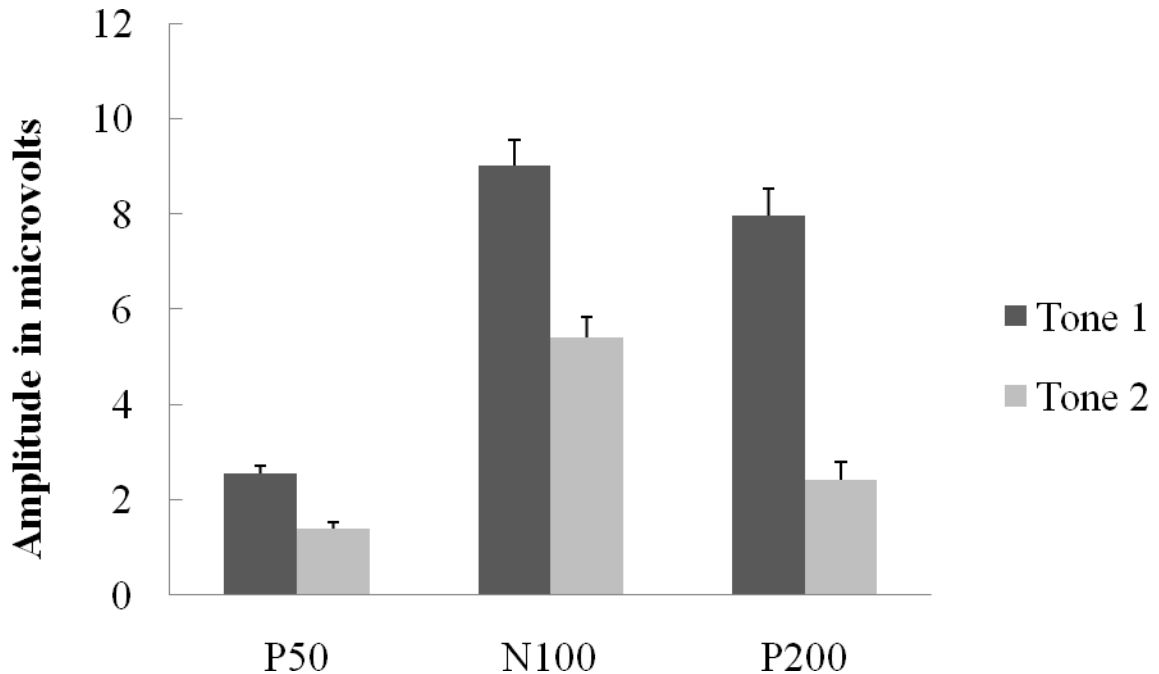
Figure 7: Amplitude for high frequency first and second tones for P50, N100 and P200 components. As was expected, there was a significant reduction in amplitude for the second tone compared to the first tone across all three components. Error bars represent standard error.

Orienting – amplitude enhancement for deviant tone

For the series with the deviant in the fourth position, the amplitude for the deviant tone ($M = 1.41$, $SD = .67$) was significantly higher than the amplitude of the third (preceding) tone ($M = .84$, $SD = .43$) for the P50 component (see figures 8,9), t (38) = 6.53, $p < .001$; the amplitude for the deviant tone ($M = 5.88$, $SD = 2.17$) was significantly higher than the amplitude of the third (preceding) tone ($M = 2.80$, $SD = 1.32$) for the N100 component, t (38) = 10.03, $p < .001$; and amplitude for the deviant tone ($M = 5.17$, $SD = 2.86$) was significantly higher than the amplitude of the third (preceding) tone ($M = 1.21$, $SD = 1.02$) for the P200 component (see figures 10,11,12), t (38) = 8.88, $p < .001$ (see table 2).

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Figure 8: Grand average ERP waveforms for the P50 component of the orienting paradigm (filtered 10-75 Hz) with the deviant tone in the fourth position, presented as amplitude (in μV) of the eight tones as a function of time (in ms). The deviant tone had significantly higher amplitude compared to the preceding tone, which represents the orienting filtering effect. Dotted line indicates stimulus onset. Single arrow points to the P50 component. All data reported from electrode Cz, n=39.
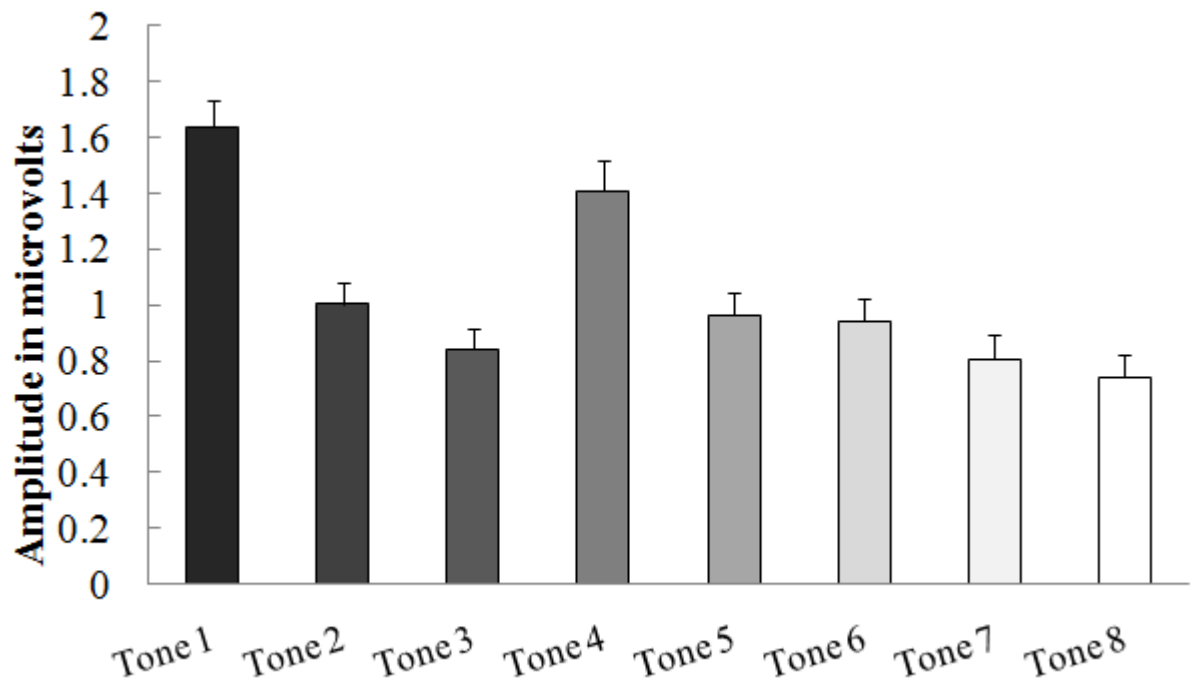
Figure 9: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fourth position for the P50 component. Error bars represent standard error.
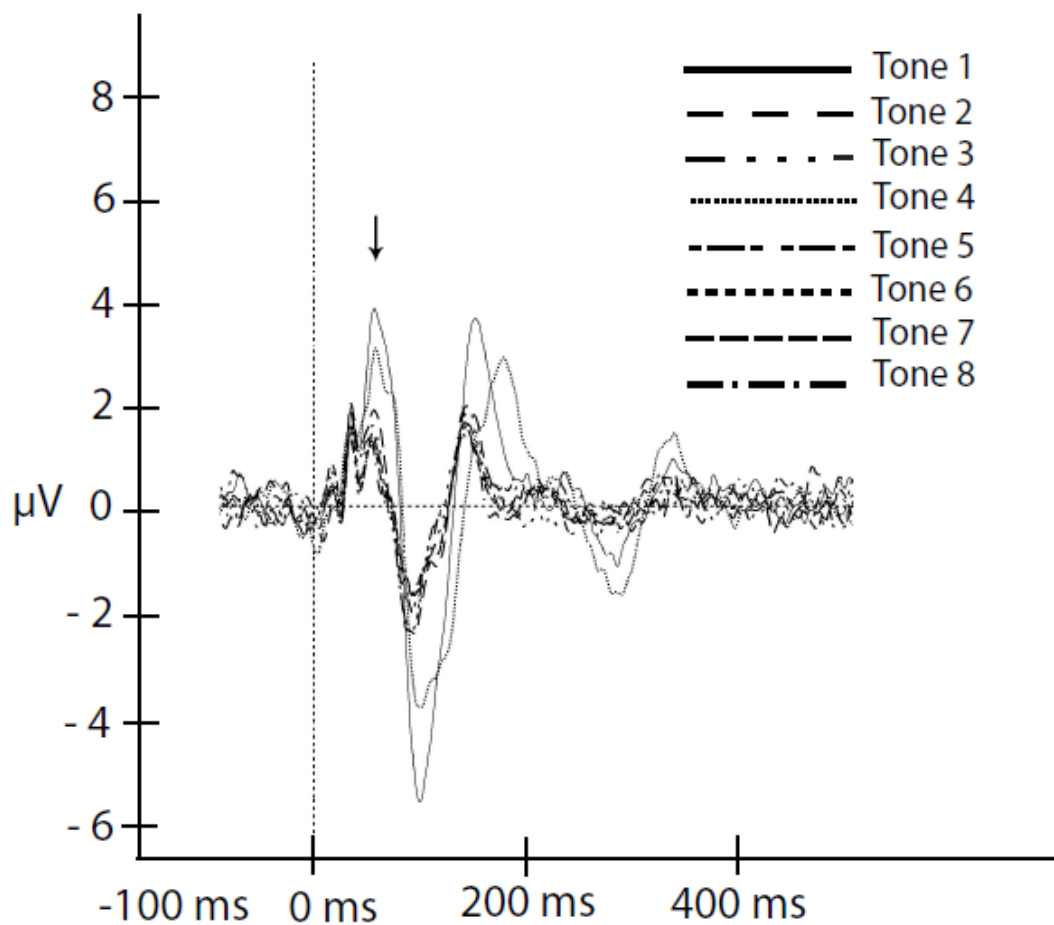
Figure 10: Grand average ERP waveforms for the N100 and P200 components of the orienting paradigm (filtered .23-30 Hz) with the deviant tone in the fourth position, presented as amplitude (in µV) of the eight tones as a function of time (in ms). The deviant tone had significantly higher amplitude compared to the preceding tone, which represents the orienting filtering effect. Dotted line indicates stimulus onset. Double arrows point to the N100 component and triple arrows point to the P200 component.   All data reported from electrode Cz, n=39.

Figure 11: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fourth position for the N100 component. Error bars represent standard error.

Figure 12: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fourth position for the P200 component. Error bars represent standard error.

Table 2

Means and (SD) for P50, N100 and P200 amplitudes for the eight tones in the orienting paradigm with the deviant in the fourth position and orienting (tone 4 – tone 3)

Components	Tone 1	Tone 2	Tone 3	Tone 4	Tone 5	Tone 6	Tone 7	Tone 8	Orienting
P50	1.64	1.00	.84	1.41	.96	.94	.81	.74	.57
	(.60)	(.47)	(.44)	(.67)	(.51)	(.51)	(.54)	(.51)	(.54)
N100	5.00	2.73	2.80	5.88	2.27	2.27	1.94	1.98	3.10
	(2.12)	(1.40)	(1.32)	(2.17)	(1.30)	(1.06)	(1.33)	(1.13)	(1.90)
P200	4.72	1.50	1.21	5.17	1.73	1.25	1.28	1.10	3.98
	(2.13)	(1.20)	(1.02)	(2.86)	(1.54)	(1.57)	(1.28)	(1.49)	(2.75)

For the series with the deviant in the fifth position, the amplitude for the deviant tone ($M = 1.41$, $SD = .64$) was significantly higher than the amplitude of the fourth (preceding) tone ($M = .87$, $SD = .53$) for the P50 component (see figures 13,14), $t (37) = 5.26$, $p < .001$; the amplitude for the deviant tone ($M = 6.01$, $SD = 2.53$) was significantly higher than the amplitude of the fourth (preceding) tone ($M = 2.83$, $SD = 1.40$) for the N100 component, $t (38) = 9.24$, $p < .001$; and amplitude for the deviant tone ($M = 5.21$, $SD = 2.71$) was significantly higher than the amplitude of the fourth (preceding) tone ($M = 1.29$, $SD = 1.29$) for the P200 component (see figures 15,16,17), $t (38) = 9.42$, $p < .001$ (see table 3).

Whether the deviant tone was in the fourth position or in the fifth position, an orienting effect was observed. This suggests that the brain had increased processing to the deviant tone.
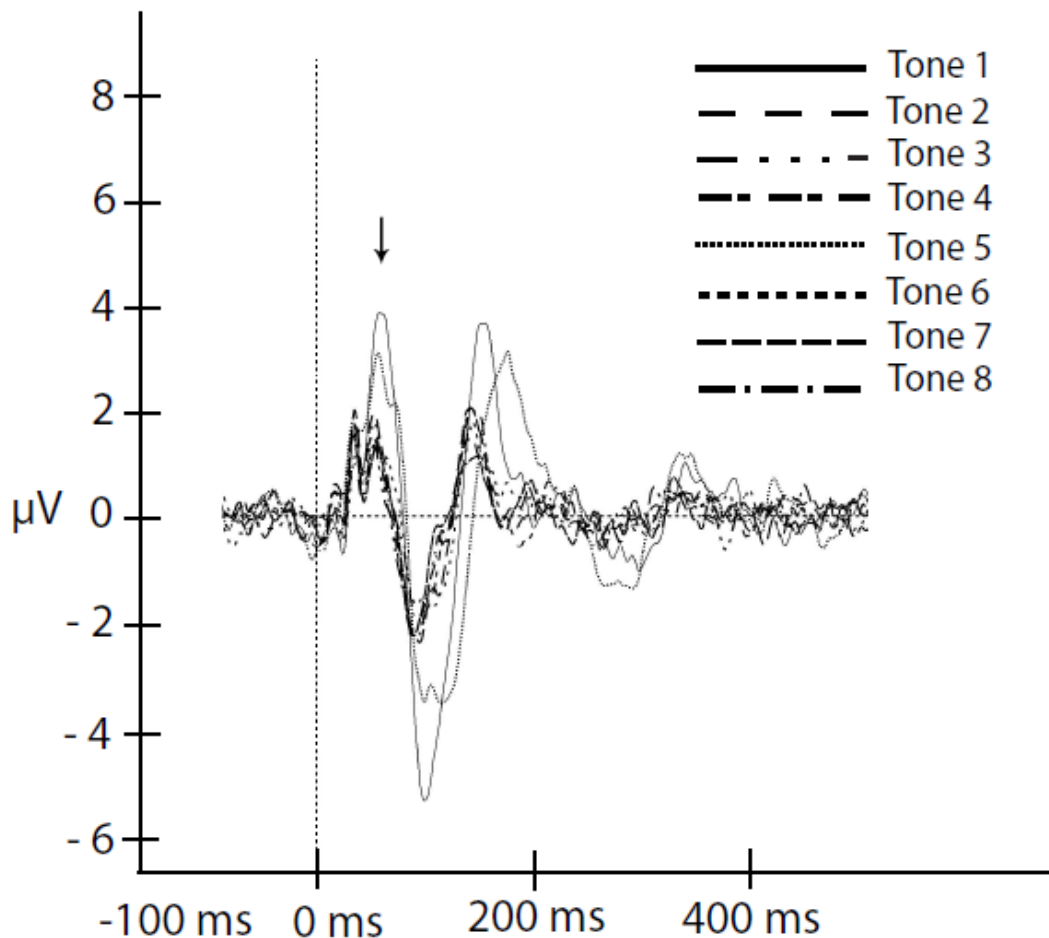
Figure 13: Grand average ERP waveforms for the P50 component of the orienting paradigm (filtered 10-75 Hz) with the deviant tone in the fifth position, presented as amplitude (in µV) of the eight tones as a function of time (in ms). The deviant tone had significantly higher amplitude compared to the preceding tone, which represents the orienting filtering effect. Dotted line indicates stimulus onset. Single arrow points to the P50 component. All data reported from electrode Cz, n=39.
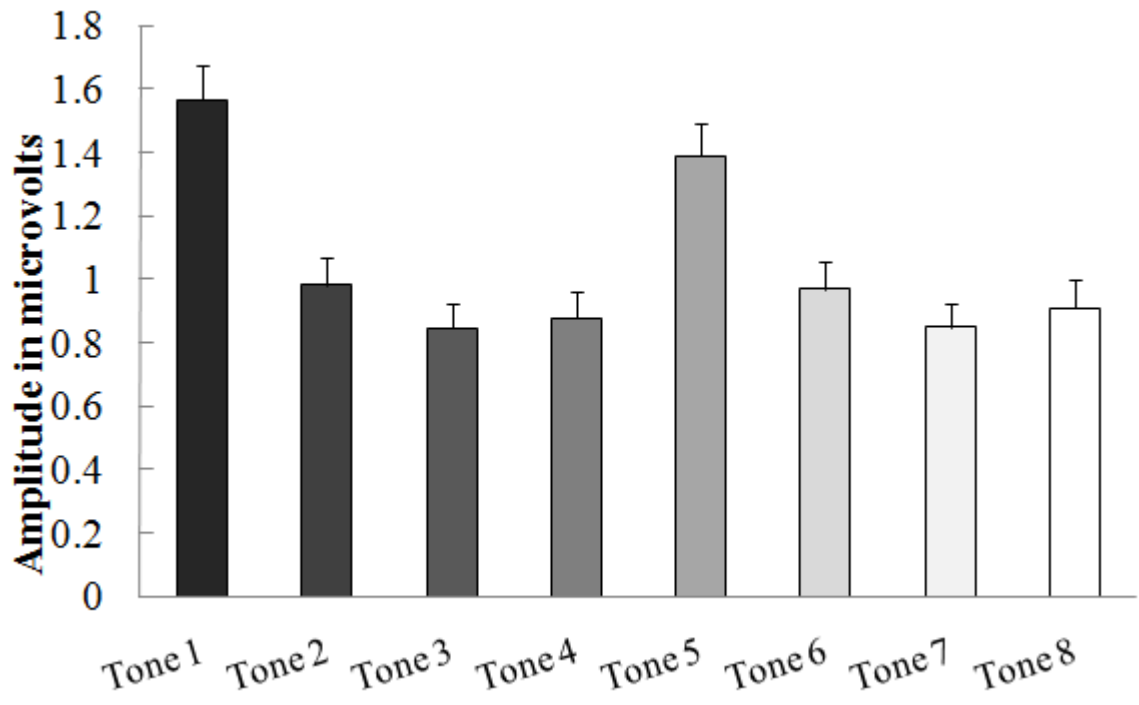
Figure 14: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fifth position for the P50 component. Error bars represent standard error.
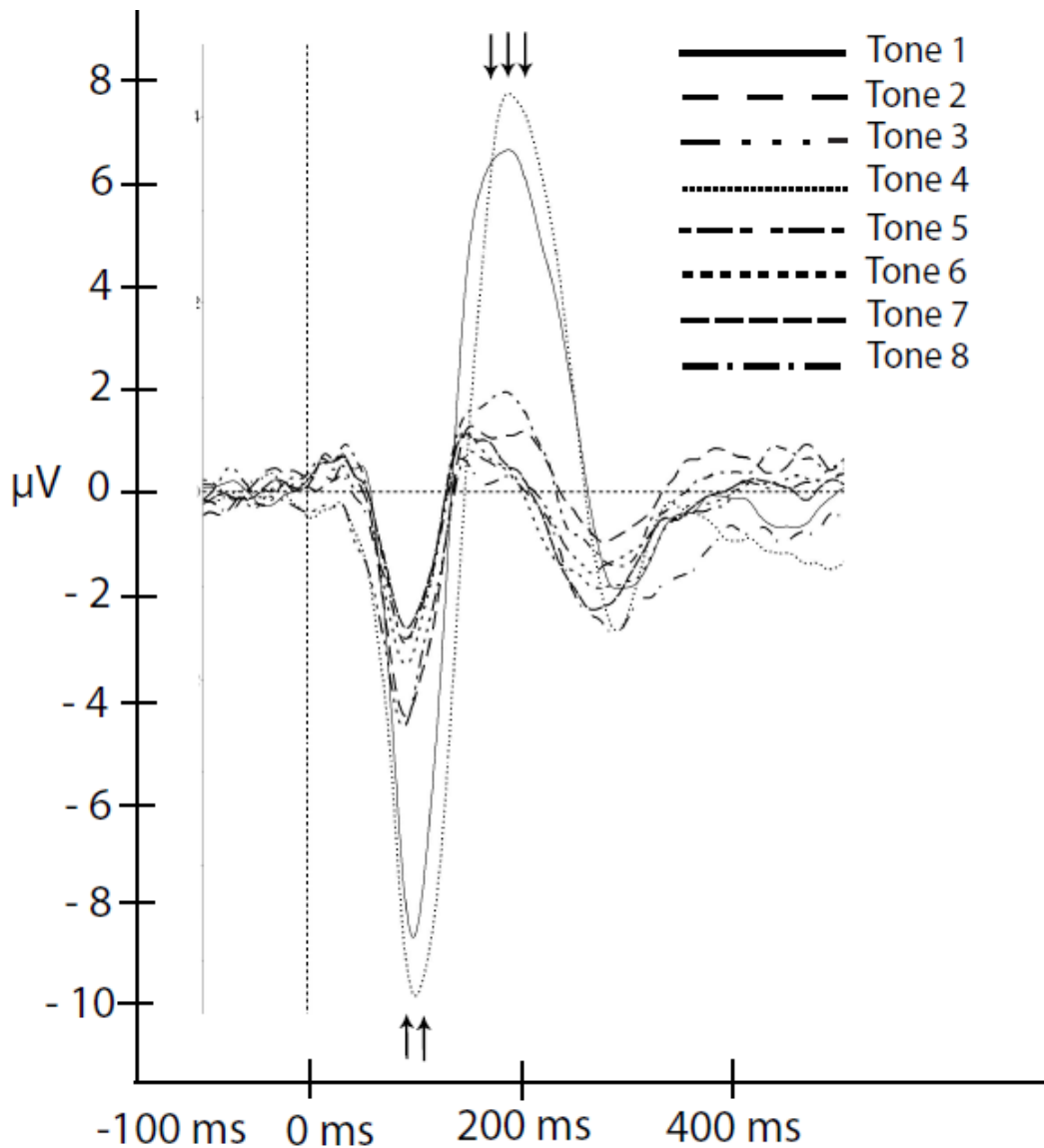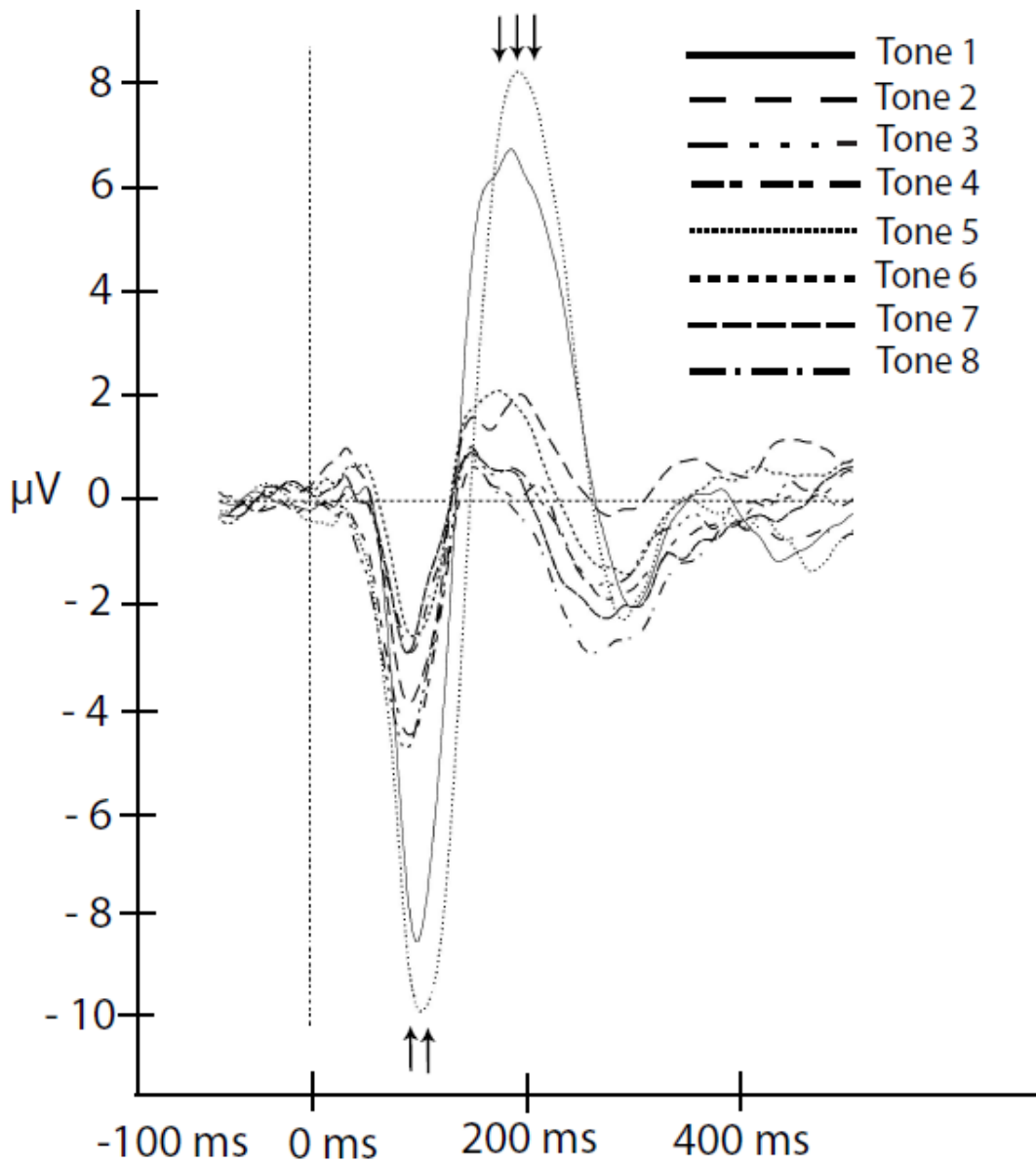
Figure 15: Grand average ERP waveforms for the N100 and P200 components of the orienting paradigm (filtered .23-30 Hz) with the deviant tone in the fifth position, presented as amplitude (in µV) of the eight tones as a function of time (in ms). The deviant tone had significantly higher amplitude compared to the preceding tone, which represents the orienting filtering effect. Dotted line indicates stimulus onset. Double arrows point to the N100 component and triple arrows point to the P200 component. All data reported from electrode Cz, n=39.
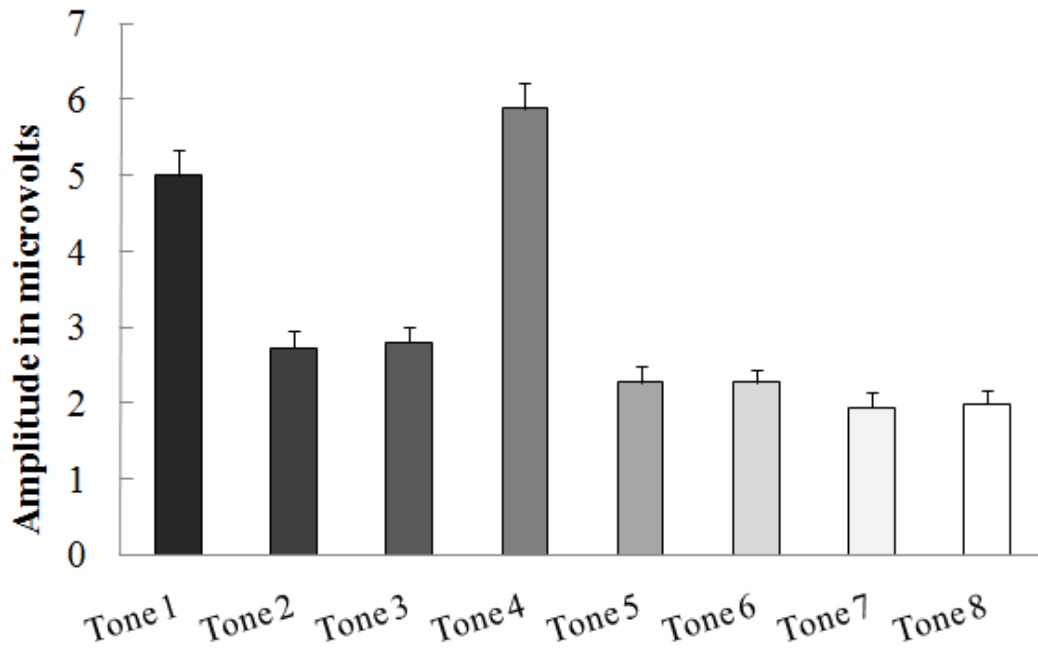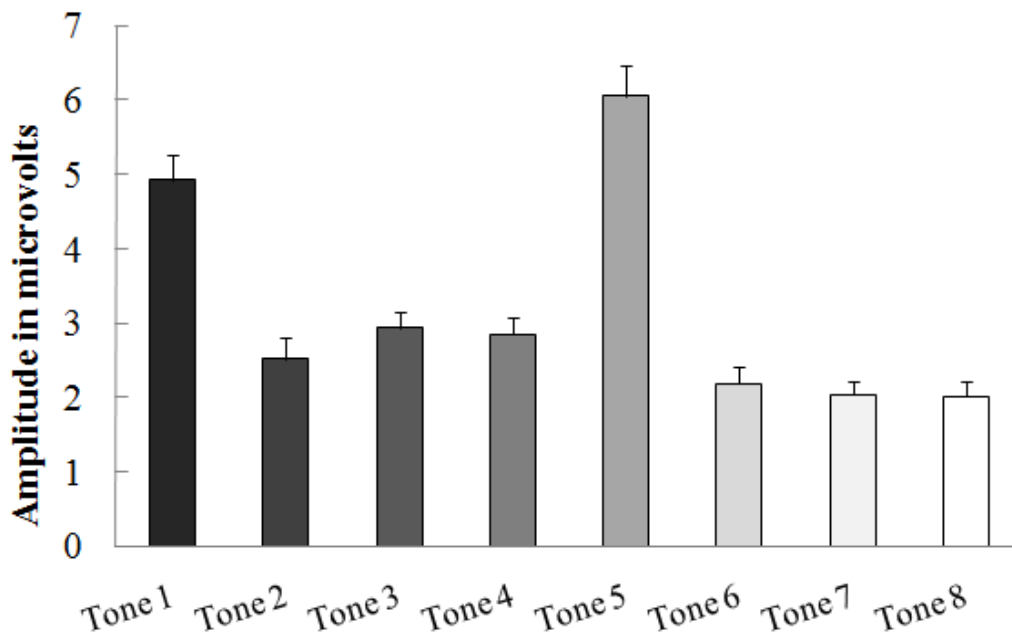
Figure 16: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fifth position for the N100 component.   Error bars represent standard error.
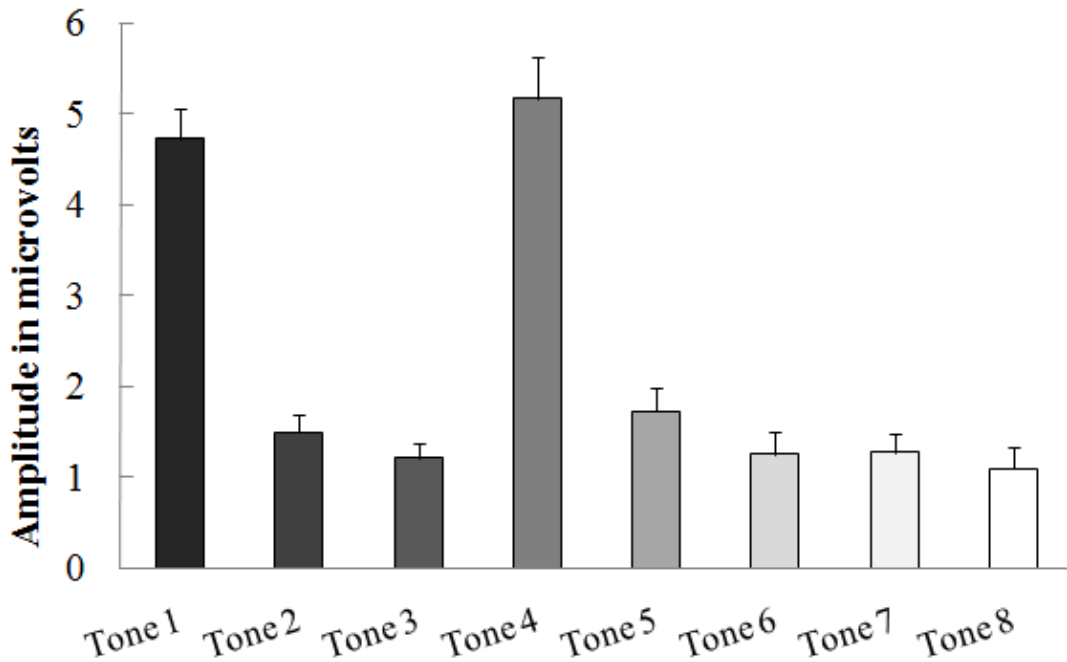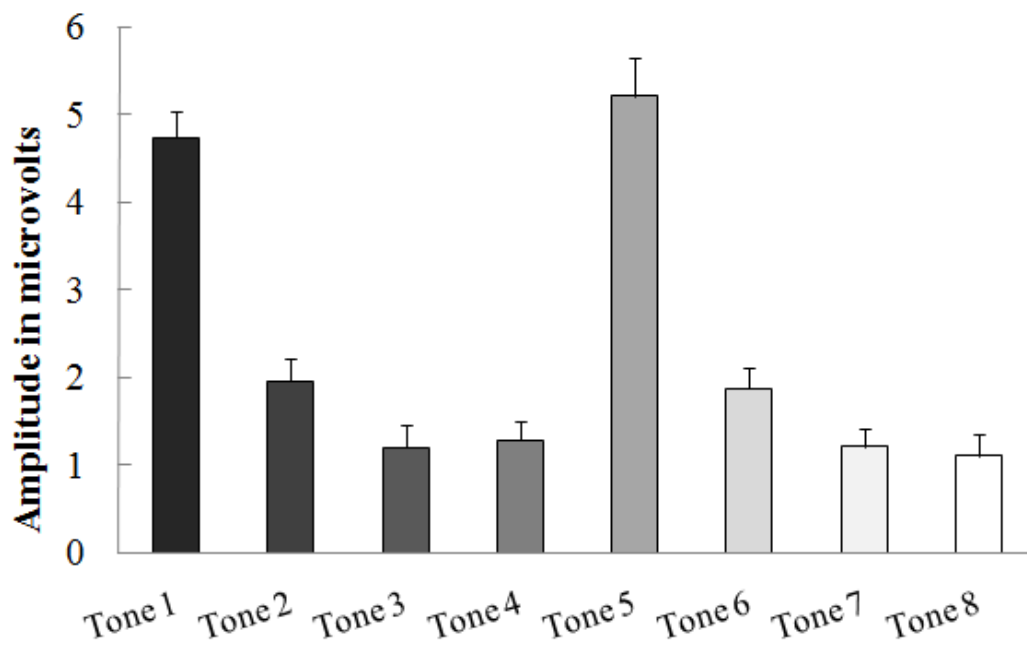

Figure 17: Amplitude for the eight tones in the orienting paradigm, with the deviant in the fifth position for the P200 component. Error bars represent standard error.

Table 3

Means and (SD) for P50, N100 and P200 amplitudes for the eight tones in the orienting paradigm with the deviant in the fifth position and orienting (tone 5 – tone 4)

Components	Tone 1	Tone 2	Tone 3	Tone 4	Tone 5	Tone 6	Tone 7	Tone 8	Orienting
P50	1.57	.98	.85	.88	1.39	.97	.85	.91	.53
	(.66)	(.54)	(.47)	(.53)	(.64)	(.55)	(.46)	(.55)	(.62)
N100	4.93	2.52	2.93	2.85	6.06	2.18	2.04	2.02	3.27
	(2.07)	(1.72)	(1.37)	(1.34)	(2.53)	(1.47)	(1.17)	(1.30)	(2.10)
P200	4.73	1.95	1.20	1.29	5.21	1.87	1.21	1.11	3.92
	(1.84)	(1.57)	(1.62)	(1.29)	(2.71)	(1.43)	(1.32)	(1.49)	(2.60)

Habituation – amplitude reduction across tones

The amplitude for the eighth tone ($M = .91$, $SD = .46$) was significantly lower than the amplitude of the first tone ($M = 1.74$, $SD = .66$) for the P50 component (see figures 18,19), $t (38) = 8.02$, $p < .001$; the amplitude for the eighth tone ($M = 1.97$, $SD = 1.25$) was significantly lower than the amplitude of the first tone ($M = 4.98$, $SD = 2.26$) for the N100 component, $t (38) = 9.87$, $p < .001$; and amplitude for the eighth tone ($M = 1.30$, $SD = 1.29$) was significantly lower than the amplitude of the first tone ($M = 5.08$, $SD = 2.13$) for the P200 component (see figures 20,21,22), $t (38) = 10.58$, $p < .001$ (see table 4). Results from the habituation manipulation verifications suggest that habituation occurred for all three components.
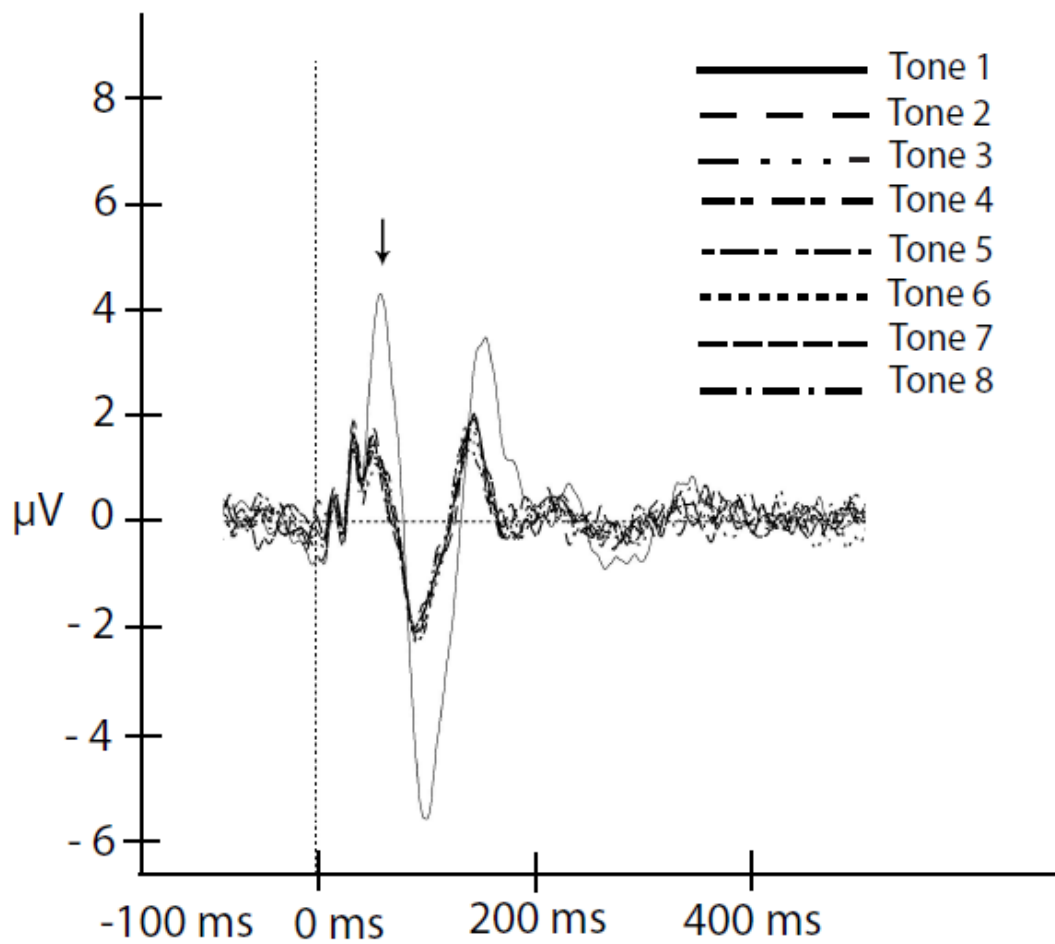
Figure 18: Grand average ERP waveforms for the P50 component of the habituation paradigm, presented as amplitude (in μV) of the eight identical tones as a function of time (in ms). The eighth tone had significantly reduced amplitude compared to the first tone, which represents the typical habituation effect. Dotted line indicates stimulus onset. Single arrow points to the P50 component. All data reported from electrode Cz, n=39.
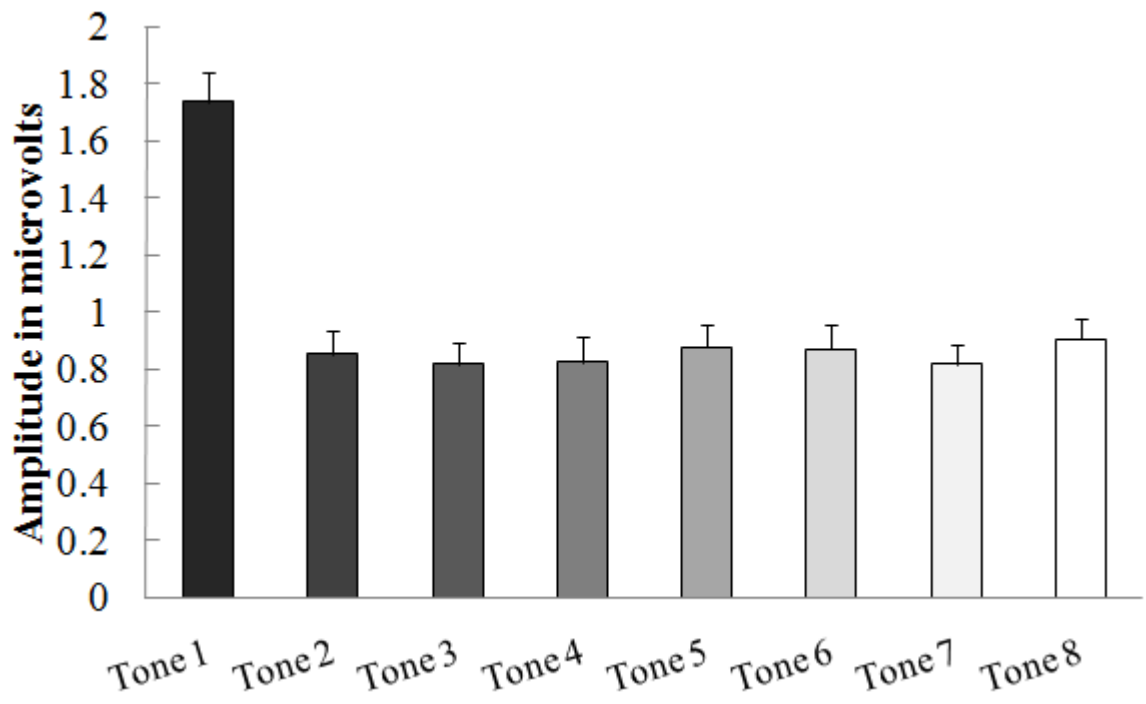
Figure 19: Amplitude for the eight identical tones in the habituation paradigm for the P50 component. Error bars represent standard error.
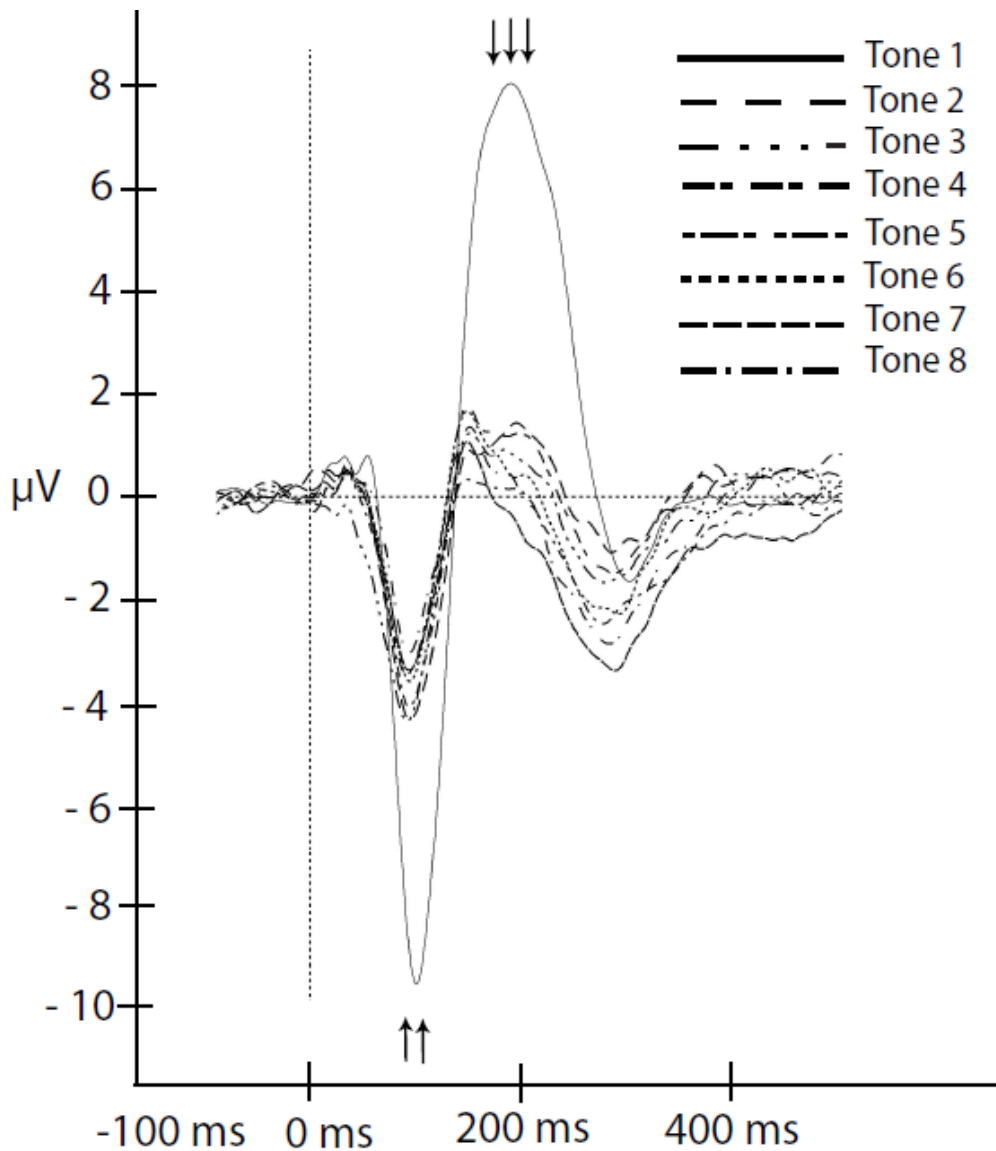
Figure 20: Grand average ERP waveforms for the N100 and P200 components of the habituation paradigm, presented as amplitude (in μV) of the eight identical tones as a function of time (in ms). The eighth tone had significantly reduced amplitude compared to the first tone, which represents the typical habituation effect. Dotted line indicates stimulus onset. Double arrows point to the N100 component and triple arrows point to the P200 component. All data reported from electrode Cz, n=39.
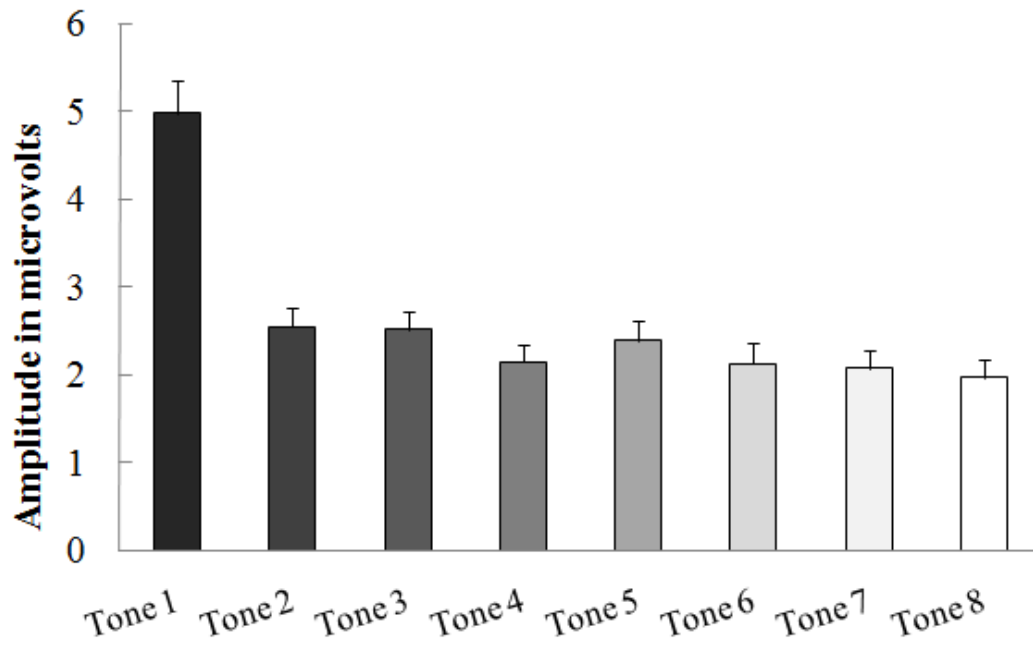
Figure 21: Amplitude for the eight identical tones in the habituation paradigm for the N100 component. Error bars represent standard error.
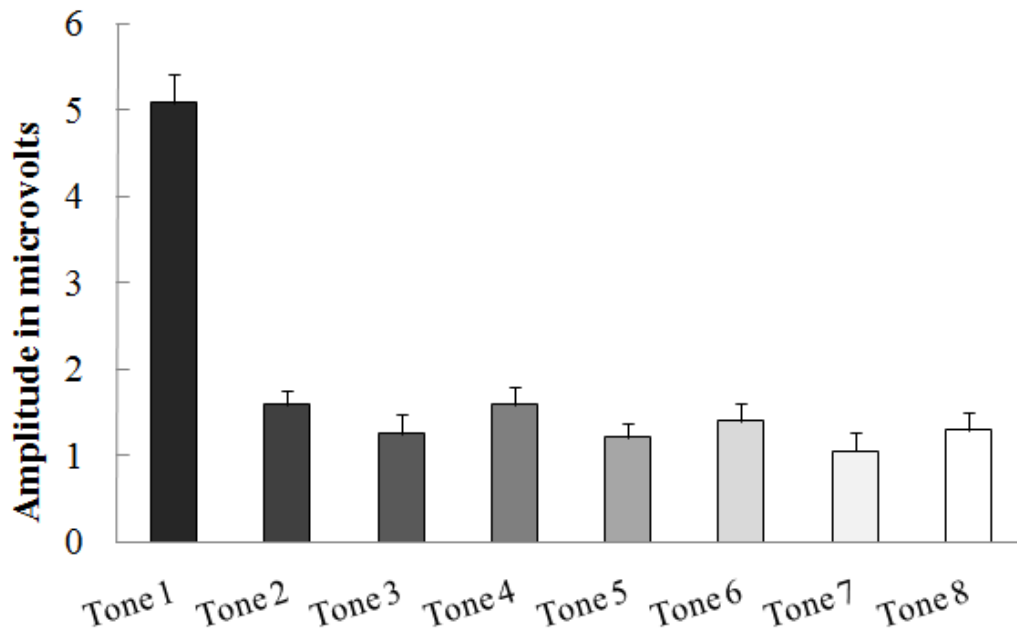
Figure 22: Amplitude for the eight identical tones in the habituation paradigm for the P200 component. Error bars represent standard error.

Table 4

Means and (SD) for P50, N100 and P200 amplitudes for the eight identical tones in the
habituation paradigm and habituation (tone 1 – tone 8)

Components	Tone 1	Tone 2	Tone 3	Tone 4	Tone 5	Tone 6	Tone 7	Tone 8	Habituation
P50	1.74	.85	.82	.83	.88	.87	.82	.91	.83
	(.66)	(.52)	(.47)	(.53)	(.49)	(.54)	(.44)	(.46)	(.65)
N100	4.98	2.54	2.52	2.15	2.38	2.13	2.07	1.97	3.03
	(2.26)	(1.38)	(1.32)	(1.22)	(1.45)	(1.54)	(1.27)	(1.25)	(1.92)
P200	5.08	1.58	1.25	1.59	1.21	1.40	1.05	1.30	3.78
	(2.13)	(1.07)	(1.38)	(1.24)	(.99)	(1.27)	(1.39)	(1.29)	(2.23)

The effects of the experimental manipulations suggest that both the auditory

registration paradigm and the sensory gating measures exhibited significant effects that

were in the predicted direction and in line with previous research.

Additional research questions

In this section, the relationship between discrimination and sensory gating and

organization and sensory gating was examined. Discrimination for low-frequency tones

in the sensory registration paradigm was not correlated with filtering for low-frequency

tones for the N100, $r(39) = -.091$, $p = .573$, and P200, $r(39) = .160$, $p = .318$,

components, or for habituation for the N100 component, $r(37) = .268$, $p = .099$, but was

significantly correlated with habituation for the P200 component, $r(37) = .381$, $p = .017$,

and orienting for the N100, $r(37) = .547$, $p < .001$, and P200, $r(37) = .551$, $p < .001$,

components.

Discrimination for high-frequency tones in the sensory registration paradigm was not correlated with filtering for high-frequency tones for the N100, $r(40) = -.224$, $p = .154$, and P200, $r(39) = .016$, $p = .920$, components, or for habituation for the P200 component, $r(37) = .255$, $p = .118$, but was significantly correlated with habituation for the N100 component, $r(37) = .371$, $p = .020$, and orienting for the N100, $r(37) = .367$, $p = .022$, and P200, $r(37) = .552$, $p < .001$, components (see figure 23).

Organization for high-intensity tones in the sensory registration paradigm was not correlated with filtering for the N100, $r(39) = .159$, $p = .320$, or P200, $r(39) = -.176$, $p = .217$, components, not correlated with orienting for the N100, $r(37) = -.153$, $p = .354$ and P200, $r(37) = -.110$, $p = .506$, components, yet was significantly correlated with habituation for the N100, $r(37) = -.347$, $p = .030$, and P200 components $r(37) = -.325$, $p = .043$ (see table 5).

Discrimination was not related to filtering, but was related to orienting and habituation. This suggests that the better the brain can discriminate between basic qualities of sound (such as intensity), the better the brain can respond to novelty and better "ignore" stimuli that are repeatedly presented. For orienting, this is not surprising because it suggests that when the brain is good at discriminating between high and low intensity sounds, it is also good at discriminating between standard and deviant sounds and thus knowing when to orient to novelty. It is less clear why habituation, but not filtering, was related to discrimination. One explanation is that for filtering, it might be adaptive to quickly reduce the amplitude between two sounds, with the trade off that the mechanism is less fine-tuned. One study found that filtering still occurred when non-identical stimuli were used, suggesting that stimuli need to resemble each other just

enough for the brain to produce a filtering response (Moura et al., 2010). On the other hand, for habituation, the brain is making subtle, gradual reductions in amplitude over time. In order for the brain to evaluate and subtly adjust amplitude each time the sound is presented it might require more fine tuned discrimination.

Organization was not related to filtering or orienting for any component, yet was related to habituation for both the N100 and P200 components. This suggests that the brain's gradual reduction in response to repeated stimuli is related to the ability to consistently respond to distinct stimuli (such as stimuli differing in frequency). The lack of relationship between organization and filtering is consistent with research that found that filtering still occurred when stimuli were somewhat different in frequency (Moura et al., 2010). The lack of relationship with orienting suggests that more similar responses in timing do not predict how strong the magnitude of the brain's response will be when a novel stimulus is introduced.

Table 5

Means and (SD) for N100 and P200 discrimination (amplitude for low-intensity tones subtracted from amplitude for high-intensity tones) and organization (amplitude of low-frequency tones subtracted from amplitude from high-frequency tones) in the auditory registration paradigm

Components	Discrimination		Organization	
	High-frequency tones	Low-frequency tones	High intensity tones	Low intensity tones
N1	3.10 (2.46)	3.43 (2.52)	4.88 (6.75)	1.44 (.13)
P2	3.77 (3.48)	2.92 (3.20)	13.18 (10.78)	1.42 (.19)
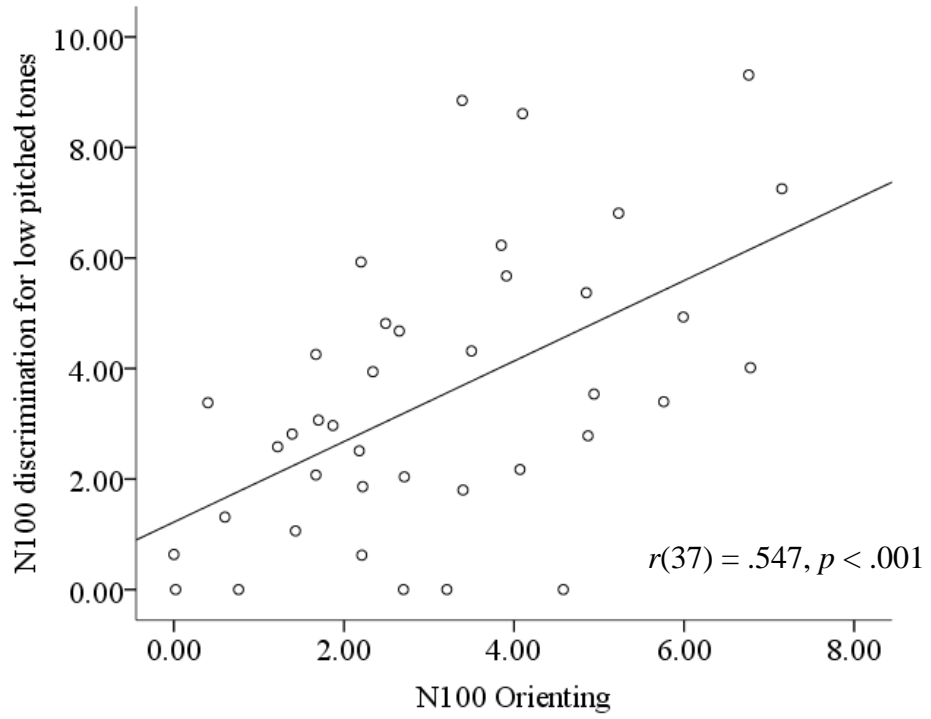
(a)
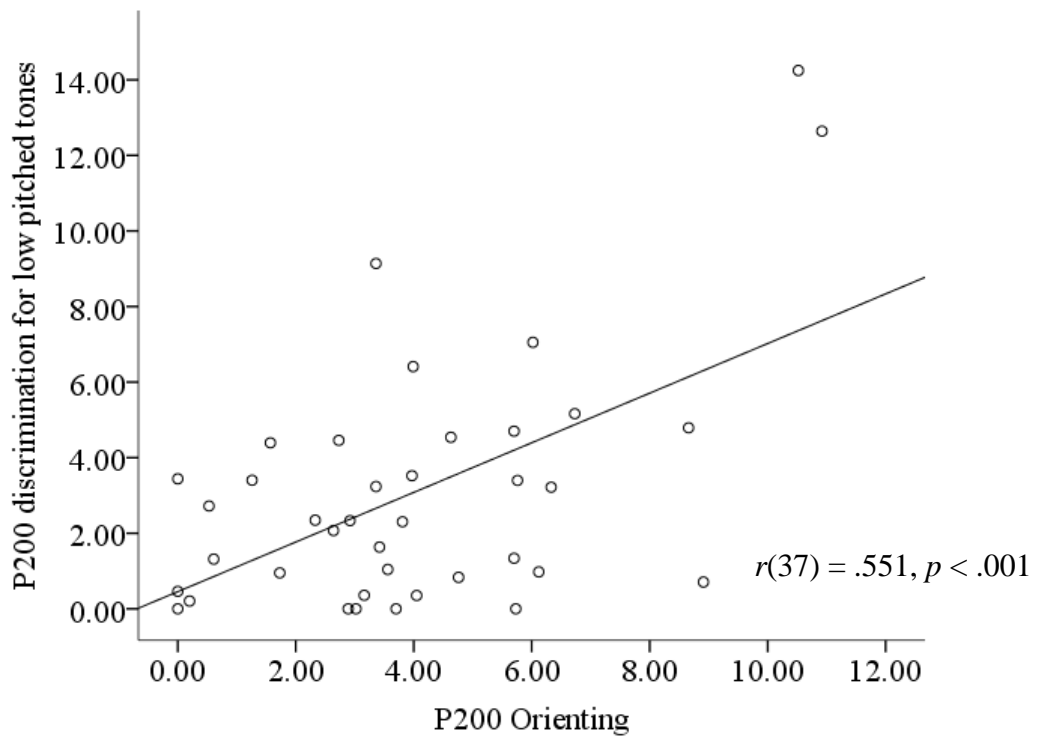
(b)
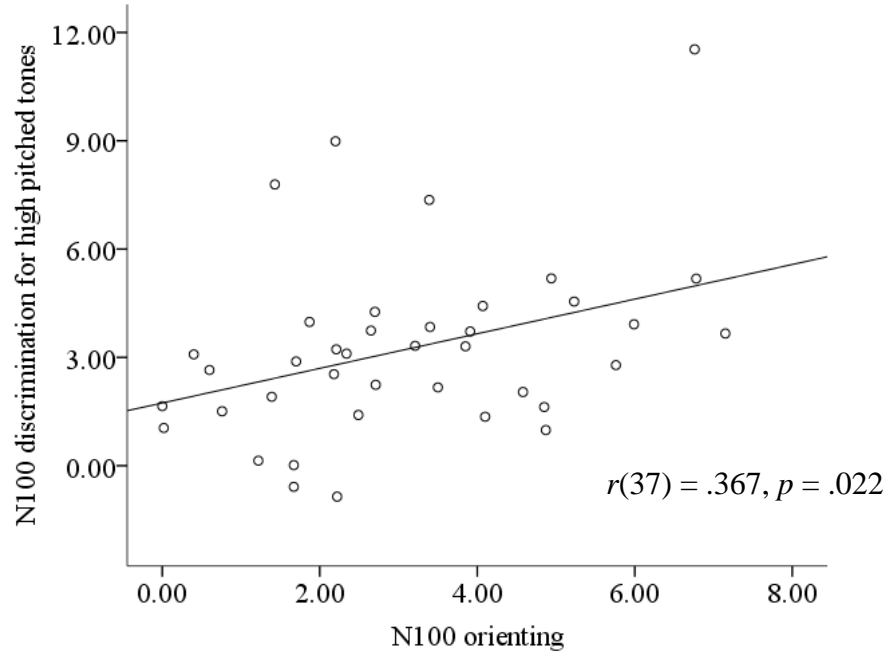
(c)
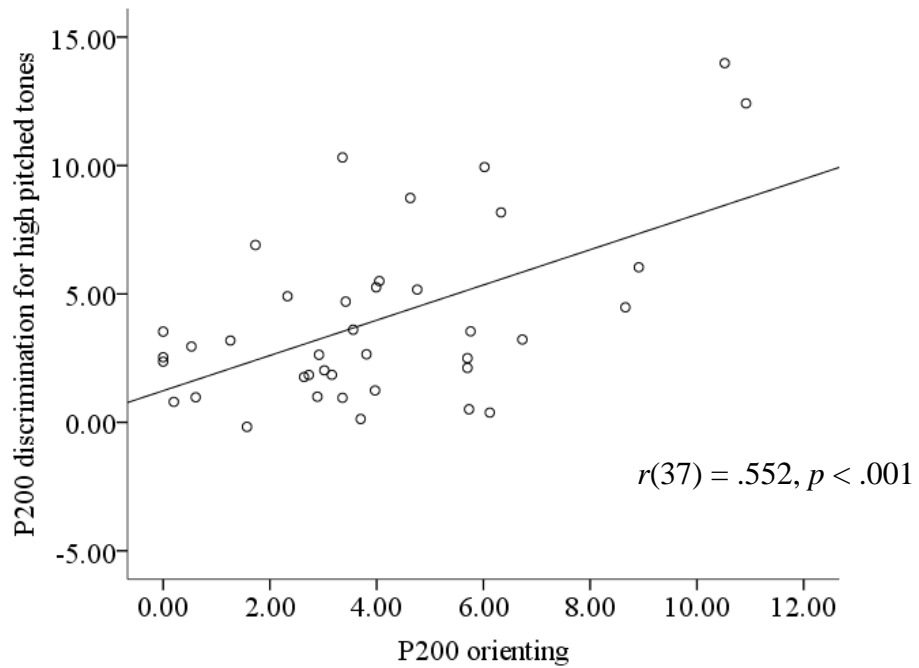
(d)

Figure 23: Relationship between N100 orienting (a) and P200 orienting (b) for low-frequency sensory discrimination and N100 orienting (c) and P200 orienting (d) for high-frequency sensory discrimination.

Chapter 4: The study of the interrelationship between different sensory gating measures

Rationale

Generally speaking, there are many studies on filtering and few studies on habituation (i.e., cortical habituation that can be measured using electroencephalographic techniques like ERPs). Therefore, the field is lacking in data for cortical habituation as measured by ERPs and even more lacking in data that compare different types of sensory gating at a mechanistic level.

Based on the available literature, evidence suggests that filtering and orienting represent different processes. For example, Hall et al. (2006) compared what genes may be in common with filtering (measured by the P50 component) and detection of a novel stimulus (measured by the mismatch negativity component). They found no genetic overlap for these two measures and suggested that they likely serve different functions that may represent unique neurophysiological mechanisms.

There is less evidence to speak to whether filtering and habituation are related. Only a handful of studies have directly compared filtering to short-term habituation by measuring ERPs at the scalp (Boutros, Belger, Campbell, D'Douza, & Krystal, 1999; Rosburg et al., 2006). Filtering was compared to short-term habitation by measuring intracranial recordings on epilepsy patients in two studies (Rosburg et al., 2004, Rosburg et al., 2006).

Results have been mixed and it remains ambiguous whether filtering and habituation are unique processes. One way to compare filtering to habituation is by comparing the amplitudes for the first or second stimulus in a filtering paradigm to the

first or second stimulus in a habituation paradigm. For example, one study found that the amplitude for the first tone in a habituation paradigm was greater than the amplitude for the first tone in a filtering paradigm (Boutros et al., 1999). Identical stimuli were used for the filtering and habituation paradigms, so the difference in amplitude between the paradigms suggests that the brain is discriminating between the different contexts – a pair of tones versus a series of several tones.

Another way to distinguish whether a habituation paradigm elicits responses that are unique from and contribute something above and beyond a filtering paradigm is to test for an amplitude reduction beyond the second stimulus. It is expected that for both filtering and habituation there would be a significant amplitude reduction between the first and second click – what can be thought of as the typical filtering effect. Yet, if there is amplitude reduction beyond the second stimulus, it suggests that that the habituation paradigm is capturing an aspect of processing that is not captured by the filtering paradigm. Rosburg et al. (2006) found that for the P50 component, there was not any significant decrease in amplitude beyond the second click, yet for the N100 component, there was a marginally significant effect such that the last stimulus in the series was less than the second stimulus in the series. However, this only occurred for data that were measured intracranially; data recorded from the scalp were in the same direction, but failed to reach significance.

Whether different types of auditory gating are distinct neurophysiological processes is important for understanding of clinical pathology. For example, individuals with schizophrenia are thought to have filtering, orienting, and habituation deficits (Olincy et al., 2000; Wynn et al., in press; Vernon, Haenschel, Dwivedi, & Gruzelier,

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2005). If these three types of gating are all unique processes, then each should be

examined in their own right because they may all uniquely relate to symptoms or higher

order cognitive processes. In other words, they may differentially affect the symptoms of

clinical disorders. On the other hand, if they are manifestations of a common underlying

mechanism, then it may be more appropriate to investigate that underlying mechanism

and how it may relate to symptoms.

Whether the P50, N100, and P200 ERP components are related to each other and

if gating at one component is better than gating at another component is also important

for understanding clinical pathology. Previous research suggests that P50, N100, and

P200 gating reflect different aspects of gating as a multistage process (Boutros et al.,

2004). As stated previously, evidence is accumulating that many individuals from

various clinical populations not only have P50 sensory gating deficits, but may also have

N100 and P200 deficits as well. If these different components do reflect different stages

of attentional allocation, then response deficits at one stage of processing may tell us

something unique about a particular clinical pathology. In an effort to understand how

different components are related to each other in healthy adults, we related responses for

the P50, N100 and P200 components for each of the three sensory gating paradigms.

In an effort to better understand the relationship among the three types of sensory

gating, we compared participants' responses across all three sensory gating paradigms.

Because the relationship between filtering and habituation is the least well understood,

we conducted more in-depth analyses examining this relationship. Similar to the studies

presented previously by Rosburg et al. (2004, 2006), we compared the brain's response

across the series of tones. If habituation is a separate mechanism, then there should be an

amplitude reduction in the habituation paradigm above and beyond the second click. If there is no further reduction in amplitude after the second click then it suggests that the habituation paradigm with eight tones is not measuring anything different than the two tones in the filtering paradigm.

The amplitudes of the first and second tones were also compared for the filtering and habituation paradigms. The sound stimuli are identical for the first two tones of these paradigms, so the amplitude should be the same if the filtering and habituation paradigms are measuring the same process. If the amplitudes of the two first tones or the two second tones are significantly different for these two paradigms, then the brain responded differently to identical stimuli, which suggests that context (i.e., tones presented in a pair or in a series of eight) has an effect.

We predict that orienting and filtering, orienting and habituation, and habituation and filtering will not be significantly correlated. We also predict that, like Rosburg et al. (2006), there will be no amplitude reduction beyond the second click for the P50 component, but there will be an amplitude reduction beyond the second click for the N100 component. Finally, we predict that amplitudes of the first and second tones will differ in magnitude for the filtering paradigm compared to the habituation paradigm. Achieving these results would suggest that filtering and habituation likely reflect different underlying mechanisms – at least as is measured by ERPs at the scalp. Regarding differential response for the three components of interest, we predict that gating responses will be different for the P50, N100 and P200 ERP components because it is thought that these components reflect different stages of sensory gating.

Data analysis

Potential relationships among the three types of sensory gating

The Pearson product-moment correlation was used to examine the relationship between the three components' amplitudes (P50, N100, and P200) and the three types of sensory gating (filtering, orienting, and habituation).

Potential relationships among the three ERP components

To determine if there were differential gating responses for the P50, N100, and P200 components, three, one-way repeated measures ANOVAs were conducted for filtering, orienting, and habituation, respectively. Also, using the Pearson product-moment correlation, responses for P50, N100, and P200 gating was related for filtering, orienting, and habituation.

Further analyses comparing filtering and habituation

Using dependent samples *t* tests, the amplitude of the second tone in the habituation paradigm[18] was compared to the amplitude of the eighth tone in the habituation paradigm, to determine if an amplitude reduction occurred beyond the second tone. We also compared the amplitudes of the third, fourth, fifth, sixth, and seventh tones to the amplitude of the eighth tone to determine the point at which habituation was completed.

Using a two (tone) by two (paradigm) repeated-measures ANOVA, amplitude for the first and second tones were compared for the filtering and habituation paradigms to determine if the typical "filtering" effect occurred for the habituation paradigm and if the amplitude magnitude was different for these two paradigms. Separate ANOVAs were

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[18] We used the habituation paradigm with eight identical tones for all of the habituation analyses in this section

run for the P50, N100, and P200 components. The Greenhouse-Geiser adjustment was used to correct degrees of freedom any time the sphericity assumption was violated. All multiple comparison procedures were computed using the Sidak method[19]

Results and Discussion

Correlations among the three types of sensory gating

Filtering was not significantly correlated with orienting for the P50, $r(36) = -.117$, $p = .484$, N100, $r(36) = .266$, $p = .107$, or P200, $r(36) = -.003$, $p = .984$, components or with habituation for P50, $r(36) = .020$, $p = .903$, N100, $r(36) = .185$, $p = .265$, or P200, $r(36) = -.094$, $p = .573$, components. On the other hand, habituation was significantly correlated with orienting for the P50, $r(37) = .410$, $p = .009$, N100, $r(37) = .345$, $p = .032$, and P200, $r(37) = .517$, $p = 001$, components.

That filtering was not significantly related to orienting or habituation for any of the three components, suggests that these types of sensory gating may be unique processes. The relationship between habituation and orienting was not a predicted effect; it suggests that better habituation responses are associated with better orienting for the P50, N100 and P200 components. One explanation is that a non-habituating orienting response is mostly useless because organisms may be orienting to all incoming stimuli (Leslie, 1996). Another explanation is that organisms have a continuous evaluation of stimuli across time, whereby responses can decrease over time with habituation and increase with orienting (we may respond to most incoming stimuli and have an even greater response to salient stimuli). Therefore, these results suggest that orienting and habituation ability are related.

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[19] The Sidak method was chosen because it is a moderately conservative multiple comparison procedure, that has higher power than the Bonferonni procedure (Blakesley et al., 2009).

Comparison of gating responses for P50, N100 and P200 components

Comparing mean gating responses for filtering revealed that there was a significant main effect for component, $F(2,80) = 17.63$, $p <.001$. Post-hoc tests revealed that filtering was significantly better for the P200 component[20] compared to both the N100 component and P50 component (see figure 4 and table 1). For orienting, there was a significant main effect for component, $F(1.32,50.11) = 33.09$, $p <.001$. Post-hoc tests revealed that orienting was significantly better for both the P200 and N100 components compared to the P50 component with no other significant differences (see figure 24 and table 2). For habituation, there was a significant main effect for component, $F(1.42,54) = 30.44$, $p <.001$. Post-hoc tests revealed that habituation was significantly better for the P200 and N100 components compared to the P50 component (see figure 25).
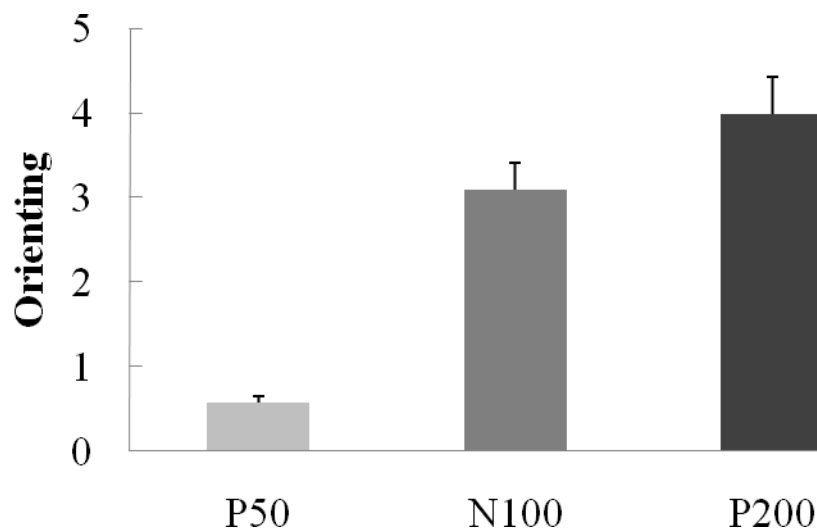
Figure 24: Orienting response for the P50, N100, and P200 components. Error bars represent standard error.

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[20] Recall that smaller numbers correspond to better responses when using ratio measurements.
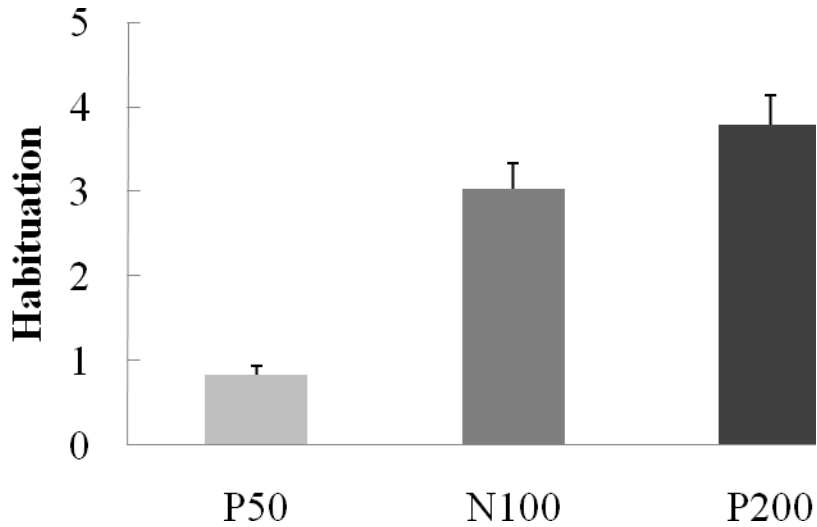
Figure 25: Habituation response for the P50, N100, and P200 components. Error bars represent standard error.

Correlating responses for the P50, N100, and P200 components within each paradigm revealed that for filtering, P50 and N100 were not significantly related, $r(39) = .066$, $p = .682$, P50 and P200 were not significantly related, $r(39) = .156$, $p = .329$, and N100 and P200 were not significantly related, $r(39) = -.256$, $p = .106$. For orienting, P50 and N100 were significantly related, $r(37) = .471$, $p = .002$, P50 and P200 were not significantly related, $r(37) = .250$, $p = .125$, and N100 and P200 were not significantly related, $r(37) = -.093$, $p = .573$. Finally, for habituation, P50 and N100 were not significantly related, $r(37) = .286$, $p = .077$, P50 and P200 were not significantly related, $r(37) = .160$, $p = .331$, and N100 and P200 were not significantly related, $r(37) = -.131$, $p = .427$.

For the most part, these results fit with what has been reported in the literature (e.g., Kisley et al., 2004; Moura et al., 2010; Boutros et al., 2004). Specifically, none of the components were related in any paradigm, except the P50 and N100 in the orienting

paradigm. Our results are consistent with Boutros et al. (2004) who also found that P50, N100, and P200 filtering were not related. That the P50, N100 and P200 components generally did not share relationships with each other suggests that they reflect different aspects of sensory processing, or that they represent different stages in the auditory processing stream.

The P50 component had the weakest degree of sensory gating across all three sensory gating tasks. For orienting and habituation, N100 and P200 had significantly stronger gating compared to P50. For filtering, the P200 had stronger gating than both the N100 and P50 components. The preattentive stage of gating had a weaker sensory gating response, and it may be because this early stage is more automatic and is less influenced by attentional state. In contrast, later stages of gating – those that are thought to be influenced by attention – had stronger gating responses. Boutros et al., (2004) did not report significant differences for P50, N100, and P200 gating and no other study is known to have compared the magnitude of these components in this fashion.

More in-depth analysis comparing filtering and habituation

Amplitude reduction beyond the second tone in the habituation paradigm

If nothing more than filtering is occurring in the habituation paradigm, then the amplitude should not decrease beyond the second tone. However, the amplitude of the eighth tone was significantly less than the amplitude of the second tone for the N100 component, $t(38) = 2.52$, $p = .016$ (see figure 21), but was not for the P50 component, $t(37) = -.59$, $p = .560$ (see figure 20). For the P200 component, the amplitude of the eighth tone was less than the amplitude of the second tone, but failed to reach significance, $t(38) = 1.44$, $p = .158$ (see figure 22, table 3).

When the amplitude for the third, fourth, fifth, sixth, and seventh tones were separately compared to the amplitude for the eighth tone, none of the differences were significant for the P50 or P200 components, but the eighth tone was significantly less than the third, $t(38) = 2.98$, $p = .005$, and fifth, $t(37) = 2.03$, $p = .050$, tones for the N100 component. The seventh tone was also significantly less than the second tone for the N100, $t(38) = 2.59$, $p = .014$, and P200, $t(38) = 2.56$, $p = .015$, components.

These results suggest that, for the N100 and P200 components (particularly for the N100 component), there is an amplitude reduction after the second tone, which reveals that short-term habituation is occurring in addition to simple filtering. The P50 component did not appear to change after the second tone in any of these comparisons, which replicates Rosburg et al. (2006). For P50, we do not seem to be measuring anything unique in the habituation paradigm. This may be because earlier components are more exogenous or stimulus driven (Luck, 2005) and therefore less likely to change from one context to another. On the other hand, for N100 and P200 we do seem to be indexing something in addition to filtering. Habituation was greater for later stages of processing, suggesting the "attentive" stages (N100 and P200) are more susceptible to habituation compared to the "preattentive" stages (P50). When it is behaviorally measured, habituation is thought to be accessible by conscious control (Sternberg, 2003). Whereas habituation does not require conscious control to work, it can be influenced by this. Our pattern of results suggests that the neural habituation we are measuring through ERPs might represent the decline in attention that is associated with habituation. Because short-term habituation seems to occur for N100 and P200 (the attentive stages of processing) but not for P50 (the preattentive stage of processing), the N100 component

and possibly P200 component might be better choices to measure short-term habituation compared to the P50 component.

Amplitude for first and second tones for habituation compared to filtering

Amplitudes of the first and second tones in the filtering and habituation paradigm were compared to confirm that the amplitude of the second tone decreased in both paradigms and to determine if the magnitude of the brain's response was different for these two paradigms. As previously stated, the stimuli and parameters were identical for these two measures. The only difference is that there were two identical tones in the filtering paradigm, whereas there were eight identical tones in the habituation paradigm.

We found that for the P50 component, there was a significant main effect for tone, where the first tone amplitude was greater than the second tone amplitude, $F(1,36) = 90.40, p < .001$. There was also a significant main effect for paradigm, where the where the amplitude for the habituation paradigm was less than the filtering paradigm, $F(1,36) = 97.16, p < .001$. There was also a significant tone by paradigm interaction, $F(1,36) = 4.44, p = .042$, such that the difference in tone one and tone two amplitude was greater for filtering than for habituation (see figure 26). For means and standard deviations, see the "Tone 1" and "Tone 2" columns for the P50 component for tables 1,2, and 4.

Figure 26: P50 amplitude for the first and second tones in the filtering and habituation paradigms. Bars represent standard error.

For the N100 component, there was a significant main effect for tone, where the first tone amplitude was greater than the second tone amplitude, $F(1,37) = 67.62$, p <.001. There was also a significant main effect for paradigm, where the where the amplitude for the habituation paradigm was less than the filtering paradigm, $F(1,37) = 149.77$, p <.001. There was not a significant tone by paradigm interaction, $F(1,37) = 1.65$, $p = .207$, (see figure 27). For means and standard deviations, see the "Tone 1" and "Tone 2" columns for the N100 component for tables 1,2, and 4.
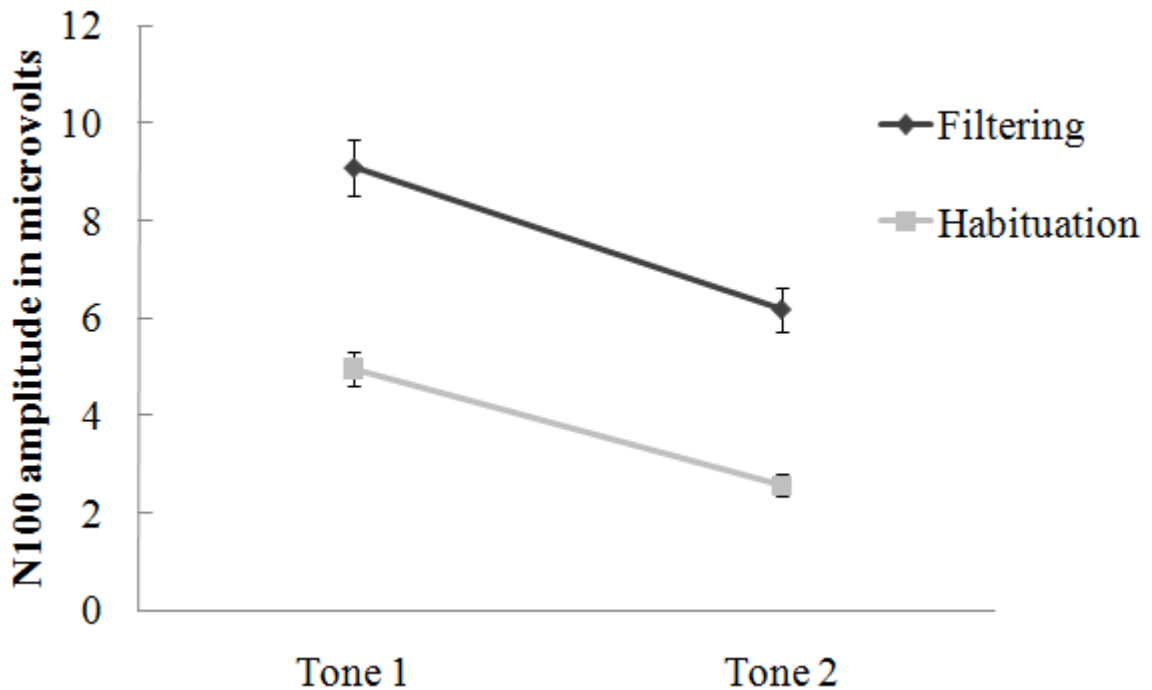
Figure 27: N100 amplitude for the first and second tones in the filtering and habituation paradigms. Bars represent standard error.

For the P200 component, there was a significant main effect for tone, where the first tone amplitude was greater than the second tone amplitude, $F(1,37) = 136.55$, p <.001. There was also a significant main effect for paradigm, where the amplitude for the habituation paradigm was less than the filtering paradigm, $F(1,37) = 43.92$, p <.001. There was also a significant interaction, $F(1,37) = 18.81$, $p < .001$, such that the difference in tone one and tone two amplitude was greater for filtering than for habituation, (see figure 28). For means and standard deviations, see the "Tone 1" and "Tone 2" columns for the P200 component for tables 1,2, and 4.

These results suggest that the amplitudes for the first two tones in the habituation paradigm for the P50, N100 and P200 components were consistently less than the

amplitudes for the first two tones in the filtering paradigm for the P50, N100 and P200 components – even when identical stimuli and ISIs were used for each paradigm. The significant interactions revealed that the magnitude of gating was greater for filtering compared to habituation for the P50 and P200 components. This provides additional evidence that suggests that habituation may be a unique mechanism from filtering. The magnitude of the reduction between the first and second tones was less for the habituation paradigm, which suggests that habituation may be a more gradual process than filtering.

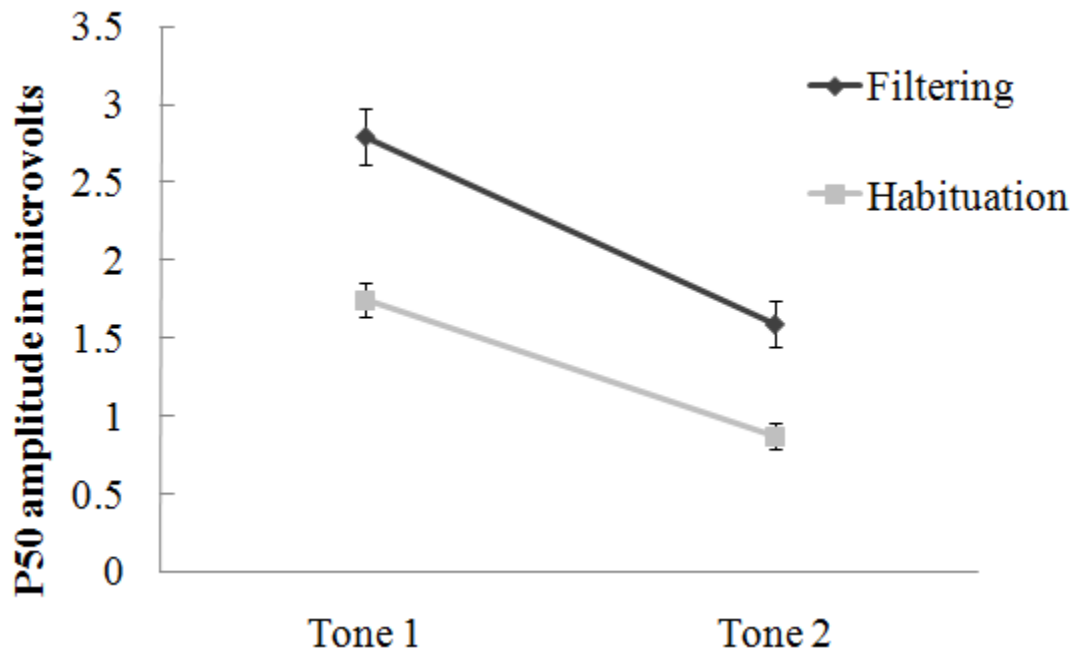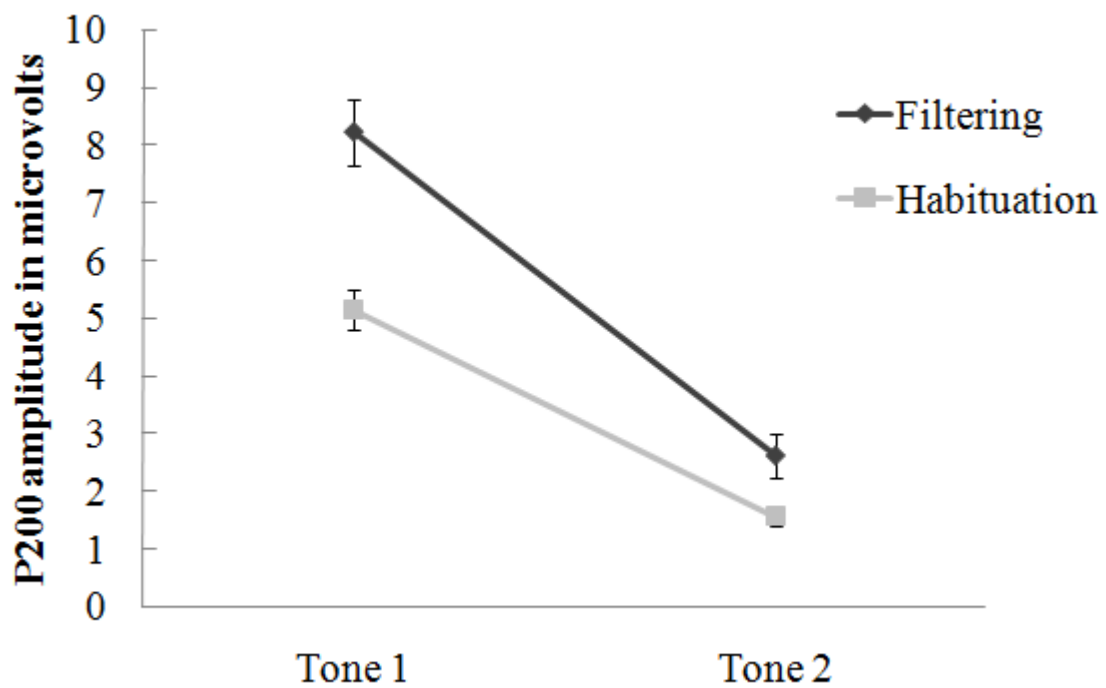*Figure 28*: P200 amplitude for the first and second tones in the filtering and habituation paradigms. Bars represent standard error.

Many of our results from this chapter are consistent with prior research as outlined above. If P50, N100, and P200 habituation were assessing the same process as filtering, there should not have been overall amplitude differences for these two

paradigms and the amplitude in the habituation paradigm should not have decreased after the second tone. We found that there was an amplitude reduction in the habituation paradigm for some tones after the second tone for the N100 and P200 components, but no amplitude reduction for the P50 component. We also found that amplitudes were consistently lower for each component for the habituation paradigm compared to the filtering paradigm. Our finding of consistently lower amplitudes for the habituation paradigm and amplitude reductions beyond the second tone for the habituation paradigm suggests that filtering and habituation are not measuring identical neural processes. In other words, the habituation paradigm appears to be providing different information from the filtering paradigm, even when identical stimuli were used. Our inclusion of the P200 component in these results is novel, as the P200 component has not yet been explored in a habituation paradigm and has only begun to be explored in a filtering paradigm. By including the P200 component in these analyses we can – at least preliminarily – establish that the P200 component provides unique data from the P50 and N100 components. For example, the P200 was not correlated with any other component, suggesting it may be reflecting a different level of processing. It also was somewhat influenced by short-term habituation and discriminated between filtering and habituation in terms of the amplitude reduction between the first and second clicks.

Chapter 5: The study of the functional significance of sensory gating

Rationale

The functional relevance of sensory gating is not well understood. It has been speculated for nearly five decades that sensory overload may affect higher level processes (Venables, 1964). One explanation is that poor gating results in an overload of sensory information, and the sensory overload, in turn, produces "downstream" effects on cognition. Along these lines, some researchers suggest that P50 filtering deficits may account for, or contribute to, auditory hallucinations of schizophrenia (Adler et al., 1998), particularly hallucinations of human voices (Hirano et al., 2010). There is also evidence to suggest that healthy adults who have poor auditory filtering feel more distracted by auditory stimuli in their environment (Kisley et al., 2004). Another explanation is that poor attention or executive function may reduce the effectiveness of sensory gating processes. A third explanation is that deficits in frontal lobe functioning impair both gating and executive function. Investigators have noted the dearth of empirical studies that have examined the relationship between sensory gating and higher-level (cognitive) processing (e.g., Potter et al., 2006).

Attention and executive function have successfully been related to sensory gating. For example, although filtering is thought to be mostly preattentive (Jerger et al.,1992; Kho et al., 2003), attentional allocation has been found to influence P50 filtering (Guterman & Josiassen, 1994; Guterman, et al., 1992). Specifically, participants were instructed to selectively attend to (count) high or low frequency clicks. In this study, attention to the stimuli resulted in worse filtering. In addition to selective attention, P50 filtering has been related to other neuropsychological measures of attention and to some

neuropsychological measures of executive functioning. For example, in one study, individuals with schizophrenia were grouped based on P50 filtering abnormalities. The high abnormality group performed worse on the Gordon continuous performance test (CPT) and Trail Making Test- Part B, and marginally worse on a digit symbol test than the low abnormality group (Erwin, Turetsky, Moberg, Gur, & Gur, 1998). Another study reported a positive relationship between digit vigilance and P50 filtering in schizophrenia (Cullum et al., 1993). Boutros et al. (2009) found that N100 filtering positively correlated with perseverative errors on the Wisconsin Card Sorting Task (WCST) in schizophrenia patients. One of their control participants had very poor scores on the WCST and they also had poor N100 filtering. The authors noted that frontal lobe deficits relating to sensory gating might not be limited to clinical group and might also be related in control participants. A few studies have found that deficits on executive function tasks were related to sensory gating deficits in healthy adults (Lijffift, Lane et al., 2009; Yadon, Bugg, Kisley, & Davalos, 2009).

Further motivation for examining a relationship between sensory gating and higher level processes is that most of the clinical groups who have sensory gating deficits also perform poorly on attentional and executive function measures (Braff and Light, 2004). For example, individuals with schizophrenia are impaired on Stroop tasks (Cohen, Barch, Carter, & Servan-Schreiber, 1999), verbal working memory tasks (Conklin, Curtis, Katsanis, & Iacono, 2000), and visuospatial working memory tasks (Chey, Lee, Kim, Kwon, & Shin, 2002). It can be speculated that there are overlapping neurological structures involved. Support for this comes from studies that implicate similar structures for both executive function and sensory gating tasks. For instance, the

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dorsolateral prefrontal cortex has been implicated in P50 filtering (Korzyukov et al., 2007) and also for executive functions (Curtis & D'Esposito, 2003).

In order to relate sensory gating to higher-level processes, we compared sensory gating to the performance on several neuropsychological measures of attention. These tasks fell on a continuum that, on one end, included the least complex tasks that only required low levels of attention and, on the other end, the most complex tasks that required high levels of attention. We administered a variety of these tasks in an effort to tease apart which degree of attentional allocation may be related to different types of sensory gating, and also the different ERP components. Based on Sternberg's additive factor model (Sternberg, 1969) we specifically chose tasks that had two parts – an easier task followed by a more difficult task. By using this additive model, we were able to investigate the relationship between lower-level attention tasks and higher-level attention tasks while using the same tasks for both.

Sensory gating has been hypothesized to protect high level functions (Lijffijt, Lane, et al., 2009), and the existing evidence suggests that frontal-lobe dependent tasks are among the few that have related to sensory gating (e.g., Lijffijt, Lane, et al., 2009). Because of this, we predicted that participants' responses on sensory gating measures would be related to higher-level cognitive processes such as the high level attention/executive function tasks. We also predicted that low level attention tasks, such as those that only required simple motor speed or naming colors would not be related to sensory gating measures (e.g., Stroop word reading, Stroop color naming, Part A of the Trail Making Task, and the Crossing off A's task.).

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An additional assessment of the functional significance of sensory gating was whether different sounds produce different gating responses. If sensory gating has a functional purpose, it is likely that the degree of gating would depend on the type of sounds that are entering the system. The vast majority of filtering studies have used clicks as their stimuli. Click sounds are brief, discrete bursts of energy that produce very clean ERPs and are widely used in this area of research. However, we live in rich environments that contain a wide variety of sounds – not just clicks. It was previously mentioned that some studies have employed brief tone sounds as an alternative to clicks and were able to achieve gating using tones (Ninomiya et al., 2000). There has been very little work that has branched out to explore how the brain filters different types of sounds, such as to real-world stimuli (Tregellas, Ellis, Shatti, Du, & Rojas, 2009). We measured filtering to high-frequency stimuli (salient) and low-frequency stimuli (less salient). We predicted that more salient tones (potentially noxious stimuli) will be filtered worse than less salient sounds (non-noxious stimuli). This finding might suggest that the brain is less likely to filter a salient sound because it may have important meaning that should not be gated-out.

Data analysis

Effects of the experimental manipulations

Testing whether higher-frequency tones have higher amplitudes

Salience refers to how noticeable a stimulus is. High-intensity or high-frequency sounds are often described as more salient than lower-intensity, lower-frequency sounds (Lehto & Buck, 2008). Sounds that are considered to be more noticeable also tend to produce a greater ERP amplitude (Brenner et al., 2009). For the present study, we

operationalized noticeability as a greater amplitude for higher frequency sounds compared to lower frequency sounds. We tested this assumption using data from the sensory registration paradigm by comparing amplitude for high intensity higher frequency tones (3000 Hz) to high intensity lower frequency tones (1000 Hz), using a dependent samples t test. More salient sounds have greater amplitudes; therefore, if the 3000 Hz tone is more salient, it should have a larger amplitude compared to the 1000 Hz tone.

Cognitive tasks performed as expected

Because we compared higher-level cognitive tasks to lower-level cognitive tasks, it was important to ensure that we achieved the typical effects for our cognitive tasks, such that our participants performed significantly worse on the tasks that were considered to be higher-level (i.e., more difficult). Using dependent samples t tests, we compared performance for the more difficult version of a task to the easier version of a task. Specifically, we compared performance on Selective A's versus Crossing off A's; Digit Span Backwards versus Digit Span Forwards; Stroop color naming versus Stroop color word naming; and Trails B versus Trails A.

Additional research questions

Potential relationship between gating and cognitive tasks

The Pearson product-moment correlation was used to explore the relationship between filtering and orienting and all of our cognitive tasks for the P50, N100 and P200 components. Hierarchical regression was used to determine if a cluster of higher level cognitive tasks predicted gating (filtering, orienting, and habituation) significantly better than a cluster of lower level cognitive tasks.

Salience and filtering

Using a dependent samples *t* test, we compared filtering for the 1000 Hz tone to the 3000 Hz tone.

Results and Discussion

Effects of the experimental manipulations

Testing whether higher-frequency tones have higher amplitudes

Although we expected higher-frequency tones in the sensory registration paradigm to have higher amplitude, we did not find that the amplitude for the 3000 Hz tone ($M = 8.35$, $SD = 3.25$) was different from the 1000 Hz tone ($M = 8.99$, $SD = 3.33$), for the N100 component, t (41) = 1.75, $p = .087$, or that the amplitude for the 3000 Hz tone ($M = 5.97$, $SD = 3.77$) was different from the 1000 Hz tone ($M = 5.44$, $SD = 3.37$), for the P200 component, t (41) = 1.65, $p = .107$.

Cognitive tasks performed as expected

As was expected, all of the higher-level versions of the cognitive tasks were significantly more difficult than their lower-level counterparts. Specifically, the Selective A's task ($M = 51.86$, $SD = 7.72$) was more difficult (i.e., participants completed fewer items) than the Crossing off A's task ($M = 149.05$, $SD = 21.16$), t (41) = 31.55, $p < .001$; Digit Span Backward ($M = 3.13$, $SD = 1.00$) was more difficult (i.e., participants completed fewer items correctly) than Digit Span Forward ($M = 5.10$, $SD = 1.07$), t (38) = 10.07, $p < .001$; Stroop color naming ($M = 66.34$, $SD = 17.41$) was more difficult (i.e., participants completed fewer items) than Stroop color word naming ($M = 54.21$, $SD = 9.88$), t (37) = 3.94, $p < .001$; and Trails B ($M = 50.87$, $SD = 14.50$) was more difficult

(i.e., participants took longer to complete the task) than Trails A ($M = 21.40$, $SD = 7.45$), t (38) = -14.51, $p < .001$.

Additional research questions

Salience and filtering

For the P50 component, we did not find a filtering difference between high-frequency ($M = .56$, $SD = .30$) and low-frequency ($M = .64$, $SD = .34$) tones, t (40) = 1.31, $p = .199$. For the N100 component, we did not find a filtering difference between high-frequency ($M = .64$, $SD = .32$) and low-frequency ($M = .71$, $SD = .31$) tones, t (40) = 1.36, $p = .181$. Finally, for the P200 component, we did not find a filtering difference between high-frequency ($M = .30$, $SD = .25$) and low-frequency ($M = .30$, $SD = .26$) tones, t (39) = .124, $p = .902$.

However, our manipulation verification failed for this analysis (no amplitude difference between high and low-frequency tones). Because the amplitude of brain response to high-frequency tones were not significantly different than the amplitude of low-frequency tones in the sensory registration paradigm, we did not expect the sensory gating to be different when comparing gating elicited by the two different frequency stimuli.

Relationship between gating and cognitive tasks

For the filtering paradigm, P50 filtering was not significantly related to any cognitive measures. N100 filtering was significantly related to performance on the Selective A's task, $r(39) = -.401$, $p = .009$, suggesting that better filtering (smaller numbers correspond to better filtering) was associated with more A's selected (see figure 29). P200 filtering was not significantly related to any cognitive measures.
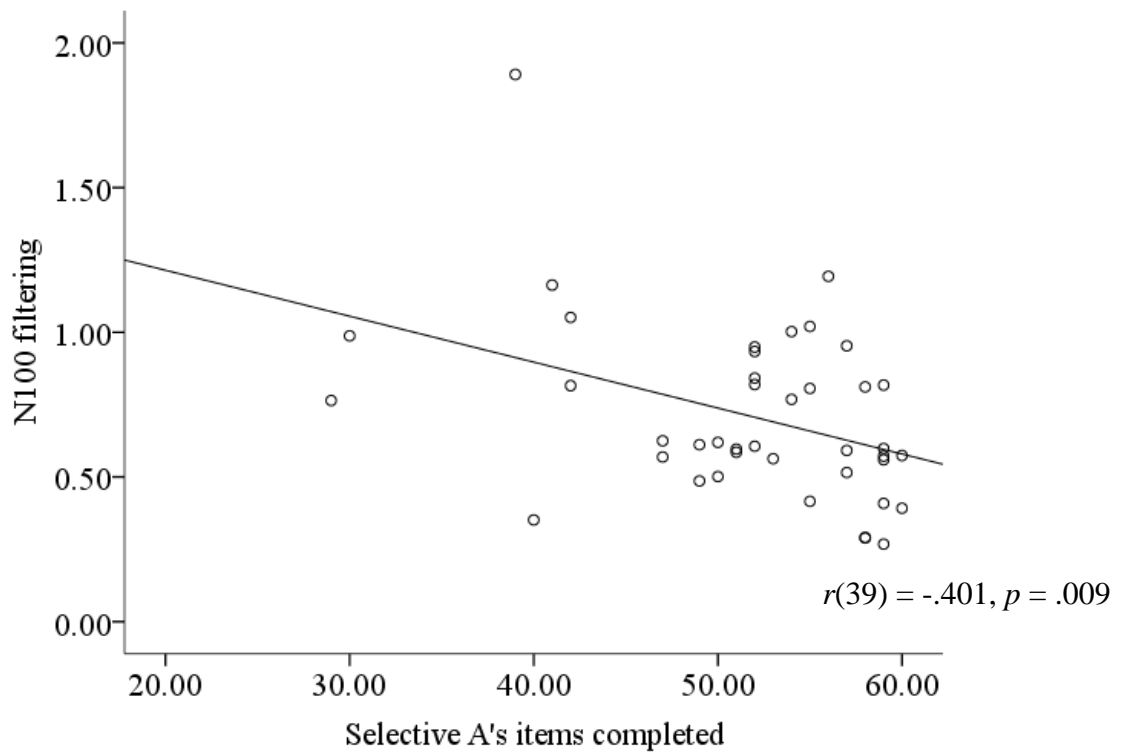
Figure 29: Relationship between N100 filtering and Selective A's performance

For the orienting paradigm, P50 orienting was not significantly related to any cognitive measures, N100 orienting was significantly related to the Selective A's task, $r(37) = .347, p = .030$, suggesting that better orienting was associated with more A's selected (see figure 30, a); and the Stroop color word performance, $r(37) = .321, p = .046$, suggesting that better orienting was associated with better Stroop performance (see figure 30, b). P200 orienting was not significantly related to any cognitive measures.
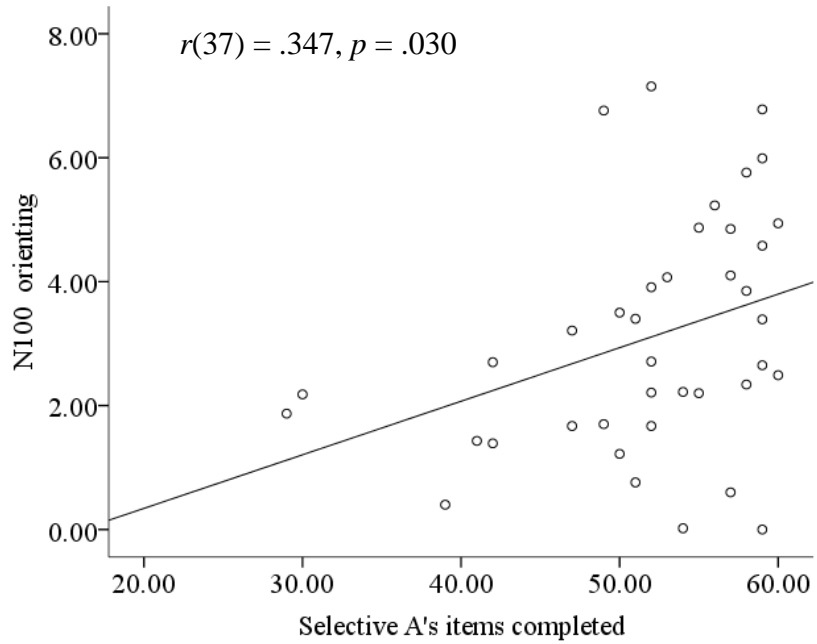
(a)
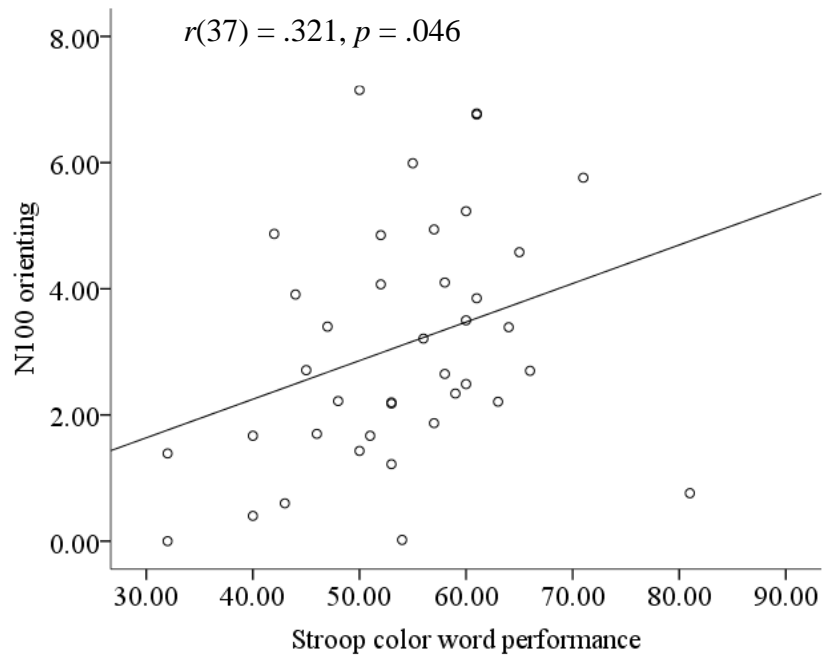
(b)

Figure 30: Relationship between N100 orienting and Selective A's performance (a), and Stroop color word performance (b).

For the habituation paradigm, P50 habituation was not significantly related to any cognitive tasks, N100 habituation was significantly related to Stroop color word performance, $r(37) = .322$, $p = .046$, suggesting that better habituation was associated with better Stroop performance (see figure 31). P200 habituation was not significantly related to any cognitive measures.
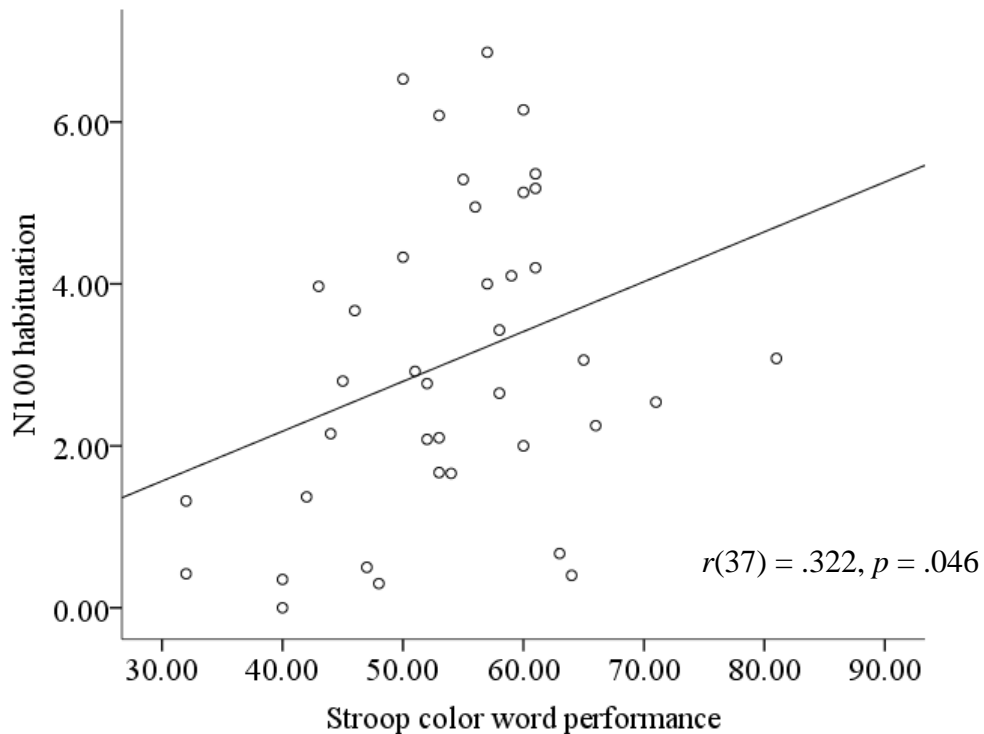
Figure 31: Relationship between N100 habituation and Stroop color word performance

Two primary results emerged from the previous analyses. The first is that sensory gating was related to cognitive tasks, which provides support that gating has a functional significance. The second is that the relationships between sensory gating and the neuropsychological tasks tended to be for higher-level attention tasks (Selective A's and Stroop Color Word performance) as opposed to lower-level attention tasks (e.g., Crossing off A's and Stroop word naming). This pattern was what we predicted. One

interpretation of this pattern of results is that freeing up resources for higher level functions is more important because higher level functions require more resources than lower level functions.

To further determine whether higher level tasks are more related to gating than lower level tasks, hierarchical regression was used to see whether a group of higher-level attention tasks was a better predictor of sensory gating responses than a group of lower level attention tasks. For Step 1 the group of lower level tasks, the control variables, (Crossing off A's, Digit Span Forward, Stroop word naming, Trails A) were entered into the model and in Step 2 the higher level tasks, the variables of interest, (Selective A's, Digit Span Backward, Stroop color word naming, Trails B) were entered into the model. In the filtering paradigm for the N100 component, there was a significant increase in predictability between the first step, $R^2 = .097$ (adjusted = -.013), F change, $F(4,33) = .88$, $p = .49$, and second step, $R^2 = .401$ (adjusted = .236), F change, $F(8,29) = 3.68$, $p = .02$ with no significant differences for other paradigms or components (see table 6).

Table 6

Cognitive predictors of filtering for the N100 component.

Step 1	β	T	p
Crossing off A's	-.211	-1.23	.229
Digit Span Forward	-.176	-1.02	.316
Stroop word naming	.006	.035	.973
Trails A	.067	.386	.702
Step 2	β	T	p
Crossing off A's	.020	.120	.905
Digit Span Forward	-.336	-1.86	.073
Stroop word naming	.095	.525	.604
Trails A	-.070	-.412	.684
Selective A's	-.509	-2.62	.014
Digit Span Backward	.352	1.93	.063
Stroop color word naming	-.287	-1.41	.168
Trails B	.180	-.798	.431

* *p* < .05

In addition to the finding that higher-level attention tasks related more to sensory gating than lower-level attention tasks, most of the relationships with sensory gating were for an attentive stage of processing, the N100 component, and not for the more

preattentive stage of processing, the P50 component. This suggests that the attention

tasks we measured at the behavioral level were related to the neurophysiological

component associated with attentional processing. These results were in the predicted

direction. If cognitive measures of attention tend to relate more to sensory gating in later

stages of the auditory processing stream (attentive) versus earlier stages of the processing

stream (preattentive), then it reasons that the P200 would also show these relationships.

However, in our results the P200 did not relate to any of our measures of attention. One

explanation for this is that the P200 component may not be specifically reflecting

attentional processing. Although some papers classify P200 as a late attentive stage (e.g.,

Wan et al., 2007) it is possible that this is not the case. For example, some work suggests

that N100 component represents selective attention, but the P200 component represents

early processing from the auditory cortex (Polich, 1993). Additional research is

necessary to understand the P200 and its relationship to attention, as there is a well

defined body of literature linking N100 component to attention, but scarce work linking

P200 to specific cognitive processes.

Chapter 6: General Discussion

This dissertation investigated several facets of sensory gating in an effort to better understand how sensory gating relates to more basic qualities of auditory processing, how different sensory gating paradigms and components relate to one another, and the functional significance of sensory gating. Gating-out was explored by measuring filtering and habituation. Gating-in was explored by measuring orienting.   We reported data across three middle-latency components – P50, N100, and P200 – which are thought to represent different aspects of sensory gating due to their differential susceptibility to attentional modulation.

In chapter three we compared sensory gating to basic auditory processing. Our first important finding was that in all three paradigms, we found significant sensory gating, which was consistent with previous research. We also found that auditory detection and organization were related to sensory gating measures. Specifically, discrimination was related to orienting and habituation whereas organization was only related to habituation. Filtering abilities did not relate to basic auditory processing.

In chapter four we investigated sensory gating as a mechanism. We found that our predictions were upheld in that the P50, N100, and P200 components tended to not be related within each of the sensory gating paradigms. Furthermore, filtering, habituation and orienting generally were not related. These results suggest that the three types of sensory gating that we explored are different processes and the three components we explored are reflecting different aspects of sensory gating. Very few studies have been conducted to determine whether habituation and filtering, measured using EPRs, are the same mechanisms. The few studies that have investigated this question produced

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inconclusive results. We found that amplitudes were less for the first two tones in the

habituation paradigm compared to the filtering paradigm and that for the N100 and P200

components amplitudes decreased significantly after the second tone, revealing a short-

term habituation effect over and above the typical filtering effect. Thus, our data provide

support that filtering and habituation are reflecting different types of neural processing,

especially in the later stages of processing. This may be because processing at the stage

of the N100 and P200 components are thought to be modulated by attentional processing.

In contrast, that attentional influence has not been strongly associated with the P50

component (Wan et al., 2007).

In chapter five we compared sensory gating to neuropsychological tasks of

attention and measured the strength of filtering to two different tone sounds. We found

that filtering, orienting and habituation were related to neuropsychological measures of

attention and that higher-level attention tasks were better predictors of gating than lower-

level attention tasks, specifically for the N100 component. We did not find a difference

in filtering for low versus high-frequency tones. Overall, the findings from this

dissertation have both theoretical and methodological implications.

Theoretical contributions

Sensory gating related to more basic auditory processes

Gating has not previously been related to more basic auditory processes in the

way that it was in the present study. One option for relating gating to simpler auditory

processes is to use single stimuli in the same paradigm. For example, amplitude for the

first or second tones could be related to the amplitude ratio in a filtering paradigm. But,

this type of comparison may be biased because both measures originate from the same

paradigm and data from the single clicks are included in the amplitude ratio. We used a

separate auditory registration paradigm that measured how well the brain could

differentiate among stimulus types and then related those responses to sensory gating.

Our findings that discrimination and organization relate to sensory gating suggest that

simple ERP responses can predict the magnitude of the sensory gating response.

However, only orienting and habituation were related to discrimination and organization;

filtering was not. This may suggest that filtering occurs regardless of the effectiveness

of the brain's early auditory processing, whereas for habituation and orienting, more

basic auditory processing needs to be functioning well. For orienting, it suggests that the

ability to process basic qualities of sound makes the brain better able to orient to novelty.

Because filtering has been shown to occur when non-identical stimuli are used (Moura et

al., 2010), filtering may be a less precise process compared to habituation. This may

explain why habituation, but not filtering, was related to more basic auditory processing.

Understanding how more basic auditory responses relate to sensory gating will allow us

to explore auditory processes in a more global context versus as isolated paradigms and

may have implications for clinical groups.

   Components as unique aspects of sensory gating in the auditory processing

   stream

   Previous research suggests that different components in ERP paradigms relate to

different behaviors. For this study, we were interested in whether the P50, N100 and

P200 components indexed different aspects of sensory gating. Prior evidence suggests

that these components are unique (e.g., Kisley et al., 2004) and it has been suggested that

we should examine these each separately in clinical groups who are known to having

gating difficulties, such as schizophrenia patients (Boutros et al., 2004). The results from the present study corroborate past research and suggest that these components are unique because they were not related to each other and because the strength of gating was different across the different components.

Habituation versus filtering

Some research has compared filtering to short-term habituation, using identical paired tones to assess filtering and a series of identical tones to assess habituation. Prior research has produced mixed results and there are only a handful of studies that have ever made this comparison. Our evidence suggests that short-term habituation is occurring after the typical filtering effect has been completed. However, this was only the case for the N100 and P200 components – the P50 component did not demonstrate an amplitude reduction past the second tone, which replicates past work (Rosburg et al., 2006). Therefore, the short-term habituation effect was revealed for later (attentive) stages of processing and not earlier (preattentive) stages. One important reason for determining whether different types of sensory gating are unique processes and which components revealed certain effects are that they could potentially be used as diagnostic tools in clinical groups. Therefore, more work should be done to understand habituation as a mechanism, how it might differ from filtering and to determine if we can achieve a dissociation for these processes among different clinical groups.

Functional significance

Most of the sensory gating research concerns filtering and scant research goes on to investigate functional significance. Relating the neurophysiological processes of sensory gating to various neuropsychological tasks of attention allowed us to speak to the

functional significance of sensory gating. We found that sensory gating was related to attention tasks and which tasks depended on which type of sensory gating was being compared. Also, as predicted, higher-level cognitive tasks were related to sensory gating as opposed to lower-level cognitive and behavioral tasks. This supports work that has related sensory gating to cognitive processing in clinical groups (e.g., Boutros et al., 2009) and healthy adults (e.g., Lijffijt, Lane, et al., 2009). In their study with healthy adults, Lijffijt, Lane et al. (2009) reported that better P50 filtering (measured as a ratio) was related to fewer commission errors on a delayed memory task. This delayed memory task was framed as a complex task and was conceptually similar to the high-level attention tasks used in the present study. They also found that better gating (measured as a difference score) was related to more correct detections on the delayed memory task. In both cases, the results are consistent with the present report – that better gating is associated with better cognitive performance. Our study provides unique contributions to the literature. For example, we used hierarchical regression analysis to predict sensory gating from cognitive performance. We also used an additive model for our cognitive tasks, which allowed us to explore what a more difficult version of a task contributed beyond a simpler version of the task. Finally, we used four different types of attentional tasks.

For both the correlation measures as well as for the hierarchical regression, only the N100 component related to the neuropsychological measures of attention. This is consistent with other research that found a relationship between sensory gating at the N100 component and cognitive measures (e.g., Boutros et al., 2009; Lijffijt, Lane, et al., 2009). One reason the N100 may be sensitive to relating sensory gating to cognition is

because it reflects an attentive stages of processing (e.g., Kisley et al., 2004; Wan et al., 2007). This may be particularly true when cognitive measures of attention were used, as were in the present study.

Neurophysiological sensory gating as a mechanism for behavioral attentional allocation

Overt behavior is often predictable when individuals are exposed to sounds. For example, when an unexpected or novel sound is presented, the typical response is an orienting response characterized by an involuntary attention switching to the sound. When redundant auditory information is presented, the typical response is a steady waning of attention with each presentation (Leslie, 1996). The sensory gating ERPs reported in the present study may be the neurophysiological underpinning of those behavioral responses. For example, our pattern of results that short-term habituation occurs during the attentive stage of processing but not for the preattentive stage of processing suggests that the neural habituation we are measuring through ERPs might represent the decline in behavioral attention that is associated with habituation. The relationship between attention and sensory gating is not well understood. Research relating the two constructs has been contradictory (e.g., Guterman et al., 1992; Jerger et al., 1992). This very complex relationship will require future studies to pinpoint how attention is related to sensory gating and how the sensory gating mechanism may be manifested in observable behavior.

Methodological contributions

Most sensory gating studies have examined filtering in isolation and typically only report from the P50 component. In this study, filtering was investigated along with

habituation and orienting and we reported from the P50, N100, and P200 components. To our knowledge, our versions of filtering, habituation, and orienting have never been measured in the same study and never directly compared. We matched the stimuli and stimulus parameters across the three types of sensory gating, which permitted a direct comparison between these measures. The only discrepancy between the paradigms was that the ITI for filtering was a fixed 8 seconds whereas the ITI for the paradigm that contained the habituation and orienting measures was a fixed random value between 8-10 seconds in increments of half a second. We do not know if this impacted our results, but cannot rule out that expectation effects influenced amplitude for the first click in the filtering compared to the habituation paradigm. For example, expectation may increase EEG amplitude (Hari, Sams, & Järvilehto, 1979) and because we had a fixed interval (leading to more expectation) for the filtering paradigm, it is possible that the filtering paradigm had greater amplitude for this reason. Another explanation why the amplitudes were consistently greater in the filtering paradigm may be because the filtering paradigm was always conducted on the first visit to the lab and the habituation paradigm was always conducted on the second visit. It is possible that after being exposed to the sounds on the first day, the amplitude was suppressed on the second visit. Our examination of three middle-latency components (P50, N100, P200) allowed us to investigate whether data from these components was very similar or suggested that we were indexing different processes.

An additional methodological contribution was our use of tone stimuli in all three sensory gating paradigms. We achieved significant sensory gating in every paradigm and these results suggests that 1000 Hz tones produce results that are similar to what has been

reported in numerous studies with clicks. One potential concern one might raise for the use of tone sounds in a sensory gating paradigm is that they are less discrete and last longer (50 ms for tones versus a few ms for clicks) and thus might produce more variable responses. However, we found that the variability for tones was not suspiciously high and we were able to achieve significant sensory gating in all three paradigms. Our results replicate the few other studies that used tone stimuli (Ninomiya et al., 2000). One benefit of using tone stimuli is that they may be more generalizable and representative of sounds heard in the real world.

Future research and overall conclusions

Future research will be necessary to replicate these findings and refine them based on the limitations presented here. For example, it will be important to compare filtering to habituation when a longer ISI is used to ensure that adequate recovery time is achieved in between stimuli[21]. It will also be important to use the same ITI for filtering and habituation to avoid potential expectation effects. More specifically, the ITI for our habituation paradigm was a random value out of five possible ITIs, whereas in the filtering paradigm the ITI was a fixed value. Expectation has been found to increase EEG amplitude (Hari et al., 1979). Therefore, there may have been more expectation in the filtering compared to the habituation paradigm leading to higher amplitudes for filtering. Because of these methodological uncertainties, the interpretation should be cautious until further evidence is reported.

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[21] A 500 ms ISI was chosen because it is typically used in filtering paradigms and produces robust suppression (Dolu, Süer, & Özesmi, 2001). Both 500 ms and 1000 ms ISIs have been used in habituation paradigms and there is preliminary evidence that a 1000 ms ISI may produce greater habituation (Rosburg et al., 2004; Rosburg et al., 2006).

Correlating the attention tasks with sensory gating produced significant effects in this study and is one way to determine if sensory gating has a functional significance. However, it will also be useful to measure sensory gating ERPs while participants are concurrently performing cognitive tasks to more directly measure what types of cognitive processing may impact sensory gating responses.

In chapter five, our prediction that high-frequency tones would not be filtered as much as lower-frequency tones was not supported. We reasoned that higher-frequency sounds would be filtered less because our high-frequency sounds (3000 Hz) were more salient and more similar to frequencies found in human speech. It is possible that the low and high-frequency sounds that were chosen for this study did not have enough saliency to produce this effect. This explanation is supported by our manipulation check for salience that compared amplitude for high and low-frequency tones. We did not find this difference and thus concluded that the higher-frequency tone was not more salient (based on the ERP response pattern) than the lower-frequency tone. It may also be that the frequencies for the two tones were too similar. In the future, comparing a high-frequency tone (such as 3000 Hz) to a tone lower in frequency than 1000 Hz might be distinct enough to produce differences.

This study investigated sensory gating in the auditory modality because nearly all sensory gating studies have explored auditory sensory gating. It is currently not known whether sensory gating is a global mechanism (e.g., there is a structure or structures responsible for coordinating sensory gating across sensory modalities) or a modality-specific mechanism (e.g., each sensory modality has its own sensory gating mechanism). Future work should help determine whether sensory gating is more of a global process or

is modality specific. One way to do this would be to examine a clinical group with a known sensory gating deficit in a given modality and test to see if their sensory gating is impaired for a different modality. In order to compare sensory gating across modalities, (such as visual filtering compared to auditory filtering) investigators must first develop paradigms that can detect sensory gating in the other modalities. Comparing sensory gating ability across modalities would be especially useful with clinical populations because at the present time we do not yet understand the scope of sensory gating deficits outside the auditory modality.

This dissertation investigated three types of sensory gating (filtering, habituation, and orienting) in an effort to better understand: how sensory gating relates to more basic qualities of auditory processing such as discrimination between high-intensity and low-intensity sounds, how the different sensory gating paradigms and components (P50, N100 and P200) relate to one another, and the functional significance of sensory gating such as how sensory gating relates to neuropsychological measures of attention. Results suggested that better orienting and habituation relate to better auditory discrimination. Also, filtering, habituation, and orienting seem to be reflecting different mechanisms and the P50, N100 and P200 components seem to be reflecting different stages of auditory processing. Finally, sensory gating was demonstrated as having a functional significance because sensory gating related to neuropsychological measures of attention, particularly for higher-level (more difficult) tasks for the N100 component, but not for the P50 or P200 components. This dissertation employed several novel methods and analyses, and provides both methodological and theoretical contributions to the literature. Most importantly, it demonstrates that filtering, orienting and habituation seem to be distinct

types of sensory gating that should be investigated more thoroughly in their own right in future studies.

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