GLOBAL PREDICTABILITY AND OMISSION DEVIANTS

NEURAL RESPONSES TO OMISSION DEVIANTS AND THE INFLUENCE OF GLOBAL PREDICTABILITY IN INFANTS AND ADULTS

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LAY ABSTRACT

Often when we expect to hear a sound, instead we “hear” silence or an omission of the sound. This thesis investigates how the brain responds to these unexpected omissions in adults and infants. Unexpected silences elicit a response similar to what we would find after an unexpected change to a sound. This seems to be true for adults and infants as young as 6-months old. Typically, predictable sound changes elicit smaller brain responses. Unlike unexpected sound changes, if the silence occurs predictably in the sequence (e.g., occurs after every 4 tones in a sequence) compared to randomly, or unpredictably, no difference is found. This lack of difference seems to be present in infants and adults. These findings further our understanding of how the brain response to unexpected omissions may not follow the same pattern as the response to unexpected changes of a sound.

ABSTRACT

The human auditory system excels at detecting patterns necessary for processing speech and music. This system is adept at detecting changes to the incoming sounds. According to predictive coding theories, the brain generates hypothesis about what the incoming tone should be, and if the incoming tone does not match the hypothesis, a prediction error response is elicited. This process can be estimated in electroencephalography (EEG) by the mismatch negativity and P3a event related potentials (ERPs) in adults or the mismatch response in infants. It remains unclear is how this system responds to unexpected absence of a sound created by silences.

In this thesis, we compared ERPs in adults (Chapter 2) elicited by infrequent sound omissions — i.e. unexpected silences or omission deviants — in various sequences of tones to those elicited by regularly occurring omissions — i.e., expected silences or predictable omissions. We found that unexpected silences elicited both the MMN and P3a, although the magnitude of these components was considerably smaller than we would expected from previous research with omission deviants and auditory deviants. We also found that infants (Chapter 3) exhibited a neural response to omission deviants similar to the mismatch response. Unexpectedly this was not influenced by the global predictability of the omission deviants, which typically attenuates the ERPs to a deviant when it is globally predictable. Adults also showed a lack of difference between globally predictable and globally unpredictable omission deviants (Chapter 4). Furthermore, in adults, we did not find the typical deviance detection ERP responses. Overall, we found evidence of robust neural responses to omission deviants in both adults and infants, but the context in which the omission deviants can change the ERP components elicited. This dissertation is the first to investigate the direct effect of global predictability on the neural responses to omission deviants, as well as 6-month-old infants' response to omission deviants.

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Table of Contents

List of Figures

CHAPTER 2

CHAPTER 3

CHAPTER 4

List of Tables

CHAPTER 2

CHAPTER 3

List of Abbreviations

μV; microvolts

ANOVA: analysis of variance

BF: Bayes factor

CFL: central frontal left

CFR: central frontal right

CFZ: central frontal midline

CL: central left

cm: centimetre

CR: central right

CZ: central midline

dB: decibels

EEG: electroencephalography

EGI: Electrical Geodesics, Inc.

ERP: event-related potential

F: F-test statistic

FL: frontal left

FR: frontal right

FZ: frontal midline

Hz: Hertz

ICA: independent component analysis

IOI: inter-onset interval

M: mean

m: metre

ms: milliseconds

MMN: mismatch negativity

MMR: mismatch response

N/n: sample size

N1: N1 event-related potential

OL: occipital left

oN1: oN1 event-related potential

oN2: oN2 event-related potential

oP3: oP3 event-related potential

OR: occipital right

OZ: occipital midline

p: p-value

P3a: P3a event-related potential response

TL: temporal left

TR: temporal right

s: seconds

SD: standard deviation

SEM: standard error of the mean

SOA: stimulus onset asynchrony

t: t-test statistic

Declaration of Academic Achievement

The following thesis contains 5 chapters and follows the format of a sandwich thesis. The first chapter is a general introduction, followed by three data chapters. The first data chapter is published, whereas the second and third data chapter have been submitted and are under review. The fifth and final chapter is a general discussion of the main findings of the thesis. I, David Prete, am the author of this thesis and the primary author for all data chapters. For all data chapters, I conceptualized the research with supervision from Dr. Laurel Trainor, organized and completed the data collection with help from Elaine Whiskin and undergraduate students, completed all the data preparation and analyses, and wrote the manuscripts. Dr. Laurel Trainor is the last author on all 3 manuscripts, as she supervised and provided funding for the research, and contributed to the manuscript preparation. Technical support was provided for all three data chapters from Dave Thompson. Two of my previous undergraduate thesis students, David Heikoop and Josh McGillivray, are coauthors on data Chapter 2, they helped with data collection and editing the manuscript. Dr. Jim Reilly listed as the fourth author on that paper as he helped advise the data analysis as well for that data chapter. Stimuli for all three data chapters was created by me using various video and audio software. The stimuli for Chapter 3 and 4 were calibrated with the help of Dave Thompson and Gary Fekete.

Chapters 4 is an extension of Chapter 3, so the methodology, stimuli, and research questions overlap.

Chapter 2 is a reprint of the published article in the European Journal of Neuroscience and has been reprinted with permission from John Wiley & Sons Ltd ("Wiley").

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Chapter 1: General Introduction

Introduction

The human brain is adept at tracking regularities in the sensory information from the environment. Detecting deviations from regularity is important for survival and detecting potentially life-threatening events, but pattern detection goes beyond survival and plays a key role in general perception. Pattern detection is critical for learning languages (Romberg & Saffran, 2010; Saffran, 2001), attention (Large & Jones, 1999), music perception (Huron, 2006; Vuust & Witek, 2014) and perceiving emotions (Barrett, 2017).

In the auditory domain, the brain tracks various types of regularities. These regularities can be simple, such as an isochronous repeating tone (Näätänen et al., 1978), or involve more complex patterns based on patterns of inter-onsets intervals (IOI; Bouwer et al., 2020; Chang et al., 2019; Fujioka et al., 2015), sequences of pitches (Barascud et al., 2016; Southwell et al., 2017), or the statistical regularities in sequences of syllables that aid in learning to extract multi-syllable words (Batterink & Paller, 2017; Romberg & Saffran, 2010; Saffran, 2001). Moreover, perceived regularities do not always stem directly from acoustic properties of the sounds. For example, rhythms in music give rise to a perceived isochronous pulse, often called the beat, that persists even when no sound occurs at the time of some beats. The steady pulse is maintained even when no sound occurs because the previously heard temporally-regular information leads to expectations as to when the next beat should occur. People can also extract multiple levels of regularity, forming hierarchies such as beat and meter in music, or syllables, words, and sentences in language.

A popular method used to investigate the perception of violations of regularities in auditory information is to measure neural activity using electroencephalography (EEG) while presenting stimuli in the oddball paradigm. The oddball paradigm consists of presenting one sound (or pattern) repeatedly, called the standard. Once the standard sound(s) have been established, some feature of the standard is changed, creating a deviant stimulus that occurs infrequently and pseudo-randomly throughout the sequence. Measuring EEG during the oddball paradigm allows us to compare the neural activity elicited by the deviants to activity elicited by standard tones or patterns, to determine if the violation caused by the deviant led to different processing. The violations can come from changing an acoustic feature such as pitch (Näätänen et al., 1978, 2007; Sams et al., 1985), loudness (Jacobsen et al., 2003), or duration (Jacobsen & Schröger, 2003; Näätänen et al., 2004; Tervaniemi et al., 1999), or from changes to more abstract or complex patterns such as a melody (Brattico et al., 2006; Putkinen et al., 2014; Trainor et al., 2002) or rhythm (Bouwer et al., 2014; Bouwer & Honing, 2015; Ladinig et al., 2009). The event related potentials (ERPs) elicited by the deviants compared to the standards have a larger negative peak between 100 and 200 ms after the onset of the deviant, and this difference is called the mismatch negativity (MMN; Näätänen et al., 1978, 2007), which is thought to index violation of expectation. Sometimes the MMN is followed by a larger positive peak between 200 and 300 ms, called the P3a, thought to index capture of attention (Horváth et al., 2008; Soltani & Knight, 2000).

Although a lot of research has been dedicated to studying the MMN, one area of research that is lacking concerns how the brain responds to the omission or absence of a sound when one is expected. Early research using omission deviants found that they can elicit an

MMN, but only if the inter-onset-interval (IOI) is less than 200 ms (Raij et al., 1997; Yabe et al., 1997, 1998). Furthermore, many early studies tended to compare the ERP elicited by the omission deviant to the ERP elicited by the standard sounds; however, it is unclear whether sounds should be compared directly to unexpected silences, since there is no auditory information for the brain to process during a silence. Thus, differences observed in such studies may not be due to processing the omission as a violation of the pattern, but rather a difference between sensory encoding and no sensory encoding.

The goal of this thesis is to investigate neural processing when the deviant in the sequence is an omission. This is important for understanding, for example, how silences within music, speech, and rhythms are processed. Specifically, this thesis compares ERPs elicited by silences presented using different types of oddball paradigms in adults and infants to further our understanding of how a lack of an expected auditory sound is processed, how predictability of the silences might affect these responses, and if the responses to omission deviants are present early in development.

Violations of expectations and the MMN

As mentioned, deviants stemming from various types of changes in the acoustic features of a sound can evoke an MMN, but the magnitude of these changes as well as non-acoustic features can influence the magnitude and latency of the MMN. The latency of the MMN decreases as the magnitude of a pitch or duration deviant increases relative to the pitch or duration of the standard sound(s) (Amenedo & Escera, 2000; Tiitinen et al., 1994). The magnitude of the MMN also increases with decreasing inter-onset intervals (IOIs) between sounds (Javitt et al., 1998; Sabri & Campbell, 2001). Furthermore, even though the MMN is a pre-attentive response, the magnitude of the MMN can increase when attention is directed towards the sounds as opposed to in a passive listening paradigm, that is more commonly used in MMN experiments (Alain & Woods, 1997; Dykstra & Gutschalk, 2015; Haenschel et al., 2005; Raij et al., 1997; Woldorff et al., 1991). Thus, the MMN indexes acoustic change detection in the brain, but it can also be influenced by non-acoustic factors.

The MMN can be elicited not only by simple acoustic deviants but also by unexpected violations in complex or abstract patterns. For example, if pairs of descending pitches are presented as belonging to the category of standard stimuli, presenting an ascending tone pair as a deviant elicits an MMN response (Saarinen et al., 1992; Zachau et al., 2005). The standard tone pairs do not have to be identical, but can consist of different absolute pitches, such that all standard tone pairs have the property that the pitch decreases from the first to second tone. In this case, the presence of MMN in response to occasional presentations of an ascending tone pair indicates that the relative-pitch property of a “falling tone pair” and a “rising tone pair” is abstracted and tracked (Paavilainen, 2013). This effect extends to longer pattens involving more than just pairs of tones (Tervaniemi et al., 1994) and has been reported for violations of chord patterns as well (Brattico et al., 2009; Virtala et al., 2011). In sum, deviance detection, as indexed by the MMN, reflects not only single tone deviations, but deviations from longer or abstract patterns.

The MMN is also sensitive to larger scale regularities in auditory information, which we will refer to as global predictability. For example, if deviants are presented with the same overall probability within a sequence, but presented randomly in one condition (i.e., globally unpredictable), but always presented after a certain number of events in another condition (globally predictable), both deviants will elicit an MMN. However, the MMN elicited by the globally predictable deviants will be attenuated compared to the more globally unpredictable deviants (Bekinschtein et al., 2009; Horváth et al., 2001; King et al., 2014; Wacongne et al., 2011). Deviations that violate multiple levels of predictability, global and local, elicit larger MMN responses. Another example involves creating a metrical structure of strong and weak pulses by alternating louder and softer tones. Presenting occasional intensity increments (deviants) on perceptually weak beats of such a rhythm will elicit larger MMN compared to increments on strong beats (Bouwer & Honing, 2015). Applying occasional intensity decrements on strong beats will also elicit larger MMN than on weak beats (Bouwer et al., 2016), Thus, people form specific expectations for the loudness of incoming tones in rhythmic patterns based on higher-order temporal structure, indicating that the brain tracks not only the regularity of the physical stimuli but also how changes fit within a hierarchy of expectations based on the complex patterns present in the auditory sequence (Friston & Kiebel, 2009; Garrido et al., 2009; Todd et al., 2021; Wacongne et al., 2012).

As mentioned, the MMN is most often studied using the oddball paradigm in which standards and deviant are different stimuli that might, on their own, elicit somewhat different brain responses, creating possible confounds (Ruhnau et al., 2012). Thus, researchers have expanded the experimental designs used to study regularity and deviance detection, by comparing the same tone presented as a deviant in one condition but a standard in another condition (Bekinschtein et al., 2009; Grimm et al., 2011; Moldwin et al., 2017; Shestopalova et al., 2015; Symonds et al., 2017; Todd et al., 2013, 2021). By comparing neural responses to the same stimulus under varying contexts, differences found between conditions cannot be explained by acoustic differences alone, but rather by the contextual differences in which the sounds were presented. Such studies have shown that even with this greater level of control between standard and deviant tones, an MMN is still elicited. Other studies have also included control conditions in which the deviant tone is presented in a sequence of random tones that all have equal likelihood of being presented, sometimes called equal probable conditions (Jacobsen & Schröger, 2003; Ruhnau et al., 2012). Importantly the occurrence rate of each tone in the equal probable condition is set to the same rate as the deviant tone in an oddball condition; for example, if 10% of the trials are deviant tones in the oddball condition then each tone in the equal likelihood condition would make up 10% of the trials. Then the ERP to the same tone is compared when the tone is a deviant, a standard, or a occurs in a sequence with no regularity, thus, controlling for acoustic features and possible effects of refractory periods due to differences in presentation rates. The MMN is still measurable when comparing the neural responses in all these control conditions, indicating that the brain is truly sensitive to violations of regularities in auditory streams.

Mismatch Response in Infants

Infants also show a neural deviance detection response in auditory sequences but, using the typical oddball paradigm, the neural response measured in young infants typically does not appear like the adult MMN, although some researchers have reported an MMN to pitch deviants in infants (Fellman et al., 2004; Hirasawa et al., 2002; Kushnerenko et al., 2002; Morr et al., 2002). Many researchers have found a slower frontally positive response to deviants that peaks around 250 to 300 ms post deviant onset, often called the Mismatch Response (MMR; He et al., 2007). This slower positive response has been observed after pitch changes (Fellman et al., 2004; He et al., 2009b), descending deviant tone pairs among ascending tone pairs (Carral et al., 2005; He et al., 2009a), and even changes in speech sounds (Dehaene-Lambertz, 2000). Systematic evaluation of the MMN and MMR responses in infants suggest adult-like MMN does not start to appear until 4 months of age, but the MMR can still be observed well beyond 6 months old (He et al., 2009b; Kushnerenko et al., 2002), with some infants showing both responses (He et al., 2007, 2009b), suggesting that they represent different deviance detection mechanisms. Whether the response is positive or negative, there is clear evidence that the infant brain has a mechanism for deviant detection in auditory streams.

Deviance detection in infants can be elicited by more complex changes to the stimuli as well. Violations based on presenting infrequent unpleasant dissonant chords in a sequence of pleasant consonant chords has evoked MMRs in newborn infants (Virtala et al., 2013), suggesting infants abstract the sound quality of the auditory information not just the absolute pitches presented to them. Deviant pitch increases embedded in melodies of descending pitches will only elicit an MMR if the pitch deviant occurs later in the melody rather early indicating that the expectation requires successive events before the overall pattern is established (Háden et al., 2015). The infant MMR will be larger in amplitude when the deviant tone occurs on a strong pulse in a rhythm compared to a weak pulse (Flaten et al., 2022; Háden et al., 2024; Winkler et al., 2009), or deviants that violate local and global predictability compared to deviants that only violate local or global predictability (Basirat et al., 2014). The MMR has even been elicited when the number of tones at a specific pitch is greater than expected (Ruusuvirta et al., 2009). Thus, even at very early stages of development the brain tracks various regularities in auditory events and reacts to deviants involving hierarchical regularities and abstract properties of auditory streams.

Omissions as deviants

Although it is important to track acoustic changes in auditory regularities, it is also crucial to know how the brain responds when expected sounds do not occur, known as an omission deviant. The lack of a stimulus can be just as important as the as the presence of a stimulus. Some of the first studies to use omissions as deviant "stimuli" employed a typical oddball paradigm to study MMN responses to omissions at various IOIs (Raij et al., 1997; Yabe et al., 1997, 1998). Omission deviants elicited an MMN, but only if the IOIs were 200 ms or shorter. Since then, omission deviants have been used many times to investigate more complex or abstract pattern learning using fast presentation rates (Bendixen et al., 2009, 2014; Chennu et al., 2016; Hughes et al., 2001; Oceak et al., 2013; Recasens & Uhlhaas, 2017; Tse et al., 2006; Wacongne et al., 2011, 2012). Using IOIs of 1 and 2 seconds, Busse and Woldorff (2003) did not find a MMN or P3a in response to an omission deviant. Instead, they found a late positive response around 300 ms that depended on deviant occurrence rate, such that higher occurrence rates led to an attenuated response.

However, only observing an MMN to an omission deviant if the IOIs are less than 200 ms does not mirror the fact that the MMN elicited by auditory deviants is commonly observed with IOIs up to a second, and can even be observed with IOIs up to 4 seconds (Näätänen et al., 2005, 2007). Furthermore, 200 ms is thought to be the temporal window of integration, in which two successive sounds can be perceived as one single event (Horváth et al., 2007; Rüsseler et al., 2001; Shinozaki et al., 2003) and shorter IOIs necessitate shorter tones, for which some acoustic information becomes ambiguous (Doughty & Garner, 1948; Oceak et al., 2013). Additionally, most studies that employ omission deviants compared omissions (deviants) to sounds (standards) (Horváth et al., 2007; Rüsseler et al., 2001; Salisbury, 2012; Shinozaki et al., 2003; Winkler et al., 2009). Comparing an omission to a sound may not be fair a comparison, as tones have acoustic features that activate the auditory neural pathway while omissions do not. A better control would be to compare omissions, or silences, under varying contexts, as more modern experimental paradigms done with auditory (sound) deviants.

Researchers who have compared omission deviants under multiple conditions have mostly employed audio-motor integration, in which button presses produce sounds, with the sound on some button presses infrequently omitted (SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013; Korka et al., 2020), or audio-visual integration, in which sounds are paired with a video of movement, such as a hand clap, and the sound is infrequently omitted from the hand clap (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). Thus, the audio-motor experiments have participants generate the sounds via button presses, comparing conditions in which, say, 12% of the button presses do not elicit a sound – these are the omission deviants – to conditions in which 50% of button presses do not elicit a sound and therefore do not violate expectations (SanMiguel, Widmann, et al., 2013). In this case, rare omission deviants elicited two negative peaks, one just before 100 ms and the other peak around 150 ms, that were not present in the ERP response to frequent omissions. Overall, this suggests omission deviants elicit specific ERP responses and omissions may isolate neural activity due to deviance detection from neural activity due to both deviance detection and processing auditory information (SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013).

These omission-related ERP components have since been called the oN1 and oN2. Some studies have found a third positive component called the oP3 (Dercksen et al., 2020; SanMiguel, Saupe, et al., 2013). The oN1 is a negative deflection in the ERP waveform between 40 and 90 ms that appears maximally around the left and right temporal region of the scalp using a nose reference. The oN2 is a fronto-central negativity that peaks around 150 ms relative the omission onset. Source analysis of both the oN1 and the oN2 indicates generators of the ERP components are located in the superior temporal gyrus, near auditory cortices (SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). The oP3 is a central positivity that peaks between 250 and 325 ms after the omission onset.

These omission-specific ERP components have also been found to be elicited in audio-visual videos of motor-generated sounds, specifically, deviants consisting of claps with no sound in comparison to standards consisting of claps with sounds (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). Rare omissions of the auditory information in this audio-visual paired context were found to lead to increased oN1 and oN2 amplitude compared to frequent auditory omissions. Interestingly, both rare and frequent omission deviants elicited an oP3 component, but the amplitude of the oP3 did not differ between conditions. Importantly, these audio-motor and audio-visual experiments included a motor only or visual only condition to remove modality-specific ERP components and isolate neural activity caused by the sound omissions. Source localization of the oN1 and oN2 for audio-motor stimuli have found generators of the component within the superior and middle temporal gyrus near auditory cortex (SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). Similar regions have also be found to be the source of the omission related components during audio-visual stimulation as well (Stekelenburg & Vroomen, 2015), and neural activity to omissions in rats have found responses in auditory regions as well (Lao-Rodríguez et al., 2023). The presence of similar ERP components and source generators across experiments suggests that these components are specific to the violation of expectations in the auditory information, not the integration of the additional sensory information, but the additional sensory modality may influence the sources of the neural activity.

While these studies shed light on the processing of auditory omissions, pure omission deviants consist of the total lack of information and thus leave open the question of whether the ERP responses are due to violations of the temporal pattern or violations of the expected sound object or, in other words, violations of "when" or "what" or a combination of the two. SanMiguel, Saupe and Schröger (2013) sought to answer this question by manipulating how predictable the identity of a sound was while maintaining the same temporal structure but omitting ~12% of the sounds in the sequences. They found the oN1, oN2 and oP3 were elicited only when the identity of the sounds surrounding the omission were predictable, but not when the sound was random, such that no predictions could be made. Korka and colleagues (2020) found similar results of attenuated oN1 when the identity of a sound associated with a specific button press was unpredictable, but the oP3 did not change. When both timing and identity were manipulated, omission of audio from audio-visual stimuli elicited attenuated omission responses during unpredictable conditions compared to predictable conditions (van Laarhoven et al., 2017). Omission responses elicited by omission deviants in complex stimuli, such as music, also seem to depend on the predictability of the stimuli, with larger responses for familiar, and thus more predictable music, compared to unfamiliar, and thus more unpredictable music (Ishida et al., 2024). Overall, omission specific responses are sensitive to the predictability of the surrounding tones and may be affected by either temporal predictions or sound identity predictions. Furthermore, this may indicate that predictive processing is responsible for the neural response to omission deviants similarly to the response to auditory deviants.

Aims of this Thesis.

Many studies using omission deviants have used methods that involve attention to be directed towards the stimuli, but research with deviant tones finds that robust deviance detection ERP components are elicited during passive listening (Näätänen et al., 2005, 2007). Violations of expected auditory information can be tracked even when attention is not directed towards the sounds, but it is unclear if the same is true for violations of expectations caused by omission deviants. Thus, the main goal of the present thesis research was to answer the question of how the brain responds to omission deviants during passive listening. This work also explores the effect of predictability on ERP responses to omission deviants, as well as the developmental origins of omission responses in infancy. The use of a passive paradigm is important for furthering our understanding of the types of patterns automatically tracked in the brain, as well as providing a way that these responses can be measured in non-verbal populations. This dissertation focuses on isochronous sequences of a repeating sound, but these findings could be extended to omission deviants within more complex auditory patterns such as language or music, although careful consideration would need to be given to the control conditions in these cases.

The first data chapter (Chapter 2) compares omissions as deviants (i.e., infrequent, unexpected silences in an auditory sequence) to omissions as "standard events" (i.e., expected silences in an auditory sequence), thus comparing brainwave activity to silences under varying contexts. If the unexpected silences are processed differently because they violate expectations set by the regularly occurring tones, then the unexpected silences should elicit different neural response than the expected silences, specifically an MMN. We found that indeed the unexpected silences elicited an MMN as well as P3a, indicating there may have also been an inadvertent attentional orientation in response to the unexpected silences.

The second data chapter (Chapter 3) investigates the response to omission deviants in 6-month-old infants to determine how early in development adult-like omission responses form. We also wanted to determine if global predictability of the omission decreased the mismatch response amplitude as it does with acoustic deviants (Basirat et al., 2014; Bekinschtein et al., 2009). Thus, we sought to look at the development of the omission deviant responses as well as the effect of global predictability. Furthermore, we added an external visual cue to mark the onset of both tones and omissions, to 1) ensure temporal alignment of the brain response to the omission as it is unclear if the violation of expectation of a response would initiate as soon as no sound occurs or if the onset of the response would have some temporal jitter across trials or across participants, and 2) to make our stimuli more like previous research using auditory omissions with a non-auditory sensory cue such as a button press or video. However, our study still employed a passive listening paradigm. Interestingly, omission deviants did elicit a response in the infants, but it was not the expected MMN, MMR, or omission-specific ERP components previous researchers have found. Furthermore, no differences were found between the global predictable omission deviants and global unpredictable omission deviants, suggesting that omission deviants may not be affected by global predictability in the same way auditory deviants are.

The third data chapter (Chapter 4) compared globally predictable and globally unpredictable omissions in adults using similar stimuli as with the infants in Chapter 3, to determine if adults, unlike infants, would show sensitivity to the global predictability of omission deviants. Unexpectedly, no specific ERP components were found but, rather, a sustained response that increased in amplitude for around 250 ms post omission onset and remained stable into the next stimulus. This sustained response did not depend on the global predictability of the omissions. Overall, our results suggest that during passive listening omission deviants are not processed in the same manner as auditory deviants, or when the omission deviant occurs during a task that directs attention toward the stimuli. The lack of an effect of global predictability between the first and second study may suggest an overall lack of an effect on global predictability on the response to omission deviants, but the sustained response was not observed within the infant data (Chapter 3).

Together this work shows that neural responses to omission deviants during passive listening appear to differ from those found during attentional listening, and that infant’s and adult’s responses appear to differ as well. This thesis contributes to our understanding of neural prediction by providing some of the first work to show omission deviant responses using IOIs larger than 200 ms, effects of global predictability on omission deviant responses, and the presence of omission responses in infants.

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Chapter 2: The sound of silence: Predictive error responses to unexpected sound omission in adults.

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Preface

Understanding how the brain processes unexpected silences is important for understanding language development and music perception. There is evidence that unexpected silences are processed similarly to unexpected changes of a sound, but previous research has not compared silences embedded in different contexts. In Chapter 2, we recorded electroencephalography while presenting adults with isochronous tones and pseudo-randomly omitting 20% of the tones to create unexpected silences. We compared the event-related responses to unexpected silences and silences that were expected in a rhythm, i.e., expected silences. Mismatch negativity and P3a were elicited by the unexpected silences in comparison to the expected silences. These results provide novel evidence for a neural deviance response when comparing silences under varying conditions. The presence of the MMN and P3a suggest that unexpected silences are processed in the brain by similar mechanism as unexpected sound changes.

Abstract

The human auditory system excels at detecting patterns needed for processing speech and music. According to predictive coding, the brain predicts incoming sounds, compares predictions to sensory input, and generates a prediction error whenever a mismatch between the prediction and sensory input occurs. Predictive coding can be indexed in EEG with the mismatch negativity (MMN) and P3a components, two ERP components that are elicited by infrequent deviant sounds (e.g., differing in pitch, duration, loudness) in a stream of frequent sounds. If these components reflect prediction error, they should also be elicited by omitting an expected sound, but few studies have examined this. We compared ERPs elicited by infrequent randomly occurring omissions (unexpected silences) in tone sequences presented at 2 tones/sec to ERPs elicited by frequent, regularly occurring omissions (expected silences) within a sequence of tones and resting state EEG (a constant silence). We found that unexpected silences elicited significant MMN and P3a, although the magnitude of these components was quite small and variable. These results provide evidence for hierarchical predictive coding, indicating that the brain predicts silences as well as sounds.

Introduction

Much of the information in auditory signals resides in their temporal dynamics. To extract relevant information, it is thought that the brain detects patterns by actively predicting incoming sounds based on the prior context (Arnal & Giraud, 2012; Bendixen, SanMiguel, & Schröger, 2012; Friston & Kiebel, 2009; Heilbron & Chait, 2017; Kumar et al., 2011). This process, termed predictive coding, is important for learning and understanding language (Romberg & Saffran, 2010; Ylinen, Bosseler, Junttila, & Huotilainen, 2017) and processing pitch and rhythm in music (Chang, Bosnyak, & Trainor, 2018; Háden, Németh, Török, & Winkler, 2015; He, Hotson, & Trainor, 2009; Trainor, 2012; Winkler, Haden, Ladinig, Sziller, & Honing, 2009; Winkler, 2007). When a stimulus violates a hypothesis, an error signal is generated, enabling updating of internal models. Models of predictive coding (Friston & Kiebel, 2009) suggest that any transient event-related potential (ERP) component could reflect prediction error response. For example, violations of self-action-generated auditory predictions have been shown to elicit an N1 response (Korka, Schröger, & Widmann, 2019, 2020; SanMiguel, Widmann, Bendixen, Trujillo-Barreto, & Schröger, 2013; Schröger, Marzecová, & Sanmiguel, 2015). When examining violations to purely auditory predictions the mismatch negativity (MMN: Näätänen, Gaillard, & Mantysalo, 1978; Näätänen, Kujala, & Winkler, 2011; Näätänen, Tervaniemi, Sussman, & Paavilainen, 2001; Winkler & Czigler, 2012) and P3a (Chang et al., 2018; Max, Widmann, Schröger, & Sussman, 2015) components are elicited. MMN typically occurs after a violation of expectation for an acoustic feature such as pitch, duration, or timbre, or a change in the pattern of sounds. However, if MMN represents all auditory expectation violations, then an omission of an expected stimulus (i.e., an unexpected silence) should also elicit MMN. Although some previous work found MNN to unexpected silences (Horváth, Müller, Weise, & Schröger, 2010; Recasens & Uhlhaas, 2017; Shinozaki et al., 2003; Winkler et al., 2009; Yabe, Tervaniemi, Reinikainen, & Näätänen, 1997), most studies report an MMN-like response only when the tones are presented at a stimulus onset asynchrony (SOA) of 200 ms or less, which is within the brain’s temporal integration window (Horváth, Czigler, Winkler, & Teder-Sälejärvi, 2007; Rüsseler, Altenmüller, Nager, Kohlmetz, & Münte, 2001; Shinozaki et al., 2003;

Winkler et al., 2009; Yabe et al., 1997, 1998). Here we examine ERPs to tone omissions outside of the integration window at an SOA of 500 ms.

MMN is typically elicited by rare stimuli (deviants) embedded in a sequence of frequent stimuli called standards (Bartha-Doering et al., 2015; Näätänen, Astikainen, Ruusuvirta, & Huotilainen, 2010; Näätänen et al., 2011; Näätänen, Paavilainen, Rinne, & Alho, 2007; Näätänen et al., 2004; Sussman, Chen, Sussman-Fort, & Dinces, 2014; Winkler, 2007). The MMN response is a frontally negative deflection peaking between 150 and 250 ms that reverses polarity at the back of the scalp, consistent with a primary generator in auditory cortex (Näätänen, 2003; Paavilainen, 2013; Trainor, 2001, 2012). The amplitude and latency of the MMN are typically extracted from the local minimum in the difference wave formed by subtracting the standard ERP from the deviant ERP. MMN magnitude increases with increased deviant tone rarity and larger physical differences, such as larger pitch deviations (Näätänen et al., 2007). MMN can be elicited without attention, suggesting that detecting regularity and violations of regularity are automatic sensory processes (Max et al., 2015; Tervaniemi et al., 1999; Todd, Provost, Whitson, Cooper, & Heathcote, 2013).

MMN can be observed when the standard and deviant stimuli are physically identical, but where the deviant violates a rule in its context whereas the standard does not in its context (Grimm, Escera, Slabu, & Costa-Faidella, 2011; Shestopalova, Petropavlovskaia, Vaitulevich, & Nikitin, 2015), or the stimulus is presented in different conditions, namely, an oddball paradigm and a condition that presents multiple stimuli all occurring with the same probability, thus controlling for context and occurrence rate (Jacobsen & Schröger, 2003; Ruhnau, Herrmann, & Schröger, 2012; Todd, Provost, & Cooper, 2011; Todd et al., 2013; Wiens, Szychowska, Eklund,

& van Berlekom, 2019). Comparing the same stimulus under different context is essential when examining MMN responses to unexpected silences, because responses to a sound will contain auditory components not in the ERP responses to silence. Specifically, we compared the ERP waveforms to silence as a standard stimulus (i.e., an expected silence) to silence as a deviant (i.e., unexpected silence).

Despite decades of research, the mechanisms that elicit the MMN remain controversial. An alternate theory to predictive coding is neural adaptation (Garrido, Kilner, Stephan, & Friston, 2009; Gu, Wong, Hu, Zhang, & Tong, 2019; Jaaskelainen et al., 2004; May & Tiitinen, 2010). According to this theory, as a tone is repeated, neurons encoding its acoustic features habituate, leading to decreased neural firing. When the deviant tone is presented, the change elicits firing from new neurons not yet habituated. In this scenario, MMN represents the recruitment of neurons to encode the deviant stimulus features.

On the other hand, both empirical and modeling research supports a predictive coding view of MMN (Chennu et al., 2016; Trainor, 2012; Wacongne, Changeux, & Dehaene, 2012; Wacongne et al., 2011). MMN can be elicited by changes to abstract features or patterns (Bouwer, Van Zuijen, & Honing, 2014; Moldwin, Schwartz, & Sussman, 2017; Paavilainen, 2013), differences in global and local probability (Basirat, Dehaene, & Dehaene-Lambertz, 2014), and disruptions to musical metric structure (Winkler et al., 2009). For example, infrequent rising tone patterns in a sequence of descending tone patterns (Carral et al., 2005; Háden et al., 2015) and relative pitch changes in melodies presented in different pitch ranges (Fujioka, Trainor, Ross, Kakigi, & Pantev, 2004, 2005; Tew, Fujioka, He, & Trainor, 2009; Trainor, McDonald, & Alain, 2002) elicit MMN. In these cases, standards and deviants differ in pattern, not stimulus features such as pitch, suggesting that MMN cannot be a result of neural habituation to acoustic features. It is possible, however, that MMN might operate at a pattern or auditory object level, with habituation occurring at these higher levels of representation. (Costa-Faidella, Grimm, Slabu, Díaz-Santaella, & Escera, 2011).

Predictive coding has also been examined in relation to the P3a ERP component, which often follows the MMN, and is related to inadvertent capture of attention (Polich, 2007; Sussman, Horváth, Winkler, & Orr, 2007). P3a increases in amplitude with decreasing deviant predictability (Chang et al., 2018; Max et al., 2015; Sussman, Winkler, & Schröger, 2003). Furthermore, P3a amplitude is inversely correlated with the power of β-band neural oscillations (Chang et al., 2018), which have been linked to auditory and motor predictive timing (Arnal & Giraud, 2012; Chang et al., 2018; Cirelli et al., 2014; Saleh, Reimer, Penn, Ojakangas, & Hatsopoulos, 2010). In sum, effects of predictive coding can be seen in various aspects of the EEG response. Here we focus on MMN and P3a.

The error signals generated by omission of an expected sound are an important, yet understudied, aspect of predictive coding. Finding MMN and P3a responses to an omission would be strong evidence against neural adaptation, as silence would not recruit any new sensory neurons. On the other hand, the absence of an MMN to unexpected silence would indicate that the neural signatures of an unexpected silence differ from those of unexpected feature or pattern deviations.

Early studies examining MMN to tone omissions only found a significant response with SOAs less than 200 ms (Yabe et al., 1997). Yabe and colleagues examined SOAs from 100 to 350 ms but did not find that omissions elicited a significantly different response from the sound stimulus at SOAs greater than 200 ms. Following this study, most studies used SOAs of less than 200 ms. Using depth electrodes, Hughes et al. (2001) found an MMN-like response to omissions in auditory sequences with an SOAs of 200 ms, but did not evaluate responses for larger SOAs because they “tended to produce responses that were dispersed in time” (p. 1078). Since these reports, most studies examining tone omissions, whether analyzing P1, N1, (Bendixen, Schröger, & Winkler, 2009) or MMN, (Bendixen, Scharinger, Strauss, & Obleser, 2014; Oceak, Winkler, Sussman, & Alho, 2013; Recasens & Uhlhaas, 2017; Wacongne et al., 2012, 2011) used SOAs shorter than 200 ms. These studies interpret the omission MMN as evidence supporting predictive coding. However, the short SOAs used in these studies fall within the auditory integration window, in which two auditory events can be perceived as one event (Yabe et al., 1998). This window is often defined, and measured, as the time window over which intensity is summated, and it spans approximately 200 ms or less (Shinozaki et al., 2003; Yabe et al., 1998). Specifically, a 200 ms tone will sound louder than a 100 ms tone of equal amplitude, whereas a 2000 ms tone will sound equally loud as a 1000 ms tone of equal amplitude. Thus, at short SOAs, omission MMNs could result from the integration of successive sounds into single percept.

Furthermore, deviant tones can elicit MMN in sequences with SOAs of up to 2 seconds or more; in general, the amplitude of the MMN decreases as SOA increases (Näätänen, Jacobsen, & Winkler, 2005; Näätänen et al., 2007), but the length of SOAs under which MMN can be observed varies greatly between individuals (Winkler, Schröger, & Cowan, 2001). Thus, if MMN reflects predictive errors related to unexpected omissions, it would be expected to be observed at SOAs larger than 200 ms. Some models of the neural architecture predict MMN responses to omissions (Wacongne et al., 2012) particularly if attention is drawn to that point in time (Wacogne et al., 2011; Chennu et al., 2016). To our knowledge only one study using EEG has found what may be an MMN or P3a-like response to a stimulus using an SOA of 1 second, but the responses were small and variable, limiting the researchers' interpretation of the ERPs (Busse & Woldorff, 2003). However, intracranial recordings (Fonken et al., 2019; Halgren et al., 1995) have found specific responses, including increased high frequency power, to sound omissions, even with SOAs larger than 200 ms. Thus, it remains an open question whether MMN and P3a measured in EEG reflect predictive errors for unexpected omissions.

Salisbury et al. (2012) examined omission deviants in the context of discrete 6-tone patterns with SOAs of 330 ms between tones. They found significant MMN to omissions of the 4th or 6th tone and interpreted this as a gestalt pattern violation. One issue in Salisbury (2012), and most studies investigating the omission response, is that they calculated the MMN amplitude by either subtracting the omission response from the standard tone response or directly compared the two responses. This is problematic because the standard tone will elicit obligatory auditory components that the omission deviant will not. Thus, a difference waveform will show peaks related to the obligatory responses present in the standard waveforms but absent in the omission waveforms, which then could be mistaken for MMN. To our knowledge this potential confound has not been discussed in the literature to date (Bendixen et al., 2014; Moldwin et al., 2017; Recasens & Uhlhaas, 2017; Salisbury, 2012). Given these questions and the importance of understanding neural responses to unexpected silences for predictive coding theories (Bendixen et al., 2014; Heilbron & Chait, 2017; Trainor, 2012), we investigated the response to unexpected silences (i.e., omission deviants), expected silences (i.e., during an expected interstimulus interval) and continuous silence (i.e., resting state). If silences that violate expectations elicit a different ERP response than silences that are expected, this could reflect predictive coding.

Methods

Participants

Thirty adults (5 males; Age: *M* = 18.7, *SD* = 1.23) were recruited via the McMaster undergraduate participant pool and given course credit for their participation. All participants reported no known hearing impairments and normal or corrected to normal vision. 70% percent of participants spoke a language in addition to English and 67% had at least one year of musical training. All study procedures were approved by the McMaster University Research Ethics Board.

Stimuli

We used a C4 piano tone from the Iowa Musical Instrument Samples database (University of Iowa Electronic Music Studios). The tone was edited using Audacity to be 250 ms in duration, including 50 ms cosine rise and decay. The tone was presented through an AudioVideo Methods speaker (P730) placed 1 meter in front of the participants' head, at 60 dB SPL-C over a noise floor of 49.8 dB SPL-C (less than 30 dB SPL-A). The tone was presented in two separate conditions, one with unexpected silences (tone omissions) and one with expected silences (Figure 1a). During the unexpected silence condition, the stimulus onset asynchrony (SOA) between tones was set to 500 ms. The unexpected silences were created by omitting 10% of tones pseudo-randomly within the sequence, with the constraint that at least two piano tones were presented between each unexpected silence.

For the expected silence condition, the same 250 ms piano tone was presented, but the SOA was doubled to 1000 ms. For this condition, the onset of the expected silence was defined as 500 ms after each tone (Figure 1a). Thus, we created two sequences with the same local context: silences occurred 500 ms after a tone onset and silences were followed by a tone occurring 500 ms after the silence onset. This ensured that the only difference between the silence conditions was the expectation of the silence from the global context of the sequence. A significantly different response to the unexpected silence compared to the expected silence would indicate a prediction violation for an unexpected stimulus omission. Finally, we also collected resting state EEG by not presenting any sound in blocks of 1 minute.

Three blocks of each of the unexpected silence condition, expected silence condition, and resting state were presented for a total of 9 blocks. Each block of the unexpected silence condition contained 600 trials (540 piano tones, 60 unexpected silences). Each block of the expected silence condition contained 60 trials (60 piano tones, 60 expected silences). Thus, we collected a total of 180 responses each of expected silences and unexpected silence.

Procedure

After obtaining consent, the participant completed a demographic questionnaire regarding language experience, musical training, hearing status, and handedness. The participant was then seated in a sound attenuating room, with the speaker presenting the sounds located 1 meter in front of their head. They were fitted with an EEG electrode net after it was soaked in a saline solution. Free field sound presentation was used to facilitate comparison to a subsequent infant study. During the experiment, participants passively listened to the tones while watching a silent, subtitled movie of their choice.

For half the participants, the order of the first three blocks was unexpected silence, expected silence, resting state; for the other half, it was expected silence, unexpected silence, resting state. Whatever order participants received, that same order was repeated 3 times to comprise the 9 blocks in total. Between blocks there was 10 seconds of silence. After the EEG testing, participants completed the Goldsmith Musical Sophistication Index (Müllensiefen, Gingras, Musil, & Stewart, 2014).

Data Acquisition and Preprocessing

EEG data was collected using a 128-channel HydroCel GSN net with Electrical Geodesic NetAmps 200 amplifier, sampled at 1000 Hz and online referenced to Cz. Raw data was saved with NETSTATION software for offline analysis. Channel impedances were kept below 50 kΩ. Any channel with impedance above 50 Ω was removed from the analysis. Channels displaying large fluctuations in amplitude, during the EEG recording, were also removed during preprocessing based on visual inspection. A total of 11 channels (see Figure 1b for details) were removed across all participants to keep the number of channels consistent for all participants.

The data were preprocessed with MATLAB 2016b (Mathworks Inc.) using the Fieldtrip Toolbox (Oostenveld, Fries, Maris, & Schoffelen, 2011). The continuous EEG data was bandpass filtered between 0.5 and 20 Hz with a 4th order Butterworth filter using the zero-phase delay filtering technique. High amplitude artifacts were corrected using the artifact blocking algorithm (ABA; Fujioka, Mourad, He, & Trainor, 2011; Mourad, Reilly, De Bruin, Hasey, & MacCrimmon, 2007), with a threshold of + 75 µV in 5 s windows, and then referenced to a common average. The data were then segmented into 750 ms segments from 250 ms before the onset of the silence to 500 ms after the onset of the silence. These trials were then down sampled to 128 Hz. Any trial in either the expected or unexpected silence condition with an amplitude range larger than 75 µV was removed from the analysis. Blinks, saccades, and heartbeat artifacts were removed using independent component analysis (ICA). ICA components containing these artifacts were determined by visual inspection conducted by author DP. The remaining data were averaged per condition, per participant. Individual ERP waveforms were baseline corrected using a 100 ms pre-silence onset window. Difference waveforms were created by subtracting the expected silence from the unexpected silence ERP waveforms individually for each participant.

Event-related Potential (ERP) Data Analysis

The difference waveforms were separated and averaged based on six electrode groups (Figure 1b) based on laterality (left, midline, right) and centrality (frontal, central). To calculate MMN amplitude for each electrode group, we used the MATLAB function findpeaks and max to find the local minimum in each participant's difference waveform between 100 and 300 ms. We then averaged the amplitude in a 50 ms window centered around the peak (25 ms on either side). We also characterized the P3a using the same peak finding and averaging method, by finding the local maximum in the difference waveform between 250 ms and 400 ms post silence onset.

We analyzed the amplitudes from the difference waveforms using two separate 3x2 repeated measures ANOVAs for laterality (left, midline, right) and centrality (frontal, central) to determine if there was a difference in ERP activity between electrode regions. To assess the presence of an MMN or P3a response, the main goal of this study, we conducted a one-sample t-test against zero based on the ANOVA results. For example, if no difference was found between the electrode regions we conducted the t-test on the average across all six regions. If there was a difference between frontal and central regions, but not between the left, mid or right regions, we conducted two t-tests, one averaged across the three central electrode regions and one averaged across the frontal regions.

For both 3x2 repeated measures ANOVAs, any violation of sphericity for main or interaction effects were corrected for using Greenhouse-Geisser correction, and only corrected p-values are reported. Significant main effects were followed up via post-hoc paired analysis. Significant interactions between laterality and centrality were followed up by one-way ANOVAs using laterality as a factor separately for the frontal regions and central regions. Significant effects in these follow-up ANOVAs were further analyzed using post-hoc paired analysis. Before conducting paired analyses, a Shapiro-Wilk test was used to assess the assumption of normality. If normality was not violated, we report values based on paired t-tests; however, if the assumption of normality was violated, we report values based on the Wilcoxon signed rank test. Multiple comparisons in the post-hoc analyses were corrected for using Holm-Bonferroni correction (Holm, 1978).

We further analyzed the power spectrum of the unexpected and expected silence conditions to assess whether potential oscillations at the stimulus presentation rates may have been present. During the expected silence condition, the SOA was 1000 ms, or 1 Hz, whereas during the unexpected silence condition the SOA was 500 ms or 2 Hz. To ensure this potential confound did not affect the ERP waveforms during the silence periods of both conditions we conduct two Bayesian repeated measures ANOVAs, one on power at 1 Hz and one on power at 2 Hz. Each included factors silence (unexpected, expected), laterality (left, midline, right) and centrality (central, frontal). Details regarding these analyses as well as the description of the results can be found in the supplemental materials. To briefly summarize, we found evidence supporting the null hypothesis that there is no difference in power between the silence conditions at either frequency, suggesting the difference in presentation rate did not affect the processing of the silences.

Results

From the grand average ERPs (Figure 2) we can see a negative peak at approximately 125 ms. There is also a positive peak within the P3a window used for analysis, although it is more spread out in time in certain region along the scalp, likely due to high variability in the latency of peak amplitude responses (supplemental Figure S1).

ERP Analyses of the MMN

The ANOVA comparing the MMN amplitude at different electrode regions reveled no significant difference in laterality ($F(2,58) = 2.19$, $p = 0.12$, $\eta^2_{\text{partial}} = 0.009$) or centrality ($F(1,29) = 0.27$, $p = 0.61$, $\eta^2_{\text{partial}} = 0.07$), nor an interaction ($F(2,58) = 1.94$, $p = 0.15$, $\eta^2_{\text{partial}} = 0.06$) suggesting a lack of difference between electrode regions analyzed (Figure 3a). Thus, to determine if there was a significant difference between the unexpected and expected silence conditions, we averaged the MMN amplitude across the 6 electrode regions for each participant and compared these averages against zero using a paired t-test. We found a significant difference ($t(29) = -3.76$, $p = 0.0007$, $CI = [-0.43,-0.126]$), such that the ERP of the difference waveform was significantly less than zero ($M = -0.277$, $SD = 0.404$). These analyses indicate a small, yet reliable MMN was elicited by the unexpected silences compared to expected silences.

ERP Analyses of the P3a

The ANOVA of the for the P3a component of the difference waveform revealed a significant main effect of centrality ($F(1,29) = 52.6$, $p < 0.001$, $\eta^2_{\text{partial}} = 0.645$), with larger P3a at frontal than central sites, a significant main effect of laterality ($F(2,58) = 23.92$, $p <0.001$, $\eta^2_{\text{partial}} = 0.452$) as well as an interaction effect ($F(2,58) = 18.89$, $p <0.001$, $\eta^2_{\text{partial}} = 0.394$). To further investigate the interaction effect two one-way ANOVAs were conducted, one for the three frontal regions and one for the three central regions. We found no significant difference in P3a between the three central regions ($F(2,58) = 1.53$, $p = 0.22$, $\eta^2_{\text{partial}} = 0.05$), whereas the three frontal electrode regions differed significantly ($F(1.4, 39.6) = 94.12$, $p < 0.001$, $\eta^2_{\text{partial}} = 0.764$). Specifically, the right frontal electrode region had a smaller response compared to the frontal midline ($t(29) = 18.1$, $p < 0.001$, $CI = [0.653, 0.820]$) and the frontal left ($t(29) = 11.5$, $p < 0.001$, $CI = [0.495, 0.709]$), while the left and midline electrodes were not significantly different (($t(29) = 1.83$, $p = 0.23$, $CI = [-0.285, 0.015]$). This suggests that the P3a response to the unexpected silence was lateralized at frontal sites, such that it was stronger in the left hemisphere compared to the right (Figure 3b).

To test the significance of the P3a response we averaged the P3a response across the frontal left and midline regions for each individual and compared this average response against zero. We found there was indeed a significant difference from zero ($t(29) = 30.89$, $p < 0.001$, $CI = [0.972, 1.11]$, $M = 1.04$, $SD = 0.18$). Conducting the same test for the right frontal region revealed a significant difference as well ($V = 465$, $p < 0.001$, $CI = [0.338, 0.421]$). Averaging across the three central regions, we did not find a significant P3a response ($t(29) = 1.17$, $p = 0.253$, $CI = [-0.077\ 0.282]$), indicating the P3a response was limited to the frontal regions.

Discussion

Although most ERP studies investigating predictive coding examine violations of expected pitch, timbre, duration, or sound patterns, a full understanding of predictive coding requires characterizing neural responses to omissions of an expected stimulus. Here we investigated EEG responses to silence under different contexts. We hypothesized that stimulus omissions (unexpected silences) would generate significant MMN and P3a when compared to conditions of expected silences. As predicted, we found an a significant MMN between 100 and 300 ms and a significant P3a response between 250 and 400 ms. Thus, we found evidence of predictive coding via the presence of MMN and P3a, suggesting multiple levels of predictive coding in response to unexpected silences. Our findings suggest that neural responses to unexpected stimulus omissions are reflected in ERP components that index auditory mechanisms of predictive coding.

Previous studies that have used unexpected stimulus omissions to investigate how MMN relates to predictive coding are limited in two respects. First, most previous studies only investigated an omission to auditory stimuli using an SOA of 200 ms or less (Bendixen et al., 2009; Chennu et al., 2016; Recasens & Uhlhaas, 2017; Salisbury, 2012; Todorovic & de Lange, 2012; Wacongne et al., 2012; Yabe et al. 1997, 1998). At such fast tempos, successive stimuli are presented within the window of temporal integration, meaning that the brain likely does not process each stimulus and silence as a fully separate events (Horváth et al., 2007; Shinozaki et al., 2003; Yabe et al., 1997, 1998). Second, previous studies compared deviant omissions (silence) to a standard tone. Tones will elicit obligatory ERP components that overlap in time with the MMN, such as the P1, N1 and P2, whereas silences do not elicit these components.

Therefore, differences between the standard and difference waveform in this case are likely due to the presence of obligatory auditory ERP components (that overlap the time of possible MMN) in response to the standard (tone) stimuli but not the deviant (silence) stimuli. To our knowledge, ours is the only study to date to overcome these limitations by comparing silences under varying levels of expectation (expected, unexpected, resting state) rather than comparing responses to tones and silence in the auditory domain alone.

Under these novel conditions, we found small, but robust, MMN and P3a responses to unexpected silences. These results strongly support predictive coding as the mechanisms underlying MMN and P3a rather than neural adaptation (Heilbron & Chait, 2018; Trainor, 2012; Wacongne et al., 2012, 2011). Furthermore, the results indicate that predictive errors can be generated without any stimulus present, and the mechanisms underlying prediction errors for stimulus feature or pattern violations are similar to those underlying the omission of an expected stimulus.

Our findings contrast with the few previous studies that examined MMN to stimulus omissions at tone sequence presentation rates larger than the temporal window of integration. Yabe et al. (1998) did not find a significant MMN to an omission with an SOA of 300 ms, although they did report a negative MMN-like ERP response under similar stimulus conditions in Yabe et al. (1997). However, both studies had very small sample sizes (less than 10) and, therefore, were likely insufficiently powered to observe a small effect size. The present study included 30 participants. Additionally, in the case of a stimulus omission, there may be temporal jitter from trial to trial and between participants as there is no stimulus to align the ERP responses precisely. This may tend to artificially diminish the size of ERP components in averaged data. Future studies could implement signal processing techniques such as temporal principal component analysis (Dien, 2012) to better align the MMN and P3a responses at the single trial level to improve overall signal to noise ratio.

Although we interpret the negative component we observed as an MMN, it is possible that it reflects a contribution of N1 or N2. Indeed, previous research has shown that when an action (button press) is associated with a sound, the omission of that sound after the action can elicit an N1 component, argued to reflect a top-down prediction signal (Korka et al., 2020; SanMiguel et al., 2013; Schröger et al., 2015). However, in the present auditory-only experiment, the mean peak latency for the negative ERP component is well beyond that of a typical N1(see Figure S3), making it unlikely that it reflects N1. It is possible that self-generated action provides a more powerful context for eliciting top-down expectations compared to auditory pattern expectations alone, as in the present study, making any N1 effects too small to observe. It is also possible that the negative component we observed reflects a contribution of an N2 component. This is unlikely, however, as N2 is typically associated with attention, whereas the present study used a passive protocol in which participants watched a silent subtitled movie while ignoring the auditory stimuli.

The P3a that we observed in response to unexpected stimulus omissions had the frontal left/midline distribution, although its latency was about 40 ms later than a typical P3a response to a sound stimulus (Escera & Corral, 2007; Polich, 2007). However, a latency delay might be expected due to difficulty in precisely locating the silence onset when there is no stimulus (Hughes et al., 2001) or a short delay before neural processes determine there is no stimulus. It is also possible that our observed response is a novelty P3 component which, like the P3a, is elicited when a novel stimulus is presented in a sequence of tones (Barry, Steiner, & De Blasio, 2016; Barry et al., 2020; Courchesne, Hillyard, & Glamabos, 1975). The novelty P3 peaks little later than the P3a (between 300 and 400 ms: Dien, Spencer, & Donchin, 2003; Dien et al., 2004; Rushby et al., 2005). However, it remains controversial as to whether the P3a and the novelty P3 are actually distinct components (Escera & Corral, 2007; Simons, Graham, Miles, & Chen, 2001).

The P3a has been characterized as an inadvertent capture of attention that typically occurs when an unexpected sound is presented in an unattended stream (Combs & Polich, 2006; Masson & Bidet-caulet, 2018; Polich, 2007; Rushby et al., 2005). Thus, the P3a has been suggested to index a prediction error signal in oddball designs similar to the current experiment (Max et al., 2015; Polich, 2007; Schröger et al., 2015). In a sense, our design could be thought of as examining temporal predictions, in that no stimulus occurred at an expected time for a stimulus. A recent study has shown that the degree of temporal prediction for the onsets of incoming sounds in a sequence (measured as the power of beta oscillations) is negatively correlated with the P3a amplitude following an unexpected pitch change. Thus, the less precise expectations are for event onsets, the greater the prediction error signals are for the deviant stimulus (Chang et al., 2018). Future studies could investigate whether individual differences in temporal tracking of tone onsets in a regular sequence, as indexed by beta power modulations, is related to the size of prediction errors as measured by P3a amplitude. This would help uncover whether predictive error responses in the case of unexpected stimulus omissions relate to temporal expectations.

During the unexpected silence condition, the standard tones were presented at a rate of 2 Hz, whereas during the expected silence condition they were presented at a rate of 1 Hz. We ruled out a possible confounding effect of neural entrainment at these rates with a Bayesian analysis that found evidence for no difference in 1 or 2 Hz power in the EEG between the silence conditions (see supplemental material and tables S1-S4 for results). However, a future study could be conducted in which the presentation rates of tones are the same across conditions with expected and unexpected omissions by having the omissions occur in either a random order (unexpected) or fixed order (expected). For example, the omissions could occur at a global rate of 20% in both conditions, but pseudo-randomly in the unexpected condition and predictably every 5th stimulus in the expected condition. We chose our current design because even though an unpredictable deviant stimulus leads to a stronger mismatch response compared to a predictable deviant, if both stimuli are rare, they both elicit an MMN response (Basirat et al., 2014; Wacongne et al., 2011).

In summary, the present study expands our understanding of predictive coding in the brain by examining predictive error responses to unexpected silences. Through careful choice of tempos under which events are individuated, and by comparing silences that were unexpected (deviant) or expected (standard), rather than comparing silence to tones, we ensured that differences were not confounded by obligatory auditory components, regardless of expectations. We found that unexpected silences elicit both MMN and P3a error signals, providing empirical support for a framework involving a hierarchical model of predictive coding (Heilbron & Chait, 2017; Trainor, 2012) in which MMN may represent a prediction error signal at the level of sensory information and P3a may reflect a top-down prediction error signal at a higher level of information processing that is related to temporal attention orientation.

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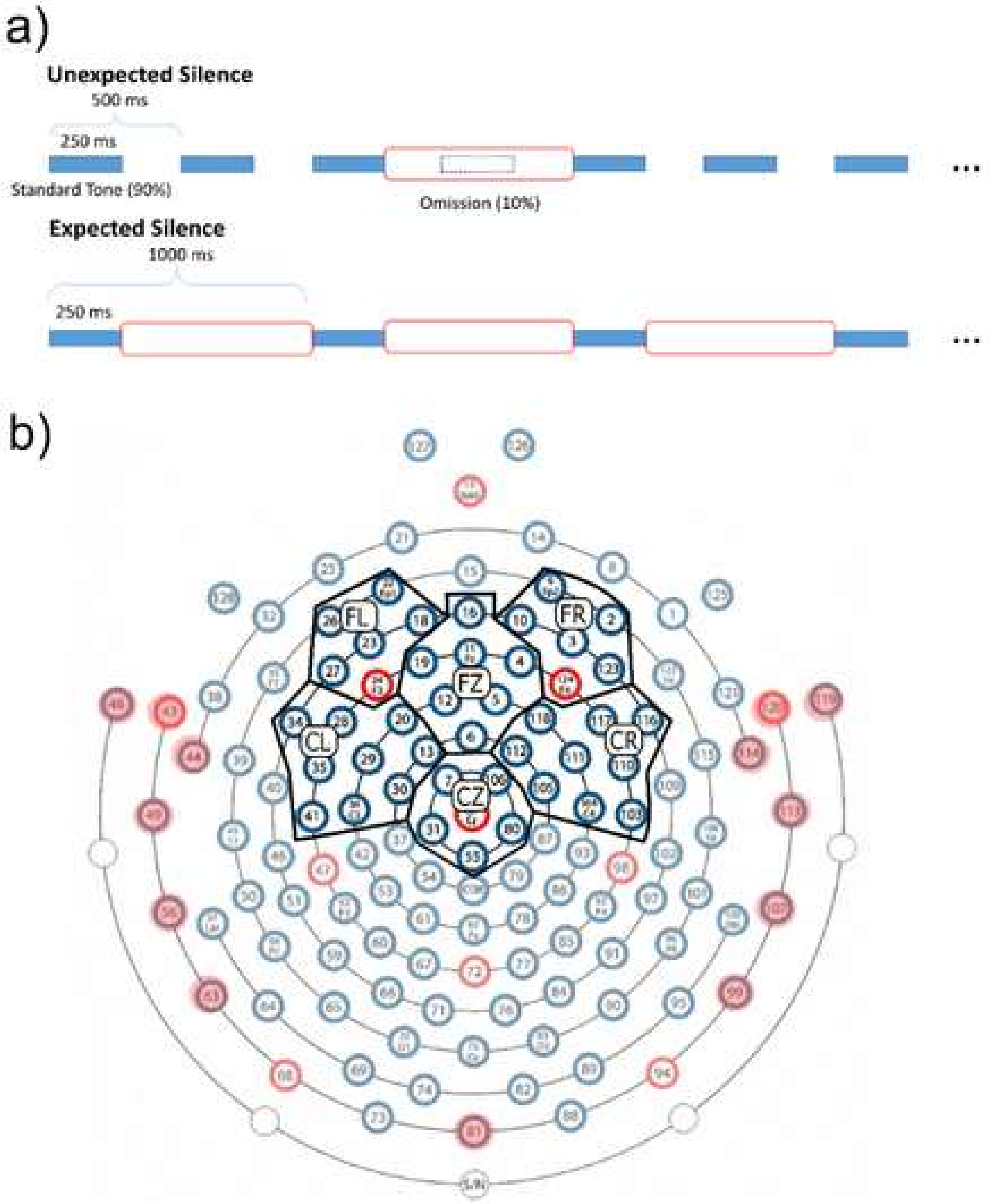

Figure 1. Experimental design and electrode placement. a) An example sequence presented during the unexpected and expected silence conditions. The filled blue rectangles represent the piano tone (C4). In the unexpected silence, the SOA between tones was 500 ms whereas in the expected silence condition it was 1000 ms. In the unexpected silence condition, 10% of tones were omitted to create the unexpected silences, represented by the blue doted square. The rounded red rectangles represent the silences of interest for comparison between the two

conditions. b) The placement of the 128 electrodes and the 6 electrode groupings used in the analysis: FL (frontal left), FZ (frontal midline), FR (frontal right); CL (central left); CZ (central midline), CR (central right). The light red shaded electrodes were removed from analysis for all participants. Specifically, they were 43, 44, 48, 49, 56, 63, 81, 99, 107, 113, 114, 119, 120.

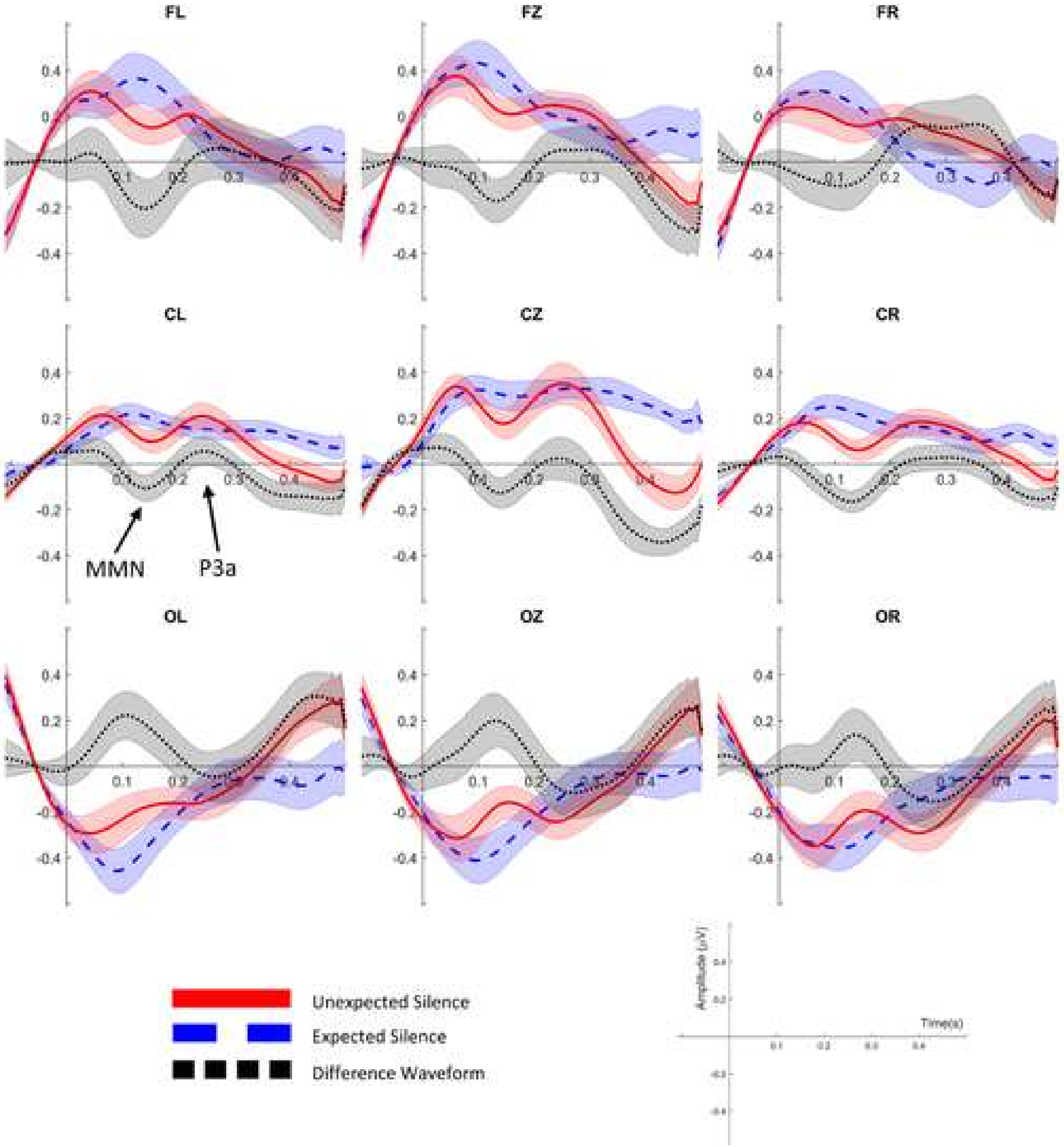

Figure 2. Grand Average ERP waveforms averaged across 9 regions of the scalp. These grand averages were filtered between 1 to 8 Hz, for visualization purposes. The unexpected waveform is displayed in a solid red line, the expected silence waveform is shown in a dashed blue line and the difference waveform is show in the dotted block line. The axis labels are displayed in the bottom right showing amplitude in microvolts on the y-axis and time in seconds on the x-axis. The shaded region around the grand average represents 1 standard error of the mean. Frontal

Left = FL, Frontal Midline = FZ, Frontal Right = FR, Central Left = CL, Central Midline = CZ, Central Right = CR, Occipital Left = OL, Occipital Midline = OZ, Occipital Right = OR. Only the Central and frontal regions were included in the ERP analyses, but the Occipital regions are shown for completeness.

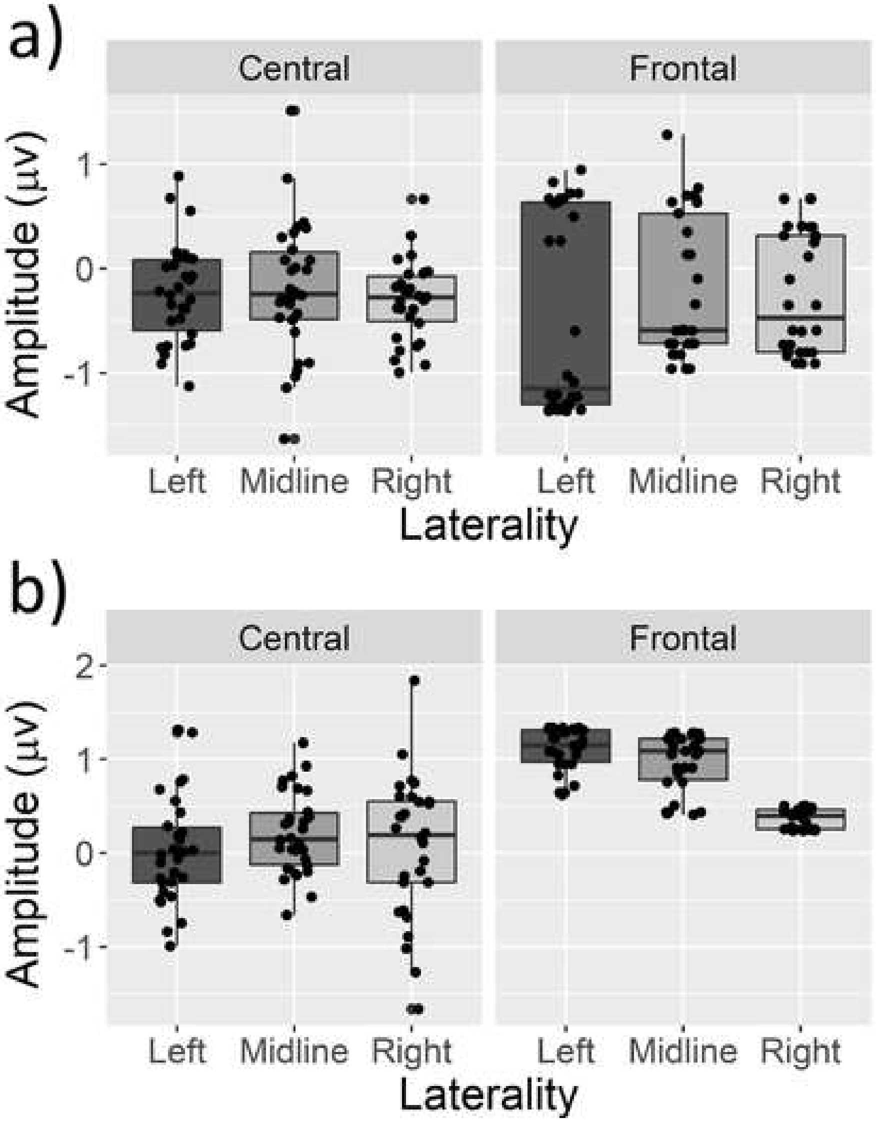

Figure 3. Amplitudes for the MMN and P3a. The MMN and P3a responses for each participant were calculated from the difference waves as the average amplitude in a 50 ms window centered on individual's peak MMN or P3a response found between 100 – 300 ms and 250 – 450 ms, respectively, for each of the six electrode regions. Individual participants are shown as black dots. The median is shown by the dark grey line within each box. The boxes and whiskers show the interquartile range and 1.5 times the interquartile range. a) The MMN peak

amplitudes from each participant's difference waveform (black dots) across the left, midline, and right regions (darkest to lightest grey) of the central and frontal electrodes. There were no significant differences across regions and MMN was significantly different from zero overall (p = 0.0007). b) The P3a peak amplitudes from each participant (black dots) across the left, midline, and right regions (darkest to lightest grey) of the central and frontal electrodes. The P3a responses were significantly greater than zero for all three frontal regions ($p < .001$), and significantly greater for frontal left and frontal midline regions compared to the frontal right region ($p < 0.001$). P3a was not significantly different from zero for the central regions (p = 0.22).

Supplemental Materials

Methods

Presentation Rates

Because the stimulus presentation rates were different in the expected silence condition (1 Hz) and the unexpected silence condition (2 Hz), we tested whether there was evidence for or against a difference in neural oscillation between the two conditions. Specifically, we wanted to ensure that ERP differences were due to whether the silence was expected or not rather than to potential lingering effects of processing the preceding tones. We computed the fast Fourier transform from -250 ms pre-silence onset to 500 ms post silence onset for each trial and channel individually, and zero padded the data to give a frequency resolution of 0.1 Hz. The trials were then averaged separately by silence condition, giving an average power spectrum for each channel per participant. The power at 1 Hz and 2 Hz was then extracted for each participant for each of the 6 electrode regions described in the main manuscript.

We then analyzed the power using a 2x2x3 Bayesian repeated measures ANOVA using JASP 0.14.1 (JASP 2020) with factors of silence (unexpected silence, expected silence), centrality (central and frontal) and laterality (left, midline, and right), separately for 1 Hz and 2 Hz power. We chose to use separate ANOVA for the two frequencies because were not concerned about the direct comparison of the power between the two frequencies, but the comparison of power between the silence conditions and electrode regions used in our main analysis. Thus, we could compare if the two silence conditions were different for a specific presentation rate without adding more complexity to our analysis. We used the default prior distribution for an ANOVA suggested by Rouder et al. (2012), and the null hypothesis that there was no evidence for a difference in power between conditions.

Given the complexity of the analysis (as seen by the 18 models compared in Tables S1 and S3) we also computed the inclusion Bayes factor (BF_{incl}) for matched models (Mathôt, 2017; Van Den Bergh et al., 2020) (Tables S2 and S4). Match models for main effects are models that include the main effect of interest excluding models that contain an interaction with the effect of interest (e.g., for the main effect of silence, interaction effects with silence such as silence * laterality would be excluded). Matched models for interaction effects consists of averaging the probability for the interaction effect excluding models that contain the main effects of the predictors that make up the interaction (e.g., for the silence *laterality interaction, models that contain the main effect of silence or laterality would be excluded). This results in inclusion prior probability [P(incl)], exclusion prior probability [P(excl)], inclusion posterior probabilities [P(incl|data)] and exclusion posterior probabilities [P(excl|data)]. Finally, the inclusion Bayes factor is then calculated by dividing the inclusion posterior probability by the exclusion posterior probability [P(incl|data)]/ P(excl|data)]. Thus, the BF_{incl} estimates the evidence for the alternative hypotheis for a main effect or interaction effect by comparing models including that effect of interest to models that do not include the effect of interest (Mathôt, 2017; Van Den Bergh et al., 2020). In other words, the BF_{incl} gives the unique estimate of evidence for an alternative hypothesis (i.e., that there is a difference between means) for a specific main effect or interaction effect across all the models within the repeated measures ANOVA.

Latencies

To demonstrate the variability in the latencies we have plotted the individual peak latencies of the MMN and P3a in Figure S1, overlayed with the boxplots to give a sense of the distribution of the peak latencies. For the MMN, the range of peaks spans about 200 ms and for the P3a, the range of peaks spans about 150 ms. This high variability in ERP responses and peak latencies is similar to that of previous findings (Hughes et al., 2001) and is likely why the grand average difference waveforms show small or temporally spread out ERP components, especially for the P3a component.

Results

Presentation Rates

The results of the Bayesian analyses of the 1 Hz power are shown in Tables S1 and S2. From Table S1 we can see there is moderate evidence supporting the null hypothesis of no difference between silence conditions (BF_{10} = 0.11), strong evidence for a difference between left, midline and right regions (BF_{10} = 12.52) and strong evidence for a difference between the frontal and central regions (BF_{10} = 3.10e ^{33}). A similar pattern of evidence is seen with the comparison for matched models (Table S2). There is strong evidence for effects of centrality, laterality, and the interaction between the two factors, suggesting differences in activity between the three frontal regions and the three central regions. This is similar to our analysis of the peak amplitudes which found differences between the central and frontal regions, and within the three frontal regions for the P3a activity (Figure 2). However, the matched model comparisons for the models that include a main effect of silence or an interaction with silence showed evidence in support of no difference in 1 Hz power between the expected and unexpected silence conditions ($BF_{incl} < 0.15$). Thus, models within table S1 that show evidence for a difference are most likely driven by differences in centrality, laterality, or both, not by differences between the silence conditions.

The results from the analyses of the 2 Hz power are shown in Tables S3 and S4. From Table S3 we can see there is moderate evidence in support of no difference in 2 Hz power between unexpected and expected silence conditions ($BF_{10} = 0.122$), but anecdotal evidence for a difference between left, midline and right electrodes ($BF_{10} = 1.27$) and strong<="" span="">evidence for a difference between central electrodes and frontal electrodes ($BF_{10} = 3.87e^{39}$). Examining the analysis of the matched models (Table S4), models including silence as a main effect or as an interaction demonstrated no evidence of a difference between the expected and unexpected silence conditions ($BF_{incl} < 0.15$). Strong evidence was found for an effect of laterality, centrality, and the interaction between the two factors ($BF_{incl} > 25.32$).

Taken together, the Bayesian analyses of 1 and 2 Hz power suggests there is little to no evidence that the difference in presentation rates led to differences in power spectrum between the expected and unexpected silence conditions. There was strong evidence to suggest the power differed based on the location on the scalp, but this did not interact with the silence condition.

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Models	P(M)	P(M|data)	BF_{M}	BF_{10}	error %
Null model (incl. subject)	0.053	2.28e -42	4.11e -41	1	
Silence	0.053	2.54e -43	4.57e -42	0.11	0.74
Centrality	0.053	7.06e -9	1.27e -7	3.10e +33	0.9
Laterality	0.053	2.86e -41	5.14e -40	12.52	1.24
Silence + Centrality	0.053	8.06e -10	1.45e -8	3.54e +32	2.54
Silence + Laterality	0.053	3.31e -42	5.96e -41	1.45	2.09
Laterality + Centrality	0.053	4.54e -6	8.17e -5	1.99e +36	1.57
Silence + Laterality + Centrality	0.053	5.02e -7	9.04e -6	2.20e +35	1.5
Silence + Centrality + Silence ✻ Centrality	0.053	1.31e -10	2.36e -9	5.76e +31	3.6

Silence + Laterality + Silence ✻ Laterality	0.053	1.8e -43	3.24e -42	0.08	2.42
Laterality + Centrality + Laterality ✻ Centrality	0.053	0.87	118.23	3.80e +41	2.05
Silence + Laterality + Centrality + Silence ✻ Centrality	0.053	7.61e -8	1.37e -6	3.34e +34	1.98
Silence + Laterality + Centrality + Silence ✻ Laterality	0.053	2.85e -8	5.12e -7	1.25e +34	2.87
Silence + Laterality + Centrality + Laterality ✻ Centrality	0.053	0.11	2.2	4.78e +40	8.72
Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality	0.053	4.84e -9	8.72e -8	2.12e +33	5.93
Silence + Laterality + Centrality + Silence ✻ Centrality + Laterality ✻ Centrality	0.053	0.02	0.3	7.17e +39	3.62
Silence + Laterality + Centrality + Silence ✻ Laterality + Laterality ✻ Centrality	0.053	0.006	0.1	2.50e +39	4.09

Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality + Laterality ✻ Centrality	0.053	8.66e -4	0.02	3.80e +38	3.49
Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality + Laterality ✻ Centrality + Silence ✻ Laterality ✻ Centrality	0.053	1.05e -4	0.002	4.58e +37	13.44

Table S1. Bayesian Model Comparison of 1 Hz Frequency Response. All models include subject. P(M|data) is the posterior probability, BF_M is the posterior odds. BF_{10} is the Bayes factor in terms of the evidence for the alternative hypothesis over the null hypothesis. Error % is an estimate of the error in computing the Bayes factor. The models are ordered from those with the largest BF_{10} to the smallest BF_{10}. P(M) is the prior probability of the data. The error percentage indicates the percentage of error in estimating BF_{10}. For example, laterality has a BF_{10} of 12.52 and error of 1.24%. Thus, the estimation of the BF_{10} for centrality for this dataset ranges from approximately 12.36 to 12.66.

Effects	P(incl)	P(excl)	P(incl|data)	P(excl|data)	BF $_{incl}$
Silence	0.263	0.263	0.11	0.87	0.13
Laterality	0.263	0.263	5.12e -6	7.99e -9	640.11
Centrality	0.263	0.263	5.08e -6	3.46e -41	1.47e +35
Laterality ✻ Silence	0.263	0.263	0.01	0.13	0.05
Centrality ✻ Silence	0.263	0.263	0.02	0.12	0.15
Centrality ✻ Laterality	0.263	0.263	1	5.15e -6	194051
Centrality ✻ Laterality ✻ Silence	0.053	0.053	1.05e -4	8.66e -4	0.12

Table S2. Analysis of Effects for the 1 Hz Frequency Response. Analysis of the various effect from the Bayesian repeated measures ANOVA of the power spectrum at 1 Hz. The analysis of effects allows us to determine the independent evidence for the alternative hypothesis for each main effect and interaction across matched model from table S5. This results in inclusion prior probability [P(incl)], exclusion prior probability [P(excl)], inclusion posterior probabilities [P(incl|data)] and exclusion posterior probabilities [P(excl|data)]. Inclusion Bayes factor is calculated by dividing the inclusion posterior probability by the exclusion posterior probability [P(incl|data)]/ P(excl|data)], estimating the independent evidence for the alternative hypothesis for a specific main effect or interaction effect.

Models	P(M)	P(M|data)	BF $_{M}$	BF $_{10}$	error %
Null model (incl. subject)	0.053	2.61e -47	4.69e -46	1	
Silence	0.053	3.18e -48	5.72e -47	0.122	5.12
Centrality	0.053	1.01e -7	1.82e -6	3.87e +39	1.29
Laterality	0.053	3.30e -47	5.95e -46	1.27	0.7
Silence + Centrality	0.053	1.12e -8	2.01e -7	4.28e +38	1.7
Silence + Laterality	0.053	3.82e -48	6.88e -47	0.15	1.4
Laterality + Centrality	0.053	2.55e -6	4.58e -5	9.77e +40	1.21
Silence + Laterality + Centrality	0.053	2.92e -7	5.26e -6	1.12e +40	2.4
Silence + Centrality + Silence ✻ Centrality	0.053	1.93e -9	3.47e -8	7.39e +37	3.89
Silence + Laterality + Silence ✻ Laterality	0.053	2.23e -49	4.02e -48	0.01	5.57

Laterality + Centrality + Laterality ✻ Centrality	0.053	0.88	126.84	3.36e +46	2.66
Silence + Laterality + Centrality + Silence ✻ Centrality	0.053	4.79e -8	8.62e -7	1.84e +39	3.48
Silence + Laterality + Centrality + Silence ✻ Laterality	0.053	1.65e -8	2.97e -7	6.32e +38	2.98
Silence + Laterality + Centrality + Laterality ✻ Centrality	0.053	0.10	2.06	3.94e +45	4.36
Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality	0.053	3.09e -9	5.56e -8	1.18e +38	13.07
Silence + Laterality + Centrality + Silence ✻ Centrality + Laterality ✻ Centrality	0.053	0.02	0.28	5.90e +44	3.12
Silence + Laterality + Centrality + Silence ✻ Laterality + Laterality ✻ Centrality	0.053	0.01	0.09	2.05e +44	2.77
Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality + Laterality ✻ Centrality	0.053	8.27e -4	0.02	3.18e +43	11.88
Silence + Laterality + Centrality + Silence ✻ Laterality + Silence ✻ Centrality +	0.053	9.72e -5	0.002	3.73e +42	12.76

Laterality ✻ Centrality + Silence ✻ Laterality ✻ Centrality

Table S3. Bayesian Model Comparison of 2 Hz Frequency Response. All models include subject. P(M|data) is the posterior probability, BF_M is the posterior odds. BF_{10} is the Bayes factor in terms of the evidence for the alternative hypothesis over the null hypothesis. Error % is an estimate of the error in computing the Bayes factor. The models are ordered from those with the largest BF_{10} to the smallest BF_{10}. P(M) is the prior probability of the data. The error percentage indicates the percentage of error in estimating BF_{10}. For example, silence has a BF_{10} of 0.122 and error percentage of 5.12. Thus, the estimation of the BF_{10} for silence in this dataset ranges from approximately 0.116 to 0.128.

Effects	P(incl)	P(excl)	P(incl|data)	P(excl|data)	$\mathrm{BF}_{\mathrm{incl}}$
Silence	0.263	0.263	0.1	0.88	0.12
Laterality	0.263	0.263	2.89e -6	1.14e -7	25.32
Centrality	0.263	0.263	2.97e -6	6.63e -47	4.48e +40
Laterality ✻ Silence	0.263	0.263	0.01	0.12	0.05
Centrality ✻ Silence	0.263	0.263	0.01	0.11	0.15
Centrality ✻ Laterality	0.263	0.263	1	2.91e -6	3440044
Centrality ✻ Laterality ✻ Silence	0.053	0.053	9.72e -5	8.27e -4	0.12

Table S4. Analysis of Effects for the 2 Hz Frequency Response. Analysis of the various effect from the Bayesian repeated measures ANOVA of the power spectrum at 2 Hz. The analysis of effects allows us to determine independent evidence for the alternative hypothesis for each main effect and interaction across matched model from table S3. This results in inclusion prior probability [P(incl)], exclusion prior probability [P(excl)], inclusion posterior probabilities [P(incl|data)] and exclusion posterior probabilities [P(excl|data)]. Inclusion Bayes factor is calculated by dividing the inclusion posterior probability by the exclusion posterior probability [P(incl|data)]/ P(excl|data)] estimating the independent evidence for the alternative hypothesis for a specific main effect or interaction effect.

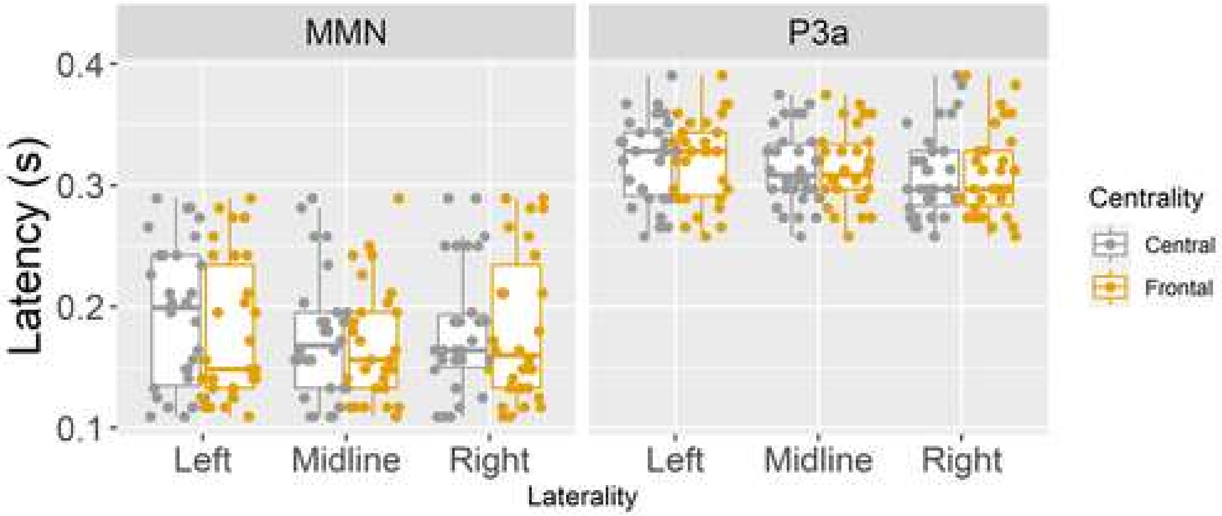

Figure S1. Individual Peak Latencies for The MMN and P3 ERP components. Boxplots of the latencies for the individual peaks (shown as black dots) plotted for each ERP component (MMN on the left side of each figure; P3a on the right side of each figure) by centrality (Central on the left figure; frontal on the right figure) by laterality (Left, Center and Right). The line represents the median value, with the box representing interquartile range. The whiskers represent 1.5 times the inter-quartile range. This suggests a highly skewed distribution along with a wide variation in peak latencies

Chapter 3: Infant Neural Responses to Omission Deviants: The Role of Local and Global Predictability

Prete, D., & Trainor, L. (2024) Infant neural responses to omission deviants: The role of local and global predictability. *OSF*. Manuscript Under Review. https://osf.io/fc6tr/

Preface

In Chapter 2 we showed that in adults, the neural response to omission deviants was similar to the response elicited by tone deviants. But little to no research has been conducted on the neural response to omission deviants in infants. Auditory deviants (i.e., occasional changes in a sound feature) typically elicit what is called the mismatch response in infants. This response is attenuated if the deviant is globally predictable but locally unpredictable, meaning the deviant is still an unexpected change from the standard tone but occurs in a predictable pattern in the auditory sequence. In Chapter 3, we recorded electroencephalography from 6-month-old infants to occasional omission deviants while manipulating the global predictability. In one condition the omission deviants were made globally unpredictable by pseudo-randomly removing 20% of the tones. In the other condition the tones were made globally predictable by removing every fifth tone. Additionally, in both conditions a dot was presented on the screen that pulsated with the onset of each tone and omission to ensure to provide an external cue for the timing of the omission. We found that the infant brain responded to omission deviants in both conditions, but this did not depend on the global predictability. Furthermore, the neural response resembled the mismatch response (MMR), elicited by tone deviants. This chapter presented the first evidence of a robust response to omission deviant in infants.

Abstract

Auditory information, such as speech and music, contains many statistical regularities that infants must make sense of. When a sound is presented that violates the regularities from the previously heard context, both adults and infants elicit a mismatch response that can be measured with electroencephalography (EEG). Mismatch responses can be elicited on the basis of either global or local violations of expectation. Much less research has examined responses to the absence of an expected sound, but processing omission violations can be informative about the world. In adults, unexpected omissions have been reported to elicit several different responses, including the mismatch response, as well as a series of omission specific responses at several latency windows. Very little is known about how the infant brain responds when an expected sound is omitted. We investigated 6-month-old infants' responses to occasional omission deviants that were either globally predictable in the sequence (i.e., removing every fifth tone in the sequence) or globally unpredictable (i.e., randomly omitting 20% of tones), with both being locally unpredictable. Overall, we found that infants responded to the omission deviants with a mismatch-like response, but no difference was found between the global predictable omissions and unpredictable omissions. Infants' neural responses to the omission of expected sounds are broadly consistent with predictive coding theory.

Introduction

Much of the information in our environment contains statistical regularities that create patterns the brain is adept at detecting. Detecting such regularities has been linked to the ability to learn and understand music (Huron, 2006) and speech (Saffran, 2001); learn motor sequences (Kilner et al., 2007); and feel emotions (Barrett, 2017). In the auditory domain, the brain’s automatic detection of an ongoing pattern of sounds can be probed by recording electroencephalography (EEG) while changing one or more of the sounds in such a way that the established pattern is violated. If the auditory pattern has been detected by the brain, the deviant sound will elicit an event-related potential (ERP) component called mismatch negativity (MMN; Näätänen et al., 1978).

However, during infancy the ERP response to a deviant sound can show up as either the MMN or a slower component called the MMR. (Themas et al., 2023; Werwach et al., 2022). The mismatch response (MMR), is a frontally positive component occurring between 200 and 400 ms post deviant sound onset (He et al., 2007). The MMR can be elicited by simple deviants such as pitch changes (Alho et al., 1990; Fellman et al., 2004; Leppänen et al., 1997), but also violations of complex patterns such as deviations in tone pairs (Carral et al., 2005; He et al., 2009a), melodies (Háden et al., 2015), and rhythmic patterns (Flaten et al., 2022; Winkler et al., 2009). The MMR to pitch violations can be measured in neonates (Ceponiene et al., 2002) up to at least 6 months of age (Flaten et al., 2022), whereas the MMN in response to simple pitch deviants does not seem to be present until about 4 months of age (He et al., 2009b). Although the MMR is often interpreted as the infant equivalent of the MMN, around 6 months of age some infants elicit both components (Trainor et al., 2003). A meta-analysis investigating the MMR throughout the first year of development found the change from a positive to negative response to be inconsistent, even citing several studies that show a change from negative to positive with age (Themas et al., 2023), which may be caused by the fact that the MMR or MMN depends not only on age, but on the acoustic feature of the deviant (Cheng et al., 2015). A longitudinal study showed that the shape of the developmental trajectory towards the adults-like MMN can be linear or an inverted-U depending on which acoustic feature is changed to create the deviant sound (Werwach et al., 2022). Regardless of which component is elicited, that deviant sounds elicit a response in infants suggests auditory deviance detection is present at very early stages of development (Moser et al., 2020).

Deviance detection in infants is also influenced by hierarchical statistical regularities in auditory stimuli. When presented with auditory patterns with a long-term global structure and deviant tones that violate either the short-term local pattern, the global pattern, or both, the amplitude of the MMR is smallest for deviants that violate only long-term global probabilities (e.g., no pitch deviant when one is expected after every 4 standard tones), largest for deviants that violate both patterns (e.g., the typical odd ball paradigm), and intermediate for deviants that violate only local patterns (Basirat et al., 2014). The MMR can also be elicited to unexpected changes in chord progressions (Virtala et al., 2013) or pitch deviations in melodies (Tew et al., 2009), indicating infants have expectations for musical patterns as well. When infants have been primed to interpret an ambiguous rhythm in groups of two or in groups of three, pitch deviants that occur on the strong beats according to their primed grouping elicit larger MMRs, showing that infants learn rhythmic structure (Flaten et al., 2022). At 9 months of age, infants who attend music classes show larger MMR to violations of musical temporal structure, compared to infants who do not attend music classes (Zhao & Kuhl, 2016), suggesting that infants use prior knowledge to process incoming auditory information into hierarchical patterns. In sum, infants not only track simple patterns but can track multiple levels of regularity.

Despite the decades of research on infants' auditory deviance detection, little research has been conducted on infants' responses to omission deviants, that is, when no sound occurs when one is expected. In adults, omission deviants (in comparison to standard tones) elicit an MMN-like response when the inter-onset interval (IOI) is 200 ms or less (Bendixen et al., 2009; Chennu et al., 2016; Wacongne et al., 2011; Yabe et al., 1997, 1998). Less research has examined omission responses with larger IOIs, but it is important to do so because with fast IOIs, less than 200 ms, successive sounds will fall within the temporal window of integration. However, a study comparing omission deviants, or unexpected silences, to expected silences in sequences with IOIs of 500 ms showed that MMN-like and P3a-like responses can be elicited for slower tempos as well (Prete et al., 2022). Additionally, when pressing a button to elicit a sound, infrequently omitting the sound to the button press elicits a specific set of omission-related responses referred to as the oN1, oN2 and oP3 that peak in windows 40-90 ms, 120-200 ms, and 250-350 ms after omission onset, respectively (SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). These ERP components have also been found when sounds paired with visual cues are occasionally omitted (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). The oN1 has also been found in children 6 - 8 years old when omission deviants occur in a sequence of action generated sounds (Dercksen et al., 2022).

However, little research has examined the omission responses in infants, partly because infants cannot be asked to do a task such as pressing a button to generate a sound. To our knowledge the only study to use omission deviants with infants presented drum rhythms containing multiple percussive instruments and compared omissions of sounds that occurred on a strong beat or weak beat in the rhythm (Winkler et al., 2009). Omissions on strong beats, but not on weak beats, elicited an MMN in newborns, indicating that omission deviants can elicit change detection responses in infants to complex auditory patterns. However, this study focused on the MMN, and did not investigate the presence of oN1, oN2 or oP3 responses. Furthermore, the IOI of the tones was 150 ms, which is within the temporal window of integration and possibly limiting the neural responses that could be analyzed.

The goal of the present study was to examine the infant response to omission deviants and to determine if predictability influences the response by comparing ERPs to globally predictable and globally unpredictable omissions. We paired sounds and omissions of those sounds with a visual cue to ensure precise time locking of when a sound was expected. Both omissions were unexpected in the local context (i.e., they would expect to hear a sound not silence at that point), but in the global predictable condition, every fifth sound was omitted, creating a global expectation of an omission deviant, whereas in the global unpredictable condition 20% of tones were omitted pseudo-randomly from the sequence. Although we expected responses to the omission deviants in both conditions, and for the globally unpredictable omissions to elicit a larger response than the globally predictable omissions, we did not have a strong hypothesis about which ERP components we would observe. From past work, we expected MMN or MMR, but it is possible infants might display some of the three adult-omission responses described above, or some infant analog of these responses as infant ERP responses do not have the same latency, or sometimes polarity, as adult responses. To our knowledge omission-specific responses have not previously been tested in infants. Thus, we compared infants' responses to globally predictable and globally unpredictable omissions in three time-windows that encompass the various ERP components we might observe.

Methods

Participants

Thirty-eight full term infants (16 male, 16 female) with normal hearing between 6 and 7 months old participated in the current study. One was removed for being beyond the age range at the time of the study and 3 were removed because they were not given all the experimental conditions. The final sample consisted of 34 infants (11 male, 13 female) between 6 months, 2 days old and 6 months, 30 days old (*M* = 6 months, and 14.7 days, *SD* = 6 months, and 8.1 days). This sample size was chosen to be comparable or larger than in previous studies that found significant MMR in infants (e.g., Flaten et al., 2022; Marie & Trainor, 2013, 2014; Trainor et al., 2012). Infants were recruited through social media posts and all methods were approved by the McMaster Research Ethics Board. Informed consent was given by the parent or primary caregiver, who also completed a questionnaire about the musical training of both parents, their language background(s), and demographic information.

Stimuli

The auditory stimuli consisted of an isochronously repeating C3 marimba tone with an inter-onset interval (IOI) of 400 ms. The tone was sampled from GarageBand and edited using Audacity® 3.2.4 (Audacity Team, 2021) to have a 100 ms duration and 15 ms cosine rise and fall times. In each block, the tone was repeated for a total of 5 minutes for 30 participants and 4 minutes for 4 participants. 20% of the tones were replaced with silence to create omission deviants. During the global unpredictable condition, omission deviants were pseudo-randomized within each block, with the constraint that at least two tones occurred before the next omission and the first 10 events in the sequence did not contain an omission, to set the expectation of hearing the marimba tone. During the global predictable condition every fifth tone was removed, creating a predictable omission deviant with the same presentation rate as the unpredictable omission deviants, but when the next omission would occur was predictable from the global context. In each 5 min block, there were 150 omissions and 600 tones for a total for 750 events per block. Within the 4 min blocks, there were 120 omissions and 480 for a total of 600 events per block.

Tones and omissions were paired with a visual cue to ensure the onset of the omissions had a clear point in time, as an omission is the lack of a sound. The visual cue was presented in a video with a format of 270 x 480 pixels. It consisted of a static dot that increased in radius by 2 cm every 400 ms such that the dot increased in size simultaneously with each tone, or omission, onset. We also manipulated the dot to change either in colour or number every 30 seconds to engage infants' attention with the visual cue. As the number of dots increased, the initial radius of each dot decreased to fit the dimensions of the video but the increase in radius remained constant at 2 cm on the monitor (see supplementary materials for an example of the stimuli). The initial radius of the dot was 4.5 cm on the monitor (increasing to 6.5 cm), and the radius of the final dots were 2.5 cm on the monitor (increasing to 4.5 cm). The auditory and visual sequences were presented to the infants as premade videos. The auditory stimuli were created using MATLAB 2020a (The MathWorks Inc., 2022) and the visual stimuli were created using SynFig Animation Studio 1.4.1 (2021). The audio and video were combined and temporally aligned using VideoPad Video Editor 13.07 (2023). The global predictable and unpredictable conditions consisted of identical visual stimuli, such that only the auditory information changed between conditions. To further engage infants' attention to the monitor presenting the pulsating dot(s), the visual cue was superimposed onto videos of baby animals (see the supplemental material for an example of the video). Videos were encoded using H264 encoder with a constant frame rate of 30 Hz and the audio was encoded as MP3 at 44100 Hz sampling rate. These settings were tested using a photo diode and oscilloscope to ensure the best synchronization between the auditory and visual stimuli.

A third visual only condition was also included that consisted of only the visual stimuli (i.e., the pulsating dots) to record neural activity related to processing the visual information alone. For 4 participants included in the analysis the visual only condition consisted of a 1 min long video whereas for the remaining participants the visual only condition was shortened to 30 seconds. This change was implemented because with 1 min long videos, infants were more likely to become overly fussy, need breaks, be unable to continue the experiment, or completely disengage with the visual cues.

Procedure

Testing took place in a sound attenuated booth and infants sat on their caregiver's lap. The sound was presented through an AudioVideo Methods speaker (P730) placed 1 m directly in front of the infants. Sounds were presented at 60 dB SPL A weighted, measured at the location of the infants' head. The videos were displayed from a Dell 2790w monitor 95 cm in front of the infants.

The three conditions were presented in each block. The order between the global unpredictable and predictable conditions was counterbalanced across participants, but the visual only condition was always presented last. Blocks of were repeated up to three times (depending on the infants' cooperation) while maintaining the counterbalanced order (i.e., unpredictable, predictable, visual only; or predictable, unpredictable, visual only). Two infants completed one repetition of all three conditions, seven infants completed two repetitions of each condition, and 25 infants completed all three repetitions.

One experimenter stayed in the booth to monitor when the infant disengaged from the videos. This experimenter initially stayed outside of the infant's view until the infant stopped looking toward the visual stimuli, at which point the experimenter would sit beside the monitor and attempt to direct the infant's attention toward the video. Both the caregiver and the experimenter wore Sennheiser 640 Pro headphones playing a mix of pop music to mask the experimental auditory stimuli. Another experimenter stayed outside the booth to monitor when the infant's gaze was not directed towards the monitor. If an infant looked away from the screen for at least 2 sec, this was noted directly in the EEG file. The infant had to be looking at the screen for at least 2 seconds after looking away to be considered looking at the monitor again. We used 2 seconds to ensure quick glances and saccades were not considered changes in attention toward or away from the screen. If the infant was not looking toward the screen for any part of a trial (i.e., tone or omission), that trial was removed from the analysis. After the visual only conditions, the infants were given a short break in which the experimenters and caregiver could interact with the infant. More breaks were given if deemed necessary by the experimenters.

EEG Data Acquisition and Preprocessing

EEG data were recorded using a 129 channel Hydrocel GSN net montage, though channels 125, 126, 127 and 128 were not connected with electrodes, for a total of 125 recording channels. NETSATION Acquisition software was used to record the data at a sampling rate of 1000 Hz online referenced to Cz. Electrode impedance was kept below 50 kilo-ohms.

All preprocessing was done in MATLAB using the Fieldtrip toolbox (Oostenveld et al., 2011). First, the data were filtered between 0.5 and 20 Hz using a 4th order Butterworth filter and using two-pass filtering to correct for phase delays. After the data were filtered, it was visually inspected to identify and remove bad channels, defined as channels showing extreme variance. On average 9.17 channels were removed across participants (min = 3, max = 15). The remaining data were then subjected to artifact blocking to minimize large amplitude fluctuations (Fujioka et al., 2011; Mourad et al., 2007), using a threshold of 60 microvolts in 10-s contiguous windows. The corrected data were offline re-referenced to the common average, and then bad channels were interpolated using an average from surrounding electrodes. The data were separated into 500 ms epochs, from 100 ms before the omission or tone onset to 400 ms post event onset. Finally, trials in which any channel had an amplitude range greater than 100 microvolts were removed before the analysis. Any infant that had fewer than 100 deviant trials in the global predictable or unpredictable condition or did not have any trials in the Visual Only condition, was removed from further analysis. This resulted in 14 more infants being removed for a final sample of 20 infants. The average trial count for the global unpredictable omissions, global predictable omissions, and visual only condition were 162.9 (SD = 42.01), 166.25 (SD = 40.67) and 63.3 (SD = 37.95), respectively. Each infant’s individual ERP for the Visual Only Condition, averaged across trials, was then subtracted from the average ERP for global unpredictable omissions and global predictable omissions to remove neural activity related to the pulsating dot.

Data Analysis

To analyze the effect of predictability on responses to omission deviants, we used a cluster-based permutation analysis in three time-windows 50 to 150 ms, 150 to 250 ms, and 250 to 350 ms. The last two windows were chosen because these are the windows in which we would expect to find an MMN or MMR, respectively. They are also windows in which we might expect to find an oN2 or oP3, respectively, given that ERP responses in children and infants tend to be later compared to the corresponding adult components (Dercksen et al., 2022; Wunderlich et al., 2006). We compared the two conditions using cluster permutation analysis based on two-sided dependent *t*-tests with an alpha of 0.05. Clusters were defined as any timepoint(s) in which at least 2 electrodes showed a significant difference, and the maximum-sum of the *t*-values was used as the cluster statistic with a cluster level-alpha set to 0.05, corrected to 0.025 for a two-sided test. The data were randomly permuted 5000 times and the maximum sum *t*-values for each iteration were used to create the permutation distribution. These parameters were used for all three time-windows.

Furthermore, to test that the omissions elicited a significant response above the noise floor, within each of the latency windows of interest, we compared the ERP in the time-windows to the 100-ms baseline using cluster permutation analysis separately for the two conditions. The same parameters as stated above were used for these permutation analyses as well.

Results

The ERPs to global predictable and global unpredictable omissions were very similar (Figure 1). In all three latency windows no differences were found between the two conditions (Table 1). Given that the global predictable and global unpredictable omissions were not significantly different we averaged each individual's ERP from both conditions together and tested whether the averaged omission responses were greater than baseline using the same cluster permutation analysis described above.

For the averaged responses, in the 50 – 150 ms window a significant difference was found between the combined results and the baseline ($t_{\text{max-sum}} = -810.12$, $p = 0.041$), that appeared to occur from about 85 ms to 150 ms at temporal left electrodes (Figure 2a). From 150 to 250 ms the averaged omission response was greater than baseline activity ($t_{\text{max-sum}} = 1030.49$, $p = 0.033$) at more frontal and central electrodes, and significantly more negative ($t_{\text{max-sum}} = -1135.89$, $p = 0.022$) at temporal left, parietal left and occipital left electrodes (Figure 2b). The duration of these differences lasted for approximately the full duration of the window. In the final analysis window from 250 to 350 ms, the averaged omission response elicited a negative component significantly larger than baseline ($t_{\text{max-sum}} = -1278.57$, $p = 0.014$) that was most prominent at left occipital and central occipital electrodes with a latency of about the full duration of the analysis window (Figure 2c). Thus, the averaged response to the omission deviants elicited responses greater than baseline activity in all three analysis windows.

To further explore the ERP results we plotted the ERP responses to the tones immediately preceding omission deviants, allowing us to descriptively compare the responses to tones and omission deviants (Figure 3). We chose tones immediately before omissions because responses to these tones should be very similar to responses, we would expect had there been a tone at the time of the omission. From the onset of both the tones and omission to about 250 ms the waveforms look very similar with a positive fronto-central peak around 175 ms that reverses at posterior scalp regions. After 250 ms, and leading into the next tone event, it appears that omission deviants had a more positive response compared to the tones, but this was not evaluated statistically.

Discussion

Omission deviants evoked responses that were greater than baseline activity at several latencies, indicating infants responded to violations of the local predictability – that is, hearing nothing when they expected to hear a sound in a sequence of repeating sounds. However, contrary to our hypothesis we did not find evidence that global predictability influenced the response elicited by the omission deviants. Cluster analyses revealed significant evoked omission responses in all three latency windows. In the first window (50-150 ms) there was a significant negative component centred at temporal left sites. It was accompanied by a positive component centred at central/parietal sites, although this component was not significant (see Figure 2). It is not clear what this component reflects as it does not appear to resemble previously reported infant or adult responses.

In the second window (150-250 ms), omission deviants elicited a positive component at frontal and central sites, accompanied by a reversal at left parietal, occipital and temporal sites. This topography is typical of the frontally-positive infant MMR, although it is slightly earlier than reported for auditory deviants such as an unexpected change in pitch (Cheng et al., 2013, 2015; He et al., 2009b; Trainor et al., 2011). The MMR and adult MMN are typically interpreted under the predictive coding framework (Friston, 2005; Friston & Kiebel, 2009), which states that these neural responses reflect prediction errors between the expected sound and the deviant sound (Chennu et al., 2013; Wacongne et al., 2012) or deviant omission (Chennu et al., 2016; Dercksen et al., 2020; Lao-Rodríguez et al., 2023; SanMiguel, Saupe, et al., 2013; van Laarhoven et al., 2017; Wacongne et al., 2011). Predictive coding theory has also been used to explain the MMR to auditory deviants in infants (Basirat et al., 2014; Háden et al., 2015) and omission responses in children (Dercksen et al., 2022). Given that the present response to omissions was earlier than is typical for MMR in infants of this age, it is possible that responses to omission deviants are faster than responses to sound deviants in infancy, perhaps because without a physical stimulus, sound characteristics do not need to be encoded and compared to the expected sound. Further studies would be needed to determine whether the infant omission evoked potentials differ in other systematic ways from ERP evoked by auditory deviants which could provide insight into how the brain learns to process an unexpected absence of an event. In any case, our results suggest infants detect deviations caused by omissions, and omission deviance detection may reflect a prediction error signal caused by hearing silence when a sound was expected (Lao-Rodrígu et al., 2023; Wacongne et al., 2012).

Interestingly, in the final window (250-350 ms), there was a negative response at left occipital sites, accompanied by a positive response at right central and temporal sites (Figure 1), although only the negative response was significant in the cluster analysis (Figure 2). Further, Figure 1 suggest that this occipitally negative/temporally positive component may build up over the entire time window between the omission onset and the next tone. It is possible, therefore, that this negativity is a slow on-going component indexing temporal expectations for the tone that follows each omission. In adults, temporal expectations can be indexed by a central negative component called the contingent negative variation (CNV; Walter et al., 1964). One existing study suggests that an adult-like CNV does not develop until 6 years of age (Cohen et al., 1967), but there is almost no research on an infant analogue of the CNV. It is possible that our results reveal an infant analog of the CNV, which, if true, would mean that infants formed some kind of global prediction about the timing of the tones following the omissions, even though infants did not appear to form expectations about the global regularity of the omission deviants. Further studies are needed to investigate the nature of this response and what it reveals about predictive coding in infants.

We found through visual inspection that the ERPs to omissions (where there was no sound) resembled the ERPs to the tones preceding omissions up to about 250 ms post-onset (Figure 3). From a predictive coding view, the similarity between the tone and omission waveforms may reflect activation of the sensory template for the predicted stimuli (Kok et al., 2014; SanMiguel, Widmann, et al., 2013). In adults, the N1 to tones and oN1 to omission deviants have similar waveforms and source localization with activity stemming from the medial temporal gyrus (Korka et al., 2020; SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). The neural activity we observed up to 250 ms to the omission deviants may thus represent, at least in part, the infant analog of the prediction model at work, and not entirely activity specifically in response to the omission deviant. Of course, this does not show up as the N1 in infants as the fully adult-like N1 does not appear until many years later (Ponton et al., 2000; Ruhnau et al., 2011; Shahin et al., 2004; Sussman et al., 2008), so the actual ERP components reflecting prediction in the infant brain will be different than those reflecting prediction in the adult brain. Neural responses after 250 ms diverge for tones and omissions, suggesting that, at least in the 250-350 ms window following omissions, the infant response likely represents expectations for the upcoming tone, as discussed above, or perhaps an infant analog of the P3a indicating infants' attention was oriented towards the omission deviant (Conroy & Polich, 2007; Polich, 2007).

Surprisingly, we did not find evidence that the magnitude of response was reduced when omissions were globally predictable, given that, according to predictive coding, prediction error responses are sensitive to hierarchical predictions. Our results suggest that the violations of hierarchal predictions seen in adults (Bekinschtein et al., 2009; Bendixen et al., 2007; Wacongne et al., 2011), and in infants in response to auditory deviants (Basirat et al., 2014; Flaten et al., 2022; Háden et al., 2024; Zhao & Kuhl, 2016), may not be fully in place yet in infants' responses to omission deviants. Infants have been shown to use statistical regularities to learn the hierarchy of syllables and words (Bosseler et al., 2016; Choi et al., 2020; Saffran, 2001; Saffran et al., 1996) and musical training enhances 9 month-old infants learning of the temporal hierarchy (i.e., rhythm, beat and meter) in music (Zhao & Kuhl, 2016). This would suggest that hierarchical predictive coding is present in infants for auditory (i.e., sound) deviants, but our current results indicate that it may not extend to omission deviants. One factor that needs to be explored is tempo. Our stimuli were presented at a relatively slow rate of 400 ms onset-to-onset, which is considerably slower than that of many of the studies cited above. Indeed, in adults, faster presentation rates lead to more robust responses to omission deviants (Raij et al., 1997; Yabe et al., 1997, 1998). Thus, future studies could explore the interaction between tempo and global predictability with infants to understand the developmental trajectory of the response to omission deviants. But in any case, the fact that we observe a response to the omission deviants greater than baseline activity is in line with a more general form of predictive coding being present in infants.

On the other hand, it is also worth considering whether neural adaptation might account for our findings. A model of neural adaptation based on adults and non-human primates that includes short term synaptic depression and lateral inhibition (May, 2021) suggests that the response to an omission deviant may be a rebound from ongoing oscillatory activity habituated to the repeating tone (Hajizadeh et al., 2019; May, 2021). Although not specifically stated or tested by the model, factors such as tempo or rate of omission deviants may be more influential than global predictability. Specifically, May (2021) tested the model for omission responses in an oddball paradigm, with stimuli presented with an SOA of 100 ms and a 10% deviant rate. As our stimuli were presented much slower, we ran the model with our parameters, specifically, an SOA of 400 ms and an omission deviance rate of 20%. With these parameters, the model produced no omission responses for unpredictable omissions. This suggests that different mechanisms may account for omission deviant responses at slower and faster presentation rates (Prete & Trainor, 2022). Further, it suggests that ongoing oscillatory activity and neural adaptation are unlikely to account for the omission responses we observed in infants, although it should be noted that the parameters of the model are not tuned for the infant brain. Both adaptation and predictive coding models need to be further developed to understand how the brain responds to omission deviants presented at a slower tempo and to account for the developmental of these responses.

In general, infant ERP responses differ dramatically from those of adults. Little research has been done on the development of neural responses to omission deviants, but one study has shown that children 6 to 8 years old produce oN1 responses (Dercksen et al., 2022), which corresponds to the age at which N1 can start to be reliably seen (Wunderlich et al., 2006). While infants in our study showed neural omission responses within the latency windows of the adult oN2 and the oP3, their components were very different than those of adults. Specifically, with a nose reference, the adult oN2 is negative around central and temporal regions (SanMiguel, Widmann, et al., 2013; van Laarhoven et al., 2017) and the oP3 is positive around central regions (Dercksen et al., 2020; van Laarhoven et al., 2017). Infants, on the other hand, using a common average reference, showed a negative posterior response predominantly at the latency we would expect the oN2 and oP3, accompanied by a positive response at fronto-central electrodes between 150 and 250 ms. While different referencing methods might account for some of these differences, it is clear that infant responses are very different from those of adults. This is not surprising as infant ERPs to sounds (Ponton et al., 2000; Shahin et al., 2004) and sound deviants (He et al., 2007, 2009b) are also very different in infants and adults. Future studies should examine how omission responses change from infancy through childhood to understand how changes in amplitude, latency, and source localization develop from infancy to adulthood.

Another difficulty in comparing infant and adult omission responses is that many adult studies investigating the response to omission deviants use a task such as pressing a button (Dercksen et al., 2020; Korka et al., 2020; SanMiguel, Widmann, et al., 2013) or detecting a visual change (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017), which draw participants' attention towards the stimuli. Thus, the adult omission responses may reflect higher-order attention or attentional capture (Korka et al., 2020; SanMiguel, Saupe, et al., 2013; van Laarhoven et al., 2017) in contrast to MMN and MMR, which does not require attention (Näätänen et al., 2007). Although the videos used in the current experiment were designed to engage infants' attention with the experimental stimuli, there was no way to ensure infants were attending; and in any case, infant attentional processes likely differ significantly from those of adults. Furthermore, directing attention toward the stimuli is not the same as having participants engage in a task. It has yet to be tested in adults whether the oN1, oN2 and oP3 are present during passive listening and, thus, it is unclear if these responses require attention or task engagement. As far as infants, it might be possible to have older infants hit a tablet with their palm to produce sounds, and occasionally omit the sound when they execute a hit, similarly to the studies where adults press a button to produce sounds (Dercksen et al., 2020, 2022; Korka et al., 2020; SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). However, it will be difficult to obtain enough trials in an infant with this approach as infants have limited attention spans; further there would likely be much more motion artifacts as infants would engage their arm as opposed to a single finger. In any case, attempting to test infants and adults with similar, yet age appropriate, paradigms could help understand differences across age and developmental trajectories of the neural response to omission deviants.

In sum, the current research was one of the first to investigate responses to omission deviants in 6-month-old infants. We found clear neural response to omission deviants indicating that infants are reacting to unexpected silences. One component in the 150-250 ms range resembled MMR, although its latency was somewhat earlier than what is typically observed in response to sound deviants. The later component of the infant omission response appears to represent an expectation for the subsequent tone. Unexpectedly, there was no evidence that omission responses were affected by global predictability, suggesting that omission responses in infancy might not be affected by hierarchical temporal structure, although this would need to be tested with faster presentation rates before reaching a definitive conclusion. Additionally, the neural mechanisms leading to the observed responses are not yet clear. Omission deviance detection is consistent with a broad predictive coding framework but could not be explained by a recent highly-specified model of neural adaptation. To understand the mechanisms producing omission responses, future research should focus on the conditions under which infants produce omission responses, and how omission responses develop with age. Combining the current experimental paradigm with other data collection methods that enable source localization, such as MEG, could also help further our understanding of the developmental trajectory for how the brain reacts to unexpected omissions of sounds.

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Analysis Time Window	**Cluster statistic (sum *t*-value)**	***p*-value**	**Latency (ms)**
50 to 150 ms	-130 - 318	*> 0.267*	64 - 134
150 to 250 ms	-22.80	0.725	240 - 244
250 to 350 ms	58.59	0.581	340 - 360

Table 1. Cluster Permutation Results Comparing Global Unpredictable Omissions to Predictable Omissions. Results from the cluster permutation analysis comparing the neural responses to unpredictable and predictable omissions in 3 time-windows. Results from each time window with multiple clusters with p > 0.05 were collapsed into a single row. The smallest p-value found, the range of the cluster statistics and range of latencies for these clusters are given instead.

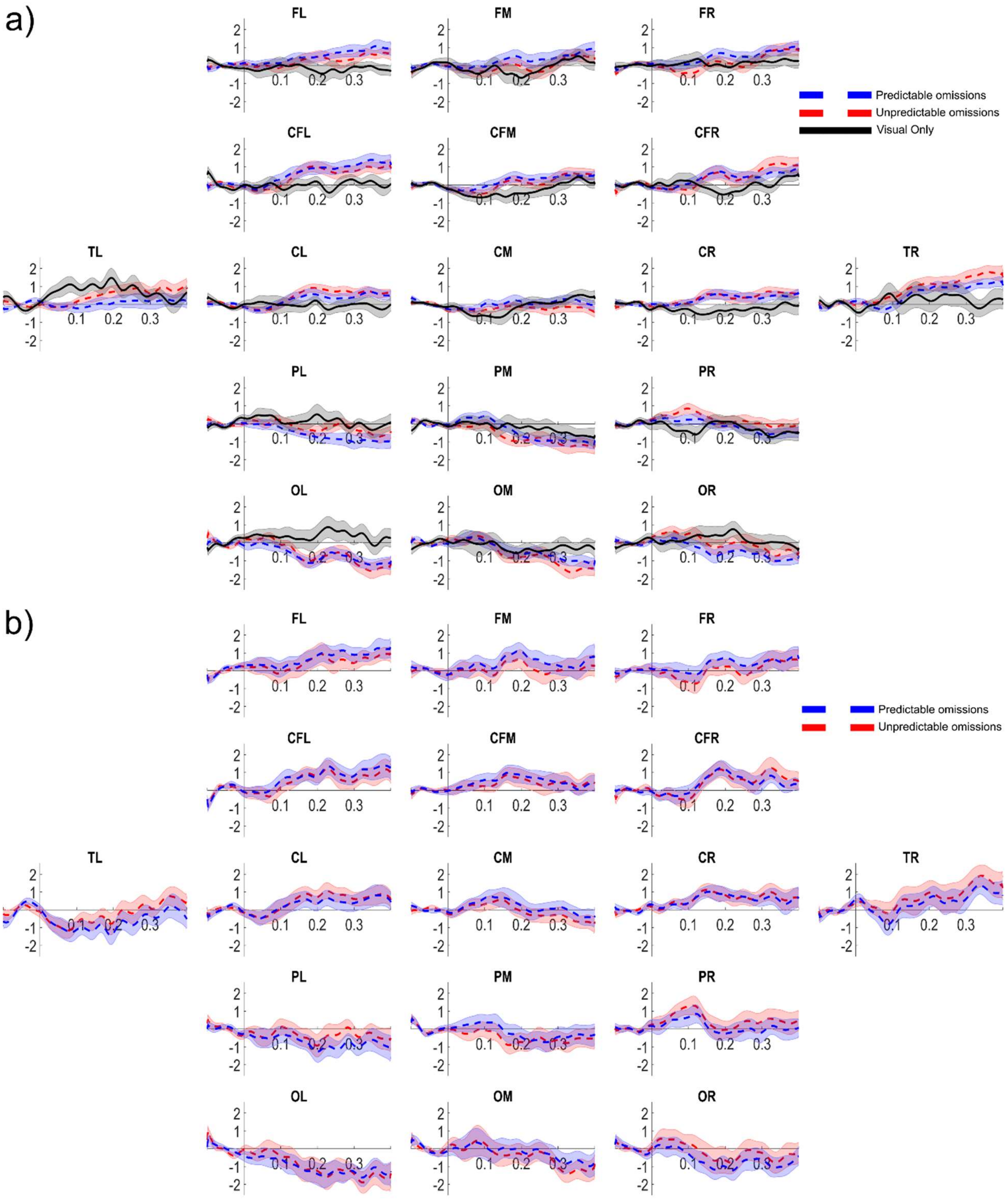

Figure 1. Grand Average ERPs Across the Scalp. a) The grand average ERPs for the three conditions: global predictable omissions (dashed blue lines), global unpredictable omissions (dashed red lines) and the visual only (solid black lines). b) the grand average ERPs for the

predictable omissions (dashed blue lines), global unpredictable omissions (dashed red lines) after the visual ERPs were subtracted at the individual level, before the grand average was calculated. Shaded areas represent +/- 1 standard error of the mean. The figures show the grand average ERPs averaged across electrodes within 14 groupings (Figure S1). The regions are split into anterior to posterior regions: frontal (F), central-frontal (CF), central (C), parietal (P), occipital (O) and three lateral regions: left (L), middle (M), right (R), and the temporal left (TL) and temporal right (TR) regions as well.

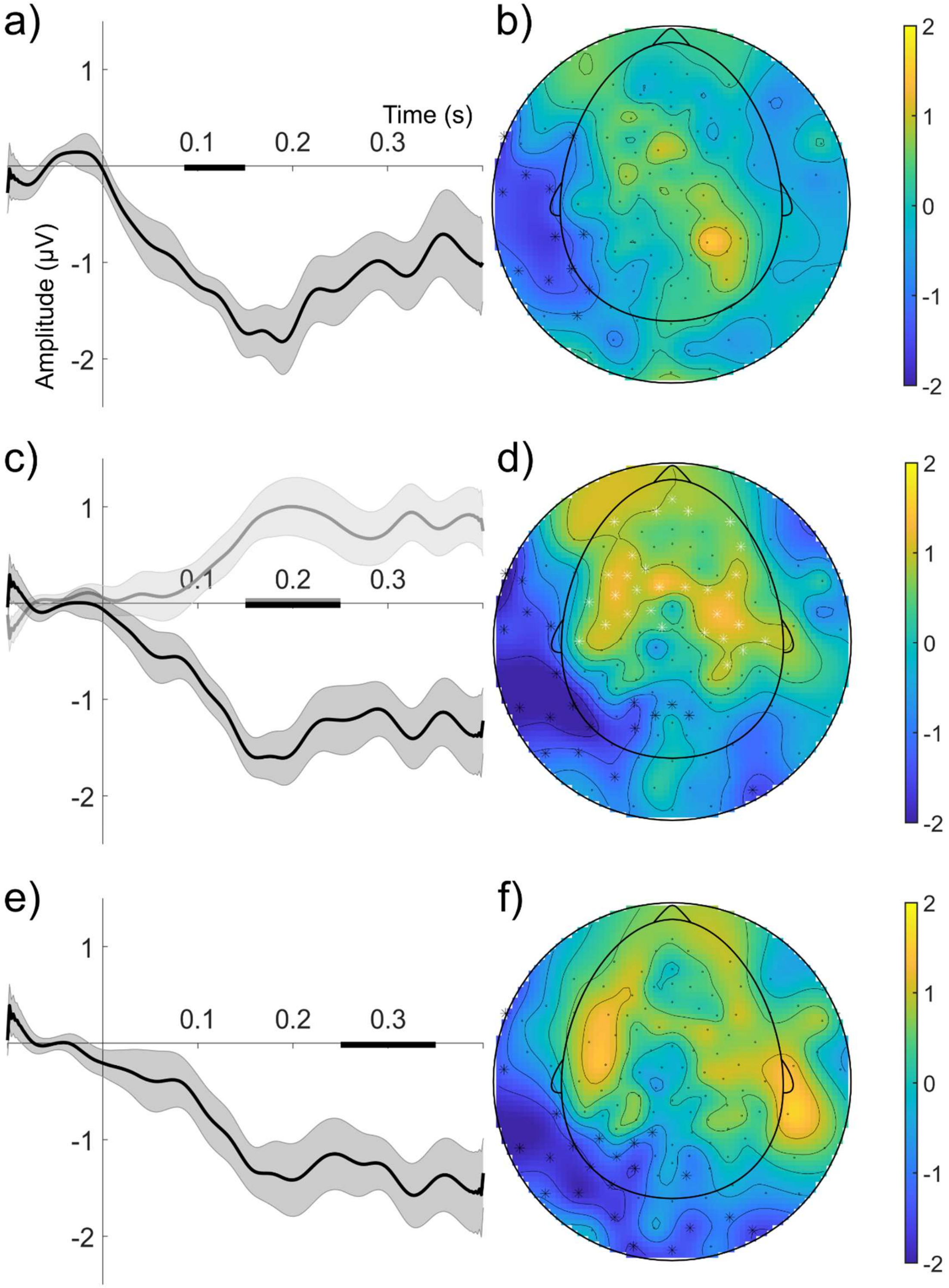
a)
b)
c)
d)
e)
f)
Time (s)
0.1
0.2
0.3
Amplitude (µV)
1
-1
-2
2
1
0
-1
-2

Figure 2. Combined Omissions Compared to Baseline. The ERP and topographic results from the cluster permutation analysis comparing the averaged ERP response to global predictable and global unpredictable omissions from 50 to 150 ms (first row), 150 to 250 ms (second row) and 250 to 350 ms (third row) to the -100 to 0 ms baseline. The shaded areas around the solid lines are +/- 1 SEM. a), c) and e) represent the grand average ERPs for the negative clusters (solid black line) and the positive clusters (solid grey line) found within each permutation analysis, when a negative and positive cluster were present. The electrodes that make-up the grand average ERPs in a), c), and e) are shown in the corresponding topographies in b), d), and f) as black asterisk for the negative cluster and white asterisks for the positive cluster. b), d), and f) are the difference topographies after the baseline activity has been subtracted from the ERP for that analysis window and then averaged over the latency of the cluster.

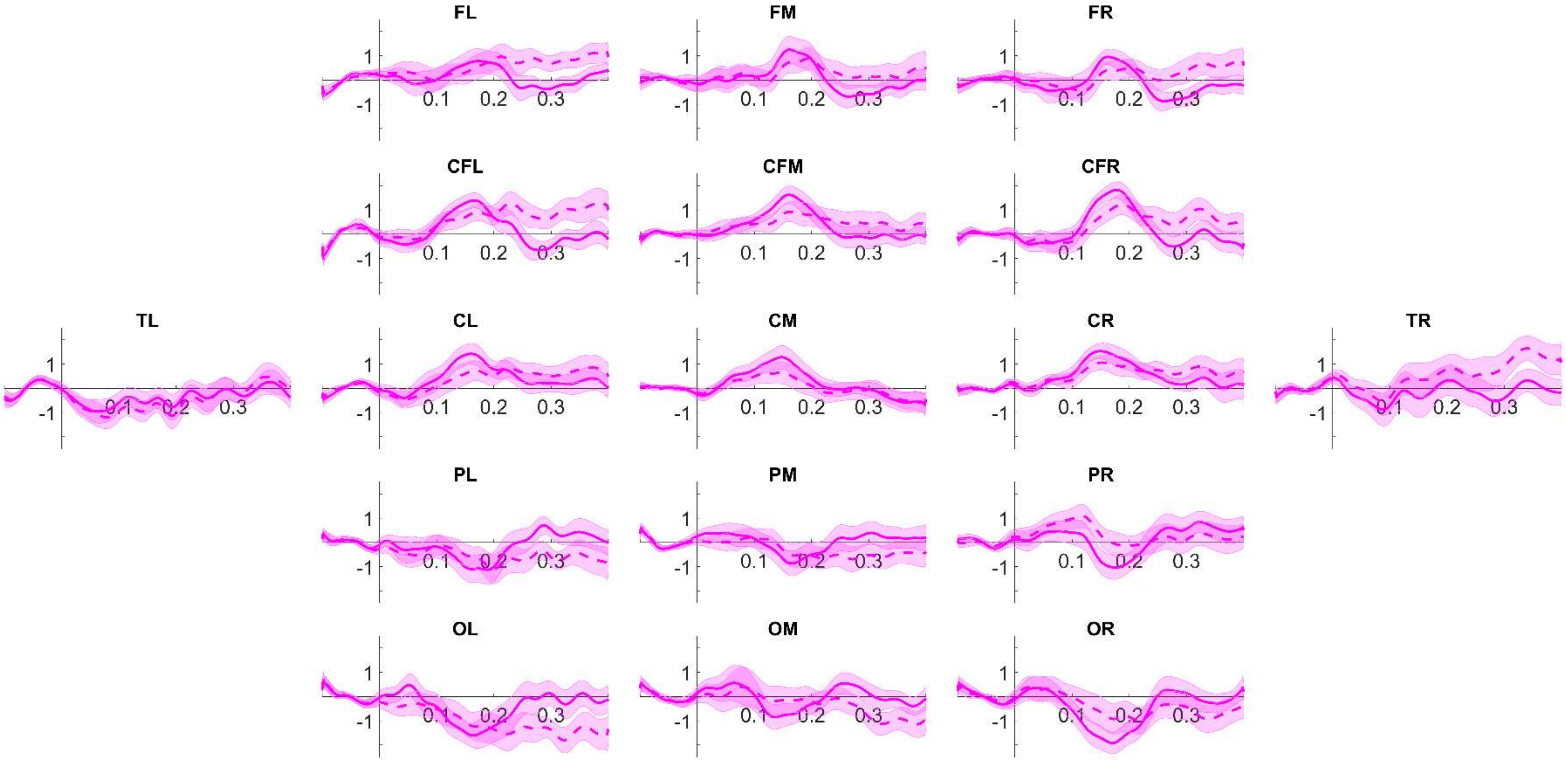

Figure 3. Tones Before Omission Deviants and Omission Deviants. a) The grand average ERPs for the omission deviants averaged across conditions and the tones occurring before (solid line) and omission deviant averaged across conditions (dashed lines) after the ERPs to the visual only condition were subtracted at the individual level, before the grand average was calculated. Shaded areas represent +/- 1 standard error of the mean. The figures show the grand average ERPs averaged across electrodes within 14 groupings (see Figure. S1 for electrode montage).

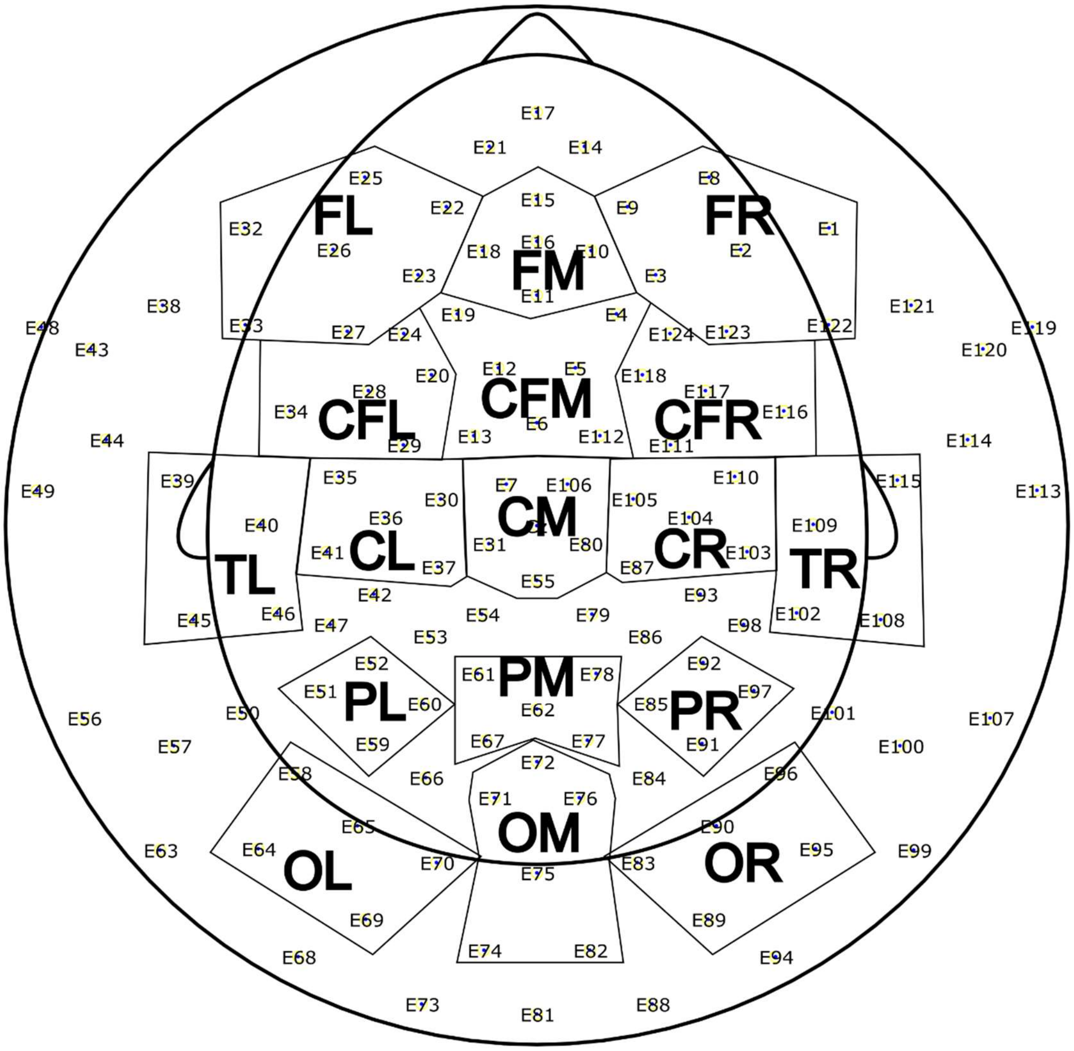

Figure S1. Electrode montage and groupings. The 129-channel montage for the Hydrocel GSN net used to record the EEG, with 14 groupings used for visualizations in figure 1. FL = frontal left, FM = frontal middle, CFR = centro-frontal right, CFL = centro-frontal left, CFM = centro-frontal middle, FR = frontal right, TL = temporal left, CL = central Left, CM = central middle, CR = central right, TR = temporal right, PL = parietal left, PM = parietal middle, PR = parietal right, OL = occipital left, OM = occipital middle, and OR = occipital right. Note these groupings were used solely for visualization and were not part of the analysis.

Chapter 4: Neural Responses to Omission Deviants: Does Globally Predictability Matter?

Prete, D., & Trainor, Laurel J. (2024). Neural responses to omission deviants: Does global predictability matter? Manuscript Under Review

Preface

In both infants and adults, omission deviants seem to elicit a reliable response indicative of a deviance detection mechanism responding to omission of an expected stimulus (as shown in Chapter 2 and Chapter 3). However, the role of global predictability on the influence of the response to omission deviants has not been directly tested. In Chapter 4 we replicated the experimental design of Chapter 3 to test how global predictability influences the response to omission deviants in adults. Because in Chapter 3 we did not find an effect of global predictability in infants, it is possible that it does not influence the response to omission deviants until much later in development, as infants and adults generally have distinct neural responses. Overall, we found responses to both globally predicable omissions and globally unpredictable omissions that were greater than baseline neural activity. However, there was no difference between the responses and the responses did not look like the typical deviance detection responses we expected from the literature or Chapter 2. We found that both omission deviants elicited a frontal positive response that lasted for the duration of the omission. These results further indicate that global predictability does not influence the response to omission deviants, similarly we found in Chapter 3 in infants, suggesting that the larger context in which the omission deviant is presented can vary the omission response drastically, as the globally unpredictable omission condition in this chapter is very similar to the unexpected silence condition from Chapter 2. Overall, more research is needed to fully understand the response to omission deviants and how global predictability, development and experimental parameters influence these responses.

Abstract

Consciously or unconsciously, we track patterns in auditory sequences. When a pattern is violated by an unexpected sound, one or more event-related components (ERPs) are elicited, demonstrating neural processing of the violation. Predictive coding theory suggests there should also be brain responses to unexpected omissions of auditory events. In a passive listening study, we presented omission deviants in two conditions while recording electroencephalography (EEG). In both, 20% of the tones in an auditory sequence were omitted, but in one case, they were omitted pseudo-randomly (globally unpredictable omissions) and in the other, every fifth tone was omitted (globally predictable omissions). Thus, we compared how global predictability influences the processing of tone omissions. We expected that globally unpredictable omissions would elicit stronger ERP responses compared to globally predictable omissions in several ERP components as predictive coding is thought to be a multi-stage process. Using cluster permutation-based analysis, we found both types of omission deviants elicited a response greater than baseline activity but no differences between the globally predictable and globally unpredictable omissions were found. Both omission deviants elicited a sustained frontal positivity for the duration of sound omission rather than the expected ERP components, such as the MMN. Thus, omission deviants elicit a robust response, but contrary to our predictions and previous research on unexpected changes in sound features, the global predictability of the omissions did not appear to influence the magnitude of the responses.

Introduction

Predicting upcoming events is vital for functioning in the world. Tracking patterns in the environment allows us to react to deviations from these patterns, helping us, for example, to attend to new information or determine if danger is present. Although models have been proposed for how the brain tracks or possibly predicts upcoming stimuli (Arnal & Giraud, 2012; Friston & Kiebel, 2009; May, 2021; May & Tiitinen, 2001; Wacongne et al., 2012; Winkler, Denham, et al., 2009), one area of research that requires more study is what happens when expected stimuli are omitted. Understanding how we respond to the absence of predicted events is necessary for a complete understanding of how the brain tracks predictability in the environment and how violations to predictability are dealt with.

Violations of patterns in auditory streams can be studied with electroencephalography (EEG). This is typically done using an oddball paradigm in which an auditory sequence is comprised of frequent, expected or predictable “standard” sounds that are randomly intermixed with infrequent, unexpected or unpredictable “deviant” sounds (Näätänen et al., 2001). The oddball paradigm has been extended to examine effects of deviant stimulus occurrence rate and sequence regularity by comparing the same stimulus presented as a deviant in one condition and as the standard tone in another (Grimm et al., 2011; Shestopalova et al., 2015), or in the situation in which a number of stimuli are presented, with no one stimulus being more probable than the others (i.e., no standard), so that all stimuli are equally unpredictable (Jacobsen & Schröger, 2003; Ruhnau et al., 2012; Todd et al., 2011, 2013).

Using different experimental designs, several ERP components have been proposed to index violations of expectation. The mismatch negativity (MMN) is the most prominently studied ERP component in this context. It manifests as a frontal negative deflection in the ERP measured at the scalp with a peak amplitude between 150 to 200 ms post onset of the deviant stimuli (Näätänen et al., 2007). The deviant tone typically deviates from the standard in an acoustic feature such as frequency, amplitude, or duration (Näätänen et al., 2004; Shröger, 2007; Tervaniemi et al., 1999). MMN can also be elicited by violations of longer patterns, such as ascending or descending tone sequences (Carral et al., 2005; Sussman et al., 1998b), violations of rhythm (Bouwer et al., 2016; Winkler, Haden, et al., 2009), or violations of more complex patterns (Alho et al., 1996; Costa-Faidella, Baldeweg, et al., 2011; Costa-Faidella, Grimm, et al., 2011; Fujioka et al., 2005; Schröger et al., 2007; Tervaniemi et al., 2014; Tew et al., 2009).

The MMN is also sensitive to local and global predictability. In a repeating 5-event pattern, such as four standard tones followed by one deviant tone, the final deviant violates the local prediction (change from the standard tone to a deviant tone) but follows the global prediction based on the 5-event pattern. Comparing deviants when a global predictable pattern is present or not, deviants that violate multiple levels of predictability (i.e., both local and global predictions) tend to elicit larger MMN compared to deviants that violate only the local or global predictability (Basirat et al., 2014; Bekinschtein et al., 2009; Horváth et al., 2001; Wacongne, Labyt, Van Wassenhove, et al., 2011). However, the deviant within the 5 event-pattern will still elicit an MMN even though it does not violate global predictions because it still violates the local predictions. Thus, the MMN indexes violations of predictions multiple hierarchical levels of the auditory stream.

Even though the majority of MMN research uses auditory deviants, there is evidence showing that omitting an expected tone, termed an omission deviant, elicits changes in the ERP as well (Raij et al., 1997; Yabe et al., 1997, 1998). Some research compared omission deviants to standard tones (Bendixen et al., 2014; Moldwin et al., 2017; Oceak et al., 2013; Recasens & Uhlhaas, 2017; Salisbury, 2012; Yabe et al., 1997, 1998). However, this paradigm leads to interpretation issues as it is difficult to be sure that any differences are due to violations of the predicted pattern and not due to auditory evoked potentials present in the ERP after a tone, which would not be present in response to omissions. In addition, most studies also presented tones very rapidly, finding evidence of omission-evoked MMN responses only for stimulus presentation rates less than 200 ms stimulus-onset asynchrony (SOA; Bendixen et al., 2014; Oceak et al., 2013; Recasens & Uhlhaas, 2017; Wacongne, Labyt, van Wassenhove, et al., 2011; Wacongne et al., 2012; Yabe et al., 1997, 1998). This is potentially problematic as it is within the window of integration in which consecutive sounds can be perceived as a single event rather than as individual tones (Horváth et al., 2007; Shinozaki et al., 2003); thus, an omission of one tone could be interpreted as a change from a two-tone percept to a one-tone percept.

To circumvent these issues, in a previous study, we compared omissions presented in different contexts rather than comparing responses to tones versus omissions, and used a slower presentation rate (Prete et al., 2022). Specifically, we presented tones every 500 ms and infrequently omitted tones, creating unexpected silences. For the expected silences, we presented tones every 1000 ms, thus creating an expected silence every 500 ms after each tone. Importantly, the immediate local context is identical in the two conditions as both expected and unexpected silences occur 500 ms following the previous tone and have a duration of 500 ms before the next tone in the sequence. Comparing the ERPs between the two types of omissions, we found that the unexpected omissions elicited MMN and P3a responses. Thus, ERP components related to unexpected omission deviants can also be found when comparing silences under different contexts that do or do not violate expectations for silence, within a sequence of tones with SOA larger than 200 ms.

However, in our previous study, expected silences, or predictable omissions of a tone, occurred more frequently (50% of the time) in their context sequence than did unexpected silences, or unpredictable omissions (20%) in their context sequence, which could have potentially affected the responses to the silences. In the current study we aimed to extend these findings by ensuring the frequency of occurrence was equal across both conditions. We created two stimulus sequences with identical immediate local contexts but manipulated the global predictability of the omission deviants within the sequence by pseudo-randomly omitting 20% of the tones in the sequence (globally unpredictable) or omitting every 5th tone (globally predictable). Thus, in both cases, we compared the omission of tones that occurred at the same rate with the same immediate local context, but that varied in predictability of the omission at the global level.

One challenge in measuring responses to omission deviants is that there is no stimulus with which to time-lock the ERP, and when a stimulus does not occur at an expected time, the brain might widen the window over which it analyzes input before setting in place the cascade of predictive error responses thought to be the mechanism for the MMN (Baldeweg, 2007; Wacongne et al., 2012), blurring the measured response when averaging across trials. In other words, because an omission is the lack of a stimulus, there is no external cue indicating exactly when an omission has occurred and therefore it is unclear when the brain will determine that a stimulus is not coming. This may explain why the majority of early research reporting omission responses used an stimulus onset interval of 200 ms or less (Chennu et al., 2016; Horváth et al., 2007; Hughes et al., 2001; Oceak et al., 2013; Recasens & Uhlhaas, 2017; Salisbury, 2012; Wacongne, Labyt, van Wassenhove, et al., 2011; Yabe et al., 1997, 1998). Furthermore, the effects from our previous study using an SOA of 500 ms (Prete et al., 2022), were small compared to typical deviant responses to a change in a sound feature. Thus, the lack of an external temporal cue and longer SOA could result in variability in the latency of responses to the violation of expectation leading to ERPs across trials that are not temporally aligned. Furthermore, there are likely both inter-individual and intra-individual latency differences. When averaged together, this would lead to smaller, more spread-out averaged ERP responses. Indeed, previous researchers who have included conditions with larger SOA have sometimes chosen not analyze those condition with larger SOAs due to the variability of the omission-related responses (Hughes et al., 2001).

One solution is to use a paired auditory-action design. If participants engage in a series of button presses, each of which generates a tone, but occasionally the tone is omitted to some button presses, these omissions deviants elicit 3 specific ERP components (Dercksen et al., 2020; Korka et al., 2020; SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013; Stekelenburg & Vroomen, 2015). The first is the oN1; it is a scalp temporal component occurring approximately 40 to 90 ms relative to the omitted stimulus. The oN2 and oP3 are more fronto-central responses, the first with a peak between 100 and 200 ms and the latter with a peak between 250 to 400 ms. However, this approach entails active sound generation on the part of the participant through self-generated movement, so it cannot examine automatic responses to unexpected omissions. An alternative to using motor generated sounds is to pair the sound events with regular visual cues, such that the visual cues are present also on sound omission deviants (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). In this way, pairing the auditory stimuli with an external pacing cue, could help to align violation of expectation responses elicited by omission deviants across trials and participants.

In the present study we used an external visual pacing cue to improve the temporal alignment of omission ERPs across trials and participants. Unlike previous research that has paired an external cue with the auditory sequence, we chose to employ a passive listening task to determine if the omission ERP responses can be elicited without any overt engagement with the stimuli, similar to research on neural responses to auditory deviants (Näätänen et al., 2007) and early work on omission deviants that also elicited MMN responses at fast tempos (Hughes et al., 2001; Raij et al., 1997; Yabe et al., 1997). Extending our previous work showing an MMN and P3a can be elicited by an omission deviant (Prete et al., 2022), here we compared omissions occurring in a regular position in the sequence to randomly occurring omissions, keeping the overall probability of a deviant the same across conditions, while always pairing the omissions with a visual pacing cue that was identical for all tones and omissions. Thus, we manipulated the global predictability of the deviant omission to be either globally unpredictable or globally predictable. Based on MMN responses to auditory deviants that were globally predictable or globally unpredictable (Basirat et al., 2014; Bekinschtein et al., 2009; Chennu et al., 2013; Horváth et al., 2001; Sussman et al., 1998a; Wacongne, Labyt, Van Wassenhove, et al., 2011) we expected that globally unpredictable omissions would elicit larger ERP responses than globally predictable omissions.

Methods

Participants

Participants were recruited through the McMaster University undergraduate participant pool and poster advertisements. A total of 28 participants were recruited (22 female, 6 male) with ages ranging from 17 to 34 years (*M* = 20.1, *SD* = 4.01). Participants completed a short demographic questionnaire, which reveal that all participants were fluent in English, 56.2**%** also spoke a second language and 56.2**%** had at least one year of musical training. All participants received course credit or monetary compensation for participating. Methods were approved by the McMaster Research Ethics Board.

Stimuli

Sequences consisted of 5 minutes of an isochronous marimba tone (C3) presented with a stimulus-onset asynchrony (SOA) of 400 ms. The tones were edited with Audacity 2.3.0 (http://audacityteam.org/) to have a 100 ms duration including 10 ms rise and fall times. During the globally unpredictable condition, 20% of the tones were pseudo-randomly removed, with the constraint that at least 2 tones were presented before the next omission. Here we use globally unpredictable to mean that participants could not make predictions about when the next omission will occur in the sequence, even if they learned that an omission will occur at some point in the sequence. During the globally predictable condition every fifth tone in the rhythm was removed to maintain the same 20% omission rate, but when the next omission would occur was fully predictable. Each 5 min block for both conditions contained 750 events in total, 600 tones and 150 omissions.

To control variability in the latency of the ERP responses to omissions (Hughes et al., 2001), we also presented a visual stimulus that pulsated in time with all tone and omission times (i.e., every 400 ms), to provide an external temporal cue for tones and omissions. The visual cue consisted of a 1.6 cm radius dot, extending a visual angle of approximately 5.06°, that increased in radius to 2.8 cm, extending a visual angle of approximately 15.41°. This increase occurred over 1 frame and the decrease occurred over 8 frames, with a frame rate set to 30 frames per second. It was presented on a black background. Every 30 seconds the dot either changed colour or the number of simultaneously pulsating dots increased, starting from one dot and increasing to 4 dots by the end of the video, to keep participants looking to the screen and for direct comparison to stimuli used in previous study with 6-month old infants. The same percentage increase between the smaller and larger radius of the pulsating dot(s) was maintained when new dots were added to the screen. The animations for the visual stimuli were created using SynFig 1.4.1 and then combined with the auditory sequence using VSCD Video Editor 6.7.5.302 (Multilab LLC, 2021). Videos were encoded with a constant frame rate of 30 frames per second using H264 encoder, whereas the audio was encoded as MP3 with a sampling rate of 44100 Hz and a bit rate of 128 kpbs. Videos were presented on an HP BIM 122 monitor with 1920 x 1080 screen resolution and 60 Hz framerate. The temporal alignment between the increase in dot size and the tone was ensured within the video editing software, but also tested after exporting the videos using a photo diode and oscilloscope. See the supplemental material for an example video. Because a visual cue was added we included a third condition that consisted of only the visual cue with no auditory information, to act as a visual control. This condition was also a 5 min video with the same changes in colour and numeracy as the predictable and unpredictable conditions.

Procedure

Participants were seated in an electrically shielded and sound attenuated booth 0.91 m in front of a HP E232 Elite Display LED monitor with a screen resolution of 1920 x 1080 and 60 Hz frame rate. The videos were presented in the upper left corner of the screen in a black square measuring approximately 8.5 cm in height and 10.5 cm in width on the computer monitor, which translates to a visual angle of ~52.2^{o}. Sounds were presented with Etymotic ER 10 insert foam headphones at approximately 68 dB SPL A weighted. Before inserting the foam tips, participants were fitted with the appropriate size of EEG cap and completed the demographics questionnaire. Participants were told they would see a visual cue on the screen and hear sounds from the headphones, but they did not need to attend to either and were given a subtitled movie of their choice to watch.

Participants were presented with either the unpredictable condition first or the predictable condition first (counterbalanced across participants), followed by the visual condition. This three-condition block was presented three times. For the unpredictable condition, a different sequence of standard and omission deviants was presented each time. The total experiment including setup, questionnaires, and the stimulus presentation lasted about 90 minutes.

EEG Collection and Analysis

EEG data was collected using a Biosemi ActiveTwo system sampled at 2048 Hz. The data were preprocessed and analyzed using the Fieldtrip toolbox (Oostenveld et al., 2011) in MATLAB 2020a (Math Works Inc., 2020). The continuous data were high pass filtered at 1 Hz and low-pass filtered at 30 Hz, using a 4th order Butterworth filter applied using zero-phase digital filtering. The high threshold for the high-pass filtered was used to improve decomposition of the independent component analysis (ICA; Winkler et al., 2015). Channels were then inspected and those with extreme variance were removed before applying a common average reference. An average of 4 channels (*SD* = 1.34) were removed per participant. Components selected to be removed were based on visual inspection of the time course and topography of the components, specifically looking for blinks, saccades or heartbeat artifacts. An average of 2.33 components were removed per participant with a minimum of 2 and a maximum of 4. Once artefactual components were removed the data was reprocessed with the same steps stated above, except the high pass filter was set to 0.5 Hz. The ICA was then re-applied using the unmixing matrix to the re-processed data, the data was then segmented into 500 ms epochs from 100 ms pre-onset of the tone, or omission, to 400 ms post-onset and trials were rejected if the amplitude range for any channel exceeded 100 microvolts. An average of 3.5% of trials were removed (*SD* = 7.87%). Finally, the previously removed channels were interpolated based on average of neighbouring electrodes using Fieldtrip templates to define neighbouring electrodes.

A cluster-based permutation test was used to determine differences between the two omission conditions (Maris & Oostenveld, 2007). Cluster analysis was restricted to 40 to 90 ms, 100 to 200 ms and 250 to 350 ms to analyze the responses in the time windows corresponding to the oN1, oN2 and oP3, respectively. The upper limit of the oP3 window was set to 350 ms to avoid expectation responses to the next tone, as the SOA was 400 ms. The clusters were defined as the maximum sum of *t*-values on dependent sample *t*-test with an alpha set to 0.05, known as the cluster-level alpha. 5000 permutations were run, and the permutation level alpha was set to 0.025 (0.05 divided by two to correct for two-tail test). The same parameters were used for each time window.

To ensure an ERP had been elicited in the three latency windows of interest, each window was compared to baseline activity from -100 to 0 ms using cluster permutation analysis. The initial window from 40 to 90 ms was increased to 0 to 100 ms, because the duration of the ERPs being compared need be the same size. Thus, the three windows compared against the baseline activity were 0 to 100 ms, 100 to 200 ms and 250 to 350 ms. The same parameters used for the previous permutation analysis were applied to this one as well. This analysis was conducted separately for the unpredictable and predicable conditions after the ERP for the visual only condition was subtracted from each participant's ERP.

Upon visually inspecting the ERPs there seemed to be a linear trend present in both globally unpredictable and globally predicable conditions (Figure 1). Thus, we preformed additional preprocessing by detrending the data at the trial level after the channel interpolation, then repeated the cluster permutation analysis described above using the detrended data.

Results

Original ERPs

The grand average ERPs for both the globally predictable and unpredictable omissions were very similar (Figure 1a). After isolating the activity due to the omission by subtracting the

ERP for the visual only condition this did not change (Figure 1) The cluster-permutation analysis comparing the two conditions across each of the three latency windows demonstrated that there were no significant differences (Table 1). Thus, global predictability had no significant effect. However, both the types of omission deviants elicited responses greater than the baseline activity.

Globally unpredictable omission deviants elicited a response significantly different from baseline in all three-time windows. In the first-time window, 0-100 ms post omission deviant, the unpredictable omission elicited a more positive response at frontal and central electrodes for approximately the whole 100 ms duration and a more negative response at temporal, parietal and occipital electrodes from approximately 5 ms to 100 ms (Figure 2a). The analyses comparing the 100-200 ms window (Figure 2b) and the 250-350 ms window (Figure 2c) show very similar results. Thus, it seems unpredictable omissions elicited a response that increased for the first 250 ms and then reached a plateau leading into the next trial.

Globally predictable omissions elicited very similar responses as the globally unpredictable omissions. In the first time window (0 to 100 ms), the response to the predictable omissions was more positive at fronto-central and central electrodes, and more negative and occipital, left and right parietal, and left and right temporal electrodes (Figure 3a). This response persisted into the 100 to 200 ms window (Figure 3b) and the 250 to 350 ms time window (Figure 3c). The Globally predictable omission deviants elicited an ERP that increased until it reached an asymptote around 250 ms post deviant onset. Although we found no difference based on predictability of the omission deviant, we found evidence that an omission deviant, whether it can be predicted or not, elicits a significant ERP response.

Detrended Data

Since the responses elicited by both conditions demonstrated a linear increase and asymptote, we explored the data further by linearly detrending and re-applying the cluster permutation analysis on the detrended data. The grand average ERPs across the scalp can be seen in Figure 4. Comparing the globally predictable and globally unpredictable conditions, we did not find any significant differences between the conditions in the 40-90 ms window, 100-200 ms window or the 250-350 ms window (Table 4). This would suggest that the predictability of the omission deviant did not affect the response to the omission deviant. Despite the lack of difference between conditions we did find significant differences between baseline activity and the omission deviants.

In all three-time windows the globally unpredictable omissions elicited a response significantly greater than baseline. In the 0-100 ms window a significant difference was found between the globally unpredictable omission deviants and the baseline activity with the unpredictable omission showing a larger positive response (p = 0.006) at fronto-central electrodes with an approximate latency of 10 to 100 ms and a more negative response (p = 0.030) at left temporal, left partial and occipital electrodes with an approximate duration of 1 to 60 ms (Figure5a) From 100 to 200 ms we also found that the globally unpredictable omissions elicited a significantly more positive response than baseline (p = 0.0004) at fronto-central electrodes lasting for about the full duration of the window. There was also a more negative response (p = 0.0008) around left and right temporal electrodes, left and right parietal electrodes and occipital electrodes also lasting for the full duration of the window (Figure 5b). In the final time window from 250 ms to 350 ms we again found that the globally unpredictable omission elicited a more positive (*p* = 0.0004) and a more negative response (*p* = 0.003) than baseline. The positive response lasted from about 250 ms to 300 ms displayed at frontal and central electrodes (Figure 5c) The negative response appears at left temporal electrodes, left and right parietal electrodes and occipital electrodes, with a duration lasting for approximating the full duration of the time window. Overall, within all three-time windows we observed the globally unpredictable omission elicited a significantly greater response compared to baseline.

The globally predictable omissions were also significantly different compared to baseline in all three-time windows (Table 6) In the first 100 ms post omission deviant, the ERP had a more positive response compared to baseline activity (*p* = 0.011) from about 13 to 83 ms, that appeared in frontocentral electrodes (Figure 6a) and more negative from about 0 to 60 ms at right temporal, central parietal and occipital electrodes (Figure 6a). From 100 to 200 ms globally predictable omissions also elicited a significantly greater response than baseline. For approximately the whole duration of the window a more positive response (*p* = 0.0004) was found at frontocentral electrodes and a more negative response (*p* = 0.0008) at central occipital, left and right temporal electrodes, and left and right parietal electrodes (Figure 6b) In the last time window from 250 to 350 ms, the predictable omission elicited a more positive response (*p* = 0.002) from about 250 ms to 320 ms at frontal and central electrodes. The ERP to the predictable omissions was also more negative (*p* = 0.011) from about 250 to 300 ms at left, right and central parietal electrodes, and occipital electrodes (Figure 6c). The globally predictable omissions elicited a significant response, even after removing a linear component from the ERP, suggesting that when the position of the omission deviants in the auditory sequence can be predicted, they still elicit a neural response that seems to be widespread throughout the duration of the omission.

Discussion

In the current experiment we presented omission deviants while manipulating their global predictability such that they were either globally unpredictable (occurred pseudo-randomly throughout the sequence) or globally predictable (occurred every fifth event). No significant difference in the ERP responses was found between the two levels of predictability, suggesting global predictability of the omission deviant had little to no effect. However, at multiple latencies both types of omission deviants elicited responses greater than baseline activity, suggesting a distinct response to the omission deviants, possibly from violating the local predictability (i.e., expecting to hear a sound). Contrary to our predictions this response did not appear as an MMN or the oN1, oN2 or oP3. We found a response to the omission deviants, but it is unclear what ERP component was elicited.

We predicted that both types of omission deviants would elicit an MMN (Prete et al., 2022; Raij et al., 1997; Recasens & Uhlhaas, 2017; Yabe et al., 1997) and that the MMN elicited by the globally unpredictable omission deviants would be larger than the MMN elicited by globally predictable omission deviants (Bekinschtein et al., 2009; Chennu et al., 2016; Wacongne et al., 2012; Wacongne, Labyt, Van Wassenhove, et al., 2011). Instead of an MMN, we found a sustained positivity that was not affected by global predictability. This response could reflect temporal expectations for an upcoming tone, as all omission deviants were of course followed by a tone. Previous EEG research investigating temporal predictions of target events, such as a tone, have found a sustained negative deflection in the EEG called the contingent negative variation (CNV; Walter et al., 1964). The CNV increases in amplitude up to the expected onset of the target tone (Cui et al., 2009; Kononowicz & Van Rijn, 2011; Miniussi et al., 1999; van Wassenhove & Lecoutre, 2015) and will begin to decrease after this latency if the target does not occur (Kononowicz & Van Rijn, 2014). Although the CNV is typically elicited when there is a task related to the target stimuli, the CNV has also been elicited during passive listening (Mento et al., 2013), suggesting that the CNV may be an index of general temporal expectations and not specifically temporal expectations during a task (Kononowicz & Penney, 2016). The sustained response we observed may index temporal expectation of the tone following the omission deviant, inadvertently creating a cue-target fore-period. However, our current results do not seem to match the CNV exactly, as the CNV is frontally negative and increases during the whole interval between the cue and target, whereas we observed an increasing positive potential that reaches a peak amplitude around 200 ms post omission onset (Figure S1). A future study might determine if this positive increase is related to temporal expectations by randomly jittering the SOA within a range so no precise expectation for the onset of the tone could be made. Alternatively, the onset of the tone following an omission could be manipulated to be later than expected latency to determine if this on-going response begins to reverse in direction when no tone appears, like the CNV.

Another possibility is that the sustained response reflects involuntary sustained attention or vigilance. But sustained attention to auditory stimuli, or omission of auditory stimuli, affects the amplitude of specific evoked potentials, like the N1 or oN1, rather than presenting as a sustained response (Alcaini et al., 1994; Oray et al., 2002). Sustained attention during visual tasks seem to result in a sustained increase in the ERP that starts around 200 ms post-onset of the stimulus, occurring after visually evoked potentials (Ruijter et al., 2000; Staub et al., 2014). The sustained response we observe may be due to sustained attention directed toward the visual stimuli the changing pulsating dot(s) used to temporally align the onsets of the tones and the omissions. Although, this seems unlikely as participants were told not to attend to the visual or auditory stimuli, given a subtitled movie to watch and no explicit task was used in the current experiment. Still, future experiments could manipulate attention towards the sounds or towards the visuals to determine if directed attention affects this sustained response or other evoked responses.

Attempting to remove the sustained response with linear detrending resulted in a frontal positive/posterior negative component that was unaffected by global predictability. This component was significantly greater than baseline activity in all three latency windows of interest. Under the predictive coding framework the remaining non-linear response may index predictive sensory template of the expected sounds (Wacongne et al., 2012). If this is the case, we would expect the response to the omission deviants to resemble auditory evoked potentials, but this is not the case. Thus, it is more likely this remaining non-linear activity represents prediction error in violating the local prediction caused by the absence of the standard tone (Friston, 2005; Friston & Kiebel, 2009). However, prediction error responses typically manifests as the MMN, and violating multiple hierarchies of predictability enhances the MMN because the violations of multiple predictions creates a larger prediction error response (Bekinschtein et al., 2009; Friston & Kiebel, 2009; Wacongne et al., 2012; Wacongne, Labyt, Van Wassenhove, et al., 2011), neither of which were present in our results. It is possible that experimental parameters such as SOA are more influential than global predictability. At short SOAs the MMN is elicited by omission deviants (Bendixen et al., 2014; Hughes et al., 2001; Raij et al., 1997; Recasens & Uhlhaas, 2017; Salisbury, 2012; Yabe et al., 1997, 1998). Behaviourally, reaction times to omission deviants presented at short and long SOAs suggests separate mechanisms for processing omission deviants when presented with shorter SOAs compared to longer SOAs (Ohmae & Tanaka, 2016). Thus, SOA is an important factor for processing omission deviants. Despite our previous finding that an MMN and P3a were elicited by omission deviants with longer SOAs (Prete et al., 2022), it seems that if the expected silences occur as the removal of a tone – i.e., a predictable omission deviant – instead of an increase in SOA the MMN is no longer present. All of this suggests that the ERP in response to omission deviants is highly influenced by the context in which the omission deviant occurs. A more thorough investigation is needed to determine how various experimental designs used to elicit the MMN to auditory deviants affect the response to omission deviants.

From a neural adaptation perspective, the remaining non-linear activity (after detrending) may be the rebound from oscillations encoding the standard sound that habituated to the repeating standard stimuli (May, 2021). However, this evidence comes from simulations of an adaption model using a fast stimulation rate (100 ms SOA) within an oddball paradigm. At larger SOAs, such as the one used in our current experiment, the neurons encoding the sound may not habituate to the same extent. To further explore this idea, we used code readily available for this adaptation model (https://github.com/pjcmay/ACtx-Model) and changed the stimuli input to match our current experiment (i.e., using SOA of 400 ms, and omission deviant rate of 20%). We found that the response to the standard was not habituated, and the omission deviants did not elicit any response. Neural adaptation based on the model proposed by May (2021) does not align with our results using stimuli with longer SOAs, possibly indicating predictive coding as a more likely explanation. However, the ERP components in our current results do not match those typically elicited by auditory or omission deviants. Even though there is a response above baseline activity the nature of this response and how it relates to previous deviance detection is unclear. Furthermore, by linear detrending we assume that the ERP is composed of a linear component and non-linear components. The slow-wave response after detrending may not be an underlying ERP component but an artifact caused by subtracting a line of best fit from an asymptotic curve. Temporal Principal Component Analysis may be better at isolating underlying ERP components, but the factors from the PCA would likely be conflated, meaning the underlying components of the ERP would not be fully separated because the sustained response is present throughout the whole epoch (Scharf et al., 2022). Improvements in approaches to decomposing ERPs into separable yet overlapping components would greatly help in the understanding of the current results.

Interestingly, we also did not find any of the reported omission evoked potentials, i.e., the oN1, oN2 and oP3. It is possible that these components are only elicited when there is a task present that guides attention toward the auditory information, such as motor generated sounds. This would explain why in our previous work, we found the omission deviants elicited the MMN and P3a but not the omission evoked potentials (Prete et al., 2022). When omission deviants are thought to be relevant to generating stimuli through a button press, such that participants should attend to them during the task, the amplitudes of the omission specific responses increase compared to when the deviants are not relevant to the task (Ishida & Nittono, 2024). Importantly, the actual presentation of the omission deviants was not related to the task, but the instructions were manipulated such that participants were told the omissions were either relevant or not relevant. Thus, attention seems to contribute to the amplitude of the omission evoked potentials. To our knowledge it has yet to be test if the omission evoked potentials are present during purely passive listening, as in the present study.

It may also be that lack of omission evoked potentials are due to, or at least partially due to, differences in preprocessing methods. Most of the work that finds the omission specific components has used a nose reference (Dercksen, 2023; SanMiguel, Widmann, et al., 2013), although the averaged mastoids have been used as well (van Laarhoven et al., 2017). Using an average reference instead would likely change the topography of the ERP response and could potentially diminish these components. Although both the left and mastoids were recorded in the current experiment, attempting to use those as a reference led to too many trials being rejected for too many participants to continue with that analysis. Further investigation is needed to understand how various preprocessing methods may influence which ERP components are observed and the polarity of these components in response to omission deviants.

Overall, we found that omission deviants, whether globally predictable or globally unpredictable, elicited a distinct response, but the exact nature of this response is elusive. The typical deviance detection responses such as the MMN or P3a as well as the omission specific responses, were not found in our current experiment. Instead, we found a sustained response above baseline activity that may represent temporal expectations for the tone after the omission deviant. Whether this was specific to omission deviants or more general temporal expectations from the isochronous tones is unclear. Further investigation is needed to understand how experimental parameters, attention and EEG preprocessing influence the various responses that can be elicited by omission deviants found in the current study and previous literature.

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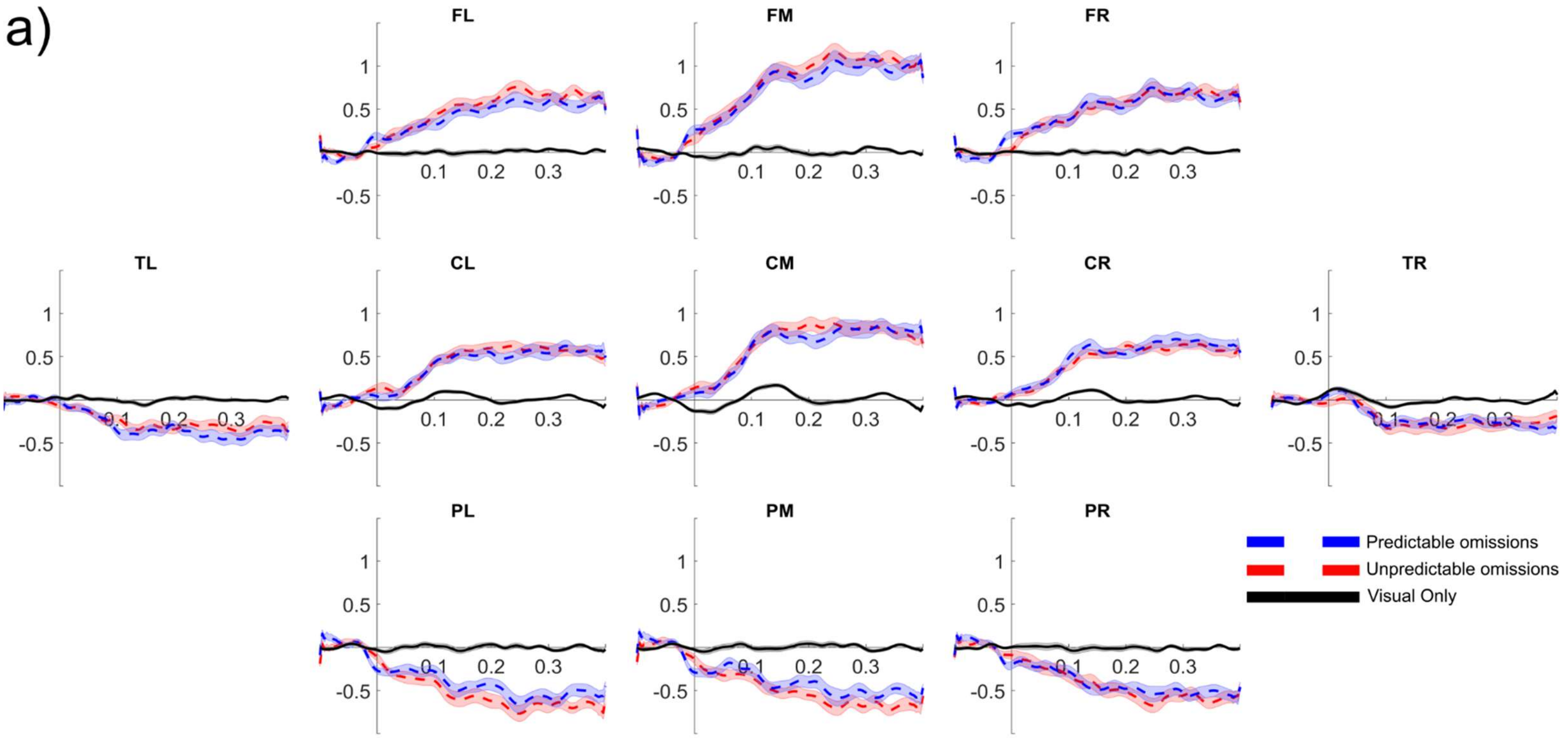
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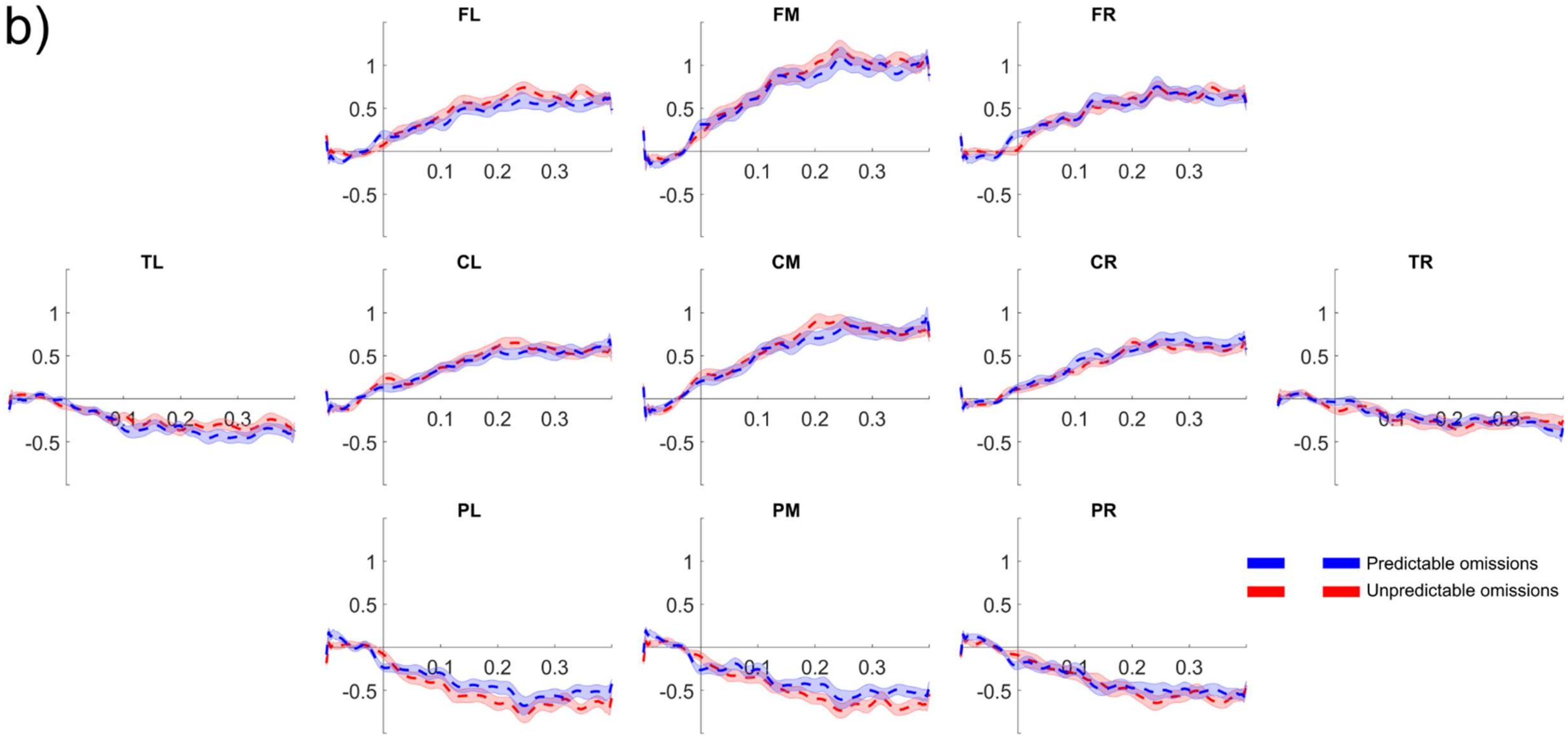
Predictable omissions
Unpredictable omissions
Visual Only

b)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Predictable omissions
Unpredictable omissions

Figure 1. Grand Average ERPs to Omissions Deviants Across the Scalp. a) the grand average ERPs for the globally predictable omissions (dashed blue line), globally unpredictable omissions (dashed red line) and the visual only condition (solid black line). The shaded regions around the grand averages represent +/-1 standard error of the mean. b) the grand average ERPs for the globally predictable omissions (dashed blue line) and the globally unpredictable omissions (dashed red line) after subtracting ERP from the visual only condition for each individual participant. For both a) and b) the ERPs are split into 11 regions representing the ERPs average across electrodes split into 11 different scalp regions. The electrode groupings are shown in FigureS1.

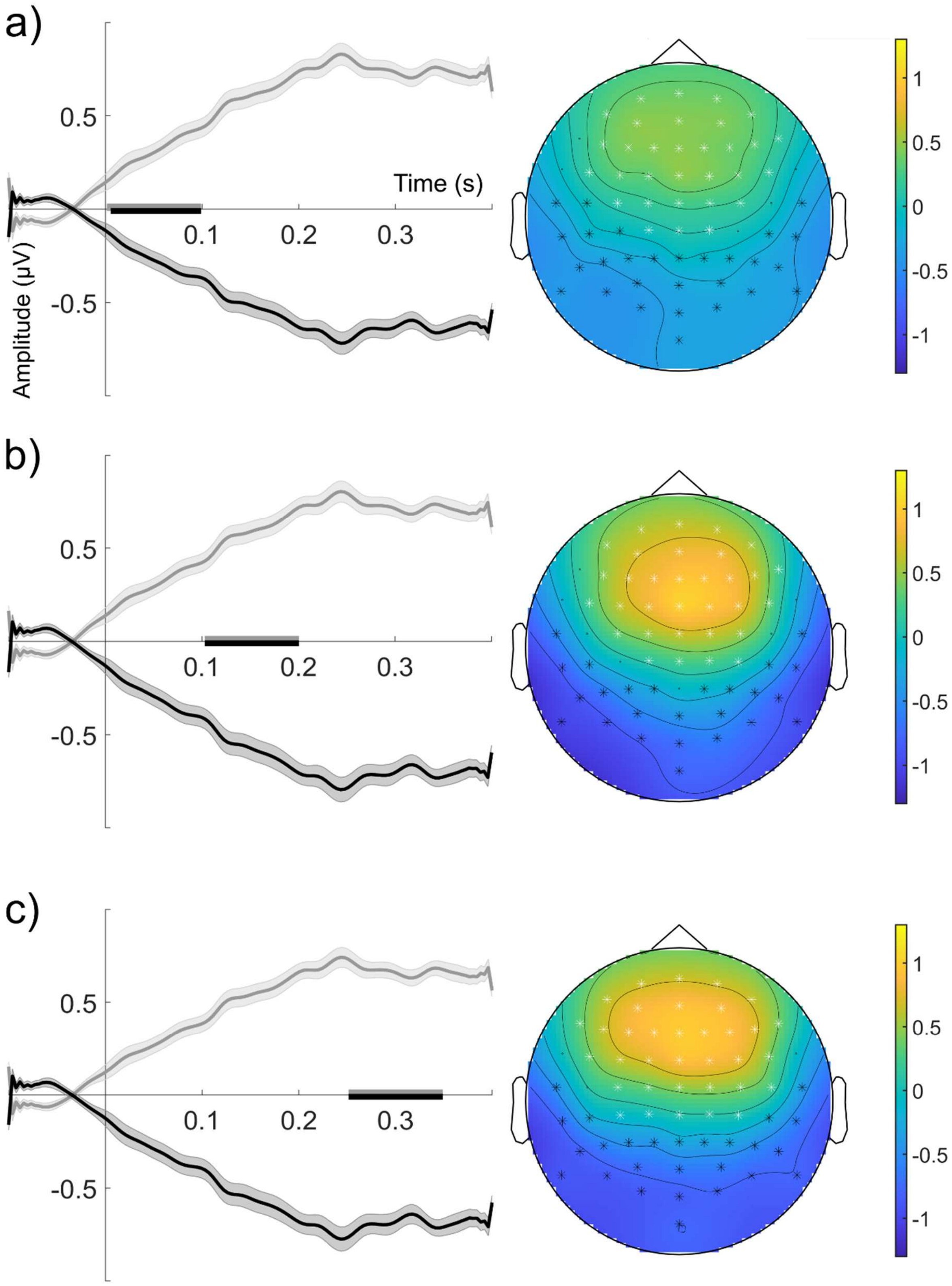
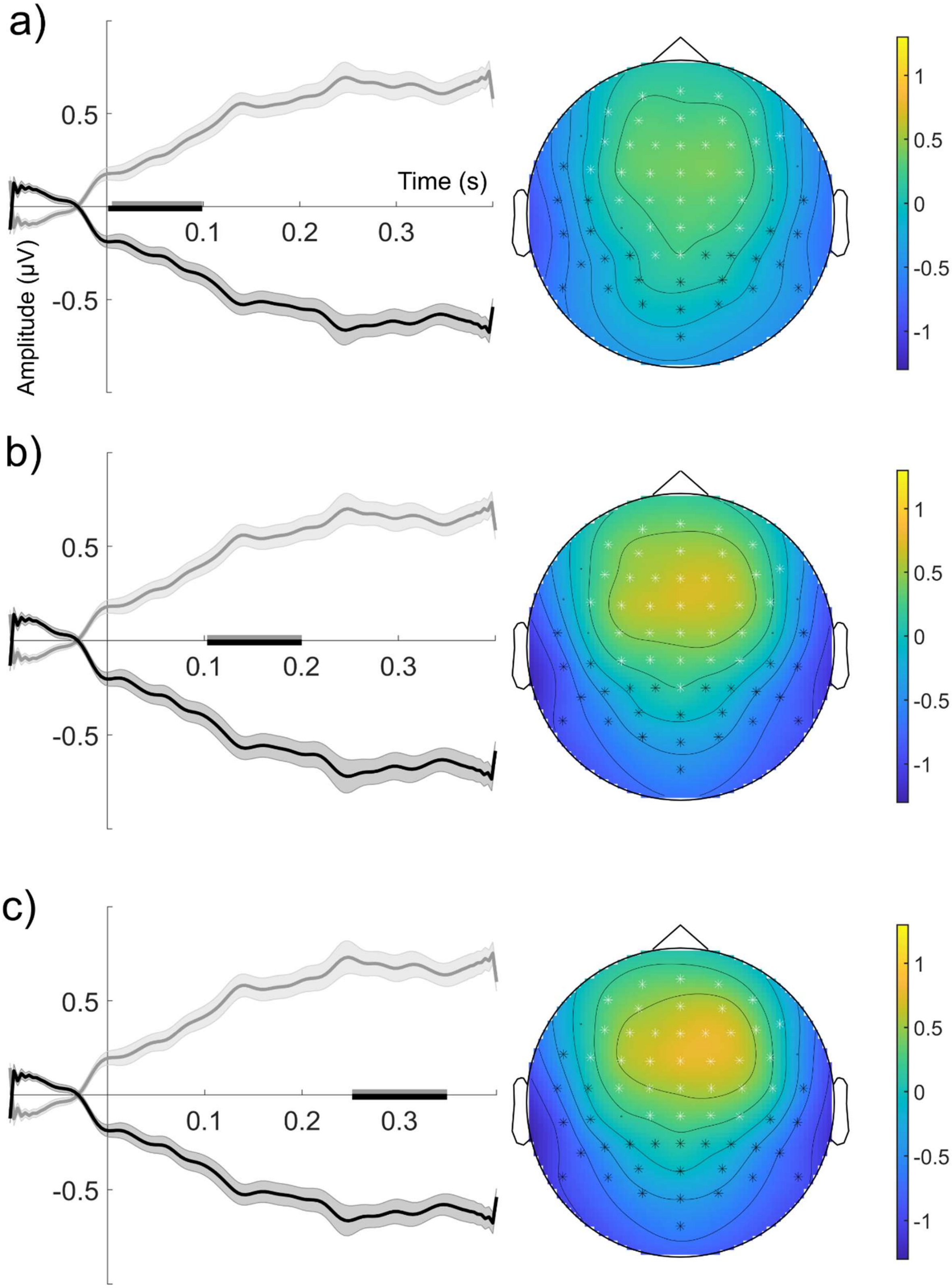

a)
0.5
Time (s)
0.1
0.2
0.3
-0.5
Amplitude (μV)
1
0.5
0
-0.5
-1
b)
0.5
0.1
0.2
0.3
-0.5
1
0.5
0
-0.5
-1
c)
0.5
0.1
0.2
0.3
-0.5
1
0.5
0
-0.5
-1

Figure 2. Globally Unpredictable Omissions Compared to Baseline Activity. Results from the comparison of the ERP to the globally unpredictable omission deviants to the baseline activity. a) the ERP and topography comparing the baseline to 0 – 100ms post omission deviant. b) the ERP and topography comparing the baseline to 100 to 200 ms post omission deviant. c) the ERP and topography comparing the baseline to 250 to 250 ms post omission deviant. Each row represents the results from the comparison in each time window with the first column showing the grand average ERPs averaged across the electrodes within the positive cluster (bold light grey line) and negative cluster (bold black line). The shaded area around the lines represents +/- 1 standard error of the mean. The horizontal black along the x-axis shows the duration of the negative cluster. The grey horizontal bar long the x-axis shows the duration of the positive cluster. The second column show the topography over the duration for the clusters for the difference from the baseline activity subtracted from the ERP to the unpredictable omission deviant. If the clusters had a different duration than the duration of the largest cluster was used. The white asterisks represent the electrodes within the positive cluster, and the black asterisk represent the electrodes within the negative cluster.


a)
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Time (s)
0.1
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Amplitude (µV)
1
0.5
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-1
b)
0.5
0.1
0.2
0.3
-0.5
1
0.5
0
-0.5
-1
c)
0.5
0.1
0.2
0.3
-0.5
1
0.5
0
-0.5
-1

Figure 3. Globally Predictable omissions compared to Baseline Activity. Results from the comparison of the response to the globally predictable omission deviants to the baseline activity from a) 0-100 ms, b) 100 to 200 ms and 250 to 350 ms. a) Each row represents the results from the comparison in each time window with the first column showing the grand average ERPs averaged across the electrodes within the positive cluster (bold light grey line) and negative cluster (bold black line). The shaded area around the lines represents +/- 1 standard error of the mean. The horizontal black along the x-axis shows the duration of the negative cluster. The grey horizontal bar long the x-axis shows the duration of the positive cluster. The second column show the topography over the duration for the clusters for the difference from the baseline activity subtracted from the ERP to the unpredictable omission deviant. If the clusters had a different duration than the duration of the largest cluster was used. The white asterisks represent the electrodes within the positive cluster, and the black asterisk represent the electrodes within the negative cluster.

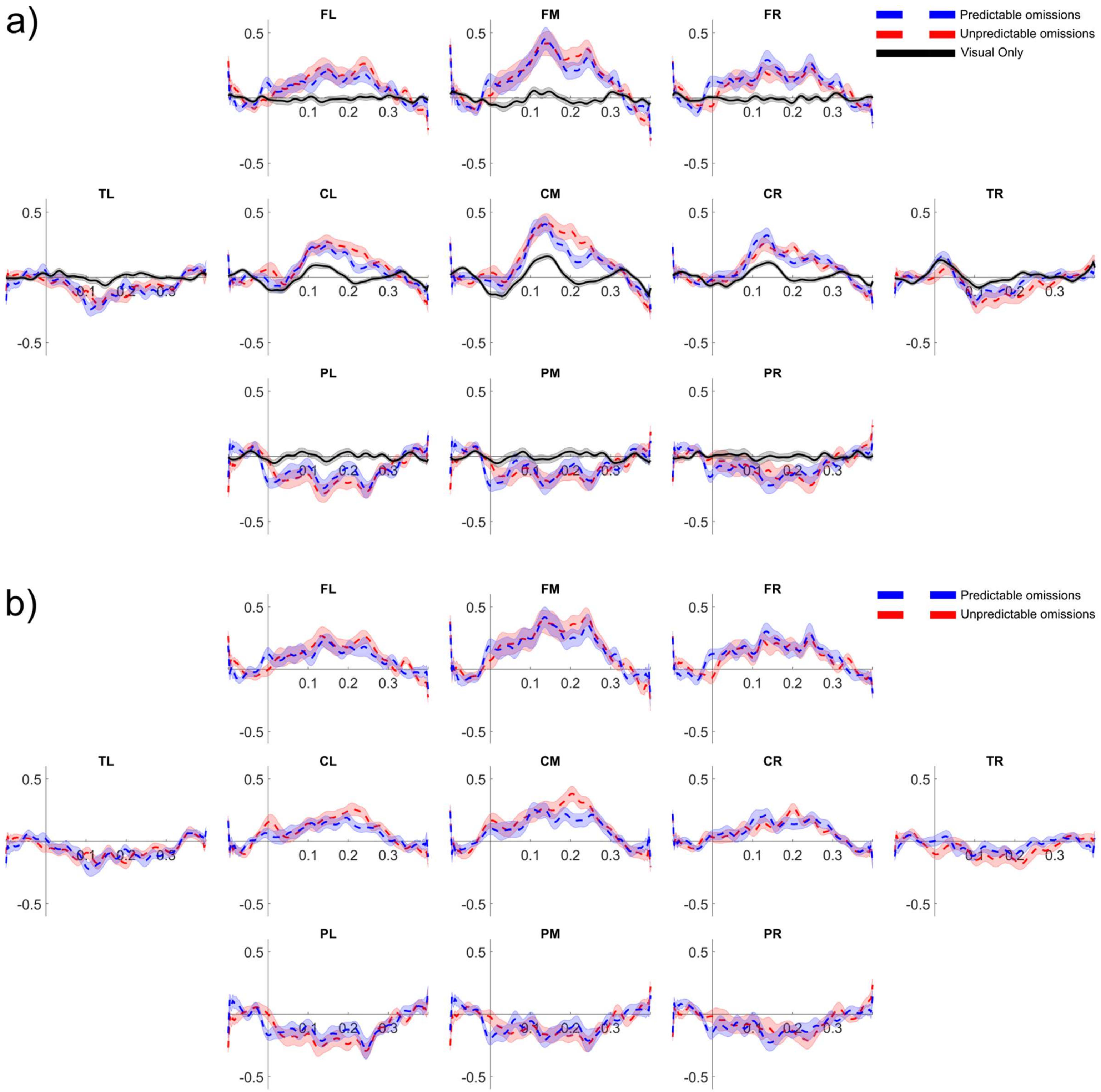

Figure 4. Grand Average ERPs to Omissions Deviants Across the Scalp of the Detrended Data. a) the grand average ERPs for the globally predictable omissions (dashed blue line), globally

unpredictable omissions (dashed red line) and the visual only condition (solid black line) after applying a linear detrend. The shaded regions around the grand averages represent +/-1 standard error of the mean. b) the grand average ERPs for the predictable omissions (dashed blue line) and the unpredictable omissions (dashed red line) after subtracting ERP from the visual only condition for each individual participant. For both a) and b) the ERPs are split into 11 regions representing the ERPs average across electrodes split into 11 different scalp regions. The electrode groupings are shown in FigureS1.

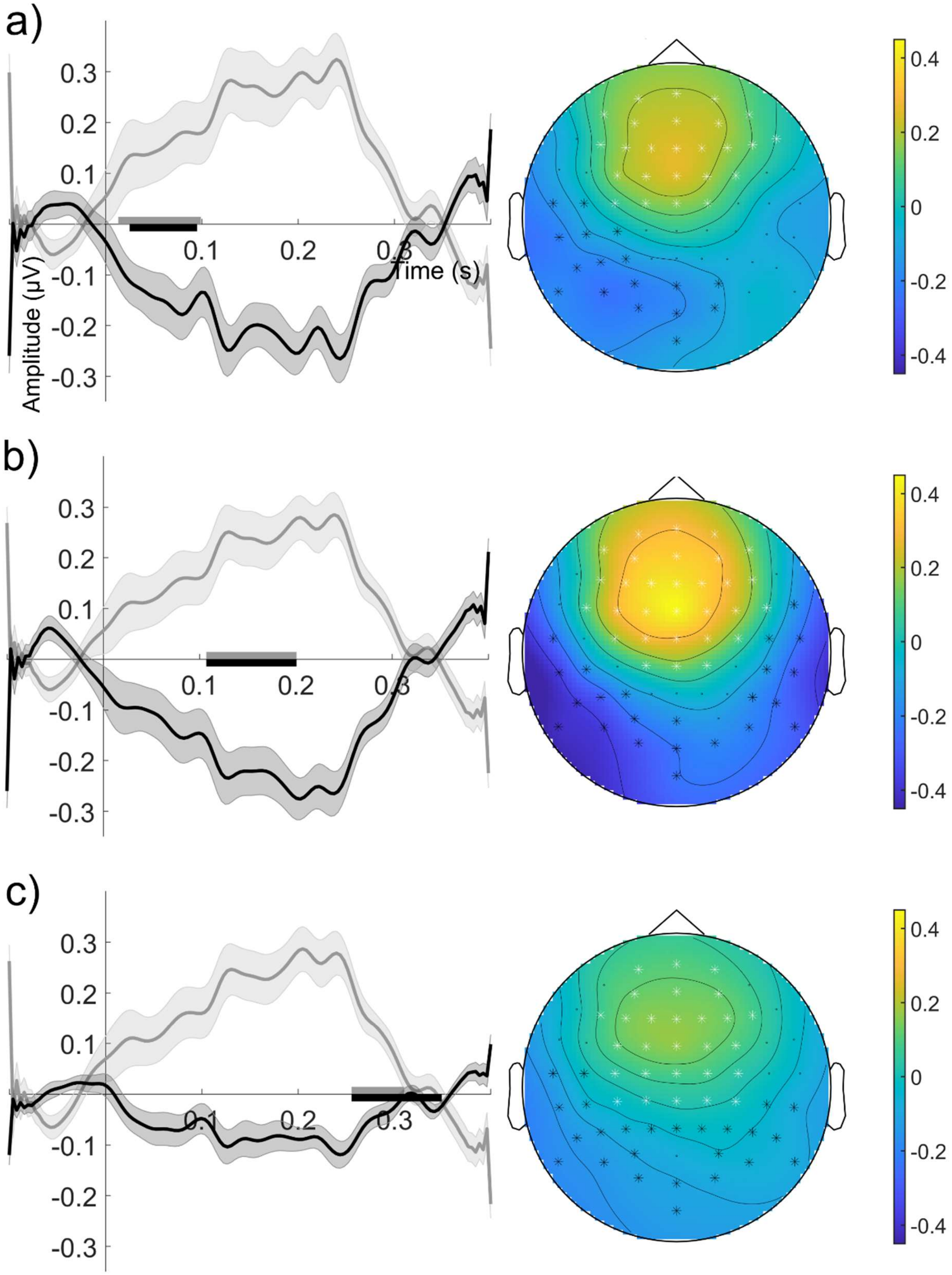
a)
b)
c)
Amplitude (μV)
Time (s)
0.3
0.2
0.1
-0.1
-0.2
-0.3
0.1
0.2
0.3
0.4
0.2
0
-0.2
-0.4

Figure 5. Globally Unpredictable Omission Compared to Baseline After Detrending. Results from the cluster permutation analysis comparing the detrended ERPs to the globally unpredictable omission deviants to the baseline activity. a) the ERP and topography comparing the baseline to 0 – 100ms post omission deviant. b) the ERP and topography comparing the baseline to 100 to 200 ms post omission deviant. c) the ERP and topography comparing the baseline to 250 to 250 ms post omission deviant. Each row represents the results from the comparison in each time window with the first column showing the grand average ERPs averaged across the electrodes within the positive cluster (bold light grey line) and negative cluster (bold black line). The shaded area around the lines represents +/- 1 standard error of the mean. The horizontal black along the x-axis shows the duration of the negative cluster. The grey horizontal bar long the x-axis shows the duration of the positive cluster. The second column show the topography over the duration for the clusters for the difference from the baseline activity subtracted from the ERP to the unpredictable omission deviant. If the clusters had a different duration than the duration of the largest cluster was used. The white asterisks represent the electrodes within the positive cluster, and the black asterisk represent the electrodes within the negative cluster.

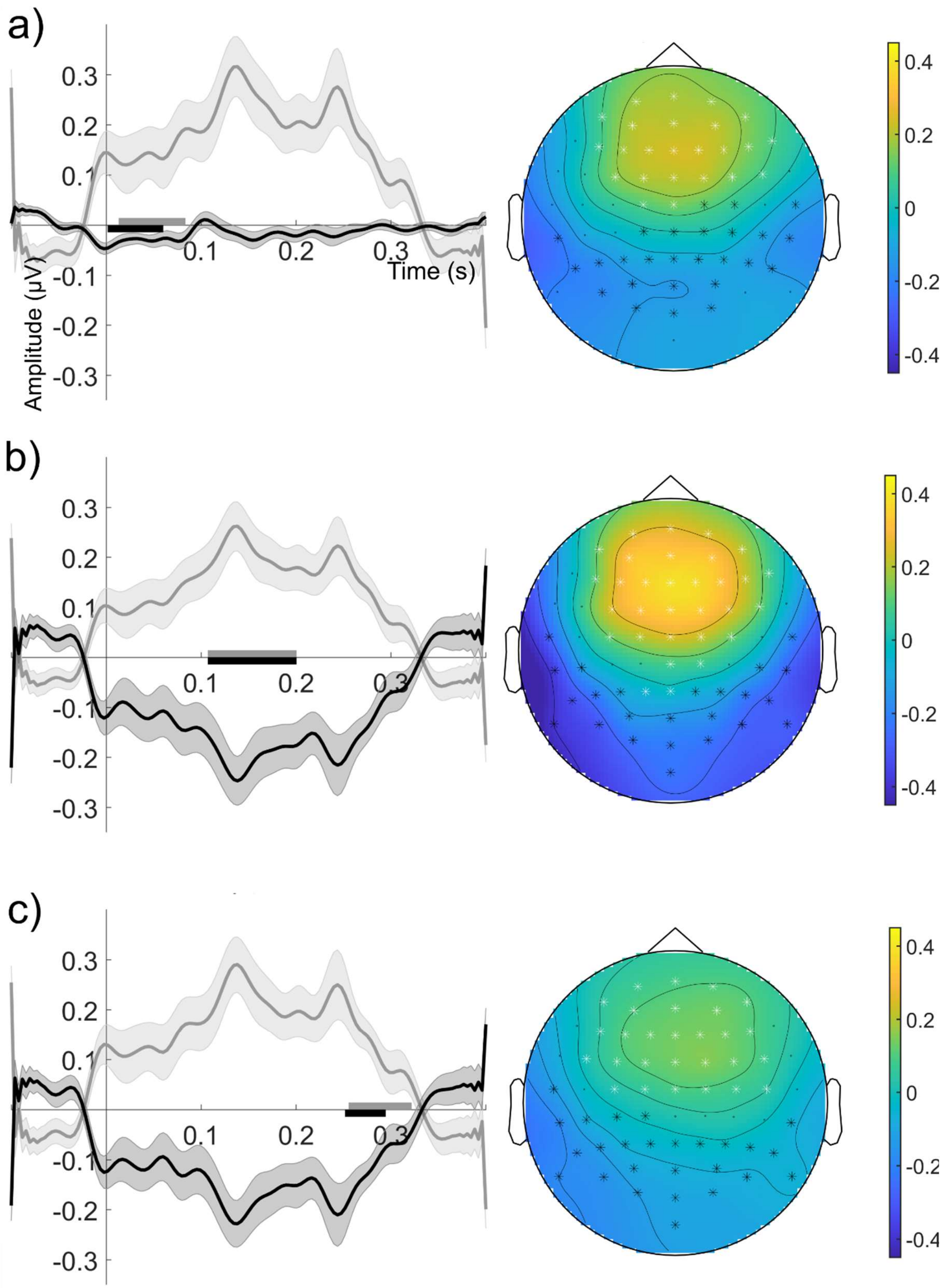
a)
b)
c)
Amplitude (µV)
Time (s)
0.3
0.2
0.1
-0.1
-0.2
-0.3
0.1
0.2
0.3
0.4
0.2
0
-0.2
-0.4

Figure 6. Globally Predictable Omission Compared to Baseline After Detrending. Results from the comparison of the response to the globally predictable omission deviants to the baseline activity from a) 0-100 ms, b) 100 to 200 ms and 250 to 350 ms. a) Each row represents the results from the comparison in each time window with the first column showing the grand average ERPs averaged across the electrodes within the positive cluster (bold light grey line) and negative cluster (bold black line). The shaded area around the lines represents +/- 1 standard error of the mean. The horizontal black along the x-axis shows the duration of the negative cluster. The grey horizontal bar long the x-axis shows the duration of the positive cluster. The second column show the topography over the duration for the clusters for the difference from the baseline activity subtracted from the ERP to the unpredictable omission deviant. If the clusters had a different duration than the duration of the largest cluster was used. The white asterisks represent the electrodes within the positive cluster, and the black asterisk represent the electrodes within the negative cluster.

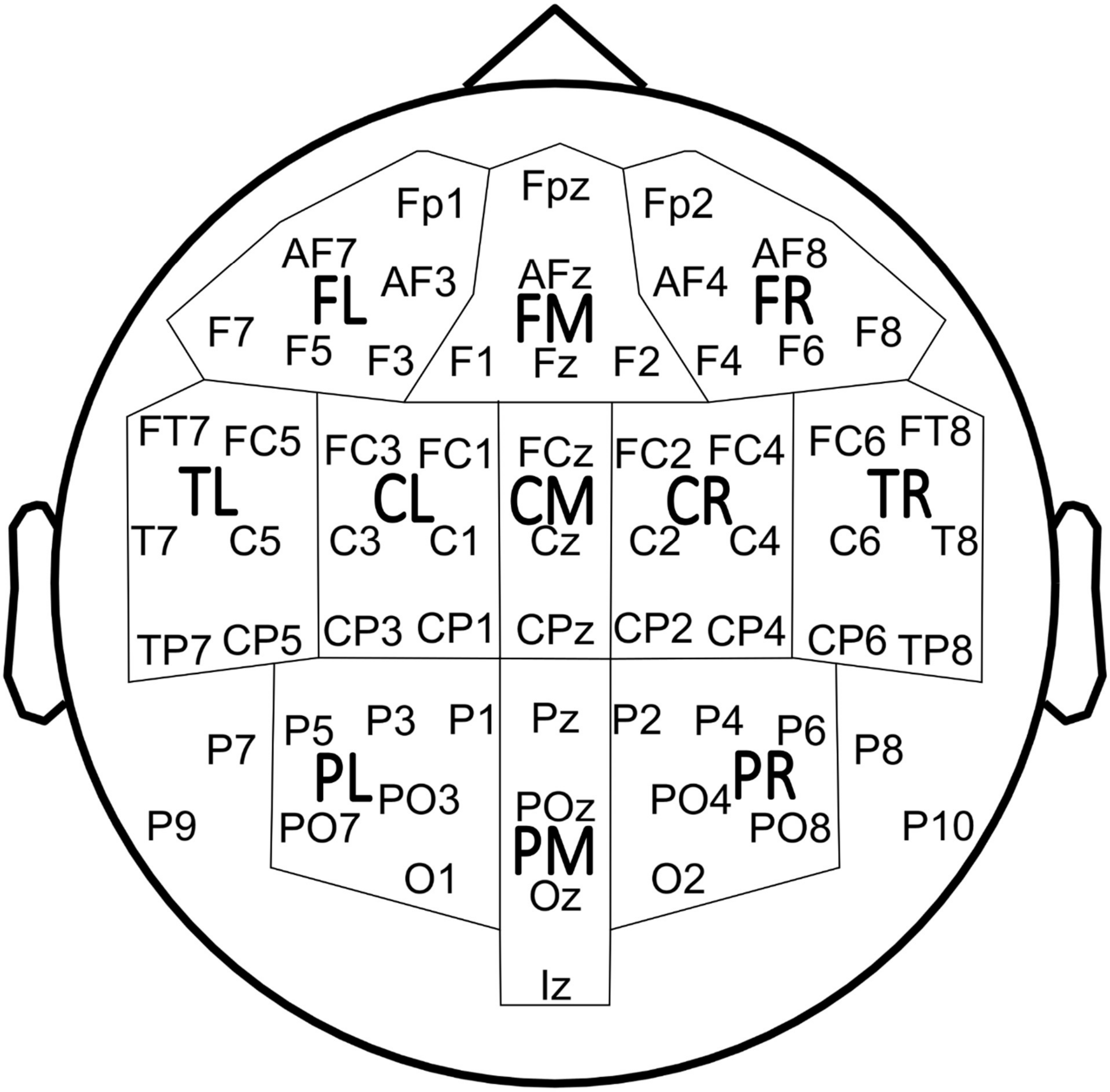

Figure S1. Electrode Montage and Electrode Groupings. The 64-channel electrode montage and the 11 electrode groupings. These groupings were used only for visualization purposes. FL = Frontal Left, FM = Frontal middle, FR = Frontal Right, TL = Temporal Left, TR, = Temporal Right, CL = Central Left, CM = Central middle, CR = Central Right, PL = Parietal Left, PM = Parietal Middle, PR = Parietal Right.

Chapter 5: General Discussion

Both adults and infants take in the cacophony of auditory information in the environment and make sense of it to understand language (Romberg & Saffran, 2010) or perceive music (Huron, 2006; Vuust & Witek, 2014). Based on predictive coding, it is a multi-stage process involving detecting patterns in the environment, making predictions about incoming sounds based on those patterns, comparing the perceived stimuli with the predicted stimuli, calculating an error for the difference between the perceived and predicted information, and finally, if needed, updating the predictions based on the error (Friston & Kiebel, 2009; Wacongne et al., 2011, 2012). The patterns can be hierarchically organized such that multiple levels of regularity are tracked, such as the relationship between beat and metre (Bouwer et al., 2020; Flaten et al., 2022; Winkler et al., 2009) or notes in chord progressions and melodies (Moldwin et al., 2017; Virtala et al., 2011, 2013, 2022). This theory is based on comparing incoming sensory information to predicted information, but what happens when an expected sound does not appear and there is a silence instead? Do we still see the cascade of neural processes indicative of predictive coding? Understanding if predictive coding is present even for unexpected silences would elucidate how the brain processes gaps in sensory information and could isolate prediction error signals from sensory encoding (Wacongne et al., 2012), furthering our understanding of the neural mechanism underlying auditory deviance detection. The goal of this dissertation was to determine if omission deviants caused by unexpected silences are processed similarly to auditory deviants, to determine if these responses are present at an early age, and if the processing is hierarchically organized.

Early research on the evoked responses to omission deviants found that an MMN could be elicited, but seemingly only when the SOA was 200 ms or less (Raij et al., 1997; Yabe et al., 1997). However, this makes the MMN difficult to measure, as it can overlap the onset of the next sound in the sequence. Further, because 200 ms is within the temporal window of integration, successive sounds might not be fully perceived as separate events (Horváth et al., 2007). Since then, most researchers have used short SOAs and compared the response to omission deviants to the response to standard tones (Bendixen et al., 2009, 2014; Chennu et al., 2016; Hughes et al., 2001; May, 2021; Oceak et al., 2013; Recasens & Uhlhaas, 2017; Tse et al., 2006; Wacongne et al., 2011, 2012). However, the MMN can be elicited by auditory deviants with an SOA up to 4 s (Näätänen et al., 2005, 2007), possibly even up to 10 s (Sams et al., 1993). Furthermore, comparison of ERPs to omission deviants and standard tones is problematic because obligatory auditory potentials elicited by a sound are not present when there is no sound, so the comparisons between omissions and sounds may lead to differences not due to deviance detection, but the absence of sensory encoding. Thus, further investigation was needed to determine if ERPs that estimate deviance detection, such as the MMN, could be elicited using larger SOAs and by comparing omissions under various contexts.

Some researchers found omission deviants elicit a cascade of response called the oN1, oN2 and oP3 (Dercksen et al., 2020, 2022; Korka et al., 2020; SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013; Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). These components appear to be present when some level of attention from the participants is directed towards the auditory sequence, either with a change detection task or by having participants press a button to generate the sounds. This in contrast to most research on the

MMN that typically uses passive listening (Näätänen et al., 2007), especially with populations that cannot do an explicit task, such as infants. To our knowledge no previous study had been conducted in which passive listening was used and the omission specific potentials were elicited. Thus, in the present thesis, I used passive listening to determine whether similar responses would be seen during passive listening, as well as a methodology that could compare infant and adult responses to omission deviants.

Additionally, the effect of global predictability on the ERP elicited by omission deviants has been understudied. Global predictability attenuates auditory deviant responses, such that when an auditory deviant occurs regularly in a sequence, an overarching global prediction can be used to determine when the next deviant will occur, and the MMN is attenuated compared to when deviants occur randomly (Bendixen et al., 2009; Horváth et al., 2001; Sussman et al., 1998). The attenuated response may be caused by a smaller prediction error from globally predictable deviants because the regularly occurring deviant becomes part of a hierarchy of sensory predictions (Friston, 2005; Wacongne et al., 2012). An MMN is still elicited because the auditory deviant still violates local predictions as it is a change from the preceding frequent standard sounds. This effect of global predictability of auditory deviants is present early in development (Basirat et al., 2014; Háden et al., 2024). However, prior to this thesis, the effect of global predictability for omission deviants had yet to be tested. Further evidence that global predictability might affect omission deviant responses comes from studies manipulating the predictability of standard sounds in an auditory sequence that contains omission deviants. Specifically, playing a different sound for every sound event attenuates the response to omission deviants, compared to playing the same sound on every trial, possibly due the a general inability to make sensory predictions regarding the auditory sequence (Korka et al., 2020; SanMiguel, Saupe, et al., 2013; van Laarhoven et al., 2017). To our knowledge, no study before this dissertation had directly tested if globally predictable omission deviants show attenuated evoked potentials compared to globally unpredictable omission deviants.

Another area lacking research is the infant response to omission deviants. Infants can detect auditory deviance as indexed by the MMN or the MMR depending on age (He et al., 2007, 2009) and the sound feature of the deviant stimuli (Cheng et al., 2015; Themas et al., 2023; Werwach et al., 2022). Winkler and colleagues (2009) found an MMN, and possibly MMR, in response to omission deviants with newborn infants. The stimuli they used were complex rhythms consisting of three different instruments, and sometimes the omission deviant consisted of removing one instrument whereas sometimes the omission deviant consisted of removing multiple instruments, but not every omission deviant elicited an MMN or MMR. Only omissions that consisted of the removal of multiple instruments that occurred on perceptual strong beat in the rhythm elicited the deviance detection responses. Understanding how the infant brain processes omission deviants and the developmental trajectory is important for understanding how the developing brain processes missing expected auditory information.

Thus, the goal of this thesis was to investigate how the brain processes omission deviants with longer SOAs during passive listening, how infants respond to omission deviants, and the influence of global predictability on the infant and adult neural response to omission deviants.

Unique Contributions and Limitations of Each Chapter

Chapter 2

Previous work on omission deviants found MMN could only be observed when the deviants were presented with an SOA of 200 ms (Raij et al., 1997; Yabe et al., 1997, 1998), while comparing the silence to the standard tone. However, given that the sound gives rise to evoked sensory responses not present for silences, the silences that create omission deviants should be compared to silences that would not be considered a deviant, rather than the standard tones. In this study we compared silences there were unexpected, i.e. omission deviants, to silences that were expected within the sequence to determine if we could observe deviance detection responses at larger SOAs.

We found that unexpected silences caused by an omission deviant elicited MMN and P3a compared to expected silences (Prete et al., 2022). Importantly, we found these responses during passive listening while using an SOA of 500 ms. Thus, even at larger SOAs, deviance-detection evoked potentials seem to be elicited by omission deviants as well as auditory deviants. However, MMN is highly dependent on context (Ruhnau et al., 2012; Sussman et al., 2014), and the expected silences used to contrast the unexpected silences were presented more frequently, occurring after every tone, or 50% of the “trials”, whereas the unexpected silences made up only 10% of the trials in their context. Thus, the differences we observe may be caused by differences in the occurrence rate of the silences rather the deviance detection itself (Busse & Woldorff, 2003; Sabri & Campbell, 2001; Sonnadara et al., 2006). In Chapter III and Chapter IV, we accounted for this issue by presenting the omission deviants at the same rate of 20% but altering the global predictability so that the omission deviants were either globally unpredictable or globally predictable.

Chapter 3

In the study from Chapter III, we investigated the evoked potentials elicited by omission deviants in 6-month-old infants, while also manipulating the global predictability. This is one of the first studies to look at omission deviants with infants and to investigate how global predictability might influence the omission evoked potentials. We found that omission deviants elicited a response greater than baseline activity, with an MMR-like response but, unlike the MMR, this ERP component was not affected by global predictability. Thus, we showed that the infant brain detected the omission deviants, but did not respond in the way we would have predicted based on infants' response to auditory deviants.

In addition to the MMR-like component, we found frontally positive ERP potentials at multiple latencies during the omission deviant. As there were no significant differences between the globally predictable and globally unpredictable omission, and both omission deviants were followed by a tone, we cannot determine if these responses are due to the omission deviant or the expectation of the upcoming tone or a combination of both. Furthermore, without additional analysis such as source localization to determine if the potentials have similar or distinct sources, we cannot determine if the negative potentials at the various latencies represent distinct responses, or one slow on-going negative potential or a combination of both. Much more investigation is need on infants' neural response to omission deviants to understand if the responses we observed are consistently elicited, how many distinct evoked potentials are present, and how these omission evoked potentials relate to auditory deviant evoked potentials.

Chapter 4

In the final study we examined the effect of global predictability in adults, to extend the findings of the first chapter investigating the omission evoked potentials during passive listening. We wanted to determine if the MMN or omission evoked potentials are present in adults using a similar experimental design as we did with infants in Chapter III, as this specific design had not been tested in adults. As in Chapter III, we found neural activity greater than baseline in adults, but we did not find the evoked potentials that we expected. Instead, the response appeared as a general increase in the ERP that reached a plateau about 250 ms post omission onset, possibly indexing temporal expectations to the upcoming tone. This increased activity was present regardless of whether the omission deviant was globally predictable or globally unpredictable. Like in Chapter III, because there was difference between the globally predictable and globally unpredictable omission deviants, and every omission deviant was followed by a tone, we cannot determine if the observed responses are due to processing the omission deviant specifically or some form of expectations for the upcoming tone, or both. It may be that under this context temporal expectations have a larger effect than global predictability.

We also did not replicate the findings of Chapter II; the globally unpredictable omission condition of Chapter IV is comparable to the unexpected silences condition of Chapter II. Two of the main differences between Chapter II and Chapter IV were an increase in the occurrence of the omission deviants from 10% to 20% and the inclusion of the visual cue. Increasing the occurrence rate attenuates the amplitude of the MMN in response to auditory deviants (Sabri & Campbell, 2001; Sonnadara et al., 2006), thus we may not have observed an MMN due to attenuation of an already small response elicited by omission deviants. Or activity from multi-modal sensory neurons may be driving the observed response in Chapter IV that are not present in Chapter II, because no visual stimuli was presented in the latter case.

Open Questions and Future Directions

Mechanism of Omission Deviance Detection

One unresolved question is the neural mechanism generating the response to the omission deviants. The most prominent theory for deviance detection for auditory and omission deviants is predictive coding, which states that any deviant stimulus that violates the established sensory predictions engages a series of neural responses that include calculating the difference between the sensory prediction and the incoming sensory information, eliciting a prediction error signal if there is a discrepancy, and updating the sensory predictions based on these differences (Baldeweg, 2007; Dercksen, 2023; Friston, 2005; Horváth et al., 2008; Lao-Rodríguez et al., 2023). Importantly, these theories state that predictive coding is hierarchical, meaning that various levels of sensory prediction can be encoded such as the local level predicting what the immediate next stimulus should be, and the global level predicting the next stimuli based on overarching patterns in the sequence. Alternatively, deviance detection could come about via neural adaptation, which suggests that the neurons that encode the specific sensory information for the incoming stimuli habituate over time, decreasing their firing rate (May, 2021; May & Tiitinen, 2010). Deviant trials then elicit a response from neurons that are not habituated as the sensory information is different, leading to the difference in the ERP response. It is important to note that these are broad overviews of the two theories. Below we will discuss some specific models based on these theories and the different interpretations they might have for the observed results.

According to a recent model of neural adaptation, the MMN can be explained by neural models of adaptation that include short-term synaptic depression and lateral inhibition (May, 2021). They found that the MMN could also be elicited by omission deviants with the SOA of 200 ms, which other researchers have argued are not possible without predictive coding (Bendixen et al., 2009, 2012; Lao-Rodríguez et al., 2023). Although not explained in detail, May suggests the response to the omission is due to rebound from oscillations. Using code for the model available online (Hajizadeh et al., 2019; May, 2021) to test if an omission deviant could be elicited using a larger SOA, specifically 400 ms, as in the present study, we found no response at all to omission deviants. Thus, this model does not seem to align with the results we found in Chapter II or Chapter III. This model also predicts a difference based on global predictability, but it is unclear which part of the adaptation model drives this effect, and if it is the same part that leads to the MMN elicited by omission deviants. Without knowing which part of the model is driving the affect of global predictability for auditory deviants, it is unclear if we should expect the same effect of global predictability for omission deviants. Furthermore, this model is based on animal and adult neurophysiology, so it is unclear if comparison between the model output and infants' responses is appropriate. But overall, this would suggest that our results do not fully align with a neural adaptation model of deviance detection for omission deviants.

One model of predictive coding suggest that all ERPs contain some activity from prediction error encoding neurons (Friston & Kiebel, 2009). Based on this, any response to omission deviants would have to be prediction error as there is no sensory encoding. This may explain the results from Chapter II as we found deviance detection responses resembling MMN and P3a, but smaller than is typically for auditory deviants, which would be expected as they would contain activity only from prediction error and not sensory encoding. This model also suggests that sensory predictions are hierarchical. Based on this we would expect globally unpredictable omissions to elicit a larger response compared to globally predictable omissions in the studies from Chapter III and Chapter IV, because unpredictable omissions would deviate from the sensory predictions more than predictable omissions. Furthermore, as predictive coding encompasses a cascade of neural responses to violations of predictions, we would expect to see several distinct, successive ERP potentials (Horváth et al., 2008). This may be present in Chapter II as we observed an MMN and P3a elicited by omission deviants. Chapter III may also have a cascade of responses as the waveform appears to have one component before 250 ms post omission onset and possibly another component after 250 ms post omission onset. However, the adult responses in Chapter IV do not display these distinct responses. Thus, the studies in this dissertation do show some aspects of predictive coding but they do not fully align with the expected outcomes.

According to a more recent model of predictive coding, the neural response to omission deviants comes from activation of the sensory template to which the incoming sensory information is compared (Wacongne et al., 2012). Based on this model we would expect the ERPs elicited by omission deviants to resemble the ERPs elicited by sounds, at least when predictions can be made regarding the sounds. SanMiguel and colleagues (2013) found evidence of this as the oN1 component to the omission deviant was very similar to the N1 component from the sounds, and furthermore the oN1 has shown to be attenuated or absent when no predictions about the sounds can be made (Korka et al., 2020; SanMiguel, Saupe, et al., 2013; van Laarhoven et al., 2017). However, as none of the studies in the current thesis observed an oN1, how much this applies to the current thesis is unclear. The sensory template response may explain the smaller MMN and P3a we observed in Chapter II in comparison to MMN and P3a elicited by auditory deviants, which would be a combination of the sensory template and prediction error, according to this model. Interestingly, in Chapter III the first 250 ms post omission onset is very similar to the response to the tone right before an omission deviant as well, further supporting this idea. However, the ERP response in Chapter IV does not follow this pattern, as neither of the responses to omission deviants presented in this study resemble the auditory evoked potentials. It may be that the differences are due to attenuation of sensory templates with development, as we learn over time which changes in the auditory environment need to be monitored and which do not. Additionally, previous studies that elicit the oN1, oN2 or oP3 use some form of task, which may cause omission deviants to be deemed a relevant change in the auditory information and engage predictive coding processing that we do not observe in as we used a passive listening paradigm. The role of attention therefore needs to be studied further.

Omission Deviants and Task Engagement

All three studies in the current thesis used passive listening. This was chosen for three reasons. Firstly, we wanted to extend the findings from past research on auditory deviance detection that have used passive listening (Näätänen et al., 2007; Sussman et al., 2014). Secondly, we wanted to determine if the omission evoked potentials, oN1, oN2 or oP3, can be evoked without preforming a task. Thirdly, we wanted to compare infant and adult responses to omissions, and infants typically need to be tested in a passive paradigm. To our knowledge, the omission evoked potentials have not been tested during passive listening. Thus, we wanted to test which ERP components we would observe during passive listening and how factors like SOA or global predictability might influence these components.

There is a growing body of research using methodologies that engages adults' attention to the stimuli by employing a task to elicit the sounds that are infrequently omitted (Dercksen et al., 2020, 2022; K. Ishida et al., 2024; T. Ishida & Nittono, 2024; Korka et al., 2020; SanMiguel, Widmann, et al., 2013). Some have employed a direct task in which participants need to respond to changes in the stimuli unrelated to the omissions (Stekelenburg & Vroomen, 2015; van Laarhoven et al., 2017). Other studies require participants to press a button at a consistent rate and the button press produces a tone that is occasionally and pseudo-randomly omitted creating an omission deviant (Dercksen et al., 2020, 2022; Korka et al., 2020; SanMiguel, Saupe, et al., 2013; SanMiguel, Widmann, et al., 2013). The button pressing task would engage some level of attention toward the sound as there is a task the requires participants to generate the sounds and omission deviants, but participants do not need to evaluate the stimuli or respond to a specific event, thus the task would not require a high level of attention or task engagement. When some task is used, rather than the MMN or P3a, the omission evoked potentials oN1, oN2, or oP3 are elicited in response to omission deviants. Although, which of these components are elicited seems depends on the context in which the omission deviants occur (Korka et al., 2020; SanMiguel, Saupe, et al., 2013; van Laarhoven et al., 2017). In the current thesis, we did not observe any of the omission evoked potentials, possibly due to a lack of task engagement. Deviance detection does not use purely passive neural processes, as the MMN can be enhanced when attention is directed to the auditory deviant (Alain & Woods, 1997; Dykstra & Gutschalk, 2015; Haenschel et al., 2005; Sussman, 2013; Sussman et al., 2002; Woldorff et al., 1991). It may be that the omission evoked potentials are also affected by attention or may require some level of attention directed to the auditory information that is omitted. If participants are told that omission deviants reflect how consistent their button presses are, the amplitude to oN1, oN2 and oP3 increases compared to when participants are told the omission deviants are random and can be ignored (T. Ishida & Nittono, 2024). Thus, changing attention via task instructions seems to be enough to elicit changes in the omission evoked potentials like the enhancement of the MMN. However, to our knowledge, no study has compared button generated responses or the omission potentials with an explicit task to a completely passive listening.

Future research should compare how different levels of attention toward the stimuli influence the omission evoked potentials. Pressing a button does not require a high level of attention, but it still engages participants with the stimuli by making their actions directly responsible for the stimulus presentation. Researchers could compare passive listening to button generated sound sequences, and/or conditions in which participants must respond to a change in the auditory sequence that is not the omission deviant. A direct comparison of different levels of attention, or task engagement on the amplitude, latency or even source localization of the oN1, oN2 and oP3 could be conducted. Furthermore, the behavioural response could be correlated to the neural response, at least in the conditions with attentional demands. It may even be possible to pair motor responses with audio or audio-visual stimuli with omission deviants in infants generating the sounds with a button press or touch sensitive tablet. This would likely entail recruiting older infants that have better motor control and more experience using the technology that would be used in the experiment, to retain enough trials for analysis. But such an experiment would be crucial for furthering our understanding of the development omission evoked potentials and the role of attention.

Omission Deviant Rate and SOA

Even though we found deviance detection ERP components in Chapter II, we did not find clear evidence of deviance detection in ERP components in Chapter III and Chapter IV. One difference between the study in Chapter II and the studies in Chapter III and Chapter IV, is the rate at which the deviants occur. In the first study the deviant rate was set to 10% of trials whereas in the last two studies, the deviant rate was changed to 20%. This increase in percent of deviant trials was done to ensure that global prediction of the 5-event pattern could be retained by infants and then kept to for comparison of ERP potentials between infants and adults under the same conditions, but the more frequent a deviant stimulus occurs in a sequence, the more attenuated the response is (Sabri & Campbell, 2001; Sonnadara et al., 2006), possibly because the deviant becomes less surprising and thus elicits a smaller prediction error response (Itti & Baldi, 2009; SanMiguel, Widmann, et al., 2013). The increase in percentage of deviant trials could contribute to the ambiguous MMR found in Chapter III, the lack of an MMN in the Chapter IV, as well as the MMN found in Chapter II. The higher occurrence rate may be limiting the ERP potentials elicited by the omission deviants that tend to be more variable (Hughes et al., 2001) and have smaller amplitude (Prete et al., 2022).

Furthermore, with omission deviants specifically, large SOAs attenuate the amplitude of the MMN even to the point where it may not be measurable (Yabe et al., 1997). Although the study in Chapter II provides evidence to the contrary, we did not find an MMN or omission evoked potentials in Chapter III and Chapter IV. We do find that omission deviants elicit some neural activity greater than baseline, but the exact nature of these responses is unclear. Having the large SOA combined with the higher deviance rate may have increased the variability in the ERPs, leading to a weaker MMN in Chapter II, an ambiguous MMR in Chapter III and no MMN or omission evoked potentials in Chapter IV. Manipulating SOA to be 200 ms, 300 ms, and 500 ms, while simultaneously manipulating occurrence rate to 10%, 12.5%, and 20%, would give a more thorough understanding of how these experimental parameters interact when the brain encounters omission deviants. It may be that with a lower occurrence rate we may start to observe a more prominent MMN in adults and MMR in infants. Additionally, using several SOAs would also allow us to determine if the slow wave observed in Chapter IV is due to temporal expectations for the upcoming sound, and thus extends to the duration of the current SOA. An alternative would be to jitter the SOA while manipulating deviant occurrence rate so no specific temporal expectation could be formed, likely mitigating the slow wave increase (if it is the result of temporal expectations) and increasing the chances of finding an MMN or MMR.

Manipulating occurrence rate or SOA while participants press a button to generate the sounds would further elucidate how varying these parameters influences the various ERP components that can be elicited by omission deviants, as the oN1, oN2 and oP3 seem to be most reliably elicited to omission deviants occurring within button generated sound sequences (Dercksen et al., 2020). If the omission specific components are similarly affected by occurrence rate or SOA, like the MMN, it might suggest similar underlying mechanism for both ERP components. However, consistently pressing a button at a specific tempo, especially a fast tempo like 200 ms, may not be possible for all participants. The variability in participants' ability to perform the task would affect tempo of the stimuli and possibly the evoked potentials. Only larger SOAs should be chosen for button generated conditions, which may make comparison to passive listening difficult. Thus, a series of studies with careful consideration to tempo and task demands would need to be conducted to fully examine the effect of experimental parameters along with the effect of attention on the omission evoked potentials.

Contingency Between Modalities

Another limitation from the studies in Chapter III and Chapter IV is that the observed ERPs may not be due to omission of the auditory information alone, but the difference in audio-visual stimuli compared to just visual stimuli, which occur when the auditory information is omitted. By this we mean that the audio-visual stimuli may activate specific neurons that encode both sensory modalities simultaneously (Burr & Alais, 2006). Cell recordings from animals have found neurons that encode audio-visual stimuli specifically (Deneux et al., 2019; Knöpfel et al., 2019), sounds or movements paired with visual stimuli alter the neural encoding of the visual stimuli within visual cortices (Vroomen & Stekelenburg, 2010; Williams et al., 2023), and multi-sensory stimuli can enhance behavioural performance (Gingras et al., 2009). It may be that the activity we observe may comes from multi-sensory encoding neurons as well as the altered activity from neurons that encode the visual and auditory information separately. Subtracting the ERP from the visual only condition would not account for such multi-sensory activity. The lack of an effect of global predictability in Chapter III and Chapter IV may be due to similar activation of these multi-sensory encoding neurons as the same information is missing in the globally predictable and globally unpredictable conditions from both studies.

Interestingly, there are also multi-sensory neurons that encode auditory and somatosensory stimuli (Foxe et al., 2002; Foxe & Schroeder, 2005; Fu et al., 2003), which may influence that ERPs elicited by button generated sounds. Comparing the oN1 and oN2 elicited by auditory omission deviants from an audio-visual stimuli and audio-motor stimuli has shown similar topography, waveform and source localization (Stekelenburg & Vroomen, 2015). This would suggest that activity coming from multi-sensory neurons do not account for most of the neural activity resulting in the omission evoked potentials, but rather the omission of auditory information may be generalized across modalities. However, we did not observe the omission evoked potentials in either Chapter III or Chapter IV, making it unclear if the same could be said for the neural activity we observed. Conducting source localization of evoked potentials to omissions of auditory stimuli from audio only sequences, audio-visual sequences, and audio-motor sequences while manipulating global predictability of the omission deviants would allow us to determine how much of the ERP is due to encoding the auditory information alone or multi-sensory encoding. Using other neural imaging tools such as MEG or fMRI could also help differentiate the sources of neural activity. Alternatively, if the latency and electrodes of the response could be hypothesized a priori, average amplitudes could be extracted for the expected responses, and the interaction could be tested statistically by including the visual only control, or motor only control, within the statistical model rather than subtracting it out, allowing for interaction effect to be estimated. Future research could be designed in such a way as to test the contribution of multi-sensory neurons both experimentally and statistically.

Summary

This thesis aimed to broaden the understanding of brain responses to omission deviants in auditory sequences. Understanding what happens in the brain and ultimately how we react to missing auditory information is important as the absence of sound could be an early sign of danger in the immediate environment or could a be an alert that kin are in danger as they are no longer making noise. Furthermore, omission deviants could isolate the prediction error signals from sensory encoding prediction signals, enabling isolation of the regions of activation for the different stages of predictive coding. Recent models of neural adaptation call into question whether predictive coding or neural adaption is the neural mechanism behind deviance detection (May 2020). Results from omission studies showing deviance detection responses at SOAs larger than 200 ms and developmental trajectories need to be incorporated in neural models of deviance detection to better understand which mechanisms reflect the observed neural response.

Across the three studies we found that the brain has a distinct response to omission deviants, but these responses were not consistent across contexts. Furthermore, global predictability did not influence the response to the omission deviants as it does with auditory deviants, suggesting that omission deviants may not be processed in the same way as auditory deviants. We were one of the first to investigate the effect of global predictability on the neural activity elicited by the omission deviants, as well as the development of ERPs elicited by omission deviants. Further research is needed to better understand the mechanisms of the neural response and the developmental trajectory.

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