

**FIRST IMPRESSIONS BIAS SOUND
SEQUENCE LEARNING ON MULTIPLE
TIMESCALES:
AN ORDER-DRIVEN PHENOMENON IN
AUDITORY MISMATCH NEGATIVITY**

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Abstract

Humans are prone to systematic biases in perception that impact rationality in judgement. First impression bias occurs when judgement is overly affected by information presented during an initial encounter. Using the amplitude of a specific brain response, the mismatch negativity (MMN), our team discovered that the brain is prone to this bias effect during the very early stages of sound sequence learning preceding knowing awareness. The aim of this thesis was to determine which experimental conditions expose or modify first impression bias effects on sound pattern learning on multiple timescales. Predictive coding models assume the brain is hierarchically-organised and uses perception to make inferences about the sensory world whilst updating predictions about incoming sensory information. Recurring comparisons between bottom-up input and top-down predictions consider environmental noise, and determine the inferential modelling process. MMN, an event-related response evoked by violating regularity in a structured sound sequence, is an example of a prediction error signal. Its presence informs on prediction model content whereas its amplitude informs on model confidence (or precision). Prediction error amplitude to a pattern violation is largest when model confidence is very high and may require engagement of additional, higher-order resources. First impression bias shows that the network uses contextual information at sound sequence onset to modulate MMN amplitude to probabilistic changes thereafter. This thesis shows that first impression bias is a remarkably robust and long-lasting phenomenon that can be interrupted if participants undertake an attention demanding task whilst hearing multi-timescale sequences or are provided with accurate foreknowledge about sound structures before sequence exposure. This thesis discusses how models assuming only local sound probabilistic information drives the MMN-generating process cannot explain bias effects on MMN amplitude. Rather, the bias is a striking example of a hierarchical inference process incorporating attentional resources that considers the potential relevance of sound information and its stability over time.

Statement of Originality

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision.

The thesis contains published scholarly work of which I am a co-author. For each such work a written statement, endorsed by the other authors, attesting to my contribution to the joint work has been included.

The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo

SIGNED:

Jade D. Frost

February, 2018

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ABBREVIATIONS

Abbreviations

ANOVA	Analysis of Variance
ART	Adaptive Resonance Theory
DCM	Dynamic Causal Modelling
DVD	Digital Versatile Disc
EEG	Electroencephalography
ERP	Event-Related Potential
EOG	Electro-Oculograms
HGF	Hierarchical Gaussian Filtering
ISI	Inter-stimulus interval
MMN	Mismatch Negativity
MRI	Magnetic Resonance Imaging
PAC	Primary Auditory cortex/cortices
PFC	Prefrontal Cortex
PT	Perceptual Task
SOA	Stimulus Onset Asynchrony
SSA	Stimulus Specific Adaptation
WM	Working Memory

Synopsis

Our team has discovered that the brain is susceptible to *first impression bias* effects during very early processing of information in sound pattern learning across time. Evidence of bias shows that the order in which sound information is heard markedly changes how pattern learning proceeds, a phenomenon comparable to primacy effects observed in psychological studies (e.g. Asch, 1946; Bargh & Pietromonaco, 1982; Baumeister, Bratslavsky, Finkenauer, & Vohs, 2001; Devine, 1989; Hamilton, 1979; Nisbett & Ross, 1980; Perdue & Gurtman, 1990; Pratto & Bargh, 1991; Rothbart & Park, 1986; Rozin & Royzman, 2001; Skowronski & Carlston, 1992; Wyer, 1973). In this thesis, we¹ apply a widely known neuroscientific psychophysiological technique, electroencephalography (EEG), and use sequences comprising patterns that emerge over multiple timescales to further expose under what conditions first impression effects are observed or are modified. We use a brain response called the mismatch negativity (MMN), a component of the auditory event-related potential (ERP) that is evoked automatically when some aspect of the sound environment unexpectedly changes. The MMN is described in the literature as a measure informing about neural states underlying central auditory processing at the cortical level. More specifically, it can be used to study the brain's capacity to 1) learn transitions statistics underlying sound patterning that emerge in environment as time unfolds, and 2) use this information to anticipate the next most likely state of neural activation.

In a series of studies, we have shown that MMN amplitude to transitional probabilities over the shorter term is modulated by contextual learning in a way that

¹ Whilst I understand it is conventional to use "I" in a thesis, I prefer to use "we" to reflect the joint venture I experienced during my candidature.

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cannot be accounted for by prominent models proposed in the MMN literature. Hence, we propose that the brain utilises hierarchically-organised inference mechanisms that are sensitive to transition statistics at multiple timescales and include sophisticated means for estimating the relevance of one sound event over another. Further, we think that the susceptibility of relevance filtering mechanisms to first impression bias occurs because estimates based on initial experience of one context (in which transition statistics are heard) has undue influence on estimating sound relevance based on probabilistic information later. This interpretation is consistent with assumptions put forward by predictive coding accounts of learning and accordingly, research questions in this thesis are formulated using theoretical principals described under this framework. In all experiments, we use variants of a sound sequence called the multi-timescale paradigm that contains transition statistics that emerge over both the shorter and longer term. The work described here is guided by a focus on specific experimental manipulations that are formulated in terms of hypotheses informing on potential mechanisms underlying first impression bias effects in auditory relevance filtering.

This thesis is organised as follows:

Chapter 1: Background and Rationale

The MMN literature is reviewed and predictive coding theory from which research questions in the present thesis are formulated is also described. In the latter half, our research findings generated by studying the first-impression bias in early relevance filtering under different conditions will be explained; the rationale for extending this knowledge in the present thesis will also be put forward.

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Chapter 2-4: Results chapters

The experimental work including the aims, hypotheses, methods and the outcomes for each study are described. In each experiment, variants of the multi-timescale experimental paradigm are used to test research questions generated about first impression bias modulatory effects on MMN amplitude. The specific goals of each study were as follows:

- To replicate patterns of first impression bias effects using a much larger sample size relative to those included in previously published studies (Chapter 2)
- To determine the effect of first impression bias on sound pattern learning following repeated exposure to more stable or more volatile sound sequences (Chapter 2)
- To determine if learned patterns of first impression bias effects remain if participants are engaged in a concurrent task that places high demands on attentional and/or working memory resources whilst hearing the multi-timescale paradigm (Chapter 3)
- To determine if knowledge about local and context-based sound structures before hearing the multi-timescale sequence affects first impression bias effects on sound sequence learning (Chapter 4)

Chapter 5: General Discussion and Conclusions

A general discussion and the conclusions of this work including contributions to the research field and possible directions for future research are provided.

Chapter 1: Background and Rationale

The environment is made up of an immense number of patterns that unfold with time. The way we perceive and learn these patterns is through our senses. In central auditory processing, translating sensory experience into something meaningful is not straight forward because the highly transient and noisy nature of the sound environment makes pattern detection and learning considerably more complex compared to other modalities such as touch. It is therefore essential that sound information is not only perceived, but is also stored and utilised in a way that allows us to interact with the environment in an adaptive way.

Over time, the brain has developed mechanisms required for learning and acting on incoming information about sound pattern probabilities that is, the statistical likelihood that an auditory event will happen. There are a number of theoretical frameworks for conceptualising this yet one, *predictive coding*, is based on the assumption that the brain models information about sound-induced patterns of neural activity and uses this information to form predictions about the likelihood of the next sound event (Winkler & Czigler 2012). This allows the brain to filter responsiveness to predictable information in preparation for instances where a sound event violates an established pattern. When a pattern violation occurs, a prediction error is registered and the model updates to accommodate sound change. This is considered optimal in terms of efficiency because it allows for the preservation of neural energy in responses to predicted sounds that can be re-distributed in preparation for any unexpected, and potentially informative, sound events (Friston, 2003, 2005). Accordingly, new predictions are formed and/or existing predictions

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are modified to accommodate this new information and perceptual learning continues in an automatic and dynamic fashion (Winkler, 2007).

Active predictions are not always formed and/or updated to be an exact replica of current experience even when something in the immediate environment has clearly changed. In studies of auditory perceptual learning during very early relevance filtering, our lab has shown that the mechanisms driving perceptual inference succumb to *first-impression bias* (Fitzgerald, Provost, & Todd, 2017; Frost, Winkler, Provost, & Todd, 2015; Todd, Provost & Cooper, 2011; Todd, Provost, Whitson, Cooper, & Heathcote, 2013; Todd, Provost, Whitson, & Mullens, 2017; Todd et al., 2014a; Todd et al., 2014b; Mullens et al., 2014; Mullens et al., 2016). Evidence of first impressions shows that what we first learn about sound probability in one context distorts learning about probabilities in a different sound context later.

In this thesis, we build upon existing research by further delineating some of the key assumptions underpinning first-impression bias in auditory relevance filtering for the purposes of developing a framework for understanding experimental conditions that facilitate or alter typical bias patterns. The mismatch negativity (MMN) is a component of the ERP understood as a prediction error response elicited after a sound pattern is violated (Friston, 2005) and is the primary dependent variable for each study reported in this thesis. As such, these data extend on our current understanding of the MMN as a prediction error signal. In this thesis, the results from four studies are presented across three chapters. All observations will be used to discuss how each contributes to existing literature on MMN from a theoretical standpoint of predictive coding. More broadly, our results provide insight into how the neural mechanisms involved in sensory inference and learning operate. Next, a

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comprehensive review of the empirical and theoretical literature pertaining to the research questions addressed in this thesis is provided before evidence of first impression bias effects on sequence learning are described. But first, an overview of central auditory processing more generally as well as the importance of MMN as a tool for measuring sound sequence pattern learning is presented.

1.1. Central auditory processing – a complex sensory phenomenon

As human beings, we interact with a rich auditory environment that is changing with each passing second, minute, day, and so forth. This means that the brain is constantly exposed to a vast number of sounds with unique and shared characteristics that may (or may not) be important for learning. From a psychological perspective, it is generally agreed that the purpose of audition is to learn the source of a sound entering the senses because this information is essential for survival (e.g. Brunswick, 1956; Gibson, 1962, 1963). Despite many types of sounds occurring simultaneously or intermittently, or both, the brain is remarkably proficient at recognising sound patterning based on probability and transition statistics, despite substantial background noise. This process involves translating the source of each individual sound event relative to other sounds and/or noise as well as monitoring the ongoing relationship between two or more sounds as time unfolds (Winkler & Schröger, 2015). As noted by Helmholtz (1867), the neurophysiological hardware underpinning central auditory processing requires elements that can use experience for computing the most likely source of sounds including relationships to determine the exact cause of incoming sensory input. The sheer complexity of the acoustic environment is what distinguishes auditory processing from other sensory modalities like smell and touch.

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The capacity to utilise sound patterning in preparation for impending sound change is underpinned by many neural events that support perception, memory, attention as well as learning processes (Escera & Malmierca, 2014). Certainly, sensitivity to sound patterning is essential for many cognitive functions such as directing one's attention to behaviourally relevant events (e.g. Berti, 2013) as well as in infant language development (e.g. Winkler, Denham, & Nelken, 2009). This type of processing can be studied using non-invasive EEG scalp recordings of brain responses generated by stimulus-relevant ERPs (Kujala, Tervaniemi, & Schröger, 2007). One key advantage of using ERPs is that each is time-locked to a sound event allowing for close examination of the time-course in which information processing unfolds with high temporal acuity.

In the present thesis, we used an ERP approach because we were particularly interested in examining the change in electrical activity during early cortical stages of temporal information processing in sound sequences containing patterning, at different timescales. More specifically, we utilise a well-known waveform derived from ERP responses called the MMN (Näätänen, Gaillard, & Mäntysalo, 1978; Näätänen, 1992; Näätänen, Kujala, & Winkler, 2011). The MMN can be used to infer what has been perceived and learned by the underpinning network over time by first establishing a sound pattern and then violating the learned pattern in some way (Näätänen et al., 1978). It has been studied in several sensory modalities including somatosensory (Kekoni et al., 1997; Shinozaki, Yabe, Sutoh, Hiruma, & Kaneko 1998; Akatsuka et al., 2005; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007), olfactory (Krauel, Schott, Sojka, Pause & Ferstl, 1999) and visual systems (Czigler, Balázs, & Winkler, 2002; Czigler, 2007; Maekawa et al., 2005; Müller, Widmann & Schröger, 2013) however most of the literature comprises examination of MMN

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following a significant change in auditory stimulus sequence (Näätänen, et al., 1978). Information processing specific to the sound modality is a key focus of this thesis.

Studies using MMN as a tool for examining auditory processing show that the remarkable capacity of the associated network to use stimulus history in anticipation of future sound change is a basic brain process. To emphasize this point, magnetoencephalography functional imaging techniques show MMN can be elicited in foetuses (Draganova et al., 2005; Draganova, Eswaran, Murphy, Lowery, & Preissl, 2007; Huotilainen et al., 2005) and in sleeping newborns (Cheour et al., 1998; Cheour et al., 2002a, 2002b), during the early stages of sleep (Atienza & Cantero, 2001; Nashida et al., 2000; Nittono, Momose & Hori, 2001; Sallinen, Kaartinen & Lyytinen, 1994; Sculthorpe, Ouellet & Campbell, 2009), and has even been observed in comatose patients (Fischer et al., 1999; Fischer, Morlet & Giard, 2000; Kane, Curry, Butler & Cummins, 1993; Kane et al., 1996).

Since its discovery, the auditory MMN has been accepted as a robust marker of perceptual integrity and learning that reflects the brain's capacity to engage in comparisons between incoming sound events and some representation of stimulus history. In the proceeding sections, we review the literature outlining the sensitivity of the MMN signal to changes in local pattern stability based on simple, abstract and more contextual-based cues whilst highlighting how such studies have contributed to current understandings of perceptual learning in audition.

1.2 The Auditory Mismatch Negativity (MMN)

The MMN is a change-specific component of the ERP that is particularly useful for examining the brain's capacity to learn patterning within sound sequences

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for anticipating the next most likely sound given stimulus history. In its simplest form, the MMN is derived using an *oddball sequence* design - the same paradigm used in its discovery (Näätänen et al., 1978; Sams, Paavilainen, Alho, & Näätänen., 1985). Participants hear a repeating series of identical sounds (called *standards*) that are occasionally interrupted by sufficiently rare sounds (called *deviants*; $p < 0.30$) that differ in some way from the established pattern. The standard is any highly probable sound whereas the deviant is a pattern violation (Winkler, 2007). Another way to conceptualise this relationship is that the brain has the capacity to monitor patterns (standard-standard) and violations (standard-deviant, deviant-standard) of transitional statistics over time (Winkler, Karmos, & Näätänen, 1996; Sussman & Winkler, 2001).

The MMN is elicited 100-250ms after a deviant violates the sound pattern and was traditionally calculated by subtracting ERP's elicited to standards from those elicited to deviants² (Kujala et al., 2007; Sams et al., 1985). In most studies, MMN amplitude (μV) is the key dependent variable used to measure sensitivity to sound events that violate established patterning and this is true of the present thesis. ERP amplitudes are largely sensitive to the physical properties of sound features and so 'genuine' MMN is typically calculated by subtracting ERP's to a sound presented as standard in one sequence block from ERPs to that same sound when presented in the deviant role in another sequence block to control for the impacts of obligatory components (e.g. N1, P2; Deacon et al., 2000; Kujala et al., 2007; Walker et al.,

² Please note, there are a number of additional experimental paradigms used to measure the MMN including the many standards (Jacobsen & Schröger, 2001) and cascade designs (Ruhnau, Herrman, & Schröger, 2012). The MMN is therefore particularly useful when used as a tool for testing specific research questions about mechanisms of the underlying system (see Todd, Harms, Schall, & Michie, 2013 for a discussion).

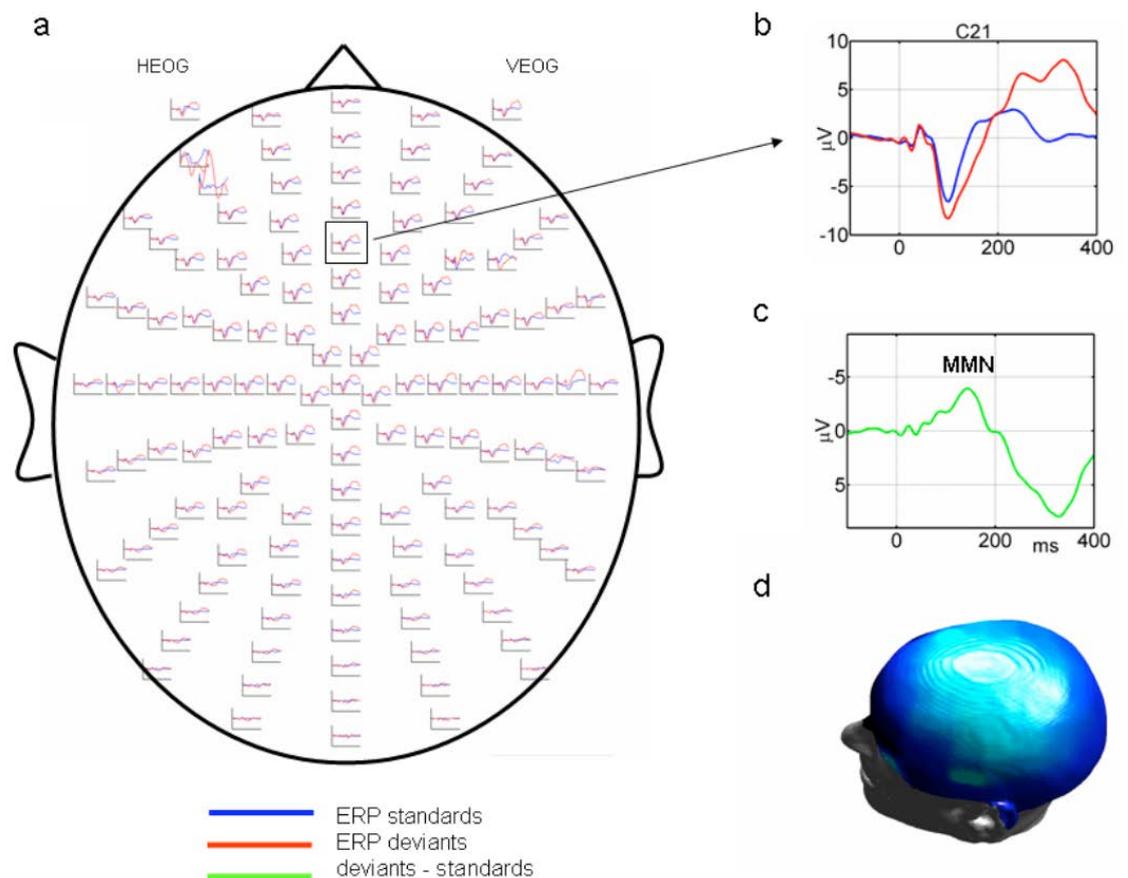


Figure 1.1. MMN scalp topography and latency. a. ERP responses to standard and deviant tones overlaid on a scalp map of 128 EEG electrodes. b. ERPs to the standard and deviant tones at a fronto-central electrode channel. c. MMN difference waveforms calculated by subtracting ERP to standards from ERP to deviants. d. MMN response averaged over a time window of 100 and 200 ms included to provide a 3D scalp topography map. (from Garrido et al., 2007b. Permission to copy and communicate this work has been granted by Marta Garrido, See Appendix 8 for evidence of permission)

2001). The maximal MMN peak amplitude (usually $<5 \mu\text{V}$) is typically measured over frontocentral scalp regions and can be distinguished from some other components of the ERP (e.g., the N2b) as it often reverses polarity in nose referenced mastoid recordings (see Figure 1.1; Garrido, Kilner, Kiebel, Stefan, & Friston, 2007; Kujala et al., 2007; Sams et al., 1985).

Näätänen and Michie (1979) first suggested that MMN comprises two sub-components: a sensory-specific component generated in the primary auditory cortex and a separate frontal component. Both bilateral supratemporal and right-lateralised frontal processes have been identified as cortical sources contributing to MMN

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generation (Baldeweg, Williams, & Gruzelier, 1999; Giard, Perrin, Pernier, & Bouchet, 1990; Rinne, Alho, Ilmoniemi, Virtanen, & Näätänen, 2000). The former is associated with relatively automatic processing of sound change whereas the latter is thought to contribute to attention-modulated processing of changes across time (Chennu et al., 2013; Opitz, Rinne, Mecklinger, Von Cramon, & Schröger, 2002; Rinne et al., 2000; Schröger, 1996; Schröger, Marzecová, & SanMiguel, 2015; Sussman, 2013; Sussman, Winkler, Huoutilainen, Ritter, & Näätänen 2002). A number of studies show that attention can modulate MMN amplitude – an effect typically studied using a dichotic listening task where attention is manipulated using explicit instruction. In one example, participants heard two alternating sounds of differing high frequencies in one ear and two of low frequencies alternating in the other ear (Alain & Woods, 1994). Repeating a sound constituted a deviant and participants were instructed to attend to one ear only and in a separate condition, stimuli were ignored altogether. MMN amplitude to the unattended ear were markedly smaller than those in the attended ear with no differences observed for the ignore group (Alain & Woods, 1994). Since Näätänen et al.'s (1978) first description of MMN however, findings regarding attention modulation of MMN have been inconsistent.

Other MMN studies show that when participants are asked to strongly focus attention towards sound sequence features (e.g. a specific sound location or specific pitch), its amplitude is markedly reduced (e.g. Alain & Izenberg, 2003; Alain & Woods, 1997; Muller-Gass et al., 2005; Winkler, Schröger, & Cowan, 2001; Trejo, Ryan-Jones, & Kramer, 1995; Woldorff, Hackley, & Hillyard, 1991; Woldorff, Hillyard, Gallen, Hampson, & Bloom, 1998) or not observed at all (Woldorff & Hillyard, 1991), relative to passive listening conditions. Another study found that

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MMN amplitude decreases with increased concurrent auditory task demand (i.e. respond to one of three rare tones via button press) suggesting that attention modulates MMN if processing resources within the same modality are simultaneously allocated to sound sequence processing (Dittmann-Balcar, Tienel, & Schall, 1999). Others find no differences in MMN amplitude between attended and ignored sounds (Paavilainen, Tiitinen, Alho, & Näätänen, 1993; Sussman, Winkler, & Wang, 2003). Thus, attention plays a role in active stimulus processing though the degree to which attention modulates MMN amplitude varies depending on the type of paradigm used. Importantly, the MMN is elicited irrespective of the participant's focus of attention (Näätänen & Michie, 1979; Näätänen, et al., 1978). In most studies, participant focus is typically redirected towards a non-relevant task (e.g. watching a film with sub-titles or reading a book) to minimise contribution of attention-related ERPs (e.g. N2b; Kujala et al., 2007; Näätänen, Simpson, & Loveless, 1982) during pattern learning. This has resulted in a widely-held assumption that although attention modulates MMN amplitude, neural generators are automatic and operate independently of attention-based mechanisms (Näätänen, 1992).

It is generally supposed that the functional significance of the MMN-generating process is to trigger recruitment of attentional resources for further processing of sound changes in the environment that are behaviourally-relevant for survival (Escera, Alho, Winkler, & Näätänen, 1998; Escera, Yago, Corral, Corbera, & Nuñez, 2003; Näätänen & Michie, 1979). A sound change that sufficiently differs from experience (e.g. approaching footsteps that stop suddenly, an air conditioner hum that begins to rattle) will capture our attention prompting conscious perception and sometimes, further assessment of whether a stimulus requires a behavioural

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response. This is consistent with studies showing that changes within an unattended sound sequence prompt attention switching away from a primary behavioural task as measured by reduced task performance (e.g. Escera et al., 1998; Giard et al., 1990; Schröger, 1997; Woods, 1992). Indeed, a component of the ERP linked to switching of attention called P3a often proceeds the MMN signal (Alho et al., 1998; Escera, Alho, Schröger & Winkler 2000; Escera & Corral, 2007; Friedman, Cycowicz & Gaeta, 2001; Knight & Scabini, 1998; Light et al., 2015; Paavilainen, Karlsson, Reinikainen & Näätänen, 1989; Rinne, Särkkä, Degerman, Schröger, & Alho 2006). Such findings support the hypothesis that the MMN-generating process is involved in directing attention, and therefore deeper processing, of the deviant sound (Näätänen, 1990). Sound change does not need to be hugely salient for an attention shift to occur as even a small variation in stimulus patterning, whether it be locally or contextually different stimuli, can attract a person's attention.

As will be discussed in subsequent sections, an understanding of exactly what the MMN component reflects about the pattern violation process is crucial because it can be used to form assumptions about the sound information held in memory and further, to infer the potential mechanisms driving perceptual learning in central auditory processing. Next, we report on studies showing that the amplitude of the MMN waveform is influenced by local changes based on stimulus history before describing how processing of changes from one sound to another can also be altered by the longer-term context in which sound patterning emerges (Dehaene-Lambertz, 1997; Näätänen et al., 1997; Sussman, 2007; Todd et al., 2011).

1.2.1 Pattern violation profiles - local and abstract sound patterns changes.

In early studies, the oddball paradigm was widely used for establishing conditions in which the presentation of a rare sinusoidal tone among a sequence of repeating tones

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with shared physical characteristic would result in MMN elicitation (Jacobsen & Schröger, 2003; Näätänen et al., 1978; Näätänen, Pakarinen, Rinne, & Takegata, 2004; Schröger, 1998). Changes in the relative probability of sound features at the local level is produced when one (or more) aspects of a deviant sound is physically different from repeating standards just heard. This means that change in local transitional probabilities is highly transient because it occurs rapidly over a reasonably short period, usually lasting no more than a few seconds. As a result of these early works, the brains capacity to respond to violations of repeating stimuli has been observed for several different deviant types including duration (Grimm, Widmann, & Schröger, 2004; Jacobsen & Schröger, 2003; Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007; Tervaniemi et al., 1999; Todd et al., 2008), frequency (Müller et al., 2002; Näätänen, Paavilainen, Titinen, Jiang, & Alho, 1993; Pakarinen et al., 2007; Todd et al., 2008), spatial location (Deouell, Heller, Malach, D'Esposito, & Knight, 2007; Deouell, Parnes, Pickard, & Knight, 2006; Jacobsen & Schröger, 2003; Paavilainen et al., 1989; Pakarinen et al., 2007; Schröger & Wolff, 1996), intensity (Jacobsen & Schröger, 2003; Pakarinen et al., 2007; Tervaniemi et al., 1999; Todd et al., 2008), tone omissions (Nordby, Hammerborg, Roth, & Hugdahl, 1994; Raij, McEvoy, Mäkelä, & Hari 1997; Tervaniemi, Saarinen, Paavilainen, Danilova, & Näätänen, 1994b), and phonemic change (Näätänen, 2001; Näätänen et al., 1997; Szymanski, Yund, & Woods, 1999; Ylinen, Shestakova, Huotilainen, Alku, & Näätänen, 2006). In one study, Näätänen et al. (2004) report on a variant oddball design in which one aspect of the standard altered between one of five deviant types (spatial location, duration, spatial location, intensity, omission and frequency). These data confirmed five MMN response types unique to each deviating property and highlights the sensitivity of this component to a range of

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sound pattern violations based on varying physical characteristics from one sound to the next. The MMN can be recorded even if the sequence does not contain a standard sound per se and rather, the invariant properties of the deviant stimuli denote a type of standard against which sound change is compared (Pakarinen, Huotilainen, & Näätänen, 2010). Irrespective of deviant type, and using a traditional computation of deviant minus repeating standard, MMN amplitude also depends on the magnitude of difference between a repeating pattern and subsequent violation, with a larger discrepancy evoking a larger differential response to the rare deviant sound (Sams et al., 1985).

The sensitivity of MMN to local probability has also been shown using roving standard paradigms in which one feature of a standard sound changes suddenly (i.e. a pattern violation occurs) and is repeated thereby coming to represent the new standard (Baldeweg, Klugman, Gruzelier, & Hirsch, 2004). ERPs evoked to a sound that matches the preceding repeating pattern show increased suppression with increased presentation of the standards relative to deviants (Baldeweg et al., 2004; Costa-Faidella, Grimm, Slabu, Díaz-Santaella, & Escera, 2011; Sams, Hari, Rif, & Knuutila, 1993). To emphasize this point, ERPs to a standard sound after 36 presentations are significantly smaller in amplitude compared to 24 presentations (Costa-Faidella et al., 2011). The opposite pattern is observed for deviant sounds that is, ERPs are more negative following exposure to 36 versus 24 standard sounds. It is therefore widely accepted that elicitation of MMN during exposure to local sound probability is dependent on changes in ERP activity to both deviant and standard sounds.

Independent of the ways in which a sound violates an established pattern, the key feature is that the violation is considerably less probable ($p < 0.30$) than the

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standard stimuli. That is, the rarer the deviation relative to standards, the larger the MMN response (Javitt, Grochowski, Shelley & Ritter, 1998; Sams, Alho, & Näätänen, 1983; Näätänen, Paavilainen, Alho, Reinikainen, & Sams, 1987). Although sound patterning in these instances may be considered relatively simple, stimuli involved can be very complex such as those required for language processing. For example, phonemes that differ slightly from a repeating sequence elicit MMN but only if the deviating phoneme is relevant to a person's native language (Aaltonen, Niemi, Nyrke, & Tuhkanen 1987). The MMN response is also elicited following a regularity violation in other temporally and spectrally rich stimuli including sequences of music (Van Zuijen, Sussman, Winkler, Näätänen, & Tervaniemi, 2004) and rhythm (Vuust et al., 2005). In other instances, standards that differ by several characteristics may share only a few similarities such as duration and frequency and again, MMN will be elicited if a sound deviates from one of these shared features in some way (Gomes, Bernstein, Ritter, Vaughn, & Miller, 1997).

The MMN has even been shown to be evoked by violations of more abstract deviations within sequences, particularly deviations from established sound relationships. The relationship between stimuli can come to signify patterning within the acoustic environment. This means that a violating sound may not differ from any physical feature of the standard sound per se, but rather occurs relative to a combination of multiple features defining sound patterning. For example, the MMN signal is observed when an established pattern based on the rule, 'the higher the frequency the higher the intensity', is violated (Paavilainen, Simola, Jaramillo, Näätänen, & Winkler, 2001); by a rare repeating sound in a sequence of descending tones (Tervaniemi, Maury, & Näätänen, 1994a); as well as by presenting an ascending tone pair in a series of descending tone-pairs (Saarinen, Paavilainen,

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Schöger, Tervaniemi, & Näätänen, 1992). The feature that therefore unites individual standard sounds is based on a shared pattern that each conforms to. In another example, a sound pattern is characterised by one of three different intensity-frequency combinations and a violation is produced when a sound comprising an intensity feature of one standard type and the intensity of another is heard (Gomes et al., 1997; Sussman, Gomes, Noursak, Ritter & Vaughn, 1998; Takegata, Paavilainen, Näätänen & Winkler, 1999). In a sequence where the pattern of alternation between two frequencies of a brief tone is constant, the occasional repetition of the first frequency type will evoke the MMN signal (Alain et al., 1994; Nordby, Roth, & Pfefferbaum, 1988). Taken together, there is robust evidence showing that the MMN is sensitive to deviations from patterning based on various relationships between tones as well as to deviations from the acoustic elements of standard sounds.

Despite the simplistic nature of oddball-like sound sequences, these findings point toward the existence of a well-organised system that can minimise responsiveness to sound patterning whilst retaining remarkable sensitivity to even the slightest change relative to experience. It is clear that the human brain can store and learn information about patterning in transition statistics presented within a few milliseconds that is, over considerably short timescales. Remarkably however, emerging evidence shows that MMN amplitude is also very sensitive to the wider context in which local sound patterning is heard.

1.2.2 Deviance profiles based on contextual change. The notion of context can take on many meanings depending on the experimental manipulation being used. Generally however, this term denotes the circumstances that form the wider setting in which multiple stimuli are heard across time. Sussman and Steinschneider (2006) note that context-dependent stimulus-driven processing describes the differential

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modulation of neural responsiveness elicited by the same sound presented in across different sound environments. That is, an individual's perception of a sound can be determined by other sounds that are nearby in time (or in space), such that any change in the wider context can influence processing of individual sounds and transitions as well as associated relationships. Next, we review evidence showing that learning about sound patterning emerging over relatively short timescales can indeed be modified depending on the temporal context in which sounds are presented.

It has been discussed in length that exposure to an infrequent oddball sound that is presented in a pseudorandom fashion amongst repeating sounds that share one or more common features elicits MMN. Remarkably however, the MMN is no longer observed if the exact same standard-deviant ratio (i.e. 80:20) is used but sounds appear in a fixed temporal order within a sequence (Scherg, Vajsar, & Picton, 1989; Sussman et al., 1998; Sussman et al., 2002; Sussman & Gumenyuk, 2005). In one study for example, no MMN was elicited to a 'deviant' sound following exposure to a repeating 5-tone pattern (AAAAB where A and B denotes the standard and deviant, respectively) suggesting that sound B was no longer coded as a change in patterning but rather, had been processed as part of the standard (Sussman et al., 1998). The key point to emphasise here is that MMN was not dependent on changes in local sound probability. Rather, the ERPs coding sound pattern information were primarily influenced by the context that in turn, determined how the deviant sound was processed. It therefore seems reasonable to assume that the associated network utilises contextual information to preserve information about relationships between sounds. This means that if MMN is sensitive to contextual features, then the system

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may also have the capacity to recognise more global structures within a sound sequences.

In line with this assumption, Sussman and Winkler (2001) used an oddball-like design to show that the MMN response to deviant sounds changed by varying the global features within the sequence. Participants heard three segments of sound consecutively. Those segments presented first and last contained double deviants (i.e. deviant varying on two physical characteristics relative to the standard) only whereas the second sound segment was composed of both single and double deviant types; the presence of single deviants reflected a change in context relative to the double deviant types. Here the MMN to the very same deviant (i.e. the double type) was altered depending on the context in which it was presented. A single-peaked MMN was elicited to double deviant stimuli in the segments containing double deviant types only whereas that to the same stimulus presented in the mixed segment elicited a MMN characterised by a double peak (or two MMN's; Sussman & Winkler, 2001). Moreover, it was found that underlying ERP responses to double deviants in the mixed segment were not immediately affected by this contextual change as the two MMN's did not emerge until the segment had lapsed for some time. These findings indicate that global sound pattern recognition accumulates with temporal stability; it also shows that a relatively longer time-course is required before the underlying network can make use of contextual-based information when processing individual sounds. Finally, it suggests that the mechanism underpinning MMN generation maintains a memory of the context for multiple sounds in a dynamic manner by updating information about change in a cumulative fashion. Taken together, results from these studies indicate that sound patterning emerging in

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the longer-term plays an important role during relevance filtering of and learning about the auditory environment.

Up until this point, we have discussed that MMN is elicited by deviants from patterns learned based on contextually invariant cues well beyond tone feature discrimination and relationships between sounds limited to sensory memory processes. Integration of more global information in central auditory processing supports that notion that the brain is sensitive to context-dependent sound patterning and this can modulate learning about local probability. Because MMN amplitude is sensitive to contextual cues, it can be used to examine how processing of patterning based on multiple stimuli occurring over time is prioritised, stored and utilised by associated mechanisms. This means that the emergence of sound patterning and associated violations can be fully understood only when the influence of contextual features on local sound probability and transitions is also considered. Schröger (2007) emphasises this point stating that auditory sensory memory is not a unique facet of memory operating in isolation per se. Rather, sensory memory is an overarching concept that includes sound representation and integration as well as short-term storage of auditory information that represents a connection between very short representations and sophisticated cognitive representations stored in the longer term. The focus will now shift to a review of the proposed neural mechanisms underlying MMN generation and modulation where it will be emphasized that earlier theoretical accounts are not fully able to explain the impact of contextual cues learned over longer periods on locally-derived pattern learning over the shorter term.

1.3 Mechanisms of Mismatch Negativity Generation

There has been extensive research on the MMN resulting in a number of assumptions about the conditions in which this ERP is elicited and its amplitude, altered. Even with this progress, we still do not understand precisely *how* the underlying network uses sound patterning recognition to filter sounds based on their relative relevance to new learning. The mechanisms that underpin MMN generation in perceptual learning remain a contentious issue in the literature. Irrespective of theoretical standpoint, it is assumed that the mechanisms depend on the relationship between the incoming and previous stimulus rather than on the violating stimulus alone.

Assumptions put forward in earlier conceptualisations have no doubt shaped current interpretations of the mechanisms underpinning perceptual learning. However, temporal processing constraints of associated MMN generators proposed in earlier accounts limits the power of this theory to provide a comprehensive account of data showing that longer-ranging contextual cues modulate local processing of sounds. We therefore explore this literature through the lens of the predictive coding framework because the research questions tested in the present thesis were based on observations (to be discussed later), indicating that mechanisms of perceptual learning are indeed sensitive to transition statistics emerging over multiple timescales. From this position, it is assumed that a hierarchically-organised cortical network underpins relevance filtering in perceptual processing allowing the system to make inferences about and therefore learn transition statistics emerging at fast and considerably slower timescales. Here MMN is conceptualised as a prediction error signal that can be used to infer and measure internal states of responsiveness and learning rates that vary depending on the temporal stability of

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sound patterning (Friston, 2005). In the next section, we selectively review early accounts of MMN before narrowing the discussion to a more recent model of predictive coding that attempts to integrate earlier explanations into one unifying theory.

1.3.1 Early Accounts of MMN. Two early accounts of MMN, namely the *model adjustment hypothesis* (Näätänen, 1984; Näätänen, 1992; Näätänen & Alho, 1997; Winkler et al., 1996) and *adaptation hypothesis* (Jääskeläinen et al., 2004; May et al., 1999; May & Tiitinen, 2010) were proposed as frameworks for interpreting MMN data that for the most part, have been generated using electrophysiological measures. The first emerged from an earlier *sensory trace* hypothesis and reflects the view that the MMN can be explained in terms of a relatively dynamic system that involves ‘online’ comparisons between current and preceding stimuli. Adaptation explanations propose that ERP responses contributing to the difference waveform do not index a distinct MMN response per se but rather, are the result of varying stimulation of differentially adapted neurons that evoke earlier obligatory responses. In general, differences between this and other theoretical perspectives of the mechanisms underpinning MMN generation are distinguished by the inclusion or exclusion of a cognitive-based function in addition to much simpler neurotransmission processes, respectively.

The model adjustment hypothesis arose from earlier conceptions of MMN as an error detection signal elicited only when the current stimulus differed from some transient auditory sensory memory “trace” of the preceding sound input (Näätänen, 1984; Näätänen, 1992; Näätänen & Alho, 1997; Winkler et al., 1996). Auditory sensory memory is a term used for describing the capacity to retain information in an accessible state for a relatively short period (approximately 10 s in healthy

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participants) and is associated with activity in primary sensory brain areas (Bottcher-Gandor, & Ullsperger, 1992; Cowan, 1984; Cowan, Winkler, Teder & Näätänen, 1993; Sams et al., 1993). Here it is proposed that the MMN points towards the existence of a memory-based comparison mechanism where the preceding stream of standard sounds is stored as a reference for comparing future experience (Alain, Woods & Knight, 1998; Näätänen et al., 1987; Näätänen & Winkler, 1999). Elicitation triggers the on-line updating of content stored within an internal representation of regularity based on the sound source. The MMN is observed only when current auditory input does not match information outlined in the active regularity representation. These representations reflect content based on the individual features of a sound as well as the relationship between sounds. The existence of a model stored in memory means that previous experience with stimuli can be used to infer future input and that the network can respond accordingly in an adaptive way when an incoming event does not conform to stored representations (Winkler et al., 1996).

After learning that the MMN signal can be observed following a “silent trace” that is, a period between standard and deviant stimuli in which no sound is heard (e.g. Cowan et al., 1993), Winkler et al., (1996) performed a study to further elucidate the parameters defining the duration of the proposed memory storage capacity. The authors substituted a train of repetitive long (450ms) standards with two, four or six new short (150ms) standard sounds before a third (300ms) probe sound, differing from both standards, was presented. The SOA was 800ms. It was found that whilst MMN elicitation ceased following the third presentation of the new relative to old standard, MMN to the probe sound relative to the old standard tone was observed even after four presentations of the new standard tone. Further, MMN

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to the probe sound was elicited after four presentations of the new standard, resulting in two successive difference waveforms. In these data, it was shown that MMN can be elicited in the absence of a stimulus trace at timescales that exceed those associated with auditory sensory memory. The authors concluded that the mechanisms driving the MMN processes are not a fixed storage system operating on a single representation of trace comparison but instead, is based on interactions between many memory representations over a longer time period (Winkler et al., 1996).

However, it was later argued that the ERP responses contributing to the difference waveform do not index a distinct MMN wave and are the result of varying stimulation of differentially adapted neurons that evoke the earlier obligatory N1 response (i.e. refractoriness; Jääskeläinen et al., 2004). Refractoriness refers to the observation that a recently activated neuron reduces responsiveness following repeated stimulation (Butler, 1968). For example, it is well-established that N1 amplitude is highly sensitive to neuronal refractoriness (e.g. Budd, Barry, Gordon, Rennie, & Michie, 1998; May et al., 1999), particularly in response to the physical properties of deviant versus standard stimuli (e.g. Winkler et al., 1996; Näätänen et al., 1997). In accordance with this view, monitoring of auditory regularities is not a requirement for recording a MMN-like waveform per se, but that a change in stimulus features would be suffice for its generation due to stimulation of new afferent neural assemblies. In a critical review of the literature, May and Tiitinen (2010) present an argument for the adaptation hypothesis that is primarily based on the finding that the amplitude of the early N1 component decreases with repeated exposure to auditory stimulation (e.g. Budd et al., 1998; Rosburg et al., 2006; Rosburg, Zimmerer, & Huonker, 2010). According to this hypothesis, subtracting the

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highly adapted ERP responses to standards from the less adapted responses to rare deviants produces a negative displacement approximately 150ms after deviant onset with no additional components elicited. Consistent with earlier proposals (Jääskeläinen et al., 2004), it was concluded that there is no evidence to support a separate MMN response and that the MMN and N1 wave amplitude enlargement are terms used to describe equivalent processes that are best understood as a measure of a relatively simple mechanism of stimulus specific adaptation (SSA; May & Tiitinen, 2010).

Although the adaptation hypothesis provides an explanation for some of the data observed when a rare deviant is presented amongst a train of repeated sounds, it cannot account for a number of findings within the MMN literature (see Näätänen, Jacobsen, & Winkler, 2005 for critical review of the adaptation hypothesis). Perhaps the strongest evidence supporting the separation of MMN from an early N1 component is the observation that the former is elicited to deviants in the absence of the latter (Hughes et al., 2001; Salisbury, 2012; Tervaniemi et al., 1994a; Yabe, Tervaniemi, & Reinikainen, 1997; Yabe et al., 1998). For example, it has been shown that a MMN-like response is observed following infrequent omission of a sound during the presentation of a series of repeating sounds (Bendixen, Schröger & Winkler, 2009; Rüsseler, Altenmüller, Nager, Kohlmetz & Münte, 2001; Tervaniemi et al., 1994; Yabe et al., 1997). These findings cannot be explained by adaptation as the neurons underpinning N1 elicitation cannot be activated in the absence of a stimulus. Further, several experimental paradigms in which SSA cannot occur have been shown to evoke a distinct MMN wave (Gomes et al., 1997; Paavilainen et al., 2001; Ruusuvirta, Huotilainen, Fellman, & Näätänen 2003; Saarinen et al., 1992; Tervaniemi et al., 1994; Winkler, Reinikainen & Näätänen, 1993). In one earlier

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study, MMN was observed following presentation of infrequent decrements in sound intensity (Näätänen et al., 1989). No stimulus repetition that could cause feature-specific adaptation is apparent in either of these studies meaning that SSA cannot account for these data.

Given that the auditory N1 and MMN typically overlap in time, it is generally accepted that SSA does indeed contribute to the MMN difference waveform to some degree (see Costa-Faidella et al., 2011; for review see Ruhnau, Herrmann, & Schröger, 2012). As noted by Winkler (2007), many early MMN studies did not control for adaption effects, which likely resulted in an over-estimation of standard/deviant contributions to the MMN waveform. In some of these earlier analyses, ERPs to the standard were subtracted from those to the deviant and physical differences between sound features were not accounted for in these ensuing data. It is acknowledged that this is a potential confound that needs to be considered when reviewing earlier studies that utilise the MMN signal as a key dependent variable. However, majority of studies since then incorporate an experimental control for estimating the contribution of earlier obligatory ERP components to the MMN difference waveform (see Kujala et al., 2007 for review). As briefly mentioned earlier, isolating the “genuine” MMN from other components that may arise is typically calculated by subtracting a sound that is physically equivalent, both temporally and sequentially, from the deviant-stimulus ERP. This control sound is normally presented in a sequence in which it does not violate a sound pattern, so the genuine MMN amplitude is not underestimated.

To date, the model adjustment and adaptation hypotheses have been largely applied to oddball paradigms containing a series of single sound features and/or relationships. As discussed however, there is clear evidence showing that

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mechanisms of MMN are not strictly limited to influences by local sound probabilities that can vary from one sound to the next. Certainly, this presents limitations for both the adaptation and model adjustment in explaining relevance filtering in central auditory processing. In these earlier accounts, standard formation was thought to arise purely as a function of sound repetition yet this cannot be consolidated with findings showing that MMN is elicited even in the absence of a frequently repeating sound. Data generated using complex sound configurations and sequences embedded with fixed temporal structures further show that a standard is characterised by sounds conforming to some form of patterning irrespective of sound change (Winkler, 2007).

A clear gap in theoretical understanding of the MMN-generating process was met with a variant of the ‘memory-mismatch’ explanation (Näätänen, 1990; Näätänen et al., 1978; Näätänen & Winkler, 1999) called the regularity-violation hypothesis (Winkler, 2007). One difference between this and earlier conceptualisations is that mechanisms are proposed to be sensitive to sound patterning that operate well beyond temporal processing capacities limited to auditory sensory memory. Another key difference is that sensory perception is more than just the passive reception of information from the environment. Rather, the brain is a predictive organ implicated in continuous information processing ‘on-line’ because it utilises past sound exposure to model regularity or patterning in anticipation of the most probable future states (Winkler et al., 1996; Winkler, 2007).

The idea that the brain has the capacity to enter an anticipatory state once exposed to highly repetitive sound sequences is not an entirely new concept per se (e.g. see Baldeweg, 2006; Deacon, Noursak, Pilotti, Ritter, & Yang, 1998; Näätänen, 1992). For example, Näätänen, (1992) proposed that neural activity following sound

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input may act as a frame of reference for comparing incoming sound deviance. This idea was however formalised by Winkler and colleagues (Winkler et al., 1996; Winkler, 2007). In the present thesis, we use said concepts to formulate hypotheses and translate our data in a way that specifically extends upon MMN literature, and contributes to more recent literature that applies these principals to inferential learning in perception more broadly. In the next section, we introduce each of these frameworks in turn. Here we describe how models of regularity representations are used for predicting future sound input, ultimately shaping the MMN generation process during auditory perception (Winkler, 2007). This will be followed by an overview of *predictive coding theory*, a generalist account of perceptual learning that uses the MMN-generating process to validate key assumptions about the mechanisms and associated brain network (Friston, 2005).

1.3.2 Regularity-Violation Interpretation of MMN - The Role of Prediction

Models. There is robust evidence showing that MMN is sensitive to the wider context in which individual sounds are heard. These results cannot fully be explained as a memory of local sound probability or differential adaptation of different neurons alone. This has prompted reconsideration of theory to better accommodate different data patterns generated under different experimental paradigms. As highlighted by Winkler (2007), this has led to the re-conceptualisation of a standard from a repeating sound to a regular inter-stimulus relationship, as well as a deviant from a sound change to a regularity violation. In agreement with this view, repeating a frequently occurring sound (e.g. in variants of an oddball sequence design) does not come to form a memory trace as such but rather, creates a representation of sound regularities used to anticipate the next sound event (Cowan et al., 1993; Winkler, 1993; Winkler et al., 1996). These regularity representations are called “prediction

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models” and contain information about individual sound properties and their relationships emerging on increasing timescales, respectively. Until the 1990’s, the notion of prediction was a relatively new concept within the MMN literature yet was quickly recognised as pivotal for testing hypotheses and interpreting results in terms of potential mechanisms of the MMN-generation process. Next, we describe the proposed role of prediction modelling using concepts outlined in the regulation-violation interpretation of MMN (Winkler, 2007).

Winkler (2007) introduced the idea that predictions about both sensory and categorical sound information emerging at increasing points in time, respectively, is modelled by the brain as part of the MMN deviance detection process. Sensory features refer to the physical characteristics of individual sounds whereas categorical information is extracted based on the temporal relationship between multiple sounds. Models are encoded in memory and reflect information about temporal regularities extracted from previous experience with sound input. Stored information is then used to generate predictions about the most likely sound event to be encountered in time, given the inter-stimulus relationship history (Winkler, 2007). If a sound relationship comes to represent a regularity, the temporal information about both stimulus characteristics as well as its category is encoded in memory (Winkler, 2007). In an earlier discussion, it was proposed that predictions about individual sounds characteristics are encoded within the context of their relationships with other sounds to minimise storage of redundant information (Winkler & Cowan, 2005). Learning about local sound cues and their relationships occurs over relatively short periods (e.g.ms-secs) and is therefore assumed to be insensitive to modulation by higher-order attentional mechanisms (Winkler & Cowan, 2005).

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Up until this point, the MMN was widely considered to be a low-level sensory process, despite evidence that MMN amplitude to dynamic changes on local timescales decreases with increased active auditory processing (Dittmann-Balcar et al., 1999). A trend towards finding an ‘optimal’ paradigm for studying MMN perhaps maintained this assumption to some degree. Indeed, MMN is typically studied using paradigms where sound regularities are violated by manipulating the physical property of one sound to the next within a relatively short time window in the absence of a cognitively demanding concurrent task. Yet, categorising temporal relationships between individual sounds involves ongoing, active monitoring and therefore requires lengthier processing and maintenance in memory over substantially longer timescales relative to local sound change. As pointed out by Winkler (2007), this means that stored categorical information may also be particularly susceptible to modulation by higher-order brain processes such as attention.

As introduced earlier (pg. 9), one proposed function of MMN is to trigger attentional resources for further processing of the deviant sound. However, Winkler (2007) took a slightly different approach emphasizing that an integral feature of the proposed MMN-generating mechanism is that any prediction modelling of sound patterning over time is achieved in a very active manner. If the network is exposed to a sound event that violates an established regularity in some way, the MMN response is elicited and this triggers the rapid updating of the associated prediction model to accommodate new information (Winkler et al., 1996; Winkler, 2007). The central function of the MMN response is to therefore direct attention and/or facilitate updating of predictions outlined in the current model so to ensure synchrony between expected and actual experience with sounds and their relationships. The capacity to

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quickly integrate new with existing information maximises the likelihood of a match between predictions modelled and actual experience before another sound event is heard. Certainly, any system (in any sensory modality) that “automatically” and rapidly filters out changes is more effective and efficient than leaving it to an active (attentional) process.

Like most inferences, confidence in predictions is used to guide the model selection process (Winkler, 2007). The MMN amplitude can be used to quantify the level of model confidence that is, the degree to which model content predicts sound input, given experience thus far. Confidence is therefore a term used to explain the predictive value or the relative “weight” of one model over another in explaining the current and/or future sensory events (Winkler, 2007). Predictive confidence increases each time a model accurately accounts for the sound experience. In the lab for example, successive presentation of several standard sounds (i.e. local reinforcement) increases the accuracy and reliability of the associated prediction model. MMN amplitude here will be considerably large if an unexpected sound violates the established regularity because high confidence in the underlying model means associated predictions are weighted above other predictions modelled that potentially inform on environmental statistics, albeit with less reliability (Winkler, 2007). Accordingly, stimuli that consistently violate predictions about regularity will lead to reduced (or no) confidence in the active model as indexed by a comparatively smaller MMN error response with each presentation. Hence, the presence of MMN can be used to infer which regularity has been encoded in the prediction model and its amplitude informs on confidence in the model’s capacity to successfully predict future experience.

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Winkler's (2007) regularity-violation hypothesis of MMN has been put forward as a variant of the earlier memory trace interpretation (Näätänen, 1990, 1992) to explain results observed in substantially more complex sound sequence paradigms. These accounts are similar in that both assume the MMN-generation process is triggered when a mismatch between a sound and some stored neural representation of earlier repeating sound stimulation occurs. Winkler (2007) neatly summarises how the regularity-violation interpretation extends on Näätänen's (1990, 1992) account in several ways. First, the brain can encode more abstract, contextual inter-stimulus relationships in addition to local sound information emerging on longer and shorter timescales, respectively. Local sound characteristics are encoded within the context of sound relationships. Second, a standard is defined as any form of regularity, irrespective of sound change, and not only by a repeating sound pattern. Here deviance occurs when a sound violates this regularity. Third, MMN is elicited if predictions about when a sound regularity should emerge misalign with the actual timing of incoming sound information and therefore considers both past and future states, and not just the deviant-stimulus trace alone. Finally, early accounts advocate MMN amplitude as fundamental to attention-switching toward sound change. From a prediction modelling perspective, however, MMN amplitude is a measure of predictive confidence that can be used to infer the active model of regularity and its associated predictive strength. Winkler (2007) therefore explains how the concept of prediction applies to MMN results thus far by emphasizing that sound information processing is future-focused.

The introduction of predictive-based accounts in the MMN literature emerged alongside a more generic account called predictive coding that is used for understanding mechanisms of inference in sensory perception and learning.

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Predictive coding provides a compelling account of phenomena observed in psychology (Knill & Pouget, 2004) as well as in electrophysiology (Rao & Ballard, 1999) and neuroanatomy (Friston, 2003, 2005). It is therefore not an explanation specific to MMN but rather, is a general model that considers both the predictable and uncertain nature of the world in its computations for perception (& action). Proponents of this view make discrete claims about how the underlying brain network implements prediction models along a structural-temporal gradient to determine the sensory cause of sound input (Friston, 2003, 2005; Friston, Kilner, & Harrison, 2006). We now provide an overview of concepts implied by predictive coding, and how these relate to MMN, because they are not directly covered in the MMN literature and further, were a source of motivation for testing hypotheses in the original body of work for which this thesis extends upon.

1.3.3 The Predictive Coding Theory. The aim of this section is to unpack general principles of contemporary hierarchical predictive coding theory - a generic framework that can be used to predict, explain and understand mechanisms underpinning inference processes in perceptual learning. The MMN offers but one indirect line of evidence fitting this approach and is arguably the most widely studied neural marker of prediction error signalling processes of inferential learning. Here we explain predictive coding concepts more broadly before translating the auditory MMN as a measure of temporal processing from this perspective. For clarity, we make note of theoretical concepts common to both MMN and predictive coding literature that for the most part differ only by terminology. It is also noted that there is a large literature on Bayesian mathematical applications and interpretations of predictive coding that is beyond the scope of this review as it is not pertinent to experimental and statistical methods used in this thesis (see Friston, 2003, 2005;

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Friston & Kiebel, 2009). Rather, we focus on concepts pertaining to 1) the hierarchical and functional organisation of the brain, 2) the mechanism of perceptual inference, and 3) the role of attention that together, operate dynamically to enable prediction modelling on multiple timescales during sound learning. This section will be followed by a discussion on the MMN from the perspective of predictive coding but first, a brief history relevant to the emergence of modern-day predictive coding perspective is provided.

In a broad sense, the notion of sensory perception and learning operating in a predictive way is not a novel idea per se. Gregory (1980) stated that these processes can be equated with hypothesis-testing where the brain continuously samples sense data from the environment that will ultimately support the null (i.e. the most highly probable sound heard thus far will be heard next) or alternative hypothesis (i.e. an improbable sound is heard). Much earlier, Helmholtz (1867) had discussed the theory of unconscious inference that is, the brain's capacity to use heuristic computational processes influenced by perception, attention, learning and behaviour to infer the cause of sensory stimulation. *Predictive coding theory* follows this empiricist tradition.

Elements of predictive coding theory as it stands today began emerging in the 1990's when Helmholtz's (1867) theory was integrated with Bayesian methods for studying perception (Kersten, Mamassian, & Yuill, 2004; Knill & Pouget, 2004; Lee & Mumford, 2003; Mumford, 1992; Rao & Ballard, 1999). The fundamental concept of the Bayesian approach is that the brain uses incoming sense data to code probability distributions in neural populations, given prior knowledge, whilst considering the relative uncertainty of each sensory cue (Knill & Pouget, 2004). In the most standard version of predictive coding, the network's underpinning

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perceptual learning reflects a hierarchically-organised cluster of models with increasing abstraction over temporal (& spatial) scales, respectively; higher level models carry predictions and can influence activity in lower levels implicated in prediction error signalling (Friston, 2003, 2005; Rao & Ballard, 1999). Such organisation minimises redundancy or “surprise” generated when predictions do not fully explain actual sensory input allowing for full use of a resource-limited brain network. Modern-day predictive coding theory aims to provide an up-to-date and unified theory of brain structure-function relationships from a probabilistic perspective.

Predictive coding asserts that cortical hierarchies are the structural architecture required for processing sound probability and their relationships, including the wider context in which these arise. This is in line with several studies showing the brain is organised hierarchically (Felleman & Van Essen, 1991; Hochstein & Ahissar, 2002; Mesulam, 1998; Rao & Ballard, 1999; Zeki & Shipp, 1988). One important feature of this network is that neurons at one level integrate information coded by neurons at the level below and vice versa, consistent with evidence showing the brain is reciprocally connected (Felleman & Van Essen, 1991; Zeki & Shipp, 1988). This is generally referred to as “backwards” and “forwards” connections, respectively. Forward connections operate from lower to higher areas and function to isolate and disseminate information about sound probabilities and their transitions, that is the relationship between one sound event to the next, in a feed-forward fashion (Friston, 2003). Backwards connections run from higher to lower brain areas and are implicated in monitoring and encoding the wider context in probabilistic information unfolds (Friston, 2003). Lateral connections also play a key role in communicating information by connecting areas within a given hierarchical

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level (Friston, 2003). Central auditory processing therefore depends on mutual neural activity within and between brain areas that together, reflect a hierarchy of ‘generative models’ of increasingly abstract states (Friston, 2003, 2005).

Not only does predictive coding explain many facets of brain organisation, it also provides a functional account for understanding a range of neural responses implicated in efficient extrapolation and coding of statistics from the auditory environment. Such sophisticated organisation allows the nervous system to reduce entropy or “surprise” by optimising the limited dynamic range of neurons (Friston, 2003, 2005; Friston & Kiebel, 2009). This is known as *free energy optimisation*. The free energy principle can demonstrate how the brain utilises inferential processes in statistical learning to maximise model evidence and make full use of a resource-limited system. Higher and lower-order resources are distributed as per the relevance of the incoming information, given a ‘prior’ to optimise neural expenditure (Friston, 2003, 2005). A prior is a type of generative model³ that reflects a probability distribution of possible sound sources given experience as well as some measure of uncertainty. Abstract information stored at higher levels informs and potentially predicts neural activity at a level below by imposing a prior (i.e. guesstimate) of their responsiveness. Functional asymmetry therefore exists between forwards (conveying predictions errors) and backwards connections (conveying predictions; Friston, 2003). Any discrepancy between predictions and actual activity evokes a prediction error signal that is communicated to the level directly above. Error signalling is then used to generate a new and improved prediction model (i.e. Bayes posterior probability distribution; Vapnik & Vapnik, 1998). This has been referred to as an

³ Friston’s (2003) generative model or prior coincides with Winkler’s (2007) notion of prediction model.

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information ‘feedback loop’ (e.g. Garrido et al., 2007). Any difference between a prior and sound input can therefore induce a cascade of ascending prediction errors that are modulated only when the most likely explanation of the sound source is attained (i.e. neural energy is optimised), and the sound is perceived (Friston, 2003).

In predictive coding, attention is involved in optimising sensory inference and is framed as a process that deduces the level of uncertainty of sound inputs (Feldman & Friston, 2010; Friston, 2009; Rao, 2005; Spratling, 2008). In actuality, the entire auditory evoked potential is a prediction-error signal meaning that even early obligatory components are prone to top-down attentional modulatory processes (Friston, 2003). Attention is used to weight or rank sensory signals by estimating their precision (i.e. inverse variance in Bayesian terms⁴; Feldman & Friston, 2010; Friston, 2005). Much like Winkler’s (2007) concept of model confidence, precision can be likened to an index of error signal reliability. This means that the brain produces prediction models that are sensitive to both error signal content *and* an estimate of its reliability as a meaningful marker of a prediction violation. When precision estimates are low, the prediction error signal is down-weighted and may be overlooked altogether. Accordingly, error signalling is magnified and prioritised for further processing when precision is high. Attention and predictive mechanisms interact in a highly dynamic way that together, reflect a relevance filtering system where processing of certain sound input is prioritised over others if it is estimated to be a very reliable explanation of sound experience.

This inference-driven, sound relevance filtering system is sensitive to temporal patterns unfolding on multiple timescales (Kiebel, Daunizeau & Friston,

⁴ Inverse variance assumes inferences are formed in a backwards manner (e.g. from observations to parameters, or from effects to causes) conferring a necessary role for backward connections in neural circuits (Friston, 2003).

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2008). As introduced above, temporal patterns in the sound environment are defined by the likelihood that one sound event will reliably follow another sound event in time (i.e. a transition statistic). Kiebel et al.'s (2008) influential work proposes that the large-scale hierarchical organisation of brain structures parallels a hierarchy of timescales where slower changes in the sound environment are the context for sound change over shorter periods. Lower levels encode transition statistics emerging dynamically on local timescales (i.e. < 1 s) whereas higher levels monitor more contextual changes that occur over longer periods of time (i.e. seconds, tens of minutes or even longer; Kiebel et al., 2008). Prediction errors can be elicited at various processing stages operating on this rostral-caudal gradient. Importantly, predictions generated over longer periods of time can dampen responsiveness in more primitive brain areas if a rare sound violates predictions modelled over a comparatively shorter timescale (Kiebel et al., 2008). The brain does this by suppressing (i.e. prediction-driven) or amplifying post-synaptic gain of stimulus-driven neural activity attuned to different acoustic elements (e.g. physical characteristics, spatial/temporal context; Bastos et al., 2010; Brown & Friston, 2012; Feldman & Friston, 2010; Kiebel et al., 2008), even when participant focus is re-directed away from sounds (Schröger et al., 2015). To summarise, the brain learns on multiple timescales by coding environmental statistics into neural states to generate predictions used for informing its operations in preparation for future neural states – a function well-suited for computing with uncertainties (Friston, 2003).

To briefly summarise the discussion thus far, predictive coding proposes that perception arises by integrating sound input with predictions modelled on multiple timescales that in turn, are used to infer sound causation based on information about sound transition statistics accumulated thus far. Importantly, this theory has a

number of core principles that motivated the experimental designs in this thesis. We shall now describe how predictive coding as a general framework that can unify earlier hypotheses described in the MMN literature (see former sections) and ultimately, to understand the mechanisms behind MMN generation and its role in inferential sound learning processes.

1.3.4 The MMN from the Perspective of Predictive Coding Theory. Apart from the adaptation hypothesis (Jääskeläinen et al., 2004), earlier accounts contend that the MMN is observed when a mismatch between predicted and actual sound experience occurs and is used to update the associated model in preparation for future experience (Näätänen & Winkler, 1999; Winkler, 2007). This resonates with predictive coding theory, where previous experience with sound (probability) is used to predict future experience (Friston, 2003). Error signalling processes arise when predictions fail to explain the current sensory experience. From this standpoint, the MMN is framed as a classic prediction error signal observed when a sound violates an anticipated sound transition statistic predicted by an internal model of regularities extrapolated from the auditory environment (Kiebel et al., 2008; Rao & Ballard, 1999).

Studies using the MMN to demonstrate the validity of predictive coding show an underlying modulation of feedforward and feedback connectivity that prompt the distribution of prediction error signals and predictions, respectively (Garrido et al., 2007, 2008, Garrido, Kilner, Stephan, & Friston, 2009; Wacongne, Changeux, & Dehaene, 2012). Perhaps the strongest evidence for backward modulation following an auditory pattern violation comes from studies showing reduced MMN amplitude in patients with dorsolateral prefrontal cortex lesions (Alho, Woods, Algazi, Knight, & Näätänen, 1994; Alain et al., 1998; Knight, 1984).

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Other results suggest that both anterior and superior temporal structures contribute to initial pattern violation processing (Giard et al., 1990; Halgren, Sherfey, Irimia, Dale, & Marinkovic, 2011; Hari et al., 1984; Jääskeläinen et al., 2004). After this point, differential activity becomes increasingly localised to the frontal lobe and may include attention-based resources (Baudena, Halgren, Heit, & Clarke, 1995; Halgren et al., 2011). This is consistent with studies showing that superior temporal generators interact with the prefrontal cortex (PFC) in considering sequence context during auditory pattern processing (see Zatorre 2001 for review). These data are compatible with predictive coding because they show that brain structures and their corresponding function are hierarchically organised to allow error signalling to inform on prediction model updating during sound relevance filtering.

MMN relevance filtering during sound sequence learning requires highly sophisticated and dynamic predictive processes that incorporate (but are not limited to) simple SSA processes. In one instance, Garrido et al., (2008) tested the feasibility of the adaptation versus model-adjustment hypothesis as well as a hypothesis that combined the two, the latter reflecting a unified predictive coding explanation of the neural network underlying MMN generation. These data showed that the mechanisms of MMN generation involve communication by way of neuroplasticity between brain areas spanning a hierarchy of increasing complexity as well as local SSA within the primary auditory cortex. It is therefore unlikely that mechanisms underpinning the MMN network are based solely on synaptic connectivity within or between brain areas but rather involves both processes operating simultaneously within a neural hierarchy consistent with predictive coding assumptions (Garrido et al., 2008). The authors concluded that predictive coding embodies both the model-adjustment and adaptation hypothesis because it predicts that updating of a

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generative model of sound regularity encompasses dynamic changes in synaptic activity proposed in each earlier account, respectively. In this regard, the MMN updates the weighting of model predictions if the model fails to explain bottom-up input and thus fails to suppress an error signal (Garrido et al., 2009).

The degree to which prediction model updating occurs can be measured electro-physiologically using MMN amplitude. The disappearance, or suppression, of MMN is observed if the network learns that transition statistics underlying sound regularity are not likely to change over the longer term (Baldeweg, 2006, 2007; Friston, 2005; Kiebel et al., 2008). For example, the simple oddball sequence is a highly stable environment because the temporal element of the repeating standard sound remains constant across the entire experimental session. Model precision, or predictive confidence (Winkler, 2007), continues to build the longer the stable-standard period remains constant (Kiebel et al., 2008). The higher the precision, the larger the MMN amplitude to deviations and this is equated with engagement of cognitive resources to update the weighting of model predictions in line with actual experience (Friston, 2003, 2005; Garrido et al., 2008; Kiebel et al., 2008).

Accordingly, a comparatively smaller MMN amplitude following a deviant is observed if it is less clear whether transition statistics underlying sound regularity will change over time (Friston, 2003; Kiebel et al., 2008). For instance, the roving paradigm is a relatively unstable sound environment because aspects of the repeating standard are constantly changing within a shorter timescale (typically <20 s). Under these conditions, model updating (i.e. higher-order resource allocation) proceeds in a cautious manner because the network cannot build a very reliable prediction model in the absence of sound pattern stability over the longer-term. A prediction model with less precision results in smaller MMN following an unpredicted sound as more

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evidence is needed to determine whether the deviant is a truly meaningful sound event (Friston, 2003). Model updating here is probably not the most efficient use of neural expenditure in what is a resource-intensive process (Friston, 2003).

Precision updating of internal models, reflected in MMN amplitude, is therefore influenced by sound learning over longer timescales and can be likened to a contextual-based, higher-order form of learning. By this account, MMN amplitude should always been larger when transition statistics underlying regularity are stable relative to unstable over time. Sound learning over longer timescales requires careful consideration of whether MMN elicited by sound fluctuations on short timescales warrants model updating given the wider context under which longer timescale information unfolds. Notably, the crux of this thesis emerges from data showing that model updating on multiple timescales is constrained by predictions formed during the very first encounter with sound probabilities.

We now narrow our focus to a series of studies that together, hold considerable implications for the field of MMN research and inferential learning more broadly. The most important outcome of this research is the discovery of *primacy bias*, of which we also refer to as *first impression bias*, on MMN amplitude during the very early stages of auditory information processing. First, we introduce the notion of ‘first impression’ as understood in popular culture before presenting a timeline of the scientific experiments contributing to the evidence-base of first-impression bias effects that together reflect the groundwork for which this thesis extends upon. To conclude, we propose that these data are a striking example of a hierarchical inference processes in which the brain uses probabilistic information on multiple timescales to weight the potential relevance of future sounds events.

1.4 First Impressions Matter

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First impression bias is a term used to describe a limitation of information processing in which people believe the first piece of information they are exposed to and are biased in evaluating subsequent information in the direction of the initial influence (Lim, Benbasat, & Ward, 2000). It is well-cited in the social and personality psychology literature where it has been shown that the very first encounter with another person, whether it be directly (e.g. upon first meeting) or indirectly (e.g. exposure to prior information about person before a first meeting), can have a long-lasting impact on our beliefs even when evidence to the contrary is presented (Allport, 1979; Anderson, 1965; Asch, 1946; Baumeister et al., 2001; Hamilton, Katz, & Leirer, 1980). To our knowledge, the revelation that first impressions can also have long-lasting bias effects on sequence learning during the very early stages of auditory information processing is a novel finding.

The discovery of *first impression bias*, by Todd et al. (2011) has resulted in a series of studies all with the shared aim of manipulating key aspects of the original experimental design to establish the conditions under which the influence of first impressions on sound sequence learning is modified. In the next section, we describe the original experiment in which first impression bias was revealed using the MMN before reporting on follow-up studies examining the bias prior to the commencement of this thesis. In respecting the author's original terminology, we will use the term primacy bias when reviewing early studies contributing to this body of work. As it stands today however, primacy bias and first impression are used interchangeably in our published studies and denote the same phenomenon. Assumptions about how the mechanisms underpinning this unexpected phenomenon may be operating will also be discussed. Finally, we use these findings as a platform for putting forward the rationale that the studies presented in this thesis contribute to ongoing effort to

elucidate how mechanisms underpinning first impression bias in perceptual learning are operating during sound sequence learning. But first, we briefly recap key points highlight in the preceding literature review that together formed the rationale for Todd et al.'s first study in 2011.

1.4.1 A Primacy Bias is Discovered. We have established that the auditory system automatically extrapolates probability information about sounds and their relationships emerging on multiple timescales in the environment. The brain learns that highly repetitive sounds events are the most likely cause of stimulation of the auditory system. The brain suppresses responsiveness to predictable sounds that provide no new information and uses this change in activity to predict future sound experience (Friston, 2005; Winkler et al., 1996). Accordingly, the auditory system becomes sensitised to sounds that violate predictions and sound deviations elicit the MMN prediction error signal. Responsiveness to deviations over the shorter term may be constrained by confidence in predictions modelled over the longer-term (Friston, 2003; Kiebel et al., 2008). Taken together, this means that predictive confidence for a given model (i.e. precision; Friston, 2003), as indexed by MMN amplitude, should always been larger when transition statistics underlying sound regularity are stable relative to unstable (Kiebel et al., 2008). In 2011, Todd et al. designed an original study to specifically explore whether this is indeed the case.

Todd et al.'s (2011) design incorporated a unique sound sequence with varying sound configurations called the *multi-timescale paradigm*. As presented in Figure 1.2, the multi-timescale sequence consists of two tones in which a short (50ms) and a long (100ms) sound that differ by duration switch roles as a highly probable standard ($p = 0.875$) and rare deviant ($p = 0.125$), creating two block-context types. In one block-context type, the short sound is the standard (hereafter

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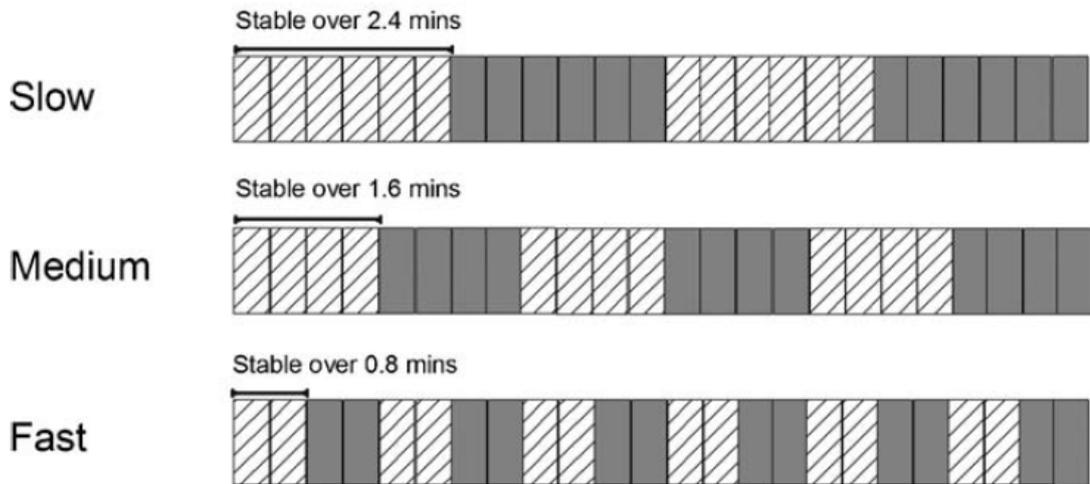


Figure 1.2. Diagram illustrating the original multi-timescale design. Three (slow, medium, fast) sequence conditions that differ only by the length of time the standard remains stable before tone roles switch. The diagonal lined rectangles represent the first block-context type (50ms standard, 100ms deviant) and the greyed rectangles, the alternate block-context type where tone roles are switched. (From Todd et al., 2011)

referred to as *first standard*) and the longer sound plays the role of deviant (hereafter termed *first deviant*). In the alternate block-context type, these tone roles switch such that the first deviant sound becomes the standard (i.e. *second standard*) and therefore forms the basis for sound patterning and the initial standard becomes deviant (i.e. *second deviant*). The notion of tone role probabilities is essentially a reframe of the notion of transition statistics and are terms that will be used interchangeably from now on.

To highlight this point with an example, the standard transition statistic in the first block-context is represented by a 50ms likely following a 50ms sound whereas the deviant is denoted by a 100ms sound rarely following a 50ms sound. Deviant sounds appeared pseudo-randomly across each block-context type and were always separated by standards. ERP responses to the first five standards at the start of each block-context and the first standard immediately following the presentation of a deviant were removed from analyses. Approximately half ($n = 10$) of participants heard the block-context with the short sound as the first standard first whereas the

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remainder ($n = 9$) heard the block-context with the longer standard sound first. To explore how confidence in model predictions accumulates over time, the length of time that the standard sound remained constant was also manipulated across three different conditions.

As shown in Figure 1.2, tone roles switched every 480 tones such that the standard remained stable for 2.4min in the *slow* condition. In the *medium* condition, the switch occurred every 320 sounds and the stable-standard period lasted 1.6min. In the *fast* condition, the switch occurred every 160 tones and the standard was stable for 0.8min. A control condition equivalent to a classic simple oddball paradigm as well as a fast-changing sequence with 2s gaps between block-context were also included in Todd et al.'s (2011) design. The former was used to ensure MMN could be elicited for a given participant and the latter was used to determine whether a brief silent period would impact on MMN amplitude; inserting a silent gap had no effect and so were omitted from further analyses. Irrespective of condition, 1920 sounds were heard in total and were presented with a 300ms stimulus onset asynchrony (SOA). Local within-block probabilities as well as sequence duration were equivalent across conditions which were presented with counterbalancing. A short 2-5min break between conditions was included. All participants were instructed to ignore the sounds being played and watch a subtitled film. It was expected that MMN amplitude to deviants would differ by standard-stable history; that is, the largest MMN was expected to emerge when the standard remained stable for the longest period (Todd et al., 2011). Accordingly, MMN was expected to be smaller with more rapid tone role switches. Here it was assumed that increasing the temporal stability of the standard increases predictive confidence in the active model

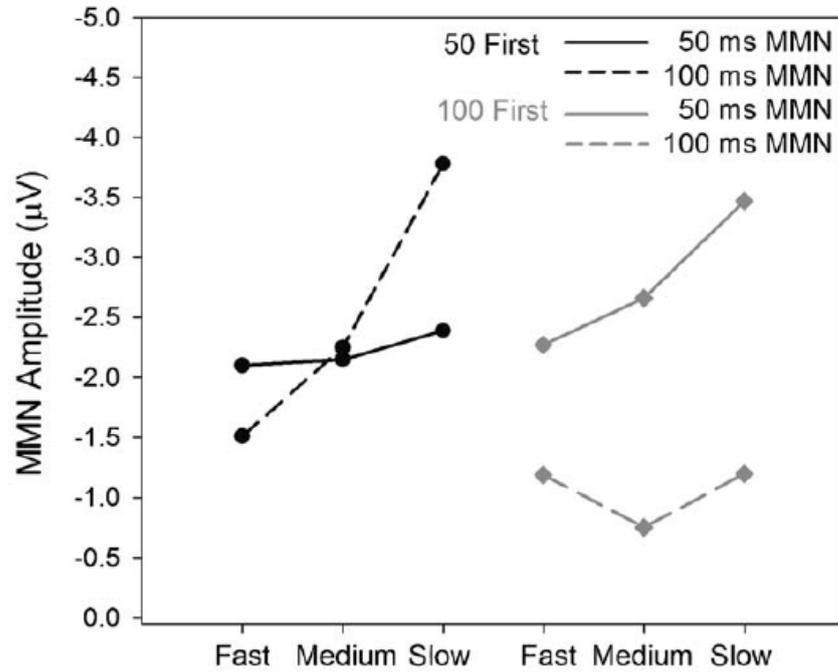
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and this would be reflected in larger MMN following a prediction-violating deviant sound (Kiebel et al., 2008).

Unexpectedly, the impact of standard stability on MMN amplitude depended on the order in which tone roles were heard. MMN was indeed larger the longer the standard sound remained stable but only for the first deviant tone presented in block-contexts that conformed to how the sequence started (see Figure 1.3; Todd et al., 2011). When tone roles switched, no significant difference in MMN size was observed between conditions. The authors also report on standard and deviant analyses showing that the differential effect of sequence stability on tone role order was predominantly driven by ERP responses to the deviants (see Figure 1.4). Todd et al., (2011) reasoned that the probabilistic information about each tone at sequence onset modulated the impact of temporal stability on MMN amplitude thereafter despite both tones being presented with equal probability across stable and unstable contexts.

The authors had discovered what they refer to as a ‘primacy-effect’ in very early relevance filtering. Learning about transition statistics in the block-context presented at the very start of the sequences was proposed to somehow impact on subsequent sound sequence learning (Todd et al., 2011). It is important to note that significant MMN was elicited to both sounds when presented as rare deviations. The brain therefore learned that the former first deviant sound had come to be the sound regularity (second standard) in the switched block-context. However, predictive confidence in the underlying model of regularity accumulated differently for the first relative to second deviant. The second deviant was not modulated by standard-stimulus history as one would expect based on widely held assumptions that

A. Tone x Condition interactions for each order.



B. Tone x Order interactions as a function of condition.

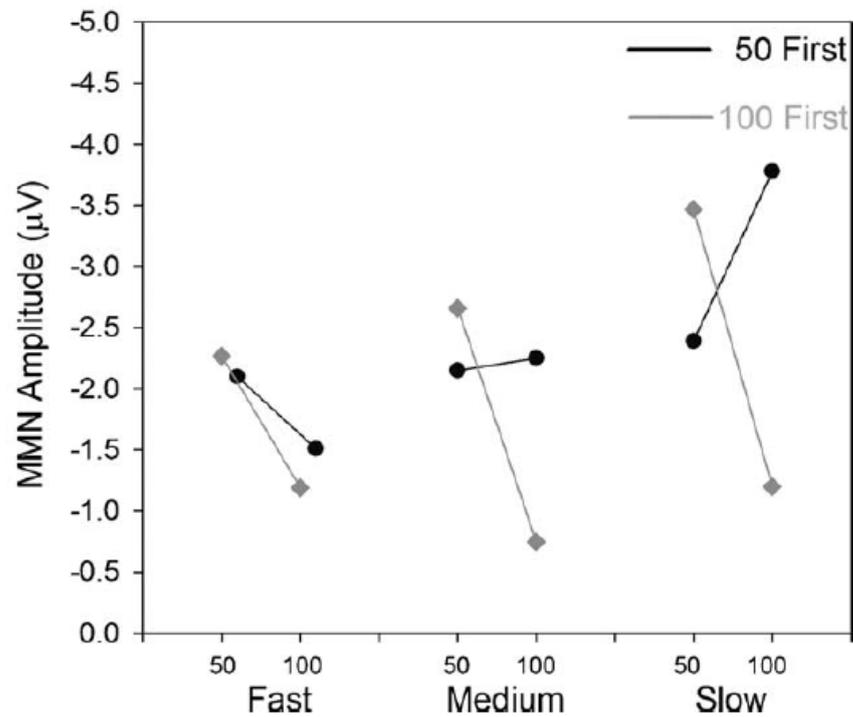


Figure 1.3. Mean MMN amplitude to each deviant tone for each condition separated by order in which tone roles were heard. The top panel A emphasises the change in MMN amplitude as a function of condition (increasing standard stability history) for each deviant tone with the group who were presented with the 50 ms standard first plotted separately to the group who received the 100 ms standard first. The bottom panel B emphasises the tone role order effects on MMN amplitude to the two deviant tone types for each condition (Todd et al., 2011).

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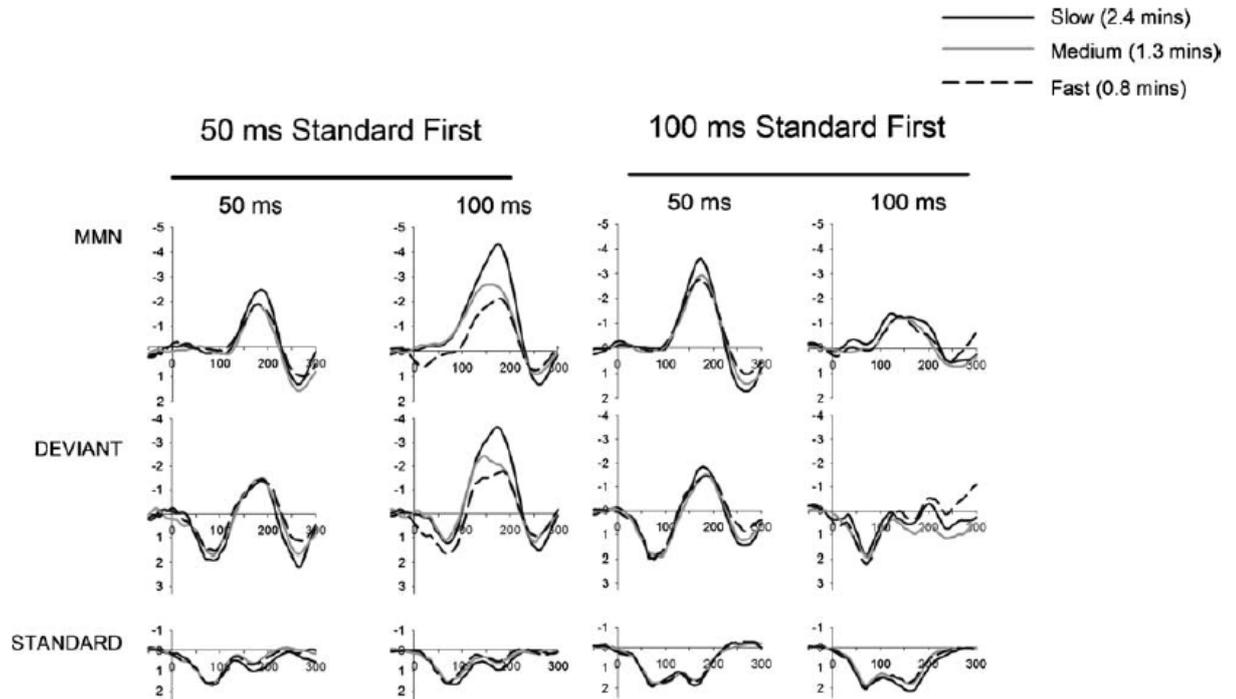


Figure 1.4. MMN waveforms to each tone and ERPs to tones when heard as deviant or standard for each condition separated by order in which tone roles were heard (Todd et al., 2011).

predictive confidence, and thus MMN amplitude, should be larger with increased temporal stability of the standard (Kiebel et al., 2008).

Evidence of a primacy bias also challenged the empirical data pertaining to the MMN literature indicating that its amplitude faithfully reflects local sound probabilities emerging on short (i.e. <30s; Baldeweg et al., 2004; Costa-Faidella et al., 2011; Sams et al., 1983) or even multiple timescales (Ulanovsky, Las, Farkas, & Nelken, 2003). If MMN were *only* sensitive to the local probability across either block-context, then its amplitude should not differ by how often the contexts switch (minimum of 0.8 min). Todd et al.'s (2011) data therefore implies a long-acting, order-driven limitation on how initial experience with sound probabilities impacts perceptual inference thereafter. Yet, one stand-out finding prompted the authors to exert caution when making claims about the emergence of a primacy-like effect; standard and deviant ERPs were more positive in those who received the 100 ms

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standard first. The sample sizes ($n = 9-10$) used in the study were recognised as problematic in explaining these group differences because smaller samples are prone to individual differences relative to examining trends across a larger data set. In a follow-up study, the authors pursued a within-subjects design to explore the longevity of the primacy bias and directly address whether the physical differences between tones could indeed explain differences in the pattern of results between groups.

In a subsequent within-subjects study, a refined and expanded version of the multi-timescale paradigm was used to test whether primacy bias was a replicable finding and further establish the impact of initial tone roles on sequence learning (Todd et al., 2013). Only the slow and fast sequence types were retained in this study; here 30ms and 60ms tones alternated standard-deviant roles. Standard ($p = 0.875$) and deviant ($p = 0.125$) probabilities stayed the same and as before; local within block probability and overall tone probability remained fixed (Todd et al., 2011). All participants heard slow then fast sequence pairs in a fixed order (called Order 1; see Figure 1.5; Todd et al., 2013). This allowed the authors to test whether Todd et al.'s (2011) findings could be repeated. After 5 min, a sequence pair in which the order of tone probabilities (i.e. block-contexts) were reversed followed Order 1 (i.e. Order 2). This allowed the authors to see whether primacy effects are affected by differences in the physical characteristics between tones. Five minutes after hearing Order 2, Order 1 was again heard (termed Order 3) to determine whether the bias is always observed when the initial sequence structure is presented.

As shown in Figure 1.6, it was found that MMN to the first deviant was larger in stable relative to unstable sequences for Order 1 with no differential impact of stability for the second deviant tone. This finding was replicated in Order 2

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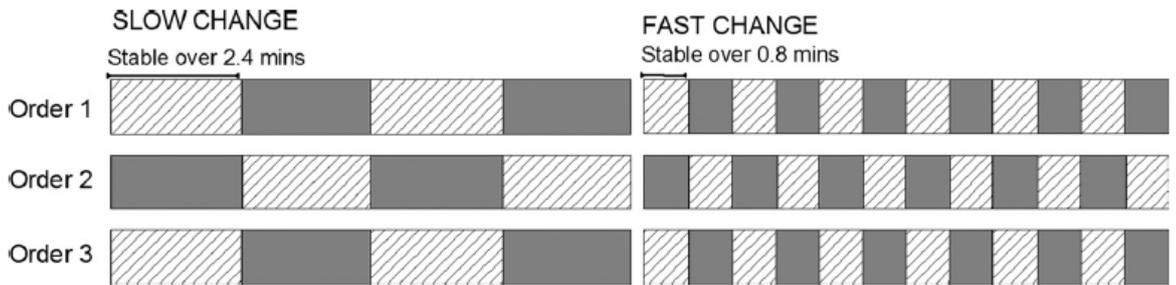


Figure 1.5. Three-order multi-timescale sequence variant. For each Order type, lined blocks indicate a 30ms standard and 60ms deviant, whereas tone roles reverse in shaded blocks. (From Todd et al., 2013)

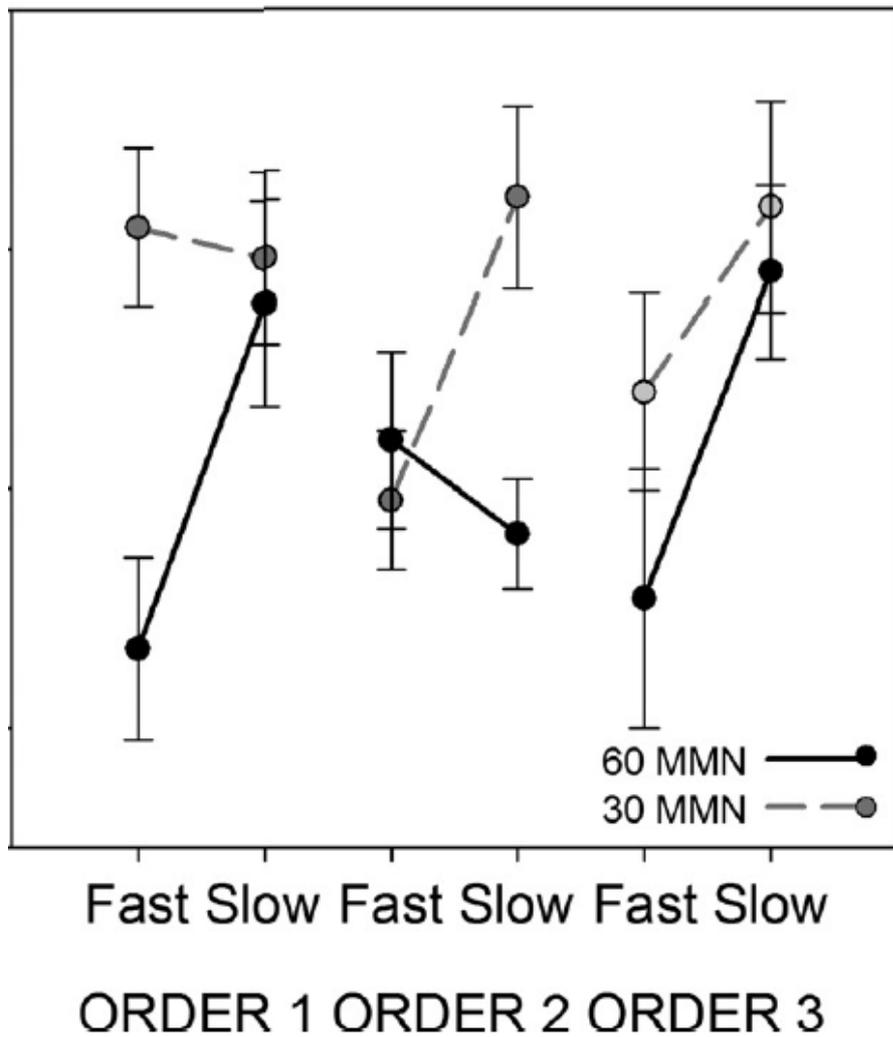


Figure 1.6. Mean MMN amplitude for three-order multi-timescale variant. MMN to 30ms and 60ms deviant sounds as a function of speed in which tone roles switch and block-context order. Interaction effects on MMN size between speed effects and tone type across each Order type. Error bars = Morey's (2008) corrected normalized within-subject standard errors (from Todd et al., 2013).

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confirming that evidence of a primacy bias cannot be explained by tone characteristics, and rather the impact of role stability on MMN amplitude is a function of the initial roles associated with each tone at sequence onset (Todd et al., 2013). Remarkably, primacy bias completely disappeared upon presentation when Order 1 was repeated after the second Order type. A reliable MMN index of primacy bias anchored to the initial structure of a sound sequence was established and could be abolished when neither block-context was exclusively associated with a first impression. Perhaps the strongest support for this phenomenon derives from a study showing that bias is most prominent at the start of block-contexts immediately after tone roles switch (Todd et al., 2014a).

Todd et al., (2014a) set out to examine how predictive confidence accumulates over time within block-contexts of the multi-timescale sequence. This was based on the rationale that equal MMN amplitudes to the second deviant irrespective of sequence stability means that prediction model confidence is maximised within 0.8min (the faster sequence block-context length). In the experimental design, only Order 1 from Todd et al., (2013) was used; the most crucial feature however was the addition of a new approach to MMN analyses. Todd et al. (2014a) further divided each block-context into the period just after tone roles switch (hereafter referred to as *first half* of block-contexts) and the period in which tones roles had been stable for some time (hereafter termed the *second half* of block-contexts; see Figure 1.7).

If confidence reaches asymptote by 0.8min, MMN to the second deviant in the slow-changing sequence should not differ from the first to second half of the block-context because the former allows ample time (1.2min) for predictive confidence levels to reach ceiling. Accordingly, MMN amplitude to the second

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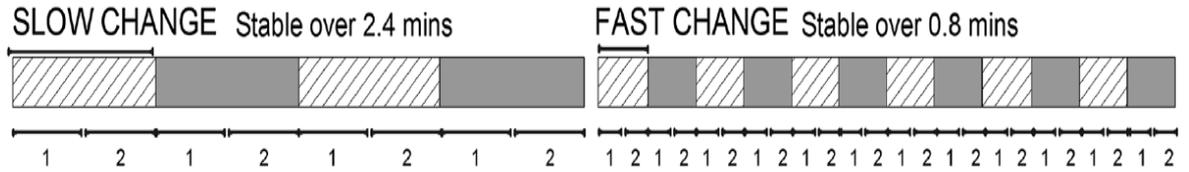


Figure 1.7. Diagram illustrating halves analysis using multi-timescale sequence. Sections labelled 1 (first half data) and 2 (second half data) show how sound block-contexts were divided for halves-analysis. Averages for MMN to first and second deviants were created for both stable and unstable sequences by pooling together the responses for first halves (i.e. the point in which tone roles switch) to produce second half 60ms and 30ms deviant MMNs. Averages for MMN to the deviants over the latter portion of the sound contexts for each condition sequences were generated by averaging together the responses for second halves to create second half 60ms and 30ms deviant MMNs. A 40ms period of silent separated stable and unstable sequence types. (From Todd et al., 2014a)

deviant should increase across within-context halves for the fast-changing sequence because 0.4 min is not quite enough time (<0.8 min) for predictive confidence to reach asymptote. In terms of the first deviant heard in fast-changing sequences, Todd et al., (2014a) reasoned that MMN would increase across halves for much the same reason as the second deviant. For this same deviant type heard in stable sequences, it was expected that MMN amplitude would indeed be larger in the first-half of block-contexts relative to those heard in the fast-sequence and the largest MMN would be observed in the second-half of this same block-context.

Once again, MMN results indicated an unexpected pattern. In the slower-changing sound sequence, MMN amplitude to the first 60ms deviant started and stayed large (MMN 0-1.2 min = MMN 1.2-2.4 min) with no significant differences between halves observed whereas that to the second 30ms deviant increased as the block-context lapsed (MMN 0-1.2 min $<$ MMN 1.2-2.4 min; refer to Figure 1.8). In the faster-changing sequence however, the differential effect of stability on deviant type was completely reversed. MMN to the first deviant started small and increased significantly by the end of the second half of the block-context (MMN 0-0.4 min $<$ MMN 0.4-0.8min) but did not change from first to second half (MMN 0.4 min = MMN 0.8 min) for the second deviant presented in the switched context (Todd et al.,

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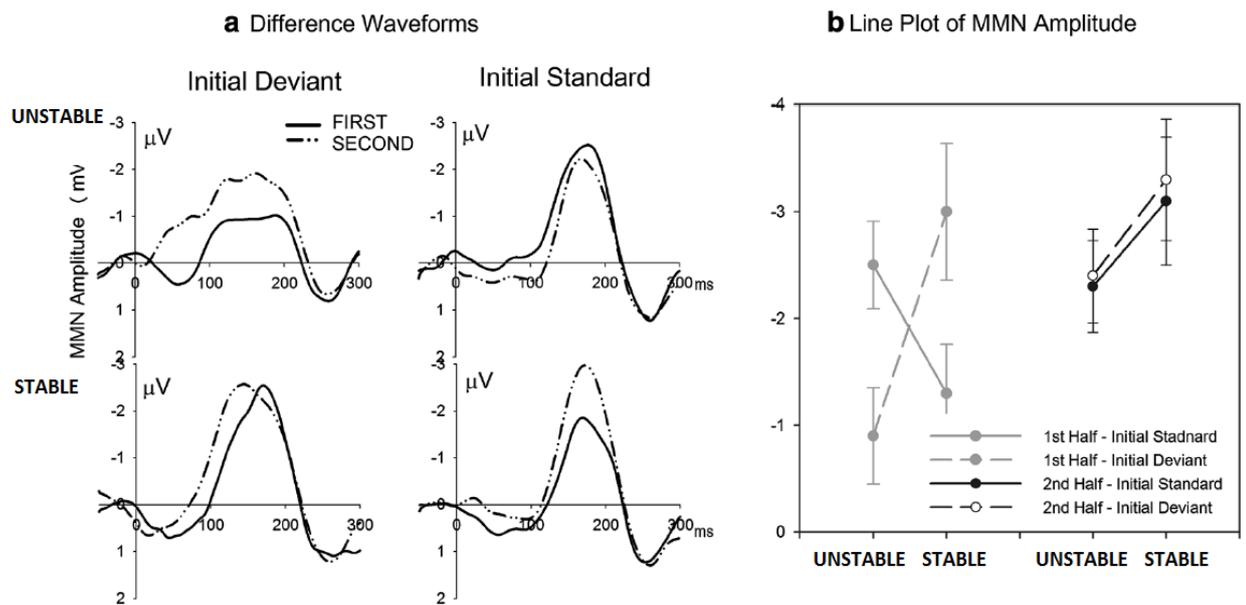


Figure 1.8. Halves analysis data. a. MMN difference waveforms in the unstable and stable sequences for the first (60ms) and second (30ms) deviant tones. MMN waveforms generated in the first-half of block-contexts (filled lines) is shown with those observed in the second-half of block contexts (broken lines). B. MMN amplitudes generated for first (grey) and second (black) half data for the first (broken line) and second (filled line) deviant sounds. Modified with permission from Todd et al.'s (2014a) published paper. (From Todd et al., 2014).

2014a). The inclusion of a halves analysis revealed that the differential impact of sequence stability on MMN amplitude was strongest during the period immediately after the tone roles switched - a finding that was masked in earlier studies due to an overall net effect of MMN size across halves within each block- context type (Todd et al., 2011; Todd et al., 2013). The finding that the MMN amplitude produced over periods of 0–0.4 min in the first-half of fast-changing sequence block-contexts was larger than that produced in periods of 0–1.2 min in the first-half of slow-changing block contexts completely falsifies assumptions that the MMN amplitude always increases with increased sequence stability (i.e. stable-standard history).

In the remainder of this thesis, we mostly refer to this phenomenon as *first impression bias*. We will also refer to slow-changing and fast-changing sequences as *stable and unstable sequences*, respectively. These terms are in-line with language used in our recent publications including that reported on in this thesis. In the next

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section, we will argue that these data are evidence that what is first learned about transition statistics and their stability has a long-lasting and disproportionate influence over later sequence learning. With each study comes a more developed understanding of how the network refers to initial experience whilst continuing to engage mechanisms of inference during perceptual learning. To communicate the most up-to-date explanation of first impression bias during sound sequence learning, we next focus on an interpretation of these data as it stands today. Using this approach means we can integrate the most up-to-date empirical data that continued to be published by our lab as the development of this thesis progressed with the literature pertaining to predictive coding models of inferential learning processes.

1.4.2 Proposed Mechanisms of First Impression Bias. Todd et al. (2014a) consider contemporary models of predictive coding (Friston, 2005; Lieder, Stephan, Daunizeau, Garrido, & Friston, 2013) in providing a comprehensive explanation for how opposing patterns of MMN amplitude modulation for stable versus unstable sequence data could emerge. The explanation is based on the premise that the brain can learn both the local sound regularity (sound probabilities), and the superordinate regularity (the rate of block-context alternations) by accruing predictions based on regularities emerging at different timescales. As reviewed earlier, all predictions are confidence-weighted (Winkler, 2007). The proposed mechanisms for the emergence of a confidence-weighted first impression bias are based on two key assumptions namely the presence of hierarchical inference (learning over multiple timescales), and the capability of higher-level predictions to modulate learning rates at lower levels when predictive confidence is high (Friston, 2005; Kiebel et al., 2008; Winkler, 2007). To explain why the stable-standard history, that is sequence stability, differentially impacts MMN amplitude as a function of tone role order, we

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integrate key theory about how the network engages in model updating as the multi-timescale sequence unfolds.

First, data patterns limited to the stable sequence support the notion that probabilistic information learned at sequence onset biases learning towards this initial information when evidence to the contrary is presented. We can see this by looking at MMN results for block-contexts that match those presented at sequence onset versus those that do not. In block-contexts that conform to those heard first, a large MMN that persists across block-context halves is observed (see Figure 1.8) indicating rapid accumulation of high predictive confidence in the underlying model. This makes sense given the considerably long stable-standard history of 2.4 min. Yet, this same result is not observed in the block-contexts that contradict transition statistics learned at sequence onset. This is evidenced by smaller MMN amplitude after tone-roles switch that substantially increases as this block-context continues (as shown in Figure 1.8). This slowed rate of learning is occurring over a timeframe that well-exceeds temporal processing limitations of auditory sensory memory indicating that higher-order brain areas involved in learning over long timescales are exerting modulatory control over stimulus-driven processes.

Hence, for approximately 1.2 min the network continues to suppress prediction error signalling, or is reluctant to engage in model updating, even though transition statistics defining tone roles emerging on shorter timescales have completely changed. As such, lower-order processes succumb to modulation by higher-order brain areas relying on predictions accumulated over the entire stable-standard period in the first block-context heard. This prediction model is presumably reactivated with the same degree of confidence when this block-context is heard again later in the sequence (see **Chapter 2** for appropriate analyses exploring the

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difference between early and later sequence portions). Taken together, these data show that the network is biased in evaluating new sound information about sound transitions over time in the direction of a strong first impression (Todd et al., 2014a). This explanation is adept in explaining the MMN results for the stable sequence, however a slightly different interpretation is applied to the unstable sequence where stable sequence data patterns are completely reversed.

Todd et al. (2014a) argue that unstable sound sequence data can also be traced to the formation of a first impression at sequence onset. The authors suggest that, as well as learning a first impression based on initial transition statistics, superordinate patterning about the stability of these statistics is also modelled with high predictive confidence when participants initially hear the multi-timescale paradigm (Todd et al., 2014a). To explain further, the superordinate pattern emerges when tone roles reliably switch every 2.4 min upon presentation of the stable sequence in its entirety. This means that when the very first block-context of the unstable sequence switches (unexpectedly) early, that is after 0.8 min instead of 2.4 min, a second-order MMN prediction error signal is evoked compromising the high confidence associated with predictions based on a first impression. This is consistent with data showing that MMN increases across halves for block-contexts in the unstable sequence that conform to those presented at stable sequence onset where the first impression (i.e. 60ms deviant, 30ms standard) is locked-in (see Figure 1.8). Subsequently, MMN to the second deviant is no longer restricted or biased by learning associated with the first impression (also apparent in Figure 1.8). This is reflected by a large MMN irrespective of block-context half indicating rapid accumulation of confidence in the underlying prediction model (Todd et al., 2014a). More recently, Mullens et al. (2016) directly tested the hypothesis that formation of

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a first-impression includes information about superordinate sequence structure (i.e. block-context length) that also informs on the relative stability of tone roles.

Mullen's et al.'s (2016) basic study design replicated Todd et al.'s (2014a) described in the previous section (see Figure 1.7 also) however the period of silence between sequence pairs was removed to create a decreasing-stability concatenation (stable to unstable block-contexts) and an increasing-stability concatenation (unstable to stable block-contexts), each lasting for 19.2 min (see Figure 1.9). Each concatenated sequence was separated by 2 min silent gap. All participants ($n = 31$) heard the decreasing-stability sequence first. Mullen's et al. (2016) limited primary MMN analyses to first-half data because the first impression bias effects are strongest at the beginning of block-contexts (Todd et al., 2014a). To very briefly reiterate assumptions underlying Todd et al.'s (2014a) explanation of the bias, a superordinate pattern violation would occur when the block-context changes length unexpectedly about half-way through the experimental session. This violation would happen when block-contexts lengths become shorter or longer during the second half of decreasing and increasing concatenated sequences, respectively. If this is the case, MMN to the first deviant should be smaller in the second half of concatenated sequences compared with the first half irrespective of relative stability because confidence in the overall first-impression diminishes when the superordinate prediction linked to the first impression is violated. This is precisely what Mullen's et al.'s (2016) data showed (see first deviant data in Figure 1.10A & B).

Furthermore, MMN to the first deviant was always larger than to the second in the earlier portions of concatenated sequences irrespective of whether stability increased or decreased offering further confirmatory evidence that the network is bias towards learning in favor of initial experience (see unstable & stable data for

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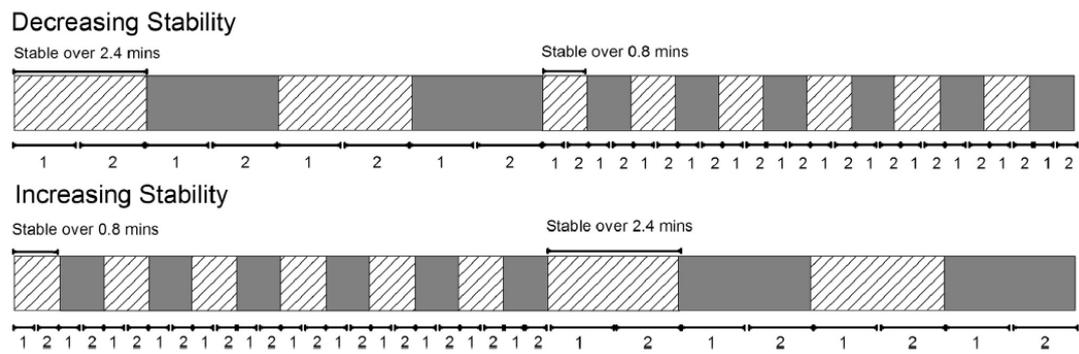


Figure 1.9. Decreasing- and increasing-stability sequence with halves-analysis. Graphical depiction of the decreasing- (top panel) and increasing-stability sequence (bottom panel) with halves-analysis under each (Mullens et al., 2016).

increasing & decreasing concatenations, respectively, in Figure 1.10A &B).

Removing the gap between sequence pairs produced data supporting the formation of a confidence-weighted first-impression that biases learning thereafter until assumptions about the temporal stability of the transition statistics are violated. Our most up-to-date explanation of data patterns underlying first impression bias is that the superordinate structure (i.e. block-context length) in the multi-timescale paradigm permits the formation of predictions about both local (tone roles) and higher-order patterning (i.e. tone role stability) with the influence of the latter revealed in predictable effects on MMN amplitude.

The authors offer an evolutionary-plausible reason for why the network may take a conservative approach to new learning when a first impression associated with high confidence is formed (Todd et al., 2014a). Upon exposure to the very first block-context heard at sequence onset, the network assigns differential relevance to sound transitions and their stability. A 30ms sound will very likely follow a 30ms sound and this is deemed unlikely to change given long stable-standard history. As such, the first standard sound is highly predictable and relatively uninformative is

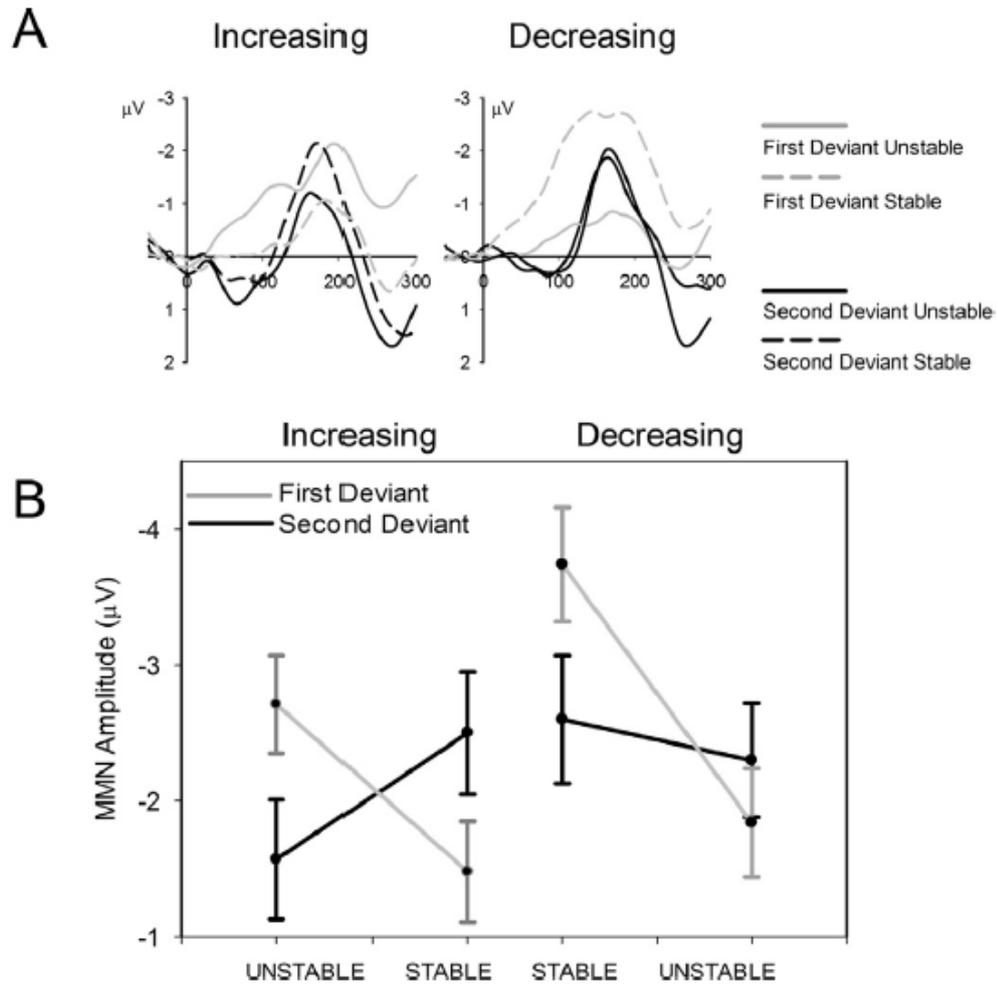


Figure 1.10. Halves analysis data. (A) First-half MMN waveforms in the increasing- (left panel) and decreasing-stability concatenations (right panel), separately for the first- (grey) and second-deviant tones (black) and for the stable (dashed line) and unstable (solid line) blocks. (B) First-half MMN amplitudes for the first- (grey) and second-deviant tones (black). Mean MMN amplitudes are shown separately for the increasing- (left panel) and decreasing-stability concatenation (right panel) for the stable and unstable sequence (x-axis). Error-bars denote standard error of the mean (Mullens et al., 2016).

terms of adaptive significance. The sound (i.e. transition statistic) is no longer informative (or ‘surprising’) because its’ source has been explained away. In stark contrast, it is very unlikely that a 60ms sound will be heard after a 30ms sound meaning this sound is potentially informative in terms of learning. A rare and ‘surprising’ sound signals that something in the environment defies our experience thus far, and may require deeper processing and/or a behavioural response (Todd et al., 2014). In this sense, the network may be reluctant to discount a first impression

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since updating a seemingly robust model of the environment requires resource engagement and therefore more energy, than retaining the model as it stands. Once the block-contexts switch, the network is wary of updating its model because of the strong belief that the first deviant is an important marker of learning that is unlikely to change and can potentially aid in self-preservation. We now refer to this concept as the information value hypothesis of first impression bias.

Todd et al.'s (2014a) proposal for why first impression bias occurs is compatible with predictive coding theory. Large MMN to the first deviant indicates that the underlying model is associated with high predictive confidence. This rare deviant sound is therefore interpreted as sufficiently different from expectations (i.e. a truly meaningful change) that warrants redistribution of higher-order resources (Friston, 2003, 2005). Put simply, the network is motivated to explain away prediction error signalling to maximise model evidence and keep the agent safe. In the multi-timescale sequence, this very reliable prediction model formed at sequence onset continues to be relied upon over the longer-term. So much so in fact, that the network will maintain predictions underlying a first impression (i.e. within stable sequence effects) even when transition statistics suddenly change. It is only when predictions about the longer-term stability of transition statistics underlying the first impression are violated upon presentation of the unstable sequence, that learning bias is absolved.

The reason why a drop in predictive confidence occurs in the switched context of stable sequences is not the same as that for the drop observed for unstable block-contexts that match those heard at the onset of the multi-timescale sequence. Predictions about transition statistics coded in a first impression are constrained by superordinate predictions about their stability formed over the longer-term (i.e. the

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entire stable sequence duration). When the environment becomes more volatile (i.e. tone roles switch earlier than predicted), predictive confidence in both first and second-order assumptions underlying the first impression is compromised. This means the network is now less certain about whether the first impression is still the best model of the environment for keeping the agent safe and thus whether the deviant is a truly meaningful sound event (Friston, 2003). Higher-order resources are presumably conserved until the network has sufficient confidence in a new and improved prediction model. Sequence learning following this superordinate pattern violation results in active sound information gathering based on dynamic changes on local timescales made evident by rapid accumulation of predictive confidence for the second deviant present in unstable block-contexts.

These data are consistent with literature showing that under typical conditions in which MMN modulation is driven by local sound statistics only (such as those used in oddball designs), this waveform is quickly observed after 2-3 repetitions of a deviant sound (Sams et al., 1993). Such explanations of order-driven effects on MMN are also consistent with assumptions put forward in Hierarchical Gaussian Filtering models of learning under uncertainty in which it is proposed that the brain can learn about local transition contingencies, the tendencies in those transition contingencies as well as the likelihood that transition contingencies will change over time (Mathys, Daunizeau, Friston, & Stephan, 2011; Mathys et al., 2014). The rate of model updating following a prediction error will depend on confidence in predictions (i.e. precision estimates) at a given level of the hierarchy and the level above. With respect to the multi-timescale sequence, this explanation would predict that model updating in the presence of an unexpected sound event will be constrained by one's model of the likelihood that transition statistics will change.

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The key message to be taken from Todd and colleagues studies is that the brain has the capacity to form first and second-order predictions during first-impression formation that impact on sound pattern extraction over many minutes. This shows that modelling of sound regularity can far exceed the temporal capacity of mechanisms associated with auditory sensory memory (i.e. 30ms; Winkler et al., 2002). These data cannot be fully accounted for by mechanisms proposed under SSA accounts of auditory mismatch processes. Furthermore, these data show that the brain is resistant to new learning, or model updating, despite a widely-held assumption that MMN should always occur within 2-3 repeats of a deviant sound (Sams et al., 1993; Winkler, 2007). These data also provide support, albeit indirectly, that higher order brain play a pivotal role in sound relevance filtering by 1) monitoring sense data over longer time-scales and 2) modulating responsiveness to dynamic sound change in the shorter-term when there is high certainty that predictions modelled over the longer-term provide a richer representation of inputs emerging on multiple temporal scales.

Evidence that the brain succumbs to first impression bias effects during relevance filtering of and learning about the sound environment underpins the rationale for each study outlined in the present thesis. In the proceeding sections, the results of four studies all with the shared aim of delineating conditions in which first impression bias effects on learning are observed and/or modified will be described. We think it is important to state here that the formatting of each chapter conforms to how it was published (e.g. Chapter 1) or how we intend to submit for peer review to publish (e.g. Chapters 2-3). As such, we express repentance that a number of introductory statements may be repetitious. In all cases, supplementary analyses of standard and deviant ERPs are presented in Appendices in the closing pages of this

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thesis. In brief, we first report on one study demonstrating that first impression bias effects are still observed when a much larger sample size is used and that effects remain despite repeated exposure to elements of the multi-timescale sequence. Next, we present data indicating that bias effects are no longer observed when increased task demand is placed on resources required for monitoring sound patterns emerging over longer timescales. Finally, we present a pilot study that aimed to explore what happens when people are informed of the temporal structures before hearing the multi-timescale sequence. Indeed, typical bias patterns were altered yet first-order learning effect remained.

Chapter 2: Surprising Sequential Effects on MMN

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Study Motivation

In this chapter, we present a published research article featuring two studies used to report on the robustness of the bias (see Appendix 1 for acknowledgement of acceptance for publication). In achieving this, we first tested whether patterns of order-driven bias *replicate* in a much larger data set compared to previous studies comprising a relatively smaller sample size. In a separate study, we tested the *longevity* of first-impression bias by examining whether patterns remain with repeated exposure to a role-alternating sound sequence.

2.1 Introduction

Research on the mismatch negativity (MMN) component of the auditory event-related potential (ERP) has flourished over the last 35 years with peer-reviewed publications on this topic exceeding 2000 and more than 200 of these have explored its characteristics in persons diagnosed with schizophrenia. The robust observation that MMN amplitude is reduced in schizophrenia has spawned a prolific effort to validate its utility as a biomarker in this group (see Atkinson, Michie, & Schall, 2012; Bodatsch et al., 2011; Stephan, Baldeweg, & Friston, 2006; Gil-da-Costa, Stoner, Fung, & Albright, 2013; Javitt, Zukin, Heresco-Levy, & Umbricht, 2012; Light et al., 2012). In both persons with schizophrenia and healthy comparison groups the MMN is elicited following the presentation of a rare, unexpected sound within a repeating stimulus pattern (Javitt et al., 1998). Yet, the signal is typically significantly smaller in schizophrenia than it is in healthy controls. Evidence suggests MMN is elicited only when a *prediction model* containing information about regularity exists and that the brain uses this model to anticipate future sensory input and minimise *prediction-error* (Winkler et al., 1996; Winkler 2007; Winkler & Czigler, 2012). It is therefore possible that smaller MMN in those with schizophrenia indexes impairment in predictive processing (Stephan et al., 2006; Todd et al., 2012). However, a necessary prerequisite for interpreting reduced MMN in those with schizophrenia is the need for a comprehensive understanding of the factors that impact MMN amplitude more generally. It is this pursuit that has uncovered highly unexpected order-driven influences on MMN in a “multi-timescale” paradigm (Todd et al., 2011). This bias contradicts the notion that MMN will always be larger in amplitude when a pattern has been stable for longer and exploring the cases and

limits of this bias can help us better understand the timescales of memory influencing MMN amplitude.

This paper features two studies designed to explore why MMN amplitude in healthy populations doesn't always increase uniformly when patterns are more stable. In study 1 we report a replication of the patterns of order-driven bias in MMN amplitude in a much larger dataset and in study 2 we demonstrate the persistence of this bias despite repeated exposure to sound sequences that should theoretically abolish its affect. Finally, we discuss how these order effects may help provide a deeper understanding of factors impacting MMN amplitude in non-clinical groups and emphasize there is still much to be learned for MMN that may influence its use as a meaningful tool in clinical groups such as schizophrenia.

2.1.2 MMN and the Multi-timescale Design. In a classic oddball paradigm, MMN will be observed in the auditory ERP when a sound violates regularity within a repetitious sequence (Näätänen, 1992). The sound may contain a rare physical feature deviation (as in most schizophrenia studies), a rare combination of features or may occur with unexpected timing (e.g., unexpectedly early or late repeat; Kujala et al., 2007). Increasingly, prominent views conceptualize the brain as capable of sophisticated hypothesis-testing and of using internal models to make predictions about future states of the sensory world (Winkler, 2007; Winkler & Schröger, 2015; Friston, 2005; Friston & Stephan, 2007). From this perspective, the MMN is considered a prediction-error signal that indicates the degree to which an expected state differs from that which is actually experienced. As models of the processes underlying MMN have matured, it is clear that MMN amplitude is tightly coupled to some quantification of “confidence” in the underlying predictions about future sound properties (Lieder et al., 2013; Winkler, 2007). Expressed simply, the confidence in

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an active prediction model will depend on the variability of incoming sensory input. A large amount of variation is apparent when the environment is highly unstable and this undermines confidence that the active model can accurately predict incoming stimuli. Predictions associated with high confidence are observed when regularity is extremely simple (e.g., a repeating identical tone) and highly stable/probable (Lieder et al., 2013). Confidence accumulates each time predictions successfully match sound input and this leads to a more accurate model with high precision. A possible ERP correlate of trace/prediction accumulation is the so-called repetition positivity (RP; Haenschel, Vernon, Dwivedi, Gruzelier, & Baldeweg 2005). Deviations from predictions that occur under conditions of high confidence will elicit a significantly larger MMN error signal (manifest as increased negativity in evoked potentials in fronto-central scalp electrodes 80-250 ms after detected deviation).

Most studies investigating MMN in schizophrenia use relatively simple sound sequences (e.g. sounds deviating on no more than a few features; see Todd, Harms, Schall, & Michie, 2013 for review). However, the exploration of MMN in alternate paradigms continues to facilitate a deeper understanding of normal predictive processes because the MMN responses elicited in stimulus paradigms with dynamically changing standard/deviant configurations reveal how the auditory system adjusts its predictions in accordance with the changing roles of the sounds (Cowan et al., 1993; Garrido et al., 2008; Winkler et al., 1996). Studies varying standard/deviant probabilities within subjects have shown that MMN amplitude plateaus at a certain point in controls and it plateaus at lower amplitude in patients with schizophrenia (Sato et al., 2003; Shelley, Silipo, & Javitt, 1999; Javitt et al., 1998) while Baldeweg and colleagues (2004) have found that the number of standard-stimulus repetitions needed to establish confident predictions correlated

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with the severity of schizophrenic symptoms. It is therefore possible that the predictive processing system is less than optimal in persons with schizophrenia (Todd, Michie, Schall, Ward, & Catts 2012). One way in which impaired processing could arise is through a limitation in the period over which confidence in a prediction model accumulates. For example, a system that can store accumulated confidence in a model over a period encapsulating 100 events could adjust response characteristics to differentially code errors as rare as 1% while a system limited to 20 events could not distinguish between an error frequency of 5% and 1% (such as in controls versus patients, see Figure 2 in Javitt et al., 1998).

The design principle in the multi-timescale paradigm was to keep local standard/deviant probabilities constant (0.875 and 0.125, respectively) and explore how changes in the longer-term stability of these patterns affected MMN in healthy people (Todd et al., 2011). The sequences within the multi-timescale paradigm contain two physically different sounds that alternate standard and deviant roles over time (see Figure 1). Previous research shows that perceptual inferences reflected in prediction models are updated very dynamically such that a model will be altered after as few as 2-3 consecutive errors causing a new repetition (Bendixen, Prinz, Horvath, Trujillo-Barreto, & Schroger, 2008; Sams et al., 1983). The properties of a former deviant will be incorporated into a new prediction model after a few repetitions, so a former standard in the multi-timescale sequence will come to elicit MMN when it occurs as a rare deviation from this new context. In separate sequences within the multi-timescale paradigm, the period of standard/deviant stability is varied such that in fast changing “unstable” sequences, the roles reverse after 160 tones (0.8 min) and in “stable” sequences, they reverse after 480 tones (2.4 minutes). The design was based on the expectation that participants affected by a

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long history of sound would show larger MMN in stable than unstable sequences. However, if participants were only affected by a short history, for example < 0.8 minutes, this should result in minimal differences in MMN amplitude in the different stability sequences. The surprise finding was that *both patterns* were in fact present in the *same participants*. MMN to deviant sounds in those periods in which the standard/deviant configuration matched the one encountered at the sequence onset (first-deviants) showed a clear stable > unstable result, while MMN to deviant sounds encountered in periods in which the roles had been reversed (second-deviants) was equivalent in amplitude for both sequences (Todd et al., 2011).

In Todd et al., (2011), role stability also had an impact on ERPs to standard sounds which emerged in the ERP as an apparent increase in positivity (although technically the combined effect of decreased N1 and increased P2) in stable relative to unstable sequences. However, this effect was consistent across tone type (i.e., no order effect) leading the authors to deduce that the bias phenomenon is driven by changes in ERPs to the deviant sound and does not modulate the RP appearing in the standard-stimulus response. In subsequent studies, the same basic pattern of bias has been observed to different feature deviations and so is clearly tied to the first-deviant, second-deviant status of the tones (Todd et al., 2013a; Todd et al., 2013b; Todd et al., 2014; Mullens et al., 2014).

A similar order-driven effect on MMN amplitude has been observed (Costa-Faidella et al., 2011) in a study designed to replicate animal work showing long timescale stimulus specific adaptation effects on standard and deviant ERPs (Ulanovsky, Las, Farkas & Nelken, 2004). Stimulus-specific adaptation (SSA) refers to the reduced spiking rate in neural response to a repeated stimulus. The paradigm used by Costa-Faidella et al. featured much shorter sequences (25 sec) containing

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two tones that switch roles as standard and deviant midway through. The authors observed that MMN amplitude to first standard when it later occurred as a deviant (after the switch) was smaller overall due to an initial “suppression” of response immediately after the roles reversed. This suppression of response to a deviant with a long prior history of repetition was attributed to the possible existence of a subgroup of auditory neurons that exhibit adaptation to sound probability on multiple timescales.

The multi-timescale paradigm revealed that MMN size following a pattern violation is susceptible to order-driven bias and is not a simple function of pattern stability and local sound statistics. An important consideration in understanding this phenomenon is whether this can be accounted for by factors sometimes referred to as “bottom-up” (meaning a modulation of response that can be accounted for by the history of sensory input) or “top-down” (meaning a modulation of response that is imposed on the auditory system by an explicit prediction-model). The degree to which bottom-up and top-down factors account for MMN has attracted considerable debate (see Näätänen et al, 2005 for discussion). Current views suggest that both can contribute to the generation of this ERP component (Sussman, 2007) and that the bottom-up contribution is required (Sadia, Ritter & Sussman, 2013). Indeed, the degree to which each contribute to smaller MMN in schizophrenia has also attracted debate (Baldeweg, Klugman, Gruzelier & Hirsch, 2004, Dima, et al., 2012). An order-driven impact on MMN amplitude could conceivably be reliant on either top-down or bottom-up effects on the ERP. The order-driven MMN modulation observed by Costa-Faidella and colleagues (2011) probably exemplifies a bottom-up effect because it mirrors the SSA finding of Ulanovsky and colleagues (2004), which

is generally accepted to be a “bottom-up” contribution to the process generating MMN.

Although the order effects in the multi-timescale sequences occur over much longer timeframes, it is likely that similar mechanisms contribute to the observed bias. However, at least two observations indicate that top-down effects must also contribute to MMN patterns in this data. Firstly, the effect of tone order on MMN amplitude in multi-timescale sequences is actually sensitive to the behavioural relevance of the sounds. In Mullens et al. (2014), participants initially heard the two sounds with equal probability and were asked to respond as quickly and accurately as possible to either the shorter sound (short-go group) or the longer sound (long-go group). The appearance of order-effects on MMN amplitude in a subsequent multi-timescale sequence differed in these two groups in a task-dependent manner. This result cannot be explained by “bottom-up” influences because the two groups heard the sounds with exactly the same probabilities and orders; the only difference was what they were asked to do in response to the sounds.

The second observation indicating that the order-effects observed in the multi-timescale sequences may reflect top-down influence is the focus of study 1 in the present paper. It was previously observed that the order effect on MMN amplitude is different in slowly changing (stable) sequences than in subsequent faster-changing (unstable) sequences in the multi-timescale paradigm. Explaining this differential pattern of data imposes a strong assumption on the bottom-up adaptation-based explanation of the order-driven effects: The strong adaptation developed for the standard in the final block of the stable sequence suppresses the response to this tone when encountered as the deviant in the following unstable sequence. If this was the case, the adaptation-based bias should diminish during the

course of the alternations of the unstable sequence. Testing this possibility requires averaging low number of trials per participant and thus requires a larger group for sufficient statistical power. In study 1, we determine whether the finding of different effects in stable vs. unstable sequences can be replicated in an expanded dataset and to test whether the differential effect is confined to the initial segment of the unstable sequence. In study 2, participants were presented with four occurrences of either the stable sequence or the unstable sequence to determine whether the order-effects would diminish with repeated exposure. We ask whether assuming the presence of top-down influences is necessary to account for the results of both studies. Implications about general factors impacting MMN amplitude are also discussed.

2.2 Method - Study 1

2.2.1 Participants. The data comprised 14 individual data sets from Todd et al. (2013b) plus an additional 21 unpublished data sets collected subsequently under identical conditions. The data therefore consisted of 35 (22 females, 18-33 years, mean = 23 years, SD = 4 years) healthy community volunteers and undergraduate students from the University of Newcastle, Australia. All data sets were collected under standards approved by the local Human Research Ethics Committee. A structured interview was conducted by one of the researchers to ensure all participants met criteria for inclusion which stipulated normal hearing, no history of head injury or neurological condition, no current mental illness or family history of psychosis and no alcohol or substance abuse. Remuneration was offered as course credit to students and cash reimbursement to community volunteers. Written informed consent was obtained from all participants consistent with standards approved by the Human Research Ethics Committee.

2.2.2 Stimuli and sequences. Sounds were 1 kHz pure tones presented binaurally over headphones at 75 dB SPL with 5 ms rise/fall times and either a 20 ms or a 50 ms pedestal to produce 30 ms and 60 ms sounds, respectively. Sounds within sequences were arranged within long-deviant and short-deviant blocks. In long-deviant blocks, 30 ms tones were highly probable ($p = 0.875$) and 60 ms tones were rare deviants ($p = 0.125$); in short-deviant blocks, the tone probabilities were reversed (30 ms and 60 ms presented at $p = 0.875$ and 0.125 , respectively; see Figure 2.1). In separate sequences, long- and short-deviant blocks were presented at either slow or fast block-alternation speeds (hereafter referred to as stable and unstable sequences, respectively) with sequences always commencing with long-preceding short-deviant (hereafter referred to as first and second-deviant, respectively). Each sequence consisted of 1920 tones in total, 960 of each duration.

Tones were presented at a regular 300 ms stimulus onset asynchrony (9.6 min per sequence). In the stable sequences, sounds were arranged in four blocks with block-type type alternating after every 480 sounds, producing a stable-standard period of 2.4 min. In the unstable sequence, sounds were arranged in twelve blocks with block-type alternating every 160 tones, creating a stable-standard period of 0.8 min. Note, full counterbalancing of sequence order and tone role as first or second-deviant was not performed here but was present in Todd et al. 2011 and counterbalancing of first-deviant identity was also present in Mullens et al. 2014 and Todd et al 2014.

2.2.3 Procedure. All participants completed a screening interview to ensure inclusion criteria were met. An audiometric screen using a pure tone audiometer (Earscan ES3S) across 500 Hz-4000 Hz was used to assess hearing thresholds (≤ 25 dB SPL) to ensure absence of hearing loss. Participants were then fitted with a

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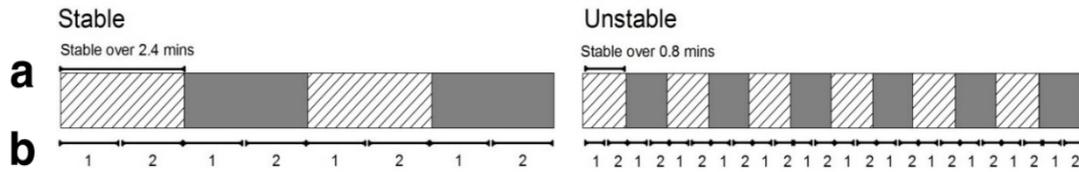


Figure 2.1. A diagram illustrating the multi-timescale sound sequences a The diagonal lined rectangles represent one deviant block type and the greyed rectangles, the other. In the blocks marked with diagonal lines, the long (60 ms) sound was the rare ($p = 0.125$) deviant and the short (30 ms) sound was the highly probable ($p = .875$) standard. In the greyed blocks, the probabilities were reversed. The block length within stable and unstable sequences were 2.4 and 0.8 min respectively, creating a difference of stability in the relative tone probabilities b Sections labelled 1 (first-half data) and 2 (second-half data) show how blocks were divided for halves-analysis as detailed in Todd et al. (2013a). Averages for MMN to the deviants were created for both stable and unstable conditions by pooling together the responses for first-halves (i.e. the point in which tone roles transition) to produce first-half long- and short-deviant MMNs (from Todd et al., 2013a).

Neuroscan Quik-Cap with Ag/AgCl electrodes. The continuous EEG was recorded on a Synamps 2 Neuroscan system at 1000Hz sampling rate (highpass 0.1 Hz, lowpass 70 Hz, notch filter 50 Hz and a fixed gain of 2010). EEG data were collected from 13 electrode locations (FZ, CZ, PZ, F3, FC3, C3, F4, FC4, C4, F7, F8 in accordance with the 10-20 system, plus left and right mastoid) and referenced to the nose. In addition, vertical and horizontal electro-oculograms were recorded using electrodes placed above and below the left eye, and 1cm from the outermost canthus of each eye to monitor eye-blinks and -movements. All impedances were reduced to below 5 k Ω . Sequences were presented over headphones (Sennheiser HD280pro) while the participant viewed a film (sound muted) with sub-titles. Participants were told they would hear sounds over the headphones but that the brain responses we were studying were automatic and best recorded if they could try to ignore the sounds and focus attention on the film.

2.2.4 Data Analysis. The continuous EEG recording was examined offline for major artefact and corrected for eye blinks using the procedures in Neuroscan Edit Software. This method applies a regression analysis in combination with artefact averaging (Semlitsch, Anderer, Schuster, & Presslich, 1986). The values generated was assessed for adequacy (> 30 sweeps in the average and < 5% variance) and

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applied to the continuous data file. Each file was epoched from 50ms pre-stimulus to 300ms post-stimulus. Epochs were baseline corrected to the pre-stimulus interval and averaged according to stimulus type. Epochs containing variations exceeding $\pm 70 \mu\text{V}$ were excluded.

Standard and deviant ERPs were created separately for the period equating to the first-half of blocks (0-1.2 minutes for blocks in stable sequences and 0-0.4 minutes for blocks in unstable sequences) and for second-half of blocks (1.2-2.4 minutes for blocks in stable sequences and 0.4-0.8 minutes for blocks in unstable sequences; see Figure 1). This was essential as Todd et al. (2013a) observed the bias effects to be prominent in first-half data only. Data for stable and unstable sequences were used to create four ERPs to standard tones and four to deviant tones (*first-half first-deviant*, *second-half first-deviant*, *first-half second-deviant*, *second-half second-deviant*). All standard and deviant ERPs were digitally filtered with a 30 Hz lowpass filter. Difference waveforms were generated by subtracting the ERP to a sound as a standard in the first- or second-half of blocks from the ERP to that same sound as a deviant in the same block period for each sequence. The majority of participants had between 50 and 60 deviant sweeps contributing to averages with a minimum of 43 for any deviant waveforms. MMN amplitude was quantified by extracting the mean peak amplitude over a 20 ms period centred on the most negative point 100-250 ms post-stimulus onset. As per Todd et al. (2013a), a total of eight MMN values were compared at F4 (where the MMN was maximal) in repeated measures ANOVA with sequence (stable, unstable), deviant (first-deviant, second-deviant) and half (first, second) as within-subject factors. Paired (two-tailed) t-tests were performed for a-priori simple effects with p-value set at .05.

2.3 Results

Difference waveforms for the first and second-deviant in stable and unstable sequences across first and second block halves are presented in Figure 2.2 and the corresponding mean amplitude values are presented in Figure 2.3. There is a clear MMN evident for each of the sequence types, for each of the deviants and for both the first and second half of sequence blocks. However, in the stable sequence (Figure 2A), MMN appears to increase more over the first to second half of blocks for the second-deviant than the first, while the reverse appears to be true for the unstable sequence (Figure 2B). Analysis revealed main effects of *sequence* (stable generally larger than unstable, $F(1, 34) = 14.84, p < .001, \eta^2 = .30$) and *half* (second-half generally larger than first-half, $F(1, 34) = 10.64, p < .01, \eta^2 = .24$) but these patterns were further modified by a significant *deviant* x *sequence* x *half* ($F(1, 34) = 7.77, p < .01, \eta^2 = .19$) interaction meaning that the stability effects reflected in sequence and half were different for the first-deviant and second-deviant MMNs.

For the first-deviant there was a main effect of sequence (stable > unstable, $F(1, 34) = 15.39, p < .001, \eta^2 = .31$) and half (second > first, $F(1, 34) = 6.02, p < .05, \eta^2 = .15$) with no interaction. However, planned analyses revealed that the MMN only increased significantly over halves for the unstable sequence ($t(34) = 2.77, p < .01$) and the effect of sequence was significant in first-half data only ($t(34) = 4.04, p < .001$) and this is clear in Figure 3A. In contrast, for the second-deviant there were no main effects but a significant sequence by half interaction ($F(1, 34) = 8.36, p < .01, \eta^2 = .20$). This was due to MMN increasing significantly over halves for the stable

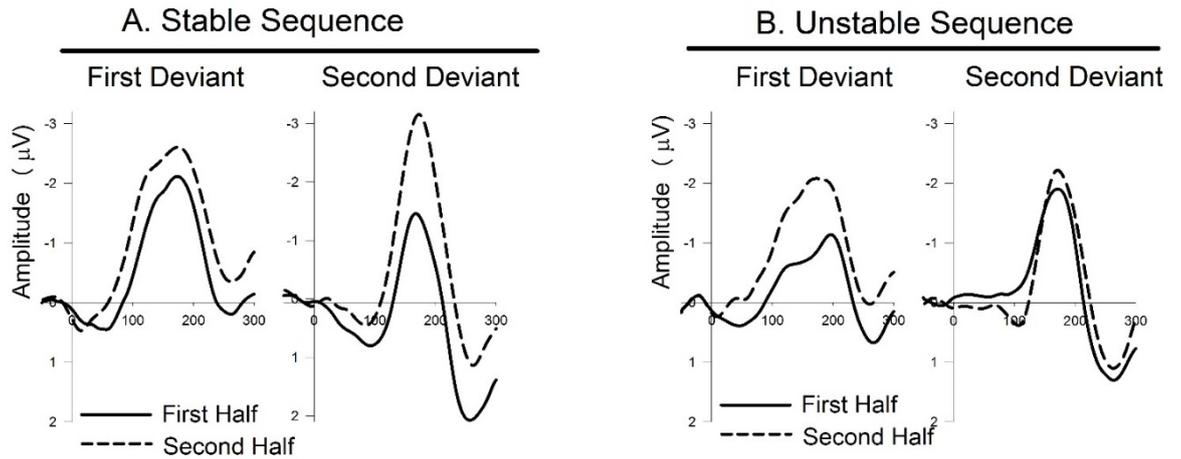


Figure 2.2. Difference waveforms in replication study. A. Stable Sequence and B. Unstable Sequence for first (60 ms) and second (30 ms) deviant. Difference waveforms for data obtained in the first-half of blocks (solid lines) are presented with those in the second-half of blocks (broken lines).

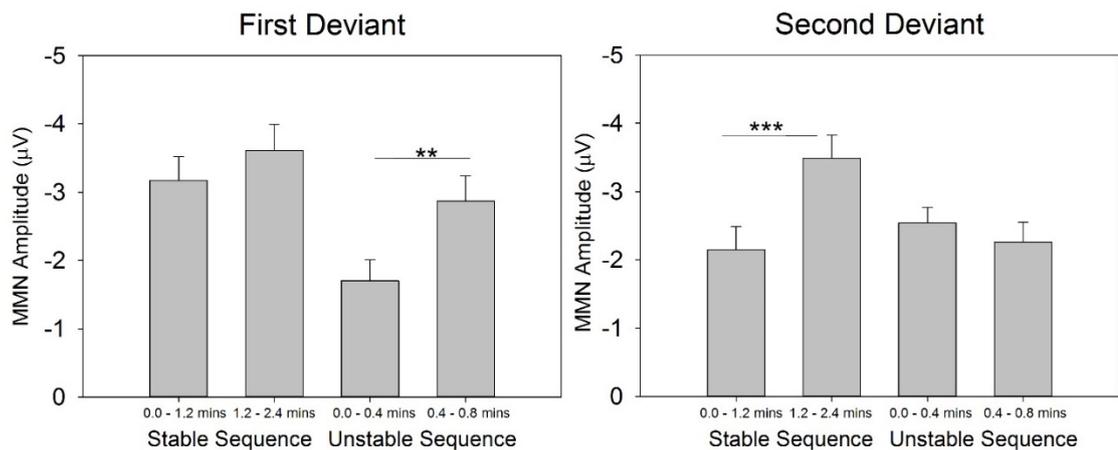


Figure 2.3. Bar graphs showing group mean MMN amplitudes. Group mean amplitude for mismatch negativity (MMN) for the first-deviant (left) and second-deviant (right) in first and second halves of stable and unstable sequences. Asterisks denote significant difference across a sequence block type. ** = $p < 0.01$, *** = $p < 0.001$.

sequence only (see Figure 2.3, $t(34) = 3.01, p < .005$) and the effect of sequence only being significant for the second half of blocks ($t(34) = 2.93, p < .01$).

The reverse pattern of block half effects in the Stable and Unstable sequences could potentially be explained by the long period of 60ms standard tones at the end of the Stable sequence leading to reduced response to these tones as deviants in the subsequent Unstable sequence. This could be expected to result in differential changes in Unstable sequence MMNs for the first and second deviants over early

versus later blocks of the sequence. Early MMN (to deviants in the first 3 blocks) versus later MMN (to deviants in the second 3 blocks) was compared over tones in repeated measures ANOVA. The analysis yielded no significant main effects nor interactions. Means for early and late MMN for the first-deviant ($M = -2.03$, $SD = 2.31$ & $M = -2.08$, $SD = 2.08$, respectively) and for the second-deviant ($M = -2.54$, $SD = 1.79$ & $M = -1.77$, $SD = 2.07$, respectively) were very similar but the evidence was not strong enough to support early and later block values coming from a sample with the same mean based on a city-block distance test (Widmann & Schröger, 1999).

2.4 Discussion.

The larger data set presented here ($n = 35$) replicates the finding that MMN amplitude is differently affected in the multi-timescale sequences for the first and second-deviant tones (Todd et al., 2013b). When examining stability effects within the stable slowly changing sequence MMN amplitude for the first-deviant is already large in first-half data and stays large over second-half data showing minimal growth from the period when roles were initially established versus later in the block when confidence has had additional time to accumulate. In contrast, MMN to the second-deviant tone is significantly smaller in first-half of the blocks than in the second-half of blocks showing a clear stability effect. This observation is consistent with that reported in Todd et al., 2013 and is also consistent with that of Costa-Faidella et al., (2011) where MMN to a deviant with a long prior history as a standard is initially very small but recovers with increasing stability in the new pattern. As per Costa-Faidella, no order-patterns were reflected in the standard ERPs, but only in deviant ERPs and resultant MMNs (see Appendix 2 for standard & deviant analyses).

The data obtained in the unstable sequence exhibits the opposite pattern even though the sequences commence with the same standard and deviant roles. For

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unstable sequences, MMN to the first-deviant is initially small but increases significantly across block halves, while that to the second deviant is actually as large during the first-half of the blocks as it is by the second-half. In fact, it is evident from Figure 2.3 that the MMN obtained after a period of 0.4 minutes stability in the unstable sequence data is as large as that obtained after 1.2 minutes of stability in the first-half of the stable sequence blocks.

Can long timescale adaptation of afferent neuronal assemblies explain the reversal of order-effects on MMN in the unstable following stable sequence? One possible explanation could relate to the first-deviant being the highly repetitious standard in the final block of the stable sequence. If a strong adaptation is developed it could potentially influence the response to this tone as a deviant in the following unstable sequence. If this were the case one might expect this effect to diminish over the course of the sequence leading to larger amplitude MMNs to the first-deviant in later blocks. There was no evidence in the data that this was the case so while we cannot rule out an adaptation explanation the data do not provide strong support for it. Incidentally the absence of a significant difference in MMN for the early and late blocks of the Unstable sequence occurs in the presence of a significant difference between the first and second halves of these blocks. Although it is difficult to draw conclusions from these subgroupings of data it is certainly consistent with Todd et al.'s (2013) suggestion that the difference over block halves is something that is repeated each time the blocks are encountered.

Todd et al., (2013) alternatively proposed that the order-effects may be explained by a lasting “first-impression”. They hypothesized that the standard and deviant roles (or probabilities) first encountered at sequence onset are “locked-in” as a type of prior; that is, an assumption about the probability distribution defining the

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likelihood and/or importance of future events (Griffiths et al. 2008). The repetitive standard tone is rapidly established to be a predictable event providing minimal new information while the deviant occurs unexpectedly as a potentially relevant violation of expectations. When the roles are encountered in the reverse order, there is initially very low confidence that the former repetitive standard is now an informative error signal. It is recognised as an error relative to the new prediction model (i.e., MMN is elicited) but it is initially “suppressed” in amplitude until later in the block when the evidence sufficiently counters the first impression. The authors suppose that the first-impression formed in the stable sequence may include a superordinate variable (or hyperprior, Bernardo & Smith, 2000) specifying the block length. The block-length model would be violated in the subsequent unstable sequence when the first block-type stops too early. As a consequence, the first-impression about tones may drop to a low-confidence weighting because the super-ordinate assumption was wrong. This could explain why MMN to the first-deviant becomes smaller at block onsets that reactivate a role assumption with low-confidence but increases over the block when counter-evidence accumulates with stability. This explanation would, in turn, imply that unstable sequences encountered in isolation (i.e., not following a stable sequence) would produce the pattern of data observed in the stable sequence above because the first-impression would simply be linked to the onset structure of this sequence.

In study 2, we used a between-subjects design to explore the longevity of the order-effects on MMN. Specifically, we exposed participants to four occurrences of either the stable sequences or unstable sequences to determine whether the patterns observed in study 1 survive repeated experience with the sequences. Repeated experience of a given sequence structure could eventually overpower any biases or

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assumptions that do not hold value in predicting the environment over the longer term (see Mathys, Daunizeau, Friston, & Stephan, 2011). Study 2 also facilitated a test of the hypothesis that the unstable sequence data produced in study 1 were due the influence of the prior stable sequence structure and an additional test of whether adaptation at the end of the stable sequences could explain the unstable sequence data. If such adaptation effects were present, repeats of the stable sequences should be subject to the same influence in which the adaptation to the standard at the end of the sequence should lead to smaller MMN to this sound as a deviant in the subsequent repeat presentation.

2.5 Method - Study 2

2.5.1 Participants. Participants included 30 (21 females; 18-27 years, mean = 21 years SD = 2 years) naive healthy community volunteers and undergraduate students from the University of Newcastle, Australia meeting the same inclusion criteria as study 1. Remuneration was offered as course credit to students and cash reimbursement to community volunteers. Written informed consent was obtained from all participants consistent with standards approved by the local Human Research Ethics Committee.

2.5.2 Stimuli and sequences. The protocol was a modification of Todd et al.'s (2013a; described in study 1) multiple-timescale paradigm comprising of four occurrences of either the stable sequence (stable condition) or the unstable sequence (unstable condition). For both conditions, a 1 min break occurred between each sequence repeat.

2.5.3 Procedure. Screening and EEG data acquisition procedure was identical to study 1. Condition allocation alternated with recruitment order (three males in the

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stable condition and six in the unstable; and mean age of 22 years in both subgroups). Sixteen participants were allocated to the stable condition and the remaining 14 participants to the unstable condition. Sequences were presented over headphones (Sennheiser HD280pro) while the participant viewed a film (sound muted with sub-titles and instructed to focus on the film as per study 1).

2.5.4 Data Analysis. EEG data analysis was identical to study 1 and generated ERPs for the period equating to the first- versus second-half of blocks for each tone, in each sequence and repeat. This resulted in 8 standard and 8 deviant ERP averages per tone (therefore 16 standard and 16 deviants per participant, per presentation). The minimum sweeps contributing to an average for any participant was 44 with the mean between 58 and 59 for all deviant waveforms. Eight difference waveforms were generated for each tone (first and second halves for each for the four sequences).

The mean-peak amplitudes were quantified as the maximum negativity in difference waveforms over a 20 ms period centered on the most negative point 100-250 ms following stimulus onset. The purpose was to determine whether the expected tone x half interactions seen in study 1 diminished with repeated presentations. Amplitudes were therefore compared in a mixed model ANOVA at F4 with *condition* (stable, unstable) as a between-groups factor and within-subjects factors of half (1st, 2nd), *deviant* (first-deviant, second-deviant) and *presentation* (Sequence 1, Repeat 1, Repeat 2, and Repeat 3). Paired t-tests were performed for planned comparisons using simple effects with p-value set at .05. Effects on deviant versus standard tones are presented in supplementary data and confirm that the bias is present in response to deviants only.

2.6 Results.

Difference waveforms for first and second-deviant, across each block half, and each presentation, are presented for stable versus unstable sequences in Figure 2.4. Analysis revealed main effects of *presentation* ($F(3, 84) = 9.24, p < .001 \eta^2 = .25$), *deviant* ($F(1, 28) = 18.15, p < .001 \eta^2 = .39$), *half* ($F(1, 28) = 17.80, p < .001 \eta^2 = .38$) and *condition* ($F(1, 28) = 27.64, p < .001 \eta^2 = .50$). While the main effect of *condition* is due to MMNs being larger overall in the stable group, the main effects of *deviant*, *half* and *presentation* were further modified by significant interactions between *deviant* and *half* ($F(1, 28) = 6.42, p < .05 \eta^2 = .19$) and *deviant* and *presentation* ($F(1, 28) = 2.83, p < .05 \eta^2 = .09$).

From Figure 2.4 it is apparent that the *deviant* by *half* interaction occurs due to MMN being smaller in the first-half than the second-half of sequence blocks for the second-deviant but not the first. This was confirmed in analyses conducted separately for the first and second deviant. For the first deviant, there was a significant main effect of *condition* (MMN smaller in the unstable group, $F(1, 28) = 18.81, p < .001 \eta^2 = .40$) and *presentation* ($F(3, 84) = 5.79, p < .001 \eta^2 = .17$), with the latter modified by a significant *presentation x half* interaction ($F(3, 45) = 6.30, p < .05 \eta^2 = .11$). This interaction was due to presentation affecting MMN size in the second-half of blocks (MMN decreasing over presentations, $F(3, 84) = 10.65, p < .001 \eta^2 = .28$) but not the first-half ($p = .76$). MMN did not differ significantly over halves for the first-deviant in any of the four presentations ($p > .09$ for paired t-tests over halves in all stable and unstable sequences). In contrast, the analysis of second-

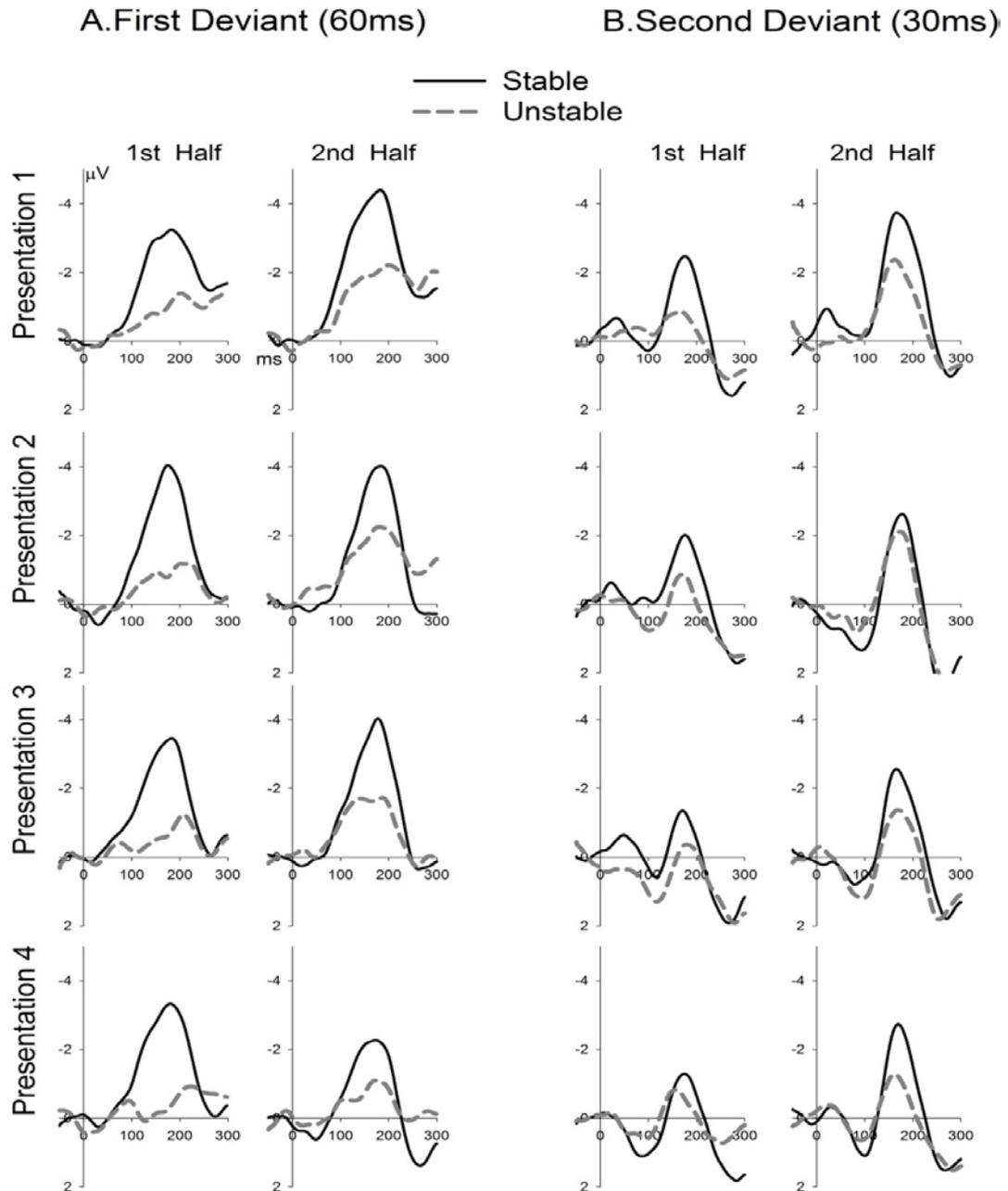


Figure 2.4. MMN waveforms in repeated sequence design study. Difference waveforms for the first (A = 60 ms) and second (B = 30 ms) deviant in the 1st and 2nd half of stable (black solid lines) and unstable (grey broken lines) sequences. Difference waveforms are presented separately for data acquired in the first, second, third and fourth sequence presentation.

deviant MMNs confirmed a main effect of *half* ($F(1, 28) = 33.12, p < .001 \eta^2 = .54$)

due to MMN incrementing across halves across all presentations. A main effect of *presentation* was also present ($F(3, 26) = 6.39, p < .001 \eta^2 = .19$) due to a reduction in MMN amplitude across repeating sequences.

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An additional analysis step was conducted on the stable sequence group data in light of the consistency of the differential effect of stability on the first and second-deviant MMNs over presentations. The data from the first and second halves of sequence blocks were further broken down into early and late blocks within the sequence. These were in turn averaged over sequences to create four MMNs per deviant type. Specifically, this produced an across-presentation average for the first-half and second-half of the early sequence block and the first-half and second-half of the later sequence block. This facilitated an examination of whether the stability patterns change from the first occurrence of the block to when the block occurred a second time. The average difference waves (minimum 90 sweeps) for each deviant and block are presented in Figure 2.5B and C along with a grand average of first-half and second-half stable sequence difference waves over the four presentations in Figure 2.5A. For transparency, the grand average deviant and standard responses are also presented in the bottom panel of Figure 2.5 (see Supplementary data on pg. 88).

It is clear from Figure 2.5B that although MMN to the first-deviant drops in amplitude from the early to the late block, the tendency for MMN to be more-or-less the same amplitude in both block halves remains constant. In a repeated measures ANOVA for first-deviant data with within-subjects factors of period (early, late) and half (first, second) these visible patterns produce main effects of period only ($F(1,15) = 23.04, p < .001, \eta^2 = .61$). In Figure 2.5C the MMN to the second-deviant does not drop over early and late sequence blocks and appears to exhibit the same significantly smaller amplitude MMN for first-half of each block confirmed in a main effect of half only ($F(1,15) = 17.18, p < .001, \eta^2 = .53$) in the corresponding repeated measures ANOVA.

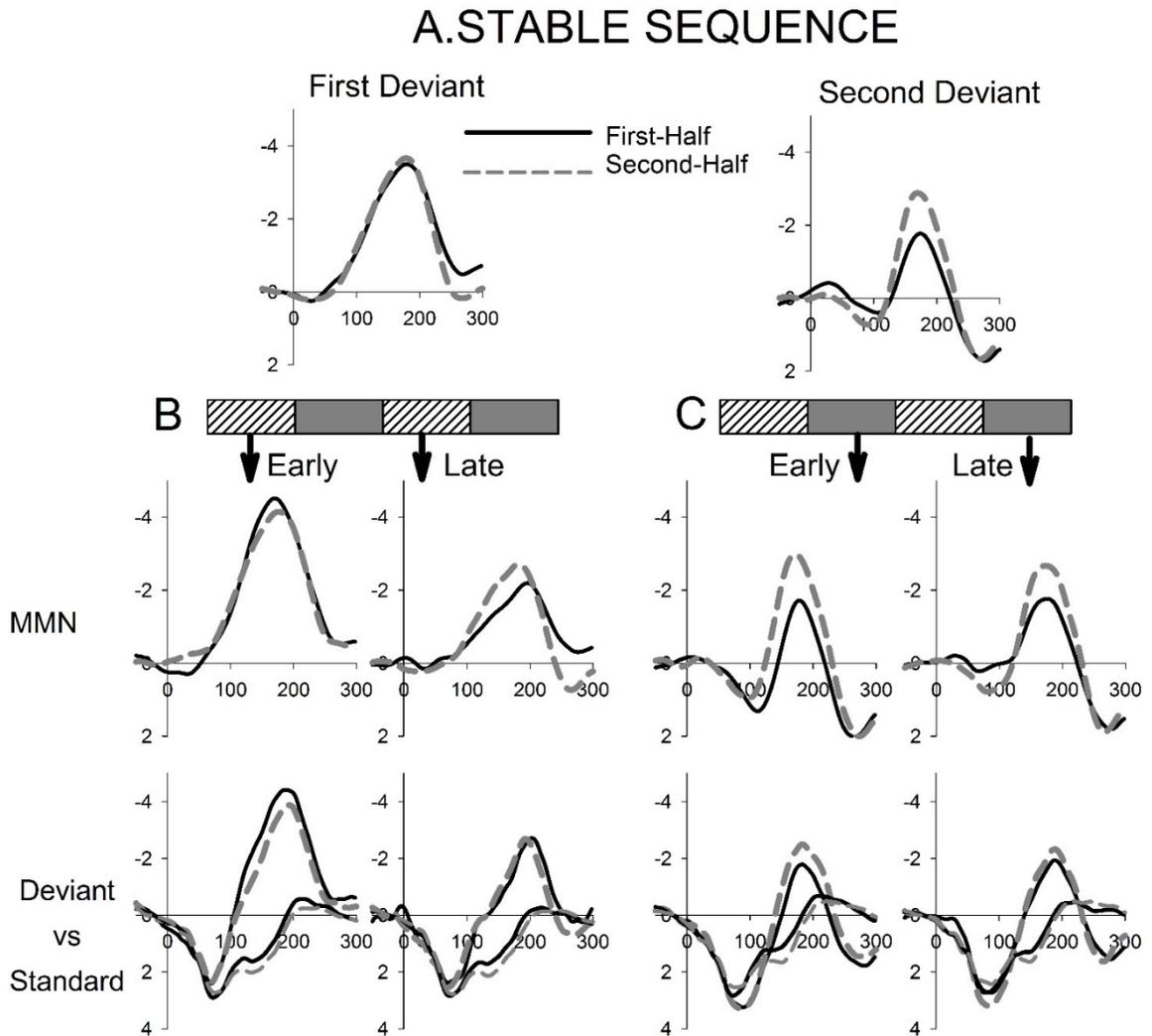


Figure 2.5. MMN waveforms in period analysis. A. Difference waveforms for the first and second-deviant in the 1st half (black solid lines) and 2nd half of stable sequence blocks (grey broken lines) averaged over the four sequence presentations. B. Same as A but for the first-deviant tone only and with the response in early and late blocks separated. The top portion shows the difference waves and the bottom the deviant and standard ERPSs. C. Same as B but for the second-deviant tone only.

2.7 Discussion.

In study 2, we used a between-subjects design to examine how the order-driven bias in MMN amplitude was affected by repeated exposure to stable or unstable sequences across time. The data reveal a remarkably persistent pattern of differential effects on MMN amplitude for the first and second-deviant. The deviant by half interaction is consistent with the pattern seen for stable sequences in study 1; similar to study 1, this difference is due to MMN amplitude being “suppressed” in

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the first-half of blocks for the second-deviant but not for the first, and this remains constant over sequence repeats. In contrast, the MMN to the first-deviant is not significantly smaller in the first-half of blocks. So, the data across presentations are very consistent for the stable sequence and show that repeated exposure does not alter the different stability effects on MMN for the first and second-deviant tone.

The discussion for study 1 raised the possibility that the long period of repetition at the end of a stable sequence could cause a strong adaptation that might impact the response to tones in the following sequence. This was proposed as a possible explanation for why the pattern of stability effects reversed in the unstable sequence when it followed the stable sequence. Observations from study 2 provide compelling evidence that this is highly unlikely. If adaptation to standards in the final block of stable sequences impacted MMN to the first-deviant in the next sequence, this would act to “suppress” MMN amplitude to the first-deviant tones when the stable sequence is repeated. It is clear from Figures 2.4 & 2.5 that this is not the case; MMN to the first-deviant is always large (Figure 2.4) and is actually largest in the early blocks of the repeating stable sequences (Figure 2.5). However, contrary to study 1, the deviant by half interaction in unstable sequences in study 2 was not significantly different to that in stable sequences (i.e., the deviant by half interaction was not modified by condition). The repeats of the unstable sequence do not replicate the modulation patterns seen in study 1 (i.e., small MMN in the first-half of blocks for the first but not the second-deviant). The effects on MMN amplitude in the unstable group in study 2 do not differ statistically from those in the stable repeat condition. It is also clear however, that the effects in the unstable group are much smaller and indeed, if analysed without the stable sequence group, produce a main effect of half only (second-half larger than first). This observation is

consistent with the proposition that the patterns in the unstable sequence in study 1 were due to the sequence being preceded by the stable sequence. When encountered in isolation (study 2), the unstable sequences produce minimal evidence of (or possible absence of) order-bias, which may reflect theory that any top-down influence on MMN amplitude will be less pronounced under conditions of low-confidence in the underlying model (Friston, 2005; Garrido et al., 2009; Lieder et al., 2013; Winkler, 2007). In the absence of any top-down bias, the results may be dominated by more local adaptation effects proposed by Costa-Faidella et al. (2011) where, with so many reversals, the adaptation effect on both tones as standards could begin to suppress the initial MMNs to the same tones as deviants leading to smaller MMNs in first-half data for both deviants.

2.8 General Discussion & Conclusions

The studies presented in this paper demonstrate robust order-effects on modulation of MMN amplitude revealed in role-alternating sequence designs. If the system were realistically computing probabilities from tone occurrences, the patterns of change in MMN for both deviants should be equivalent. Instead, the evidence pertaining to the two tones and/or block types appears to be weighted differently. Although long time-scale adaptation could contribute to these order-effects (Costa-Faidella et al., 2011), it cannot account for why such effects can be altered by changing the behavioural relevance of the sounds (Mullens et al., 2014) and it does not appear to account for why the order-effects reverse if an unstable rapid role alternating sequence follows a stable slow role alternating sequence (study 1 and Todd et al., 2013).

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It was hypothesised that repeated exposure to sequences (study 2) could result in diminishing bias as the auditory network learns over time that tones and block-types are equally probable. Instead, the pattern of bias remained. This suggests that the learning that generates the bias is stable or may even be reinforced with repeated exposure to sequences with the same initial structure (see Todd et al., 2013a for reversal of bias with reversal of deviant order).

We have elsewhere suggested (Todd et al., 2013a) that the “first-impression” bias we expand on in this paper is akin to the formation of an instantaneous prior with a lasting impact that is reactivated each time the roles reverse. MMN has generally been considered to reflect a very low-level relevance filtering system, however this is challenged by the observation that these apparent instantaneous priors (biases) can have profound affects that are altered by previous experience with sound. As reviewed in the introduction, Mullens et al. (2014) showed that the appearance of the bias was a function of the behavioural relevance of sounds in a previous go-no-go task. The results suggest that the MMN prediction-error signal can reflect an integration of sound meaning or relevance with sound probability information (e.g. first-deviant is rare and potentially important; first standard is predicted and provides no new information). The observation that previous familiarity can affect MMN amplitude is also evident in studies showing larger MMN to recognised language (Jacobsen et al., 2004; Pulvermüller & Shtyrov, 2006) and non-linguistic stimuli (Jacobsen, Schröger, Winkler, & Horváth., 2005) than those with equivalent physical distinctiveness. Our observations indicate that these effects may not be solely related to familiarity but instead to what participants have to do in response to the sound (i.e., sound relevance). These propositions require additional investigation but invite the intriguing possibility that applications of

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MMN can be used to study how priors interact with evidence to influence predictive processes that filter relevance in the unattended auditory environment.

Although order biases have emerged in (and could be confined to) studies employing role-reversing paradigms, what the data clearly reveal is that we do not yet understand all of the factors that significantly impact MMN amplitude. It is therefore imperative that continued efforts are made to explore such phenomena, particularly those that challenge current assumptions about the conditions in which smaller MMN is observed. Certainly, current models of the inferential process appear incomplete because they would not predict the present data. Studies using the multi-timescale paradigm have shown very long lasting cumulative effects of learning that appear to distort confidence in automatic perceptual inferences. A deeper understanding of how this learning impacts MMN amplitude in healthy populations will ultimately advance our understanding of the many ways in which the system underlying sensory predictions and MMN amplitude can be impaired in a variety of clinical groups including those with schizophrenia. Furthermore, paradigms that can dissociate adaptation effects on ERPs from those that might be attributed to active prediction-models can contribute to identifying the contribution of each of these elements to smaller MMN in clinical populations.

Chapter 3: Increased task demand on cognitive resources abolishes effects of first impression bias on sound sequence learning

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Study Motivation

This chapter is the outcome of multiple revisions following three rounds of peer reviews. The purpose of our research study and associated rationale has remained consistent throughout each version that is, we wanted to examine whether first impression bias is altered under conditions that place increased demand on cognitive resources. In the first version, one group of participants completed a concurrent 2-back WM task whilst hearing the multi-timescale paradigm revealing basic stability effects on MMN. Reviewers recommended we add a comparison group who completed a simple perceptual task to control for attentional influences and validate our conclusion that contributions from cognitive brain areas are likely involved in learning biases on longer time-scales. We complied with this request and found basic stability effects on MMN irrespective of task type. In a second submission, we were

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advised to add another control group of participants who heard the multi-timescale sequence under typical low-demand conditions (i.e. whilst watching a DVD). We followed this recommendation and found that each task type differed significantly relative to the low-demand condition with differences most pronounced between the low-demand and WM conditions. Upon our third submission, the paper was rejected because “The discussion shows that there are too many buts to prevent a clear straightforward conclusion”. We have since asked two independent researchers with almost 50 years of experience in MMN research combined to provide an opinion on the prepared manuscript – both agree that our interpretations of these data are conclusive. Although the data remain unpublished, we have presented these studies in line with our original interpretation.

3.1. Introduction

First impressions are thought to occur when the first instance encountered is allocated greater weight relative to later experience (Birnbbaum, 1974; Tetlock, 1983). These impressions typically persist despite evidence to the contrary (Baumeister et al., 2001; Nisbett & Ross, 1980; Rothbart & Park, 1986; Rozin & Royzman, 2001). A wide range of studies including those in learning (e.g. Jacoby, Wahlheim, Rhodes, Daniels, & Rogers, 2010; Shteingart, Neiman, & Loewenstein, 2013), resistance to stereotypes and attitude to change (e.g. Allport, 1979; Bargh & Pietromonaco, 1982; Devine, 1989; Hamilton, 1979; Pratto & Bargh, 1991; Wyer, 1973) as well as judgement and decision-making (Carney & Banaji, 2012; Collins & Shanks, 2002; Dennis & Ahn, 2001; Hertwig, Barron, Weber, & Erev, 2004; Hogarth & Einhorn, 1992; Mantonakis, Rodero, Lesschaeve, & Hastie, 2009) have been used to demonstrate how order-effects impact on information acquisition across time. These forms of first impression bias are inferred from patterns of information recall or are otherwise exposed in overt behaviour. However, there is evidence that first impression bias can be observed in neural activity that reflects automatic relevance filtering processes in the brain, a much earlier stage of information processing compared to the previous examples (e.g. Frost et al., 2016; Todd et al., 2011; Todd et al., 2014a). In the present study, we test the hypothesis that the formation and/or maintenance of this bias depends on access to cognitive resources, and therefore would be altered if participants were engaged in a concurrent cognitively demanding task.

The first impression bias to which we refer has been exposed in participants passively listening to sound sequence compositions. Using evoked potentials, we have demonstrated that the amplitude of the response to rare pattern deviations is

impacted by the way the sequence begins (Fitzgerald et al., 2017; Frost et al., 2016; Mullens et al., 2014; Mullens et al., 2016; Todd et al., 2011; Todd et al., 2013; Todd et al., 2017; Todd et al., 2014a; Todd et al., 2014b). The bias is indexed using the amplitude of the mismatch negativity (MMN) component of the auditory event-related potential (ERP). MMN is a negative deflection typically observed at fronto-central scalp sites 100-250 ms following the presentation of a sound that violates a learned regularity (Näätänen et al., 1978; see Näätänen et al., 2011, for review). MMN parameters (amplitude, latency, etc.) are calculated from a difference waveform by subtracting ERPs to pattern-conforming sounds (hereafter referred to as *standards*) from those elicited to pattern-violating sounds (hereafter referred to as *deviants*). Sound information associated with MMN pattern violation detection is said to be represented in the brain by an internal prediction model outlining the likelihood of encountering a sound that conforms to a regular repeating pattern established in the present context (Winkler et al., 1996; Winkler, 2007). In this regard, MMN can be considered a prediction error signal because it is observed when a mismatch between predictions outlined in model content and actual input occurs (Friston, 2005).

MMN amplitude increases with increasing temporal stability of pattern repetition within a sequence and this reflects accumulated “confidence” in the underlying internal model (Winkler, 2007; Winkler & Schröger, 2015). Confidence is used to ‘weight’ or rank the probability for one prediction model to explain a future sound source over another (Winkler, 2007; Winkler & Schröger, 2015). While exposure to a rare model violation always elicits MMN, the system is highly dynamic and repetitions of this same sound will stimulate new learning as indexed by progressively smaller ERPs with each repeat (Winkler et al., 1996; Sams et al.,

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1993; see extension to temporal patterns in Barascud, Pearce, Griffiths, Friston & Chait, 2016). These observations have been interpreted as evidence that learning based on local sound probabilities (i.e. in a single short oddball sequence) rapidly updates internal models to better anticipate future sound experience.

The first impression bias refers to the observation that new learning based on sound transition statistics does not always unfold in a uniform manner as one might predict based on local statistics. Instead, it appears that initial learning has a disproportionate influence over subsequent sound responses in a way that is consistent with predictions based on shorter timescales being constrained by assumptions about how stable sound statistics should be in the current environment (Frost et al., 2016; Todd et al., 2011; Todd et al., 2013; Todd et al., 2017; Todd et al., 2014a; Todd et al., 2014b; Mullens et al., 2014; Mullens et al., 2016).

The bias has been observed in participants presented with a sound sequence containing regular patterning on multiple timescales (coined the *multi-timescale paradigm*; Todd et al., 2011). Sequences comprise two different sounds that are organised into two block-contexts (an example is available in Figure 3.1 in Methods). In one block-context, one sound is a highly probable standard and the other a rare deviant (hereafter referred to as *first deviant*). In the other block-context, sound probabilities switch such that the once rare sound is now probable and the once probable sound is now rare in this new context (hereafter referred to as *second deviant*). In both cases, the rare deviant sounds elicit MMN. The sequences comprise multiple blocks that alternate between these two states, and the block length varies between either shorter or longer durations across two different sequence types, respectively (Todd et al., 2011). This means that patterns can emerge on a dynamic local timescale when a standard is heard repeatedly within each block-context but

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also on a slower timescale when the block-context reliably switches after exposure to the entire stable sequence typically heard first. In the stable sequence, MMN amplitude to first deviants has equivalent amplitude throughout the early and later portions of the block-contexts, while that to the second-deviant begins smaller at the beginning of the block-context and increases over time. This differential pattern of change in MMN amplitude over time has been observed to completely reverse in a subsequent sequence comprising 12 block alternations of shorter length (0.8 min, Todd et al, 2014a).

To explain why these order effects might occur, Todd et al. (2014a) draw upon contemporary models of predictive coding (Friston, 2005; Lieder, Stephan, Daunizeau, Garrido, & Friston, 2013). The explanation relies on two key elements: the existence of hierarchical inference (learning over multiple timescales), and the influence of higher-level predictions over learning-rates at lower levels. Todd et al. (2014a) propose that the brain can learn about both the local sound patterning (recent sound probabilities), and the super-ordinate pattern (the rate of block-context alternations) by accumulating predictions based on regularities present on different timescales. Such ideas have been formalised in Hierarchical Gaussian Filtering (HGF) models of learning under uncertainty. In these models, it is posited that over time the brain can learn not only about local transition contingencies, but also the tendencies in those transition contingencies and furthermore, the likelihood that transition contingencies will change (Mathys, Daunizeau, Friston, & Stephan, 2011; Mathys et al., 2014). The rate of model updating following a prediction error will depend on confidence in predictions (or Bayesian precision) at a given level and the level above. This formulation would stipulate for the multi-timescale paradigm that model updating in the presence of an unexpected event (a deviant tone), will

ultimately be constrained by the modelled likelihood that transition statistics (i.e. tone roles) will change.

Thus, the following explanation of the first impression bias effects on MMN can be proposed: Participants rapidly accumulate high confidence in the model formed at sequence onset (first block-context), and because this is highly stable, they also form a higher-order belief that transition statistics are unlikely to change (Mullens et al. 2016). Model updating and therefore, the rate of learning about transition statistics in the new context is slower because the associated network requires time to overcome this higher-order belief. Over time, confidence in the new context accumulates and MMN amplitude to the second deviant increases. Although these differential patterns may diminish slightly in the second encounter of each block, data suggests the different levels of confidence are reactivated in later encounters (Frost et al, 2016).

Mullens et al. (2016) further tested the assumption described above (Todd et al., 2014a) that cumulative learning over a longer time course enables predictions for longer term regularities in the sequence: i.e., the system should be able to learn that the two different contexts always alternate, and even learn the rate at which they alternate (the block lengths). If this was the case, the system would be ‘surprised’ if a block-context changed earlier or later than expected, thus creating a type of second-order prediction error. When the first-context block ended sooner than predicted in the unstable sequence heard during the second half of the experiment, confidence associated with this context appeared to drop as was attested by the finding that MMN amplitude increased more slowly in this case compared to the reversed (second-deviant) context (Mullens et al., 2016). This interpretation was further supported by the observation that the same reversal in MMN amplitude

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accumulation also occurs in the stable sequence immediately after the twelve-block unstable sequence (i.e., as the first block of the stable sequence violates predictions by changing later than anticipated compared to the preceding unstable sequence). In summary, these distortions of development of the MMN amplitude over time appear to depend on both the tone roles at sequence onset and the large-scale structure of the overall sequence.

The mechanisms of learning proposed to explain the first impression bias require learning of sound structures that emerge over longer timescales (Todd et al., 2014a). Kiebel, Daunizeau and Friston (2008) posit that regularity extraction over different timescales is processed in a rostral-caudal fashion. The PFC is proposed to be involved in encoding the temporally more stable contexts relative to primary sensory areas that are sensitive to rapidly changing transition statistics. This is consistent with data generated in both electrophysiological and neuroimaging studies showing that changes in cortical responsiveness to sound is the result of neural dynamics operating within a temporo-frontal network (Doeller et al., 2003; Giard et al., 1990; Opitz et al., 2002; Rinne et al., 2000). The MMN response receives contributions from both the auditory and the frontal cortex (Alho, 1995; Alho, Woods, Algazi, Knight, & Näätänen, 1994; Baldeweg et al., 1999; Escera et al., 2003; Giard et al., 1990; Näätänen, et al., 1978; Rinne et al. 2000). There is evidence to suggest that the temporal component is activated before the frontal, forging the possibility that the latter is involved in additional processing following sound change (Rinne et al. 2000). Others report that frontal MMN generators facilitate automatic allocation of attentional resources to deviations from the detected regular sound patterning (Escera et al., 2003). Taken together, these findings indicate that the PFC is likely involved in forming predictions about the potential relevance of incoming

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sound input over longer timescales (Kiebel et al., 2008) and/or fine-tuning the distribution of attentional resources to better prepare the network for impending sound change (Opitz et al., 2002).

Although previous studies show that the formation of predictive models based on short-timescale regularities is generally not dependent on attentional capacities (for a detailed discussion, see Sussman, 2007), predictions based on information gleaned over longer time periods might be. In line with early propositions (Desimone, 1996; Maunsell & Treue, 2006), it has more recently been shown that mechanisms of attention are involved in enhancing prediction error signalling during statistical pattern learning in an environment characterised by constant noise and uncertainty (Feldman & Friston, 2010). To date, the multi-timescale paradigm has only been studied when participants hear the sound sequences whilst engaged in a simple task (i.e. watching a DVD with subtitles) that placed relatively low demand on perceptual and cognitive resources. It is not known whether first impression bias in sound information-processing is observed when task demand is increased, therefore reducing access to resources presumably required for sequence learning on multiple timescales.

The aim of the present study was to determine whether first impression bias is dependent on the availability of cognitive resources. Performance on tasks reliant on sustained attention and/or working memory is known to depend on frontal brain areas (Buschman & Miller, 2007; Corbetta & Shulman, 2002; Courtney, Petit, Haxby, & Ungerleider, 1998; Courtney, Petit, Maisog, & Ungerleider, 1998; Fritz, David, Radtke-Schuller, Yin, & Shamma, 2010; Fuster, 1988; Owen, McMillan, Laird, & Bullmore, 2005; Stuss & Benson, 1984). To test this, we compared MMN amplitude modulation in three separate groups: those who heard the multi-timescale

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paradigm while (1) watching a DVD with subtitles (low cognitive demand DVD condition); (2) performing a visual 2-back working memory task (high cognitive demand working memory [WM] condition); or (3) performing an attention-demanding visual inspection time task (high cognitive demand perceptual task [PT] condition). The latter group were included as a means for testing whether first impression bias would be differentially affected by a task that required attention but not WM per se as in the WM condition, compared with a relatively low demand condition. The DVD group reflected typical experimental conditions under which learning biases reliably emerge and was included as a crucial control condition against which the demanding task groups were compared. If first impression bias patterns revealed in MMN amplitude depend on attentional and/or cognitive resources, we expect that participants performing concurrent demanding cognitive tasks would show reduced or absent first impression bias.

3.2 Method

3.2.1 Participants. Participants were 46 healthy community volunteers and undergraduate students from the University of Newcastle, Australia aged 18-34 years. Participants formed three groups, distinguished by the task condition: the *DVD condition* ($n = 14$, 7 female, $M = 25$ years) the *WM condition* ($n = 17$, 10 female, $M = 22$ years) and the *PT condition* ($n = 15$, 11 female, $M = 26$ years). Groups were tested at separate times within the same laboratory. The data from the DVD condition is a subset of data published previously (Todd et al., 2013, Order 2) and is included here for comparison purposes. Recruitment methods and age range of participants was similar across conditions. Volunteers were included if they were between the ages of 18 and 35 years, had normal hearing and were naïve to multi-

timescale sequence exposure. Those meeting these criteria were excluded only if they had a history of head injury, neurological condition, family history of psychosis, or they were currently being treated for mental illness or engaged in alcohol or substance abuse. Remuneration was offered as course credit to students and gift voucher to community volunteers. Written informed consent was obtained from all participants consistent with standards approved by the Human Research Ethics Committee.

3.2.2 Stimuli and Sequences. Figure 3.1 features a schematic illustration of the sound sequences used in this study. Sequences were made up of sound blocks that presented either long-deviant or short-deviant tones. In blocks with long-deviants, 30 ms tones were highly probable standards ($p = .875$) and 60 ms tones were rare deviants ($p = .125$). In blocks with short-deviants, the probabilities of the two tones were reversed (30 ms as deviant and 60 ms as standard presented at $p = .875$ and $.125$, respectively). Blocks were organised into two sequence types. In the stable sequences, sounds were arranged in four blocks with block-type alternating after every 480 tones producing a stable-standard period of 2.4 min. In the unstable sequence, sounds were arranged in twelve blocks with block-type alternating every 160 tones creating a stable-standard period of 0.8 min. Overall tone probability (1920 tones in total, 960 of each duration) and sequence length (9.6 min) were identical across the stable and the unstable sequence. Experimental conditions were equivocal irrespective of task demand conditions that is all participants heard stable followed by unstable sound sequences separated by a 40s period of silence and the longer sound was always heard as the first deviant.

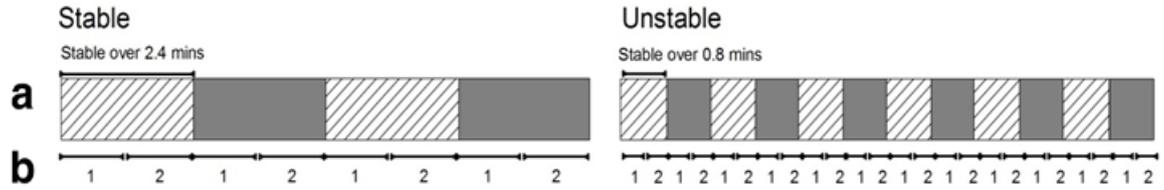


Figure 3.1. Multi-timescale sound sequences and the block halves analysis a. Lined rectangles represent long (first) deviant block-contexts; solid rectangles short (second) deviant block-contexts. b. Sections labelled 1(1st half data) and 2 (2nd half data) show how blocks were divided for halves-analysis as detailed in Todd et al. (2014a).

All tones were 1000 Hz pure tones presented at 75 dB SPL with 5 ms rise/fall times and either a 20 ms or 50 ms pedestal to produce 30 ms and 60 ms sounds, respectively. All sounds were presented binaurally over headphones (Sennheiser HD280pro). Tones were presented at a regular 300 ms stimulus onset-to-onset interval.

3.2.3 Concurrent Task. For all groups, stimuli for the concurrent task were presented on a video monitor (60cm x 34cm) at a viewing distance of approximately 150cm. The concurrent task was always initiated 1 minute before the onset of the auditory stimulation. In the DVD condition, participants viewed a silent movie with subtitles (Todd et al., 2013). Participants in the WM condition were asked to monitor the identity of a series of visual stimuli (a letter of the English alphabet) and respond (by way of button-press) only when the current stimulus was the same as that presented two trials before. For this visual version of the *2-back WM task* (Owen et al., 2005), we used 13 uppercase letters (S, W, P, V, D, B, R, X, E, C, J, K & L) subtending a vertical visual angle of 1.0° and a horizontal visual angle of 1.2°. The letters were white in colour and presented at the centre of a black screen. A white fixation cross (vertical and horizontal visual angles of 5° and 4°, respectively) was presented at the centre of the screen between successive letters. Letters were presented for 500 ms at an average stimulus onset-to-onset interval of 2 s with onsets

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falling between 1.5 - 2.5 s on any given trial (uniform distribution). Each experimental session consisted of 10 practice trials followed by two test blocks separated by a 40 s break. Before testing commenced, a researcher first provided scripted instructions of the *2-back WM task* to each participant. The onset of the task preceded the tones by one second and ran for the full duration of the auditory sequence resulting in the presentation of 158–160 targets (2-back matches) and 408–423 non-targets (2-back mismatches). Task performance (correct and incorrect trials and misses) for both practice and testing sessions was recorded for each participant.

The visual 2-back task requires participants to constantly update information stored in WM to include new information about the most recently presented stimulus while at the same time, ignoring temporally irrelevant stimuli (Owen et al., 2005). This task has been found to robustly activate dorsolateral PFC regions associated with higher-level cognitive processes (Owen et al., 2005) and has no significant impact on MMN amplitude to deviations from simple regularities (e.g., the auditory oddball paradigm with no dynamic changes in the make-up of the sequence; see e.g., Winkler et al., 2003).

The remainder of participants performed a vertical line PT task in which they had to decide whether the left or right line within a visual stimulus was longer. In this task, a centrally positioned fixation cue (a small white plus [+] sign measuring 6.6 mm with vertical and horizontal visual angles of 5° and 4°, respectively) preceded all trials. A trial commenced when this cue was replaced by a stimulus figure consisting of two vertical lines (one 15 mm other 30 mm long) subtending a visual angle of 0.6° and 1.2°, respectively, joined at the top by a horizontal line of approximately 18 mm subtending a visual angle of 1.1°. A flash mask immediately replaced this figure after a visual inspection time of 150 ms, and consisted of two

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vertical lines 35 mm in length, shaped as lightning bolts. The mask was presented for 375 ms. Duration of exposure was not varied as a function of performance to control for task difficulty. On each trial, the participant was required to indicate which line was longer by pressing a left or right button on a game console response pad (equal probability across trials). Participants were told to emphasise accuracy and speed when responding. A stimulus to stimulus trial time of 1250 ms was used for both practice and test trials. PT is demanding on sustained attention with performance reliant on lateral and medial frontal brain areas recruited by the demand of attempting to process a visually degraded percept in addition to a fronto-posterior network that includes sensory areas (Deary et al., 2004).

3.2.4 Procedure. A screening interview was conducted prior to testing to ensure that all participants met inclusion criteria. Next, a pure tone audiometer (Earscan ES3S) was used to assess individual hearing thresholds (≤ 25 dB SPL separately for each ear) across 500-4000 Hz and exclude participants for hearing loss. Participants were fitted with a Neuroscan Quik-Cap hosting tin electrodes. Continuous EEG was recorded using a Synamps 2 Neuroscan system at 1000 Hz sampling rate (high-pass 0.1Hz, low-pass 70 Hz, notch filter 50 Hz and a fixed gain of 2010). The EEG data were collected from 32 electrode locations (Fz, FCz, Cz, CPz, Pz, Oz, FP1, F3, FC3, C3, CP3, P3, O1, FP2, F4, FC4, C4, CP4, P4, O2, F7, FT7, T7, TP7, P7, F8, FT8, T8, TP8 & P8 in accordance with the 10-20 system, plus bilateral mastoids) and referenced to the nose tip. Vertical and horizontal electro-oculogram were also recorded using electrodes placed above and below the left eye, and 1 cm lateral to the outer canthi of both eyes to monitor eye blinks and movement. Electrode impedances were accepted below 5 k Ω . Once a cap was fitted, a researcher provided participants with both verbal and written instructions for completing the session.

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Irrespective of group (DVD, WM, PT), all participants were asked to focus on the instructed task and ignore the sound sequence heard.

For the WM and PT tasks, responses provided during practice sessions were closely monitored and the practice block was repeated if performance was low to maximise engagement during testing. Once participants successfully completed the practice session (response accuracy > 90%), testing commenced and sound sequences were presented over headphones while the participant concurrently completed the task. Participants in the WM and PT groups then completed a two-item post-test questionnaire designed to capture feedback regarding awareness of sound sequence structure. The first item, “Were you aware of any patterning in the sound sequences?”, was formatted as a yes-no question. The second question enquired, “If YES, please briefly describe what you noticed about the sounds”. The questionnaire took approximately 5 min to complete. Data regarding sequence awareness were not obtained for the DVD group.

3.2.5 Data Analysis. Participant performance for the WM task was measured to ensure that all participants were engaged in the task and was quantified using standard signal detection measures including hit-rate (correct 2-back target) and false-alarm rate (target stimulus response to non-target stimulus) percentages. For PT data, line length discrimination performance was measured by examining the percentage of correct responses and errors (including both commission and omission types). The response to the sequence awareness question was coded (0 – not aware, 1 – aware) to calculate percentage of yes/no responses.

For all groups, continuous EEG recording was examined offline to correct for major artefact and eye blinks using procedures in Neuroscan (4.5) Edit Software: regression analysis in addition to artefact averaging was applied (Semlich, Anderer,

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Schuster, & Presslich, 1986). The average eyeblink artefact response algorithm was assessed for suitability (> 30 samples with < 5% variance in samples contributing to the average) and applied to the continuous data set to maximise data quality and remove unwanted noise. Each data set was epoched from 50 ms pre-stimulus to 300 ms post-stimulus. Epochs with a voltage change that exceeded $\pm 70 \mu\text{V}$ were excluded. Separate averages were created for responses to the standard and deviant tones for the early (first-half) and later (second-half) portions of the stable and unstable sequences in line with the methods previously established in our group (Todd et al., 2014a). The first five standards in a block and the first standard after each deviant were excluded from averages to control for ERPs affected by a recent stimulus change (Sams et al., 1983). The practice of combining data from the first half versus second half of a block is used to emphasise differences in MMN amplitude at transition points (i.e. period after block-contexts/tone roles alternate) compared to later periods when the roles have been stable for some time, respectively. From this follows that a maximum of 60 epochs are included in an average deviant-stimulus response. In the present study, the minimum number of epochs contributing to an average for any participant was 45 with the mean between 55 and 58 for all deviant waveforms. Average ERPs were digitally filtered with a 30 Hz low-pass filter to exclude high frequency noise.

Difference waveforms were created by subtracting the ERP to a sound when presented as a standard from the ERP to that same sound when presented as a deviant in the corresponding sequence, block, and half. Quantification of MMN amplitude was achieved by extracting the mean peak amplitude over a 20 ms period centred on the most negative point in the difference waveform within the 150-250 ms post-stimulus interval. This facilitated a reliable measure for capturing the peak

amplitude (Kujala et al., 2007). Right frontal (F4) MMN measures were compared in a mixed model ANOVA with sequence (stable, unstable), deviant (first deviant, second deviant) and half (first half, second half) as within-subject variables and condition (DVD group, WM group, PT group,) as a between-subject variable. The alpha level was set at .05; η^2 effect sizes are shown. All significant main effects and interactions are described.

3.3 Results

3.3.1 WM and PT Task Performance. Mean hit- and false-alarm rates for the 2-back task were 76.5% (range: 41-92%) and 3% (range: 1-7%), respectively. Two participants maintained relatively low hit-rate scores (41% and 47%) but were not excluded due to low false-alarm rates indicating that neither person was responding in a random fashion. All other participants demonstrated high hit-rates and low false-alarm rates. In the PT task, the mean hit rate was 90.7% (range: 76-98%) and the error rate 6.5% (range: 1-14%). Taken together, assessment of task performance indicated that all participants were sufficiently engaged in the instructed task.

3.3.2 Mismatch Negativity. The deviant minus standard difference waveforms for the DVD, WM and PT group are presented in Figures 3.2. The omnibus mixed model ANOVA produced main effects of sequence (stable > unstable, $F(1, 43) = 31.52, p < .001, \eta^2 = .42$), block half (second half > first half, $F(1, 43) = 39.49, p < .001, \eta^2 = .48$), deviant (first > second, $F(1, 43) = 12.25, p < .01, \eta^2 = .22$) and group (DVD < WM, PT, $F(1, 43) = 4.43, p < .05, \eta^2 = .17$). However, these main effects were subject to modification by a significant group x sequence x half x tone interaction ($F(2, 43) = 3.70, p < .05, \eta^2 = .15$). Additional analyses were therefore conducted to explore precisely how MMN amplitude patterns differed between groups.

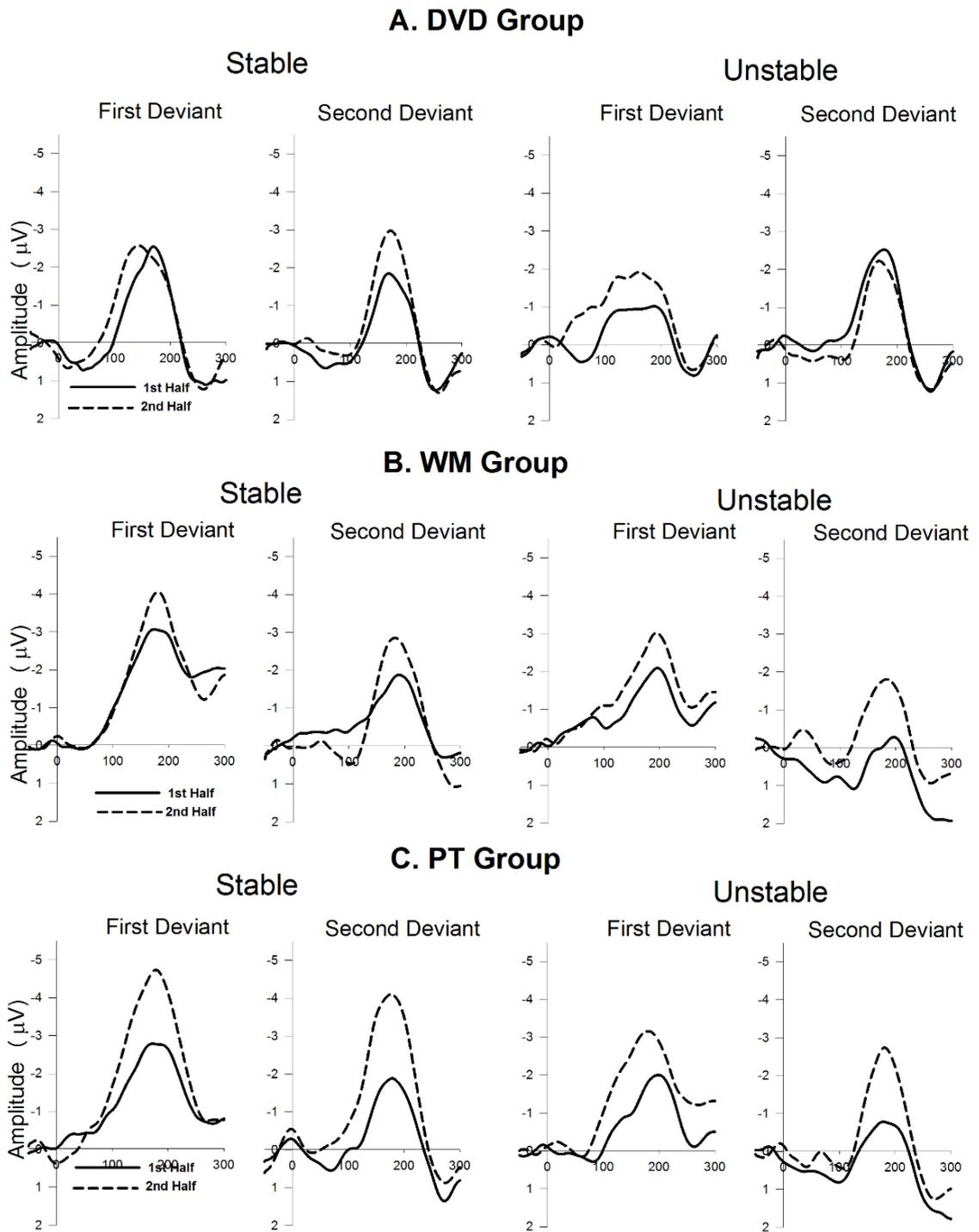


Figure 3.2. MMN difference waveforms separated by task demand. A. DVD group (undemanding conditions), B. WM group, and C. PT group for the first (60ms; left within panel), and second (30ms; right within panel) deviants for the stable (top left panel) and unstable (top right panel) sound sequences. The MMN waveforms for data obtained in the 1st half (solid lines) and 2nd half (broken lines) of the sound blocks are over-plotted.

The DVD group displays the MMN modulation patterns typical of the first impression bias. Although there is a main effect of half overall (second half > first half, $F(1, 13) = 6.02, p < .05, \eta^2 = .32$), this is modified by a significant sequence x

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deviant x half interaction ($F(1, 13) = 7.75, p < .05, \eta^2 = .37$). In the stable sequence, the deviant MMN was modulated differently by half for the two deviants ($F(1, 13) = 4.72, p < .05, \eta^2 = .27$) – increasing over time for the second deviant ($t_{13} = 3.03, p < .05$) but not for the first. In the unstable sequence, the opposite trend was present ($F(1, 13) = 3.84, p = .07, \eta^2 = .23$) with MMN increasing over time for the first deviant ($t_{13} = 3.11, p < .05$) but not the second.

These MMN modulation patterns tended to differ from those in both the WM and PT groups with the sequence x deviant x half interaction significantly modified by group in the DVD/WM comparison ($F(1, 29) = 7.63, p < .01, \eta^2 = .21$) and marginally in the DVD/PT comparison ($F(1, 27) = 3.57, p = .07, \eta^2 = .12$). The pattern of MMN modulation did not however differ between the WM and PT groups. Visual inspection of Figures 3.3 and 3.4 show that in those performing the WM and PT tasks, MMN amplitudes elicited by first and second deviants appeared to increase from the first to the second half of the stimulus blocks in both stable and unstable sequences. This was confirmed when these two groups were compared in a mixed model ANOVA with the analysis producing a significant effect of sequence (stable > unstable, $F(1, 29) = 16.30, p < .001, \eta^2 = .36$) half (second half > first half, $F(1, 29) = 16.34, p < .001, \eta^2 = .36$) and deviant (first deviant > second deviant, $F(1, 29) = 6.08, p < .05, \eta^2 = .17$) but no significant interactions. MMN amplitude increased with increasing stability, both in terms of a stable > unstable and second half > first half MMN amplitude. For completeness, we note that the main effects of sequence, half, and deviant were significant within both the WM ($F(1, 16) = 26.62, p < .001, \eta^2 = .63$; $F(1, 16) = 11.12, p < .01, \eta^2 = .41$; $F(1, 16) = 14.14, p < .01, \eta^2 = .47$, respectively) and the PT group ($F(1, 14) = 16.32, p < .01, \eta^2 = .54$; $F(1, 14) = 26.02, p < .001, \eta^2 = .65$; $F(1, 14) = 7.52, p < .05, \eta^2 = .35$, respectively) with no

significant interactions present in either group. Separate analyses of the standard and deviant responses revealed that amplitude effects in the MMN difference waveform were reliant on responses to deviants only (see Appendix 3).

3.3.2 Participant Awareness. In the WM condition, all but three participants reported that they were aware of sound patterning. However, they were not fully able to articulate exactly what type of sound patterning they heard. Of the 14 participants who reported sequence awareness, 12 did not provide a description of what they heard. One person provided a description that indicated some awareness of patterning stating, *“The sounds had a pattern of low frequency clicks followed by high frequency beep. Sometimes it would switch with high frequency beeps followed by one low frequency beep”*. Similar reports were made by those who completed the PT task. There were eight out of 15 participants who indicated they were aware of sound patterning though did not fully describe actual sequence structure in detail (e.g. *“Long sounds and short sounds”*, *“Rapid paced quick sounds with a short interval between each”*).

3.4. Discussion

The first impression bias observed under passive listening conditions was absent in those who performed either a WM or a PT task. Groups that performed these tasks did not show differential patterns of MMN amplitude to the first and second deviant tones in the stable and unstable sound sequences. Instead, MMN to both deviants was modulated in the same way, increasing over time with increasing period of local pattern stability. That is, MMN showed characteristics of a system fully governed by local transitional probabilities (see, e.g., Mittag, Takegata, Winkler, 2016). Both the WM and the PT task were similarly effective in cancelling out the first impression bias evident in those who simply watched a DVD with

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subtitles. These data provide compelling evidence that the presence of first impression bias is dependent upon some capacities that can be taken away by the cognitive demands of a task concurrent to the sound sequences. Below we discuss how concurrent task demand might interact with the mechanisms thought to be responsible for the bias.

Our proposition has been that the bias is reliant on 1) learning the large-scale structure of the first encountered sequence and 2) assumptions about its stability. These identify two entry points for a concurrent task to interrupt the first impression bias. One pathway is through preventing the system from learning the longer-term structure of the sound sequences. Indirect support for this pathway comes from a recent study in which the four stable sequence blocks and twelve unstable sequence blocks used in the current study were presented in a pseudorandom order with no fixed large-scale temporal structure (Todd, et al., 2017a). Participants heard this sequence under the same conditions as the DVD group did in the current study, and yet the data resembled those obtained in the WM and PT groups: i.e., no first impression bias while MMN amplitude increased with local stability for both first and second deviants (Todd, et al., 2017a). It is therefore possible that whenever there is either no higher-order longer-term predictability in the sequence (as in Todd et al., 2017a), or reduced capacity to learn this structure (as in WM & PT groups in the present study), only the local stability affects the MMN amplitude.

As reviewed in the introduction, the frontal cortices are implicated as being essential for an inferential network that allows us to extrapolate patterns occurring over longer timeframes (Kiebel et al., 2008). Given the proposed reliance of the bias on this longer-term learning, any reduction in access to resources that could support this type of learning could explain its disruption. This is in-line with findings

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showing that MMN amplitude to rare deviants in simple oddball paradigms decreases with increasing task demands, particularly if processing resources within the same auditory modality (versus visual) are simultaneously allocated to sound sequence processing (Dittmann-Balcar et al., 1999). Although the present study does not include explicit measures of PFC engagement, prior neuroimaging studies have demonstrated WM task performance to be reliant on this region (Buschman & Miller, 2007; Corbetta & Shulman, 2002; Courtney, Petit, Haxby, & Ungerleider, 1998; Courtney, Petit, Maisog, & Ungerleider, 1998; Fritz, David, Radtke-Schuller, Yin, & Shamma, 2010; Fuster, 1988; Owen, McMillan, Laird, & Bullmore, 2005; Stuss & Benson, 1984). There is also evidence showing engagement of frontal cortical areas in participants performing a PT task like the one used in the present study (Deary et al., 2004; Waiter et al., 2008; Waiter et al., 2009). Yet, it remains unclear as to what extent different MMN generators (e.g. frontal versus temporal) contribute to MMN modulation in active stimulus processing of patterning and associated violations on shorter and increasing timescales.

A second possibility is that the commencement of the attention-demanding task prior to the onset of sounds dampens or prevents the influence of initial sequence structure by strongly directing limited attention resources away from sound input. Although the group watching the DVD are instructed to ignore the sounds presented, there is no consequence for not filtering the sounds out of the focus of attention effectively. In contrast, suboptimal filtering during selective attention to visual stimuli appearing for only a short time by the WM and PT group would have negatively impacted their task performance. It is therefore possible that access to attention resources was more effectively gated in the WM and PT groups, in turn altering the encoding of the large-scale sequence structure of the first tone sequence.

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Access to attention resources was presumably reduced throughout the WM and PT tasks relative to the DVD task, consistent with the high level of task performance.

Within a hierarchical predictive coding system, attention increases the precision weighting assigned to models and thus modulate the system's response to both expected and unexpected stimuli (Auksztulewicz & Friston, 2015; Feldman & Friston, 2010; Kok & De Lange, 2015; Schröger et al., 2015). If high confidence/precision being assigned to the internal model of the first context is a critical determinant of first impression bias, its absence in the WM and PT groups could reflect reduced access to this source of modulation. This suggestion is consistent with the observation that MMN elicited to the first deviant in these groups starts at lower amplitude and increases over time rather than assuming its maximal amplitude already in the first-half of stable blocks as observed in the DVD group both in this study and in previous studies. Attention resources may therefore be critical not only to learning at the start of a new context, but also to the maintenance of differential precision weightings that contributes to the longevity of the resulting bias effect.

Finally, although we consider it unlikely, the present data do not necessarily exclude the possibility that the higher-order structure was learned together with its first-encounter based confidence/precision, but that access to attention resources is required for MMN amplitude to be affected. The attention-dependent augmentation of high-level prediction-errors involves the basal forebrain (Colder, 2015; Doya, 2002; Iglesias et al, 2013; Sarter, Bruno, & Turchi, 1999; Sarter, Parik, & Howe, 2009; Yu & Dayan, 2002, 2005). If this mechanism has limited capacity, and this capacity is reserved for the primary task, the pathway to express modulation based on longer-term pattern extraction may be limited. However, we consider it more

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likely that the deprivation of attention resources interfered with learning about sequence structure generally, leaving only the local deviance sensitivity and stability effects intact.

Two additional observations of the data tangential to primary hypotheses should also be discussed. Firstly, both the WM and PT group produce an overall effect of deviant where MMN is larger to the first deviant tone. This order effect is of course confounded with tone property as the first deviant was always the longer tone. It has previously been shown that larger MMN is elicited by long duration deviants compared with short duration deviants (Catts, Shelley, Ward, & Liebert, 1995; Jaramillo, Alku & Paavilainen, 1999; Jaramillo, Paavilainen & Naatanen, 2000; Naatanen, Paavilainen & Reinikainen, 1989). Sounds of short duration can be subject to loudness summation, which is the tendency for longer sounds to be perceived as louder relative to shorter sounds (<150 ms; Scharf, 1978; Zwislocki, 1969). Further, rare long duration tones have two points of deviance; the point at which they exceed the short tone duration (in this case at 30 ms) and the accumulated difference at the point at which they cease (in this case 60 ms). It is therefore possible that the first deviant MMN is larger overall in these groups because of the asymmetry in the changes from short-to-long versus long-to-short contexts.

However, earlier work by our group challenges this interpretation. Mullens et al (2014) exposed participants to the same multi-timescale paradigm as that used here, but there were three pairs of stable and unstable sequences with the first deviant changing from the long tone in the first pair, to the short tone in the second pair, and finally back to the long tone in the third pair. Participants completed a task with the tones before hearing the multi timescale paradigm under passive listening

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DVD task conditions. In the task, the short and long tones were presented randomly with equal probability. One group were asked to respond with a button press only to the short tones (short target group), and the other to the long tones (long target group). There was no first impression bias evident in the first sequence pair, but the bias appeared in the second pair for the short target group (this pair had the short tone as first deviant), and for the third pair for the long target group (this pair had the long tone as first deviant). So, the bias eventually returned when the first deviant was the target in the prior task. Importantly, when the bias returned, MMN amplitude was larger overall to the first deviant tone regardless of whether the tone was short (within the short target group) or long (within the long target group). This finding is consistent with the notion that the mechanisms of bias interact with perceived stimulus relevance in the longer term. If that is the case, it remains possible that the first>second deviant MMN in the WM and PT groups reflects the presence of a simpler form of order-effect remaining in the data – that is, the perception of potentially higher information value for the first deviant tone.

Finally, the observation that MMN amplitude was overall smaller in the DVD group relative to both the WM and PT groups is inconsistent with previous studies that have explored the effect of concurrent task as a within-subjects' manipulation (see Wiens, Szychowska, & Nilsson, 2016). MMN amplitudes observed in the DVD group are however like those reported in previous published studies using the same paradigm (e.g., Mullens et al., 2014, 2016) and we consider it likely that these group differences reflect coincidental sampling differences. In terms of limitations, it is possible that the sample sizes used in the present study are underpowered. Indeed, this may explain why the PT task did not emerge as a statistically significant modifier of the sequence by tone by half interaction when

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comparisons were made with those who watched a DVD only, though a trend in this direction was observed. The sample reproduced here from Todd et al.'s (2014a) study was specifically selected because the overall participant number is of a comparable size relative to both the WM and PT groups thereby mitigating effects of inequality of variances associated with unequivocal sample sizes. The sequence by deviant by half interaction within the DVD group has a large effect size suggesting that the WM and PT groups should have had sufficient power to show the effect if the same influences were present. Although this is the first study in which the multi-timescale paradigm was presented simultaneously with a cognitively demanding task, typical patterns of first impression bias have been detected in samples as small as 11 (Todd et al., 2013) and were robust when a substantially larger group of participants was tested ($n = 35$; Frost et al., 2016 or see Chapter 2, Study 1). Nevertheless, incorporating a larger sample size for each group would likely strengthen the present results.

In summary, the results provide empirical support that first impression bias reflects a hierarchical inference process that is no longer observed when access to higher-level network resources is compromised by a demanding concurrent task. The study employed an experimental manipulation to test the hypothesis that the bias would show sensitivity to the availability of cognitive resources. Our hypotheses regarding exactly how the bias is impacted by reduced access to brain areas required for longer-term learning and/or attention resources remain speculative, and invite further exploration using tools that can disentangle the likely mechanisms.

In conclusion, the present data add to a body of work that indicates that local relevance filtering based on dynamic models of statistical input is robust to participant engagement in a concurrent cognitively demanding task in the sense that

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MMN is reliably elicited to sound characteristics that are locally improbable. However, MMN amplitude is clearly modulated by influences that appear to reflect learning over much longer timescales (Frost et al., 2016; Mullens et al., 2014; Mullens et al., 2016; Todd, Provost et al., 2013; Todd et al., 2014a; Todd et al., 2014b; Todd et al., 2017a, 2017b) that are shown here to be sensitive to manipulation of available resources. This conclusion is in line with the currently widely accepted views regarding the role of attention in MMN elicitation (Auksztulewicz & Friston, 2015; Sussman, 2007). The results also contribute to our argument that differential modulation of MMN amplitude seen in the multi-timescale paradigm cannot be explained by local effects, such as SSA (for discussion see Frost et al., 2016, Mullens et al., 2016, Todd et al., 2017b; also see **Chapter 1, 1.3.1 Early Accounts of MMN** of this thesis). The present study provides additional, albeit indirect, support for a network model of the underlying learning system in which different timescales of information may be reliant on different levels of a cortical hierarchy, and that this learning and implementation is resource intensive. These findings also imply that attention-based modulation of MMN may be an important driver of the first impression bias effects.

Chapter 4: Foreknowledge about the auditory environment abolishes first impression learning bias

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Study Motivation

We hypothesize that learning biases arise because the system relies on a strong first impression about tone roles and when these roles will change to evaluate surprise in relation to model-based predictions during multi-timescale sequence processing. If so, then first informing participants about sequence structures should eliminate the surprise generated when these patterns are violated. To test this, we recruited naïve participants who had never heard the multi-timescale sequence. Study conditions were equal to typical experimental protocols with one important exception. We explicitly told participants about the local and superordinate pattern structures before presenting sound sequences. Foreknowledge reduced or eliminated surprise about when tone roles changed but not when a first-order pattern violation about the relative informative value of sound probabilities occurred. Results are interpreted with caution due to experimental limitations. Tentatively speaking however, we think these data provide yet another striking example of dynamic top-down modulation over sound processing by cognitive brain areas that determines how the brain accomplishes sound sequence learning over time.

4.1. Introduction

The human brain is remarkably apt at extracting simple and abstract rules from explicit instruction and applying this information during frank experiential learning (Ruge & Wolfensteller, 2010). Such a feat presumably relies on successful processing of foreknowledge from a highly abstract, potentially verbally encoded sound representation toward a more ‘experience-based’ representation (Nakayama, Yamagata, Tanji, & Hoshi, 2008; Sussman et al., 2002). This allows us to compare explicit knowledge with actual experience and quickly adapt to fluctuating environmental demands. In this study, we used the MMN error response signal to investigate whether explicit foreknowledge about sound sequences alters a strong first impression learning bias that can be traced to the very first encounter with sound probabilities and their stability. We achieved this by first informing participants about the local and global characteristics of sound patterning on short and long timescales, respectively, before presenting multi-timescale sequences. Here we present evidence showing that prior knowledge about sound structures alters first impression bias effects on MMN when sequences are heard.

Todd et al., (2014) discuss elsewhere why a first impression is formed stating that a regular versus rare sound at sequence onset is evaluated for information value. We have also discussed this in depth across previous chapters of this thesis (pg. 56-58, 111). The predicted nature of the standard tone in the absence of an ecologically-relevant linked consequence results in high-confidence (i.e. precision) that this sound is less important. In comparison, the information value of the rare pattern-violating deviant is unknown and potentially more salient because it signals that the environment may have changed. The respective information values are modelled with high-confidence in the context of a stable environment indicating that tone roles

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are unlikely to change. The result is the formation of a robust precision-weighted first impression that impacts how predictions about each sound are modelled as the multi-timescale sequence unfolds. To date, first impression bias has only been studied in participants who have never heard and know nothing about sound transition statistics or overarching temporal structures embedded within the multi-timescale sequences. Yet, Todd et al.'s (2014) explanation implies that the bias should not occur if participants have foreknowledge about sequence structures that negates relative information value and stability of transitional probabilities at sequence onset within the broader context of the over-arching sequence design.

Here we further test the hypothesis that this learning bias can be traced to learning probabilistic information about the differential relevance of sound transition statistics and their stability at sequence onset (Todd et al., 2013). We use the multi-timescale paradigm comprising block-contexts with two different duration tones that switch probabilities as the common “standard” ($p = 0.875$) and rare “deviant” event ($p = 0.125$) every 2.4 min then every 0.8 min across stable and unstable sequences, respectively. We propose that differential patterns in MMN modulation depend on assumptions formed at sequence onset about 1) sound information value, and 2) how stable transition statistics defining information value should be based on the very first encounter. If this is the case, then accurate foreknowledge about sequence structures prior to exposure should alter or eliminate first impression bias because the network is less “surprised” when tones reverse roles and/or when block-contexts start alternating faster in the unstable sequence. If this is not the case, we expect learning bias patterns to be uninterrupted by sequence foreknowledge.

4.2. Method

4.2.1. Participants. Participants were 15 (10 female, 18-37 years, mean = 22 years, SD = 4.8 years) healthy community volunteers or undergraduate students from the University of Newcastle, Australia. Volunteers met inclusion criteria if they were aged 18-35 years, had normal hearing and were naïve to multi-timescale sequence exposure. Those meeting criteria were excluded if they reported on a history of head injury or neurological disorder, current diagnosis or treatment of mental illness, family history of psychosis or heavy alcohol/substance use. Remuneration was offered as course credit to students and cash reimbursement to community volunteers. Written informed consent was obtained from all participants consistent with standards approved by the Human Research Ethics Committee, University of Newcastle.

4.2.2. The Multi-timescale Paradigm. In accordance with earlier studies (Frost, Winkler, Provost, & Todd, 2015; Mullens et al., 2014; Todd, Provost, & Cooper, 2011; Todd, Provost, Whitson, Cooper, & Heathcote, 2013; Todd et al., 2014a; Todd et al., 2014b) and those experimental protocols presented in Chapters 1 (pg. 48-51), 2 (Study 1, pg. 69) and 3 (pg. 97), participants heard the multi-timescale paradigm binaurally over headphones (Sennheiser HD280pro; see Figure 4.1). Participants always heard the stable before unstable sound sequence separated by 40 sec of silence and the long 60ms deviant was always heard first.

4.2.3. Procedure. Participants were first interviewed to screen for exclusion criteria. This included an audiometric assessment that was administered using a pure tone audiometer (Earscan ES3S) to exclude for hearing loss and establish individual hearing thresholds (≤ 25 dB SPL) across 500 Hz -4000 Hz. Suitable participants were then fitted with a Neuroscan Quik-Cap comprising tin electrodes. Continuous

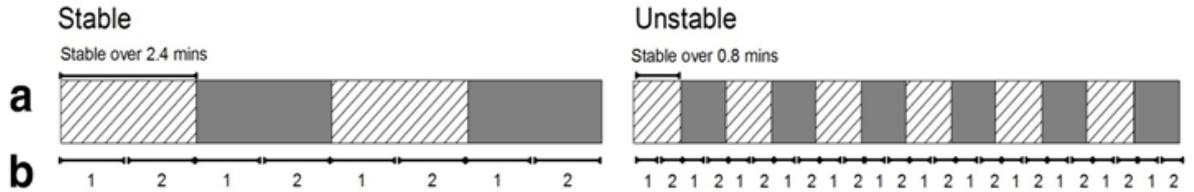


Figure 4.1. Diagram illustrating the multi-timescale design (Todd et al., 2013a) a In the contexts marked with diagonal lines, the 60 ms sound was the rare deviant ($p = 0.125$) and the (30 ms) sound was the regular standard ($p = .875$). In the contexts marked in grey, the probabilities (i.e. tone roles) were reversed. The context length within stable and unstable sequences were 2.4 and 0.8 min respectively, creating a difference of stability in the relative tone roles b Sections labelled 1 (1st half data) and 2 (2nd half data) show how sound contexts were divided for halves-analysis as detailed in Todd et al. (2013a).

EEG was recorded on a Synamps 2 Neuroscan system at 1000 Hz sampling rate (highpass 0.1 Hz, lowpass 70 Hz, notch filter 50 Hz and a fixed gain of 2010). The EEG data were collected from 32 electrode scalp sites (FZ, FCZ, CZ, CPZ, PZ, OZ, FP1, F3, FC3, C3, CP3, P3, O1, FP2, F4, FC4, C4, CP4, P4, O2, F7, FT7, T7, TP7, P7, F8, FT8, T8, TP8 & P8 in accordance with the 10-20 system, including left & right mastoids) and referenced to the nose tip. Vertical and horizontal electro-oculograms were also recorded using electrodes placed above and below the left eye, and 1cm from the outermost canthus of each eye to monitor eye blinks and movement. Impedances were reduced to below 5 k Ω .

Immediately prior to multi-timescale sequence exposure, participants were shown an image of the sound sequences identical whilst a researcher verbally conveyed a standardised script (see Appendix 4 for sequence image & script) informing each person on local and superordinate sequence structures. In short, participants were told that a long and a short sound would alternate roles as a repetitive standard and rare deviant at slow (2.4 min) then fast (0.8 min) speeds. The multi-timescale sequence was then presented over headphones as the participant viewed a film of neutral content with sub-titles (sound muted). All participants were asked to ignore sounds and focus on the film. After the sequences were played,

participants were given approximately 5 min to complete a post-test questionnaire to assess awareness of auditory tones and sequence structures. The questionnaire was made up of two items. Item one, “How aware were you of the patterning in the sound sequence”, required participants to choose one of three response options (Not Aware, A Little Aware, or Fully Aware). Item one was followed by a second question namely, “If YES, please briefly describe what you noticed about the sounds”. Participants were encouraged to provide a response if they reported being aware of sequence structure however this was optional.

4.2.4 Data Analysis. The continuous EEG recording was examined offline to correct for major artefact and eye blinks using procedures in Neuroscan (4.5) Edit Software. Using this technique, a regression analysis in addition to artefact averaging was applied (Semlich, Anderer, Schuster, & Presslich, 1986). Output values were then assessed for suitability (> 30 sweeps in the average and $< 5\%$ variance) and applied to the continuous data set. Each data set was epoched from 50 - 300 ms pre- and post-stimulus, respectively. Epochs were baseline corrected to the pre-stimulus interval and averaged depending on stimulus type. Any epoch comprising variations that exceeded $\pm 70 \mu\text{V}$ were not included for analysis. All standard and deviant ERPs were digitally filtered with a 30 Hz low-pass filter.

Standard and deviant ERPs were averaged separately for the period corresponding to the first-half of block-contexts which immediately followed point when tone roles switched, and 2) the second-half of blocks-contexts when tone-roles have been stable for some time in comparison (see Figure 4.1b). This analysis is the crucial comparison as we have consistently shown that evidence of first impression bias is maximal immediately after tone roles switch relative to the period before roles switch (Frost et al., 2015; Todd et al., 2014). Difference waveforms were

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created by subtracting the ERP to a sound when presented as a standard in any given block-context period (i.e. first or second half) from the ERP to that same sound when presented as a deviant in the corresponding block-context period for each sequence. Sequence awareness data generated from responses to item one was merged into either aware (Fully or A Little Aware data combined) prior to analysis and examined by plotting the distribution (%) of responses (0 – not aware, 1 – aware). The minimum sweeps contributing to an average for any participant was 45 with the mean between 57 and 58 for all deviant waveforms. Standard and deviant ERPs for the period equating to the first- versus second-half of sound block-contexts for each tone, in each sequence were generated to calculate MMN difference waveforms.

Mean amplitude for standard ERPs was extracted over two time windows occurring after stimulus onset. The first corresponded to the window used to define repetition positivity (50-150 ms) and the second to isolate differences over the P2 period (140-170 ms). Mean-peak deviant ERP and difference waveform amplitudes were quantified as the maximum negativity over a 20 ms period centred on the most negative point (70-270 ms) following stimulus onset. This allowed for a reliable measure of the peak amplitude (Kujala et al., 2007) and resulted in eight MMN difference waveforms. The first five standards in a sound block and the first standard after each deviant were excluded to control for ERPs affected by a recent stimulus change (Sams et al., 1984). Standard and deviant ERPs and difference waveform amplitudes were compared separately in a repeated measures ANOVA at F4 with sequence (stable, unstable), deviant (first deviant, second deviant) and half (first, second) as within-subject factors.

4.3. Results

4.3.1. Participant Awareness. All participants reported awareness of sound sequence patterning as indicated by a yes response to item one as well as a

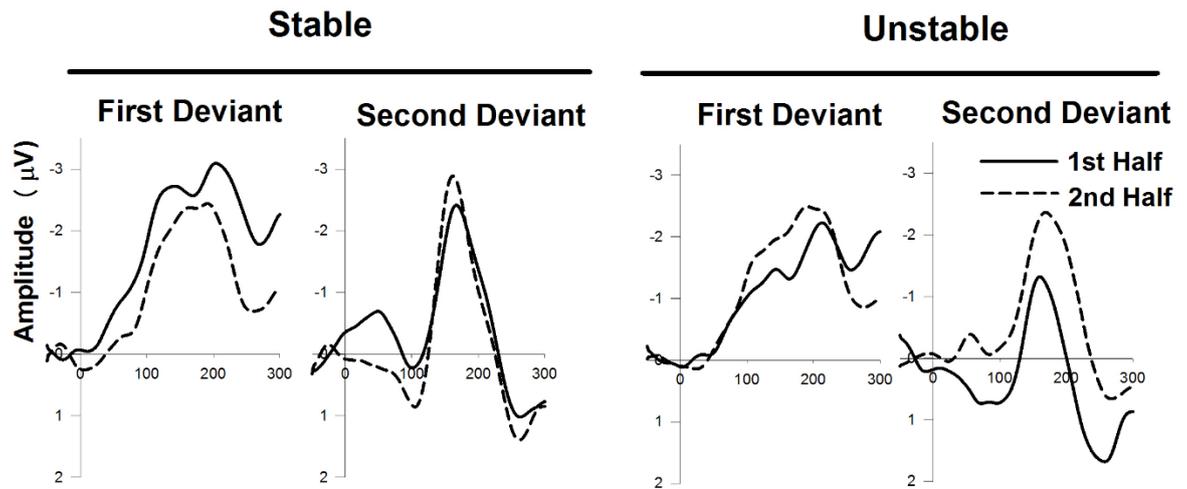


Figure 4.2. MMN difference waveforms to the first (60ms) and second (30ms) deviant tone for A. Stable and B. Unstable sound sequences. The MMN waveforms for data obtained in the 1st half (filled lines) and 2nd half (broken lines) of sound block-contexts are displayed. In contrast to statistical evidence of first impression bias (significant half x tone x sequence stability interaction), no differential effect of sequences stability on MMN size to each deviant sound was observed.

description of what was heard. Three participants provided a description that indicated some awareness of sound patterning (e.g. “*The sounds alternated between two lengths one short one long. Sequences of mostly short sounds with rare long sounds, and sequences of mostly long sound with rare*”). However, most participants (80%) were not able to articulate the patterning based on the description structure (e.g. “*I didn't notice the pattern too much. I could not tell how much time was going by either. Overall I would say that the sounds were noticeable but I was not fully aware*”).

4.3.2. The Mismatch Negativity. Difference waveforms for both deviant types in stable and unstable sequences across block-context halves are presented in Figure 4.2. MMN was elicited to both first and second deviant across block-context halves of stable and unstable sequences. Repeated measures analysis showed that MMN was larger for the first relative to second deviant only ($F(1, 14) = 6.41, p < .05, \eta^2 = .314$). No other main effects or interactions were observed indicating that typical first impression bias effects on MMN were not observed when foreknowledge about

sequence structure was first provided before sounds were heard. Standard and deviant analyses are present in Appendix 5

4.4 Discussion

In previous first-impression bias studies, we present the multi-timescale paradigm to participants naïve to sequences without informing them about sequence composition and ask them to ignore the sounds (e.g. Fitzgerald et al., 2017; Frost et al., 2016; Mullens et al., 2014; Mullens et al., 2016; Todd et al., 2011; Todd et al., 2013; Todd et al., 2014). In this experiment, conditions were identical except that we first provided participants with information about sound patterning and change emerging at shorter and longer timescales, respectively. It was anticipated that foreknowledge could attenuate or even eliminate first impressions based on information value and the element of “surprise” generated when tone roles match those presented at sequence onset as well as when tones reverse roles earlier than expected once the very first sound block-context in the unstable sequence is heard. The data are consistent with these hypotheses in that they do not replicate the bias pattern observed previously. In brief, MMN was larger to the first relative to second deviant tone. Neither half nor deviant type was modified by sequence stability indicating that relatively high-precision estimates about tone role stability are maintained even when tones started switching faster in the unstable sequence.

We propose that, in the absence of foreknowledge about future input, the network relies on direct experience with sound contingencies and their stability at sequence onset to ‘lock in’ a first impression that transition statistics underlying differential information value are unlikely to change (Frost et al., 2016; Todd et al., 2011; Todd et al., 2014). If so, an ‘explicit prior’ holding information about potential

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causes of future states on increasing temporal scales could explain its disruption when it reliably informs the perceiver on exactly what will be heard in future.

Mullens et al., (2014) used the multi-timescale paradigm to show how an existing prior could impact inferential learning in sound sequence processing (Mullens et al., 2014). The authors manipulated the behavioural relevance of tones by instructing participants to respond to one sound feature (i.e. short vs. long duration sound) to determine whether this impacted order-driven learning bias. The bias was indeed prevented (i.e., MMN to both sounds affected in the same way by sequence stability) if participants initially performed a task in which the sounds are heard with equal probability. These data together with the present findings clearly show that we can experimentally remove the bias by explicitly creating a prior that counters the first-impression of difference in standard and deviant probabilities and their stability embedded within the multi-timescale paradigm.

The proposition that an explicit prior disrupts first-impression bias is in accordance with hierarchical learning processes and rests on the assumption that using probabilistic information to create a ‘prior’ provides a frame of reference against which impending surprise is quantified (Friston, 2005, 2012). Higher-order brain areas utilise contextual information over the longer term to modulate the degree to which dynamic changes in the shorter-term impact error signalling in learning. The presence of an explicit prior might interrupt first impression learning bias because the network is “less surprised” when structural patterning on multiple timescales eventually emerges and conforms to inferences formed indirectly through foreknowledge. Given that the learning of rules based on overt verbal instruction is typically adaptive (Doll, Jakobs, Sanfey, & Frank, 2009; Galizio, 1979; Hayes et al., 1986; Hayes, 1993), keeping an explicit prior active for the purposes of directly

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testing its veracity against environmental causes seems a worthwhile strategy for optimising efficiency in a network constrained by limited resources. This is in line with functional imaging data showing that utilising prior information in the MMN sequence learning process is attributable to top-down modulation over auditory cortical areas (Schröger, 1997; Sussman et al., 2002). Utilising an explicit prior based on foreknowledge may therefore exploit the ensuing computational efficiency during direct sequence exposure in what is a resource-intensive process (i.e. *the free energy principle*; Friston, 2005).

The proposition that the bias emerges when the associated inferential hierarchy deems first learning, and the wider context in which learning occurs, a benchmark for measuring surprise identifies two, and perhaps overlapping, entry points for an explicit prior to interfere with this process. First, an explicit prior pre-empts automatic allocation of differential information value based on the initial encounter with sound probabilities and their stability that subsequently biases learning thereafter under naïve conditions (Frost et al., 2016; Todd et al., 2014). If so, associated inferences are ‘blocked’ when foreknowledge about sound probabilities and their stability is provided because the perceiver receives information that both first and second deviants hold equal informative value or relevance in their respective block-contexts. The MMN elicited to either deviant was not modified by sequence type in first-half data acquired from the period immediately after the tone roles switched indicating that learning in both block types unfolded in a similar manner. Equivalent learning rates across block types therefore persisted across the entire experimental session even when the superordinate structure was violated once the tone roles start switching more often in the unstable sequence. Given that the first-impression bias is proposed to be linked to the

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likelihood of initial sequence compositions changing (Fitzgerald et al., 2017; Frost et al., 2016; Todd et al., 2011; Todd et al., 2013), this may explain why the bias is not observed when we know exactly when and how compositions will emerge over the entire experimental session.

Another way to conceptualise the present findings is that the network was engaged in a type of “confirmation bias” that favoured sequence foreknowledge first and foremost. The network may have actively sought to confirm information outlined in an explicit prior following learning, albeit indirectly, by way of foreknowledge. Confirmation bias toward prior information is observed even when foreknowledge is inaccurate (Doll et al., 2009; Galizio, 1979; Hayes, 1989, 1993; Hayes et al., 1986). Misinformation about future experience with stimuli probabilities has been shown to drive response behaviour despite direct evidence to the contrary resulting in reduced task performance (Doll et al., 2009). It is therefore possible that the network sampled and/or processed information in a way that confirmed pre-existing beliefs associated with an explicit prior. One way of testing this is by priming participants with inaccurate foreknowledge about sequence structures or omitting foreknowledge about first deviant/block-context relevance prior to multi-timescale exposure and examining whether this impacts on precision-weighted MMN error signalling (i.e. learning rates) during actual sequence processing.

In considering the wider MMN literature, the present results indicate that the MMN network can utilise instruction during multi-timescale sequence processing over the longer term, and this alters how MMN amplitude is modulated relative to that elicited to the same sounds when participants are uninformed (Frost et al., 2016; Todd et al., 2011; Todd et al., 2014). This challenges the assumption that MMN

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cannot be used to study more abstract, contextual influences on pattern learning (Jääskeläinen et al., 2004; May et al., 1999; May & Tiitinen, 2010; Wacongne et al., 2011). Our results are like Sussman et al.'s, (2002) who found that foreknowledge about the local and global aspects of sound structures prior to sequence exposure impacts MMN elicitation. MMN was not observed to a locally deviant sound in participants primed with prior information relative to those fully naïve to sequence structures indicating that this sound was processed as part of an overarching repeating tone pattern (i.e. 11112; Sussman et al., 2002). The authors attributed this to an interaction between predictive and more cognitive-based, attentional mechanisms where prior information changed how top-down processes affected the information used in the MMN prediction error signalling process. Broadly speaking, these interpretations are much like those described here; in that sound structure foreknowledge influences how higher-order brain areas modulate very early stimulus-driven ERP responses and very likely play a crucial role in modulating MMN error signalling that adapts to suit demands imposed by varying experimental conditions.

We also think it is important to expand on the present finding showing larger MMN to the first deviant tone type than that to the comparatively shorter, second deviant tone. We observed this same result in Chapter 3 when participants were engaged in a concurrent cognitively-demanding task whilst hearing the multi-timescale sequences. Much like the present finding, MMN was always observed when a rare sound violated the locally regular pattern. The formation of internal models and their dynamic updating is therefore not disrupted by foreknowledge per se in-line with studies showing that providing participants with prior information about sound sequence probabilities does not eliminate MMN (e.g., Rinne, Antila, &

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Winkler, 2001; Horváth et al., 2011). In Chapter 3, we referenced bias data published by Mullens et al. (2014) to explain simple deviant effects; the authors showed that MMN is always larger to the first versus second deviant, irrespective of whether the shorter or large tone is the first deviant at sequence onset (see pg. 110 for discussion). This clearly shows that differences in the physical sound properties cannot fully account for differential tone effects on MMN amplitude in our program of bias studies. Given that the perceived higher importance of the first deviant tone emerges even when concurrent task demand increases (see Chapter 3), it is possible that this same mechanism of bias is activated when participants are fully informed on sound sequence structures. That is, the initial rarity of the first deviant may have a powerful impact on the system such that first-order inferences about the potentially higher and lower information value of first deviant and first standard tones, respectively, prevail despite foreknowledge that both sounds are equally informative markers of pattern violations in their respective contexts. The reduced or eliminated “surprise” when tone roles change is therefore probably more malleable to sequence foreknowledge and likely explains the elimination of the remaining bias patterns (i.e., the differential modulation of MMN to the two tones in the two different sequences).

In terms of whether participants were knowingly aware of sound sequence patterning in this study, our findings are like Sussman et al.’s, (2002) who found that participants could not describe any patterns after hearing an oddball paradigm even when they attended to tones and/or were informed on the sound structures before hearing sequences. There are clear limitations associated with using self-report to measure sequence awareness that compromises test validity. For example, participants can utilise memory retrieval strategies based on explicit communication

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of sequence structures delivered by researcher (e.g. recall; Graf & Birt, 1996).

Sequence structures embedded within the multi-timescale paradigm are considerably more complex, and therefore much harder to explicitly detect relative to an oddball sequence like that used by Sussman et al., (2002). We are therefore confident that participants were not fully aware of sound patterning in this experiment. Rather, we suspect that participant focus naturally fluctuated between sounds being played and watching the film.

First impression order effects on perception and the context effects that inform learning arise from and are constrained by carefully considering previous experience with sound information over time. When information reduces surprise about the likelihood of future sources of sound compositions, it changes how perceptual learning unfolds and explains why accurate foreknowledge about future sound experience alters perceptual learning. Equivocal MMN amplitude regardless of block-context or overall sequence stability indicates that the network was ‘unsurprised’ by changes in both the lower and higher-order structures over the longer term. Yet it seems that the relative weighting, in terms of potential sound relevance, placed on sound probabilities presented first persists throughout sequence learning.

Our interpretations of prior information preventing first impression order effects on sound pattern learning need to be verified in future studies that include a sufficiently large sample size with the aim of determining whether the present results hold true in analyses that include a control group comparison. The proposed reasons for why the bias disappears in the presence of an explicit prior that precedes direct experience with sound probabilities and their transitions remain theoretical, and invite further opportunities for studying potential mechanisms involved. There is

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increasing evidence that mechanisms underpinning sound relevance filtering based on dynamic models of statistical information involve cognitive brain areas in the sense that prediction error signals are reliably elicited to sound events that are probable over multiple timescales, yet are modulated differently depending on demands and/or provisions imposed by the external environment. Future studies can help to isolate the impact of one or more constraints on the learning process under which order-driven biases emerge. ERP responses to sounds with benefit of sequence foreknowledge point toward top-down involvement with primary sensory processing, as inferences stored using an explicit prior increase in and/or maintain predictive power once the network validates this information through direct sound experience.

Chapter 5:

General Discussion and Conclusions

The previous three chapters described the empirical work undertaken in this thesis. This chapter presents a summary of the experiments conducted and discusses the general implications for understanding the role of first impression bias mechanisms in perceptual inference and learning including relevance to MMN literature. These data show that order-effects are robust and long-standing except when we undertake an attention-demanding concurrent task or know exactly what we will hear before sound sequence exposure. We propose that data generated in response to the MMN multi-timescale paradigm are a striking example of a dynamic and hierarchically-organised inferential learning process that assists the brain in minimising its free energy. In terms of major theoretical contributions, this thesis adds to the proposition that cognitive processes influence perception and that attention weights the precision of our inferences during perceptual learning. We first outline the key findings of this thesis supporting these contributions. A critical assessment on the limitations of theory and methodology is then presented before directions for future research are considered.

5.1. Short Synopsis

The experiments reported on in this thesis were designed to test mechanistic hypotheses, conceptualised in terms of hierarchical inference processing that explain the generation and modulation of auditory evoked brain responses underlying first impression bias in MMN. Predictive coding theory asserts that relevance filtering in

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perception arises with processing of current information from the sound environment, and precision-weighted predictions about the cause of this input; this assumption motivated us to develop and test hypotheses about mechanisms of learning biases revealed using MMN. The working hypothesis of this thesis was that first impression bias is evidence that the brain has the capacity to implement, monitor and adapt learning over much longer timescales during relevance filtering than those recognised in conventional literature of this field. Our primary hypothesis is that first learning about sound probabilities (local sound patterning) and their stability (superordinate sound patterning) slows learning rates when tone roles later switch contradicting initial experience, and also when subsequent experience violates superordinate patterning determining when tone roles should switch. The studies conducted provide further tests of this hypothesis by exploring: 1) whether the effects hold in a replication study using a much larger sample size compared with previous studies, and 2) how the effects are altered by different experimental manipulations used to probe brain mechanisms.

First impression bias was found to be a robust phenomenon in a larger sample and the differential modulation patterns for first and second deviant tones remained over multiple encounters with the same sequence type (**Chapter 2**). Manipulations that interfere with more cognitive than perceptual abilities interfere with the bias in various ways (**Chapters 2-4**). First impression bias was altered if concurrent task demand increased (**Chapter 3**), or if foreknowledge about sequence structures was provided prior to hearing the multi-timescale sequence (**Chapter 4**). We shall now highlight the importance of these findings one by one.

5.2. Implications of this Thesis

5.2.1. What have we learned about first impression bias? The aim of the work described in the first results chapter, **Chapter 2**, was to determine the replicability and longevity of first impression bias by testing whether associated patterns are robust when examined in an expanded dataset (**Study 1**) or following repeated encounters with stable or unstable sound sequences (**Study 2**), respectively.

Additional analyses were also performed on datasets generated from each study to test whether adaptation-based explanations could account for order-driven effects observed.

Successful replications of previous results can provide greater confidence about the veracity of a hypothesized effect (Brandt et al., 2014). When a relatively large sample of participants ($n = 35$) heard the multi-timescale paradigm (**Study 1**, **Chapter 1**), we replicated the same order-effects on MMN amplitude revealed in comparatively smaller datasets produced in earlier studies ($n = 14-20$; Todd et al., 2011; Todd et al., 2013; Todd et al., 2014a; Todd et al., 2014b). These findings are important because they establish the reliability of first impression bias. That is, we can say with confidence that first impression bias in sequence learning reflects *a reliable phenomenon* that cannot be attributed to random variation due to insufficient statistical power (Brandt et al., 2014).

In **Study 2** of this same chapter, we investigated the longevity of first impression bias on MMN amplitude to first and second deviant tones and found that a slowed learning rate for the second but not first deviant was remarkably persistent across both stable and unstable sequence types. Participants who heard four occurrences of either sequence showed MMN modulation patterns equivalent to those generated in the stable sequence of Study 1 with rapid learning evident in

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responses to deviants in block-contexts that matched those at sequence onset, with learning rates to the second deviant markedly slower in comparison. To emphasize, repeated exposure to sound probabilities in both block-contexts did not override order-effects on MMN amplitude modulation.

A key difference concerning the Chapter 2, Study 2 variant of the typical multi-timescale design is that the superordinate pattern was not violated across conditions because the same stable or unstable sequence was presented four times and block-contexts lengths appeared at fixed intervals across the entire experimental session. One explanation of these data is that *first impression bias persists if higher-order predictions about the stability of local transition statistics continue to hold true* with continued experience. This is important because it indicates that predictions about tone probabilities and their stability anchored to a first impression bias prevail with recurring experience if assumptions about the latter are not violated. It also suggests that higher-order predictions consistently slow local pattern learning when sound probabilities do not match those stored in a first impression, even after 30 min of sequence processing.

Across both **Study 1** and **2 (Chapter 2)**, we directly tested whether SSA effects could explain key data patterns we attribute to longer-term learning bias anchored to a first impression. We asked whether SSA mechanisms could account for the reversal of order-effects on MMN between sequence types (**Study 1**) and/or between deviant types in the unstable sequence immediately after tone roles switch (**Study 2**). In both analyses, we revealed particularly robust *evidence against SSA being able to fully account for first impression bias effects on sound sequence learning*.

Chapter 3 reported on the impact of increased concurrent task demand on the MMN modulation patterns typical of first impression bias during exposure to the multi-timescale paradigm. The initial rationale was that engaging participants in a cognitively or attention-demanding task could reduce availability of higher-level attentional resources, interfering with the network's capacity to utilise high-precision longer timescale predictions to modulate (or bias) bottom-up information. We showed that *increasing task demand eliminates first impression bias*. Those who completed an attention-demanding WM task or perceptual task showed basic stability effects in which MMN amplitude increased both from earlier to later periods within a block and from shorter compared to longer block types. This is important because it indicates that some level of cognitive and/or attentional capacity is needed to acquire and/or implement the assumptions derived from first-impressions. This also means that when attention-based cognitive resources are depleted, learning about transitional probabilities may be limited to local sound patterning emerging on shorter timeframes only.

In **Chapter 4**, we showed that fully informing participants about sequence structures before they heard the multi-timescale paradigm dramatically alters order-driven bias effects on MMN amplitude. In this study, we wanted to test whether bias would be eliminated by preventing surprise when tones reverse probabilities or when blocks lengths change in the multi-timescale sequences. *First impression bias was not observed when prior information about transitional structures underlying local and superordinate regularities was provided*. Instead, foreknowledge facilitated rapid adjustment to changes within the sequences supporting the conclusion that first impression order-driven bias emerges only when accurate information about

sequence structures has not been learned already. This is important because it indicates that the MMN signal in addition to patterns of bias are sensitive to explicit verbal instruction about what will be heard in future.

We acknowledge that the sample size used in the **Chapter 4** study is modest relative to those reported on in **Chapter 2** and **3**, and this study requires replication to increase validity of our interpretations. Importantly however, first impression bias has been shown to emerge in sample sizes comparable to those reported on in **Chapter 3** and thus we remain confident that learning biases are impacted by foreknowledge. Collectively, the studies in this thesis support our overarching assumption that first impression bias arises with active and dynamic interactions between simple sensory and higher-order cognitive mechanisms spanning multiple levels of processing.

5.2.2 A final comment on the role of SSA in first impression bias. In

disseminating our work across multiple contexts (e.g. national/international conferences, manuscript reviews), we are often asked to defend against assertions that the patterns evident in differential modulation of MMN amplitude in multi-timescale sequences are examples of very simple SSA mechanisms (May & Tiitinen, 2010). Knowledge claims in science are defended by making the best argument possible for that claim given the data, and are imperative in scientific progress (Shuell, 1987). As such, it important to emphasize that we do not discount the contribution of adaptation effects to results implicated in this thesis. SSA and short-term plasticity are frequently observed in the cortex (for review, see Calford, 2002), particularly in the auditory cortex (Brosch & Schreiner, 2000; Condon & Weinberger, 1991), and a comprehensive theory of MMN should take these effects into account.

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As introduced earlier (see **1.3.1 Early Accounts of MMN**), Näätänen et al. (2005) neatly summarise several phenomena measured using the MMN signal that cannot be accounted for by the adaptation hypothesis. We think first impression bias is another such phenomenon. With increasingly complex patterns like those used in our paradigm, we are seeing effects on transition statistics over minute-long time frames. This is because the network needs more time and sufficient regular occurrences to build a prediction model of tone role stability (i.e. block-context length). We directly tested the SSA hypothesis of first impression bias across both studies in **Chapter 2** and found that exposure to the long sound as a repeating standard could not explain the differential response to deviant tones in neither the stable or unstable sequence (as discussed on pp.'s 90, & 98-100). Furthermore, if bias effects were solely driven by stimulus-driven information embedded within sequence configurations they should not be altered by manipulating cognitive resources and/or prior knowledge about sequence structures as clearly shown in **Chapters 3 & 4**, respectively. Together, these studies challenge *any* model that assumes the first impression bias phenomenon can be accounted for by purely bottom-up influence. This thesis therefore adds to an increasingly convincing case that cognition plays an important role during incidental (i.e. task independent) learning about regularities on multiple timescales in sound sequences.

5.3 How cognitive is perception in inferential learning?

In this thesis, we extend upon current understandings of MMN and sound sequence processing by demonstrating that inferential learning mechanisms adapt to experimental demands that expend attentional and/or cognitive resources (as in **Chapter 3 & 4**). The notion that perception is more than just the passive receipt of

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sound information is not a novel concept per se – it has long been supposed that perception is shaped by attention, learning, memory and expectations (e.g. Helmholtz, 1902/1962; Kienker, Sejnowski, Hinton, & Schumacher, 1986). Yet, the degree to which the brain utilises cognitive resources to compute meaning and uncertainty from sensory input whilst maximising redundancy is an area of increasing interest across the empirical and theoretical cognitive neuroscience literature (e.g. Avena-Koenigsberger, Masic, & Sporns, 2018; Clark, 2017; Cocchi et al., 2016; Parr & Friston, 2017; Ransom, Fazelpour, & Mole, 2017). In this thesis, we have learned that first impression bias effects observed in earlier studies will not always reflect the structures embedded within the multi-timescale sequences under conditions that place varying demands on cognition (as discussed on pp. 122-124, 155). We shall now consolidate this proposition by discussing why explanations of attention in the MMN literature are limited in this regard. We finish by considering the role of attention-based cognitive resources in learning biases and how these ideas fit with models of human cognition more broadly.

In the MMN literature, there has been debate regarding the degree to which attention influences the MMN response. Mäntasylo and Näätänen (1987) and Näätänen (1992) were first to propose that MMN elicitation is insensitive to manipulations of attention and is therefore a useful measure for unveiling mechanisms of implicit information processing. The MMN has since become described as an established marker of “pre-attentive” learning about regularities mainly because attention is not required to generate it. Yet assumptions about how attention modulates MMN amplitude are less clear and inconsistent not well formulated (as discussed on pp. 20-22). Here we emphasize that explanations are conflated by mixed findings and argued that understanding attentional effects on

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MMN in absolute terms (i.e. either there is an effect of attention on MMN elicitation or not), as is often the case in conventional interpretations, undermines the potential significance of these findings and omits understanding the relative effects of attention on MMN amplitude. Winkler (2007) expands on earlier accounts by advocating that “categorical” information interacts with top-down effects yet auditory sensory information is still assumed to be processed independently of attention. Views that top-down processes can influence which sensory information receives additional processing during the MMN deviance-detection process (Chennu et al., 2014; Sussman, 2013; Sussman, Ritter, & Vaughan, 1998; Sussman, Winkler, Huotilainen, Ritter, & Näätänen, 2002), but do not impact the actual deviance-detection process itself (Rinne et al., 2001; Ritter, Sussman, Deacon, Cowan, & Vaughan, 1999; Sussman, Winkler, & Schröger, in press) are only partially consistent with the results in this thesis. Thus, a hierarchical pattern recognition system in the brain is the most plausible assumption whereby a higher level in the hierarchy encodes for a higher level of pattern complexity.

We developed studies in this thesis with the assumption that attentional mechanisms can modulate processing of *all* input during MMN sound relevance filtering albeit the level of contribution depends on a multitude of factors: attention effects in learning could be influenced by the types and timing of patterning and violations that emerge within the auditory stream, resource availability, experience, concurrent task demands, network integrity and so forth. We also assumed that attention is a limited and valuable cognitive resource pertinent to inferential learning on multiple timescales (as discussed on pp. 46, 109, 124, & 128). These assumptions form part of predictive coding view and shaped our understanding of how attention and predictive mechanisms interact in the MMN-generating process. These

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assumptions do not support MMN amplitude being a marker of “pre-attentive” sensory learning, although to do not challenge the idea that MMN elicitation is. In actual fact, we emphasize that applying the term “pre-attentive” to MMN is misleading; in that its elicitation is clearly a very automatic process because it is observed in sleep and coma, but its amplitude is not. Rather, we think attentional resources are selectively used based on environmental variability over the longer-term, informative value of transition statistics and associated precision estimates that together determine how the prediction error signal processing unfolds (as discussed on pp. 14, 31 & 70).

In explaining first impression bias effects on MMN amplitude, we argue that the brain categorises one sound as relatively redundant and the other has as being potentially more meaningful in terms of information value following exposure to two sounds of high and low probability, respectively (i.e. the information value hypothesis as discussed on pp. 68-70, 100, 127, & 151-153). Elements of this hypothesis were introduced in the very first published paper by Todd et al., (2011) who revealed primacy effects on MMN amplitude. Our most up-to-date understanding is that this feature, together with the overarching assumption that the transition statistics defining the binary state behaviour at sequence onset is very stable, causes top-down attention-based cognitive mechanisms to modulate learning and error signalling in a way that reveals long lasting biases. Strong support for the importance of the information value hypothesis was obtained when Mullens et al. (2014) demonstrated that first impression bias disappears when sequences are manipulated such that the binary state properties (i.e., being 30 ms and 60 ms in length) belong to both common and rare sounds at sequence onset, yet will

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eventually emerge if a binary distinction can be gleaned from information over the longer-term (as discussed on pg. 111, 148).

The first-impression bias reported in this thesis shares similarities with phenomena observed in human cognitive information processing models more broadly such as computational applications of Adaptive Resonance Theory (ART; Carpenter & Gaddam, 2010; Carpenter & Grossberg, 2017). In terms of theoretical assumptions, there are many commonalities between ART and other learning models including predictive coding and early accounts of MMN, despite the former denoting a purely cognitive model of human categorical learning and reasoning. These models are similar in that they all assume: 1) the neural network is equipped with a top-down predictive element and a bottom-up input driven element, that interact to generate prediction errors, and 2) attention operates on representations of input. In ART, the default network encodes features as distinct categories of a binary relationship allowing it to act upon relative neural states whilst enduring variability inherent to more absolute states of learned input (Carpenter & Grossberg, 2017). The system categorises input into that which is consistently present versus absent to form an expectation about a ‘critical feature pattern’ and compares this with bottom-up information (Carpenter & Gaddam, 2010; Carpenter & Grossberg, 2017). Computational examples of ART show that the network is prone to errors that delay new learning because it pays ‘too much’ attention to category features critical during early learning (Carpenter & Gaddam, 2010).

Such assumptions are just like our proposition that attentional resources are used to ‘lock-in’ a first impression of information value based on a binary distinction between a sound that is predicted and uninformative versus that which is unexpected and potentially important. This means that depleting attention-based cognitive

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resources (**Chapter 3**) or providing exclusive foreknowledge (**Chapter 4**) that either disables or removes the capacity to categorise input into a binary distinction disrupts the tendency to prioritise early pattern learning over later novel experience.

ART networks will eventually learn a new categorical representation in response to prediction errors but only after a bias is introduced into the network; bottom-up input thereafter predisposes the network against prioritising attentional resources toward earlier feature pattern learning (Carpenter & Gaddam, 2010). We see similar effects on our data with learning biases diminishing by the second-half of block-contexts once the network learns that the source of input has changed. Models of human cognition that assume attentional resources bias learning away from new input corroborate our position that attention-based cognitive mechanisms modulate high precision-weighting of sensory input resulting in learning bias thereafter. In this regard, perhaps we are seeing more cognitive effects on perception under conditions that elicit or alter patterns of first impression bias in sound sequence processing. Understanding more about the role of cognition in perception is therefore imperative for understanding the mechanics of hierarchically-driven inferential learning.

The studies comprising this thesis add to the multi-timescale study program, contributing to an increasing appreciation of the potential role of attention-based modulatory processes in the first impression bias phenomenon. We conclude that MMN is impacted by top-down influences and assert that 1) modulations of MMN amplitude are impacted by availability of attention resources, and 2) the emergence and/or altering of a strong first impression bias observed under different experimental conditions is mediated by attention-based augmentation of prediction error signaling. The results add to a growing literature indicating that although MMN is elicited under altered levels of consciousness, its amplitude is very sensitive to

experimental conditions that place demand on attentional resources. We therefore endorse modern re-conceptualisations of traditional views that are open to the possibility that the entire evoked-potential is susceptible to modulation by attention (Auksztulewicz & Friston, 2015; Feldman & Friston, 2005; Friston, 2005). The revelation that cognitive manipulations affect the bias phenomenon highlights that learning more about the role of cognition in perception is paramount in helping us reach a more holistic understanding of inferential learning, and invites opportunity for considering more cognitive models of learning and their implications for human sound processing.

5.4. Sensitivity to superordinate patterning on slower timescales

Not only have we learned that increased concurrent task demand interferes with learning patterns on slower timescales, this thesis shows that bias patterns prevail if we do not violate the superordinate sequence structure and that differences in MMN amplitude to first and second deviants in the unstable sequence may be traced to learning the superordinate structure once the entire stable sequence is heard. The aim of this section is to comment on studies indicating that MMN is insensitive to global regularities and highlight why this does not necessarily denote evidence that the underpinning network cannot extrapolate and utilise higher-order regularities to modulate learning about local sound patterning.

The term global patterning is comparable to the concept of superordinate patterning discussed in our papers and has been used to describe probability information evident over longer timescales than local stimulus transitions. The former is generally used in studies examining long-term effects on MMN to global sound regularities over several tens of seconds whereas we emphasize that

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superordinate learning includes these timescales and extends to those operating across many minutes (Kiebel et al., 2008). Network sensitivity to global patterning has been studied recently using computational modelling of data generated in oddball sequences. For example, Wacongne et al., (2012) modelled thalamic input to layer 4, with prediction error units in more superficial layers 2/3 within primary auditory cortices that together simulated a three-tier circuit embedded within an entire cortical hierarchy. Predictive coding simulations were modelled on data generated using a five-tone repeating standard (i.e. AAAAB) occasionally violated by replacing input B with input A (i.e. AAAAA, $p = .20$, SOA 1200 ms; Bekinschtein, Dehaene, Rohaut, Tadel, & Cohen, 2009). The repeating AAAAB sequence is therefore standard at the more superordinate or *global* level (i.e. over the entire experimental session) and deviant at the *local* level (i.e. from one sound to the next). Wacongne et al.'s (2012) model indicates that the inferential process reflected in MMN is "blind" to global transition probabilities and rather, is dominated by the local prediction of an A sound following an A (Wacongne et al., 2012), replicating earlier findings generated using the same paradigm (Bekinschtein et al., 2009; Wacongne et al., 2011).

Wacongne et al., (2012) conclude that a relatively simple hierarchical architecture can account for the major empirical properties of the MMN including an apparent insensitivity to the global context of sound sequences when the timescale exceeds temporal processing capacities of primary auditory cortices. One might argue that this is evidence against our proposal that the network is sensitive to the super-ordinate structure embedded with the multi-timescale sequence. We however contend that Wacongne et al.'s (2012) conclusions apply only to the sequence structure used in their study, and that generalising results based on one type of

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sequence design to other complex sound sequences risks over-simplification of the neural network.

Predictive coding assumes that each level within a hierarchy sends prediction errors in a feed-forward fashion whereas predictions are sent down the hierarchy (Friston, 2005). The network modelled by Wacongne et al. (2012) is based on processing capacities limited to primary sensory areas only and therefore it does not model potential engagement of rostral brain areas in modulating stimulus-driven responses during exposure simple sequences. Put simply, we do not know what happens to the prediction error signal after it is processed by layer 4 in Wacongne et al.'s (2012) model. Indeed, each level of the hierarchy is specifically tuned to be most sensitive to a particular temporal scale. The primary auditory cortex is most sensitive to information gathered over relatively short timescales whereas higher levels may extract regularities over tens of seconds to minutes, days, weeks and so forth (Kiebel et al., 2008). Wacongne et al.'s (2012) model reflects only one timescale associated with pattern extraction in the shorter term and so is an insensitive measure of changes in neural states modelled over much longer timescales. This is because the time span over which the sound transitions can be learned is strictly limited by the processing capacity of the memory associated with a given level of the cortical hierarchy (Kiebel et al., 2008).

Wacongne et al.'s (2012) finding contradicts those found by Sussman et al., (1998) who essentially used the same sequence albeit with a considerably shorter SOA (100 ms) and found that MMN to the B in the AAAAB sequence disappeared indicating that the final B sound in the five-repeating sequence was processed as part of a global standard. However, Sussman and colleagues did not violate a global pattern per se and rather, concluded that lack of MMN suggests the network had

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coded the fifth tone as part of the five-tone repeating standard pattern (Sussman et al., 1998). It has however been argued that establishing a regularity in the absence of a violation is a less sensitive measure of the type of regularity coded in the internal model (Herholz, Lappe, & Pantec, 2009).

Herholz et al. (2009) used a similar paradigm to both Wacongne et al., (2011) and Sussman et al., (1998) and found that violating global regularities elicits a MMN response. One key difference in Herholz et al.'s (2009) study is that global pattern violations were frequent ($p = 0.50$), the SOA of tones was quite long (1000 ms) and the pattern therefore had to be extracted based on a longer time range. It was suggested that 1) higher-order pattern extraction occurs at much slower rates and do not necessarily “pop out” straight away relative to very rare pattern violations, consistent with Kiebel et al.'s (2008) findings, and 2) that responses to violations of patterns reflect a more sensitive measure for detecting this. These conclusions also imply that Wacongne et al.'s (2011) paradigm failed to elicit MMN because of the relative probabilities of the global versus local patterns embedded within their sequence; in that increasing the likelihood of experiencing a global pattern over the longer-term, compared with encountering local sound patterning on shorter timescales, could have elicited a MMN following a global pattern violation. In terms of whether the MMN is a sensitive measure of the networks sensitivity to superordinate regularities, or any complex patterning for that matter, results clearly differ by experimental design.

Todd et al., (2013) emphasize that there is “no ideal paradigm” for using the MMN signal to study perceptual learning. The multi-timescale sequence design confirms the brains capacity to learn and utilise global or superordinate temporal structures because MMN amplitude is affected when we violate/reinforce this

pattern. We continue to learn more about this phenomenon because we purposefully use the time-scales of sensory input as an experimental factor to study how learning transitional probabilities in the shorter term is constrained by learning the stability of these statistics over the longer term. Yet we would never have uncovered evidence of network sensitivity to superordinate patterning if we never satisfied our curiosity about whether MMN amplitude changed across block-context halves (in studies succeeding Todd et al., 2011). Predictive coding simulations and ERP studies show differing results and we think this is because different protocols place different demands on the underpinning network. Interpreting potential mechanisms of the MMN process are therefore bound by each novel study design and analysis techniques. To conclude this discussion, we think that generalising explanations to other paradigms risks undermining the complexity of the network as well as devalues the unique contributions that can be made by different experimental designs.

5.5. Limitations and Future Directions

One point of controversy stemming from this thesis concerns the degree to which mechanisms of attention control the weighting, or gain, of MMN signals under conditions in which first impression bias effects are observed, altered or eliminated. Our experimental methods are limited in that we cannot directly determine how top-down predictions and attention-based precision estimates interact for each of our given experimental conditions. We therefore acknowledge that our current methodologies indirectly test the information value and superordinate pattern learning hypothesis and remain theoretical for now.

With increasingly complex sound patterns, extracting enough regular instances of the superordinate pattern to build up an internal model with high

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precision also increases. To test the superordinate patterning hypothesis of first impression bias it would be ideal to precisely track how MMN to the proposed superordinate pattern violation changes over time (Friston, 2005; Kiebel et al., 2008; Todd et al., 2011, 2013). A limitation of our study design is that we cannot directly measure this because ERPs used to calculate MMN require averaging over many trials. Our data is constrained by too few data points resulting in low statistical power and so conventional MMN methods used to test the networks sensitivity to superordinate sound patterning cannot be applied to multi-timescale sequence data. Adopting explicit biologically plausible neuronal models such as dynamic causal models (DCMs; David et al., 2006; Friston et al., 2003) may provide a fruitful avenue for directly examining the causal architecture of neuronal interactions between lower and higher-order brain areas during multi-timescale sequence processing. The aim of DCM's is to test a-priori hypotheses about both the coupling among brain areas or sources as well as how that coupling changes with different experimental factors. Applying computational models to our multi-timescale data may therefore afford a better understanding of attention-based augmentations of first impression learning bias under typical and varied experimental conditions.

The emergence of sophisticated computational tools expands the questions we can ask about how auditory systems engage in learning biases when modelling the cause of sound sources from the acoustic environment. Explaining the first impression bias as evidence of precision- or confidence-weighted predictions modelled on multiple timescales is a working hypothesis and needs to be confirmed by more studies that continue to test assumptions predicted by our interpretation. For example, Mullens et al., (2016) rightly point out that it is important to test if the superordinate structure is somehow encoded in memory with high-confidence during

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first impression formation and, when the higher-order structure of the sequence changes, high-confidence in predictions about the original structure are re-adjusted in response. We are unsure at this stage whether a superordinate pattern violation fully releases subsequent learning about tone roles in switched contexts from bias thereafter or triggers the formation of a new first impression, albeit possibly weighted by lower-precision, that then biases sequence learning for the remainder of the unstable sequence. As discussed in **Chapter 3**, the notion that first impression bias indicates tiers of learning with increasing abstraction can be accommodated by the recent development of an influential mathematical modelling tool – the HGF model of individual learning under uncertainty (Mathy's et al., 2011).

The HGF is a generic analytical approach within the hierarchical Bayesian framework and as this thesis neared fruition, our lab has become increasingly convinced that the HGF model can accommodate key assumptions of first-impression bias (as discussed on pp. 71, 92, & 107). We think this model could predict at least some of the data patterns we observe when participants hear the multi-timescale sequence. More specifically, it could predict that model updating upon exposure to an unexpected event (i.e. a deviant tone), is always constrained by the modelled likelihood that transition statistics (e.g. tone roles) will change (e.g. sound sequence stability; Mathys et al., 2011). The HGF model therefore reflects a potentially valuable tool for testing mechanistic hypotheses about the bias because it can be applied to our data to confirm the presence of bias effects in evoked-potentials as well as elucidate how the bias is modified under different experimental conditions, including those induced in this thesis.

There is a movement to study the effects of deviance from sound patterning using complex sound sequence configurations that are arguably a more ecologically

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valid measure of sound processing across time. At present, we do not know whether other observations (Mullens et al., 2016; Todd et al., 2011, Todd et al., 2013, Todd et al., 2014a) or those generated in this thesis are specific to a relatively simple two-tone context or alternatively, indicate a fundamental order-dependent phenomenon that extends to more complex sound environments. One future experiment could determine whether first impression bias occurs when a third tone in the role of a second equally probable standard (i.e., deviant $p = 0.141$, both standards $p = 0.425$) is introduced. This means the role of the deviant would alternate between three tones across block-contexts of sequences creating a first, second and third deviant and two initial standards. Here two of the three sounds would signify the regularity in any given block-context making two tones equally redundant in the first block. This study design additionally creates a difference in stability for the first two standards (i.e. when one switches to become the second deviant and the other continues as a standard for a second consecutive block). It is possible that this additional period of “redundancy” could affect responses in the stable sequence. If this additional redundancy has an effect we would expect this to show up in more prolonged suppression of the growth in MMN to this sound when it becomes a deviant in the stable sequence data. Such a design introduces random background noise to the sound environment during sound sequence processing, and could better establish the ecological validity of first impression bias. This could provide insight into whether the bias is a phenomenon that extends to experience with more complex transition statistics underlying auditory input over time rather than just a two-tone sequence which is far removed from the complexity of the real-world auditory environment.

5.6 Concluding Remarks

This thesis examined mechanistic hypotheses of first impression bias that were tested using a specific auditory evoked response, the MMN. This work has been conducted under assumptions of predictive coding (& empirical Bayes) as a general theory for understanding inferential learning in perception. Put simply, sound inputs, predictions and prediction error signals (discrepancy between sound input & predictions) interact across different levels of a hierarchically-organised cortical network. The research described in this thesis provides experimental evidence that first impression bias is a robust and long-lasting default processing mechanism that requires naivety to sound sequences as well as some level of resource availability to be observed.

Importantly, these results support the overarching working hypothesis of this thesis - that first impression bias is a striking example of a hierarchical inference process at play. Moreover, the results show that MMN amplitude is clearly sensitive to manipulation of attention-based cognitive resource availability. It demonstrates the usefulness of utilising unique sequence designs to test specific questions about how underlying mechanisms adapt to demands induced by different experimental designs in addressing core problems in neuroscience such as perceptual inference and learning in the brain. Finally, results in this thesis have implications for how the human brain processes sound patterns. Evidence of learning bias in such a basic process introduces the potential to study aspects of learning without laborious pre-training or the need for a motivated learner. It further offers the opportunity to examine the developmental trajectory of these learning biases as well as whether they are altered by different clinical disorders (e.g. schizophrenia) or age and even its evolution over species.

References

- Aaltonen, O., Niemi, P., Nyrke, T., & Tuhkanen, M. (1987). Event-related brain potentials and the perception of a phonetic continuum. *Biological Psychology*, *24*(3), 197-207.
- Akatsuka, K., Wasaka, T., Nakata, H., Inui, K., Hoshiyama, M., & Kakigi, R. (2005). Mismatch responses related to temporal discrimination of somatosensory stimulation. *Clinical neurophysiology*, *116*(8), 1930-1937.
- Akatsuka, K., Wasaka, T., Nakata, H., Kida, T., & Kakigi, R. (2007). The effect of stimulus probability on the somatosensory mismatch field. *Experimental brain research*, *181*(4), 607-614.
- Alain, C., & Izenberg, A. (2003). Effects of attentional load on auditory scene analysis. *Journal of Cognitive Neuroscience*, *15*(7), 1063-1073.
- Alain, C., Woods, D. L., & Ogawa, K. H. (1994). Brain indices of automatic pattern processing. *Neuroreport*, *6*(1), 140-144.
- Alain, C., & Woods, D. L. (1997). Attention modulates auditory pattern memory as indexed by event-related brain potentials. *Psychophysiology*, *34*(5), 534-546.
- Alain, C., Woods, D. L., & Knight, R. T. (1998). A distributed cortical network for auditory sensory memory in humans. *Brain research*, *812*(1), 23-37.
- Alho, K. (1995). Cerebral generators of mismatch negativity(MMN) and its magnetic counterpart (MMNm) elicited by sound changes. *Ear and Hearing*, *16*, 38-51.
- Alho, K., Winkler, I., Escera, C., Huottilainen, M., Virtanen, J., Jääskeläinen, I. P., ... & Ilmoniemi, R. J. (1998). Processing of novel sounds and frequency changes in the human auditory cortex: magnetoencephalographic recordings. *Psychophysiology*, *35*(2), 211-224.

REFERENCES

- Alho, K., Woods, D. L., Algazi, A., Knight, R. T., & Näätänen, R. (1994). Lesions of frontal cortex diminish the auditory mismatch negativity. *Electroencephalography and clinical neurophysiology*, *91*(5), 353-362.
- Allport, G. W. (1979). *The Nature of Prejudice*. Basic books.
- Anderson, N. H. (1965). Primacy effects in personality impression formation using a generalized order effect paradigm. *Journal of Personality and Social Psychology*, *2*(1), 1
- Asch, S. E. (1946). Forming impressions of personality. *The Journal of Abnormal and Social Psychology*, *41*(3), 258.
- Atienza, M., & Cantero, J. L. (2001). Complex sound processing during human REM sleep by recovering information from long-term memory as revealed by the mismatch negativity (MMN). *Brain research*, *901*(1), 151-160.
- Atkinson, R. J., Michie, P. T., & Schall, U. (2012). Duration mismatch negativity and P3a in first-episode psychosis and individuals at ultra-high risk of psychosis. *Biological psychiatry*, *71*, 98-104.
- Auksztulewicz, R., & Friston, K. (2016). Attentional enhancement of auditory mismatch responses: a DCM/MEG study. *Cerebral Cortex*, *25*(11), 4273-4283.
- Baldeweg, T. (2006). Repetition effects to sounds: evidence for predictive coding in the auditory system. *Trends in cognitive sciences*, *10*(3), 93-94.
- Baldeweg, T. (2007). ERP repetition effects and mismatch negativity generation: a predictive coding perspective. *Journal of Psychophysiology*, *21*(3-4), 204-213.

REFERENCES

- Baldeweg, T., Klugman, A., Gruzelier J. H., & Hirsch, S. R. (2002). Impairment in frontal but not temporal components of mismatch negativity in schizophrenia. *International Journal of Psychophysiology*, *43*, 111-122.
- Baldeweg T, Williams J. D, Gruzelier J. H. (1999). Differential changes in frontal and sub-temporal components of mismatch negativity. *Int J Psychophysiol*, *3*, 143–8.
- Baldeweg, T., Klugman, A., Gruzelier, J., & Hirsch, S. R. (2004). Mismatch negativity potentials and cognitive impairment in schizophrenia. *Schizophrenia research*, *69*, 203-217.
- Baudena, P., Halgren, E., Heit, G., & Clarke, J. M. (1995). Intracerebral potentials to rare target and distractor auditory and visual stimuli. III. Frontal cortex. *Electroencephalography and clinical neurophysiology*, *94*(4), 251-264.
- Barascud, N., Pearce, M. T., Griffiths, T. D., Friston, K. J., & Chait, M. (2016). Brain responses in humans reveal ideal observer-like sensitivity to complex acoustic patterns. *Proceedings of the National Academy of Sciences*, *113*(5), E616-E625.
- Bargh, J. A., & Pietromonaco, P. (1982). Automatic information processing and social perception: The influence of trait information presented outside of conscious awareness on impression formation. *Journal of personality and Social psychology*, *43*(3), 437.
- Bastos, A. M., Usrey, W. M., Adams, R. A., Mangun, G. R., Fries, P., & Friston, K. J. (2012). Canonical microcircuits for predictive coding. *Neuron*, *76*(4), 695-711.

REFERENCES

- Baumeister, R. F., Bratslavsky, E., Finkenauer, C., & Vohs, K. D. (2001). Bad is stronger than good. *Review of General Psychology*, 5(4), 323.
- Bendixen, A., Prinz, W., Horváth, J., Trujillo-Barreto, N. J., & Schröger, E. (2008). Rapid extraction of auditory feature contingencies. *Neuroimage*, 41, 1111-1119.
- Bernardo, J. M., & Smith, A. F. (2001). Bayesian theory.
- Berti, S. (2013). The role of auditory transient and deviance processing in distraction of task performance: a combined behavioral and event-related brain potential study.
- Birnbaum, M. H. (1974). The nonadditivity of personality impressions. *Journal of Experimental Psychology*, 102(3), 543.
- Bodatsch, M., Ruhrmann, S., Wagner, M., Müller, R., Schultze-Lutter, F., Frommann, I., ... & Brockhaus-Dumke, A. (2011). Prediction of psychosis by mismatch negativity. *Biological psychiatry*, 69, 959-966.
- Bottcher-Gandor, C., & Ullsperger, P. (1992). Mismatch Negativity in Event-Related Potentials to Auditory Stimuli as a Function of Varying Interstimulus Interval. *Psychophysiology*, 29(5), 546-550.
- Brown, H. R., & Friston, K. J. (2012). Dynamic causal modelling of precision and synaptic gain in visual perception—an EEG study. *Neuroimage*, 63(1), 223-231.
- Brunswick, E. (1956). Perception and the representative design of psychological experiments (2 ed.). Berkeley, CA: University of California Press.
- Budd, T.W., Barry, R.J., Gordon, E., Rennie, C., & Michie, P.T. (1998). Decrement of the N1 auditory event-related potential with stimulus repetition:

REFERENCES

- Habituation vs. refractoriness. *International Journal of Psychophysiology*, 31, 51–68.
- Buschman, T. J., & Miller, E. K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science*, 315(5820), 1860-1862.
- Butler, R. A. (1968). Effect of changes in stimulus frequency and intensity on habituation of the human vertex potential. *The Journal of the Acoustical Society of America*, 44(4), 945-950.
- Carney, D. R., & Banaji, M. R. (2012). First is best. *PloS one*, 7(6), e35088.
- Catts, S. V., Shelley, A. M., Ward, P. B., & Liebert, B. (1995). Brain potential evidence for an auditory sensory memory deficit in schizophrenia. *The American journal of psychiatry*, 152(2), 213.
- Cheour, M., Ceponiene, R., Lehtokoski, A., Luuk, A., Allik, J., Alho, K., & Näätänen, R. (1998). Development of language-specific phoneme representations in the infant brain. *Nature neuroscience*, 1(5), 351-353.
- Cheour, M., Čeponienė, R., Leppänen, P., Alho, K., Kujala, T., Renlund, M., ... & Näätänen, R. (2002a). The auditory sensory memory trace decays rapidly in newborns. *Scandinavian journal of psychology*, 43(1), 33-39.
- Cheour, M., Martynova, O., Näätänen, R., Erkkola, R., Sillanpää, M., Kero, P., ... & Savela, J. (2002b). Psychobiology: Speech sounds learned by sleeping newborns. *Nature*, 415(6872), 599.
- Colder, B. (2015). The basal ganglia select the expected sensory input used for predictive coding. *Frontiers in computational neuroscience*, 9.
- Collins, D. J., & Shanks, D. R. (2002). Momentary and integrative response strategies in causal judgment. *Memory & Cognition*, 30(7), 1138-1147.

REFERENCES

- Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature reviews neuroscience*, 3(3), 201-215.
- Costa-Faidella, J., Grimm, S., Slabu, L., Díaz-Santaella, F., & Escera, C. (2011). Multiple time scales of adaptation in the auditory system as revealed by human evoked potentials. *Psychophysiology*, 48, 774-783.
- Courtney, S. M., Petit, L., Haxby, J. V., & Ungerleider, L. G. (1998). The role of prefrontal cortex in working memory: examining the contents of consciousness. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 353(1377), 1819-1828.
- Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science*, 279(5355), 1347-1351.
- Cowan, N. (1984). On short and long auditory stores. *Psychological bulletin*, 96(2), 341.
- Cowan, N., Winkler, I., Teder, W., & Näätänen, R. (1993). Memory prerequisites of mismatch negativity in the auditory event-related potential (ERP). *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 19(4), 909.
- Czigler, I. (2007). Visual mismatch negativity: violation of non-attended environmental regularities. *Journal of Psychophysiology*, 21, 224-230.
- Czigler, I., Balázs, L., & Winkler, I. (2002). Memory-based detection of task-irrelevant visual changes. *Psychophysiology*, 39(6), 869-873.
- Deacon, D., Nousak, J. M., Pilotti, M., Ritter, W., & Yang, C. M. (1998). Automatic change detection: does the auditory system use representations of individual stimulus features or gestalts? *Psychophysiology*, 35(4), 413-419.

REFERENCES

- Deary, I. J., Simonotto, E., Meyer, M., Marshall, A., Marshall, I., Goddard, N., & Wardlaw, J. M. (2004). The functional anatomy of inspection time: an event-related fMRI study. *Neuroimage*, 22(4), 1466-1479.
- Dennis, M. J., & Ahn, W. K. (2001). Primacy in causal strength judgments: The effect of initial evidence for generative versus inhibitory relationships. *Memory & Cognition*, 29(1), 152-164.
- Dehaene-Lambertz, G. (1997). Electrophysiological correlates of categorical phoneme perception in adults. *NeuroReport*, 8(4), 919-924.
- Deouell, L. Y., Heller, A. S., Malach, R., D'Esposito, M., & Knight, R. T. (2007). Cerebral responses to change in spatial location of unattended sounds. *Neuron*, 55(6), 985-996.
- Deouell, L. Y., Parnes, A., Pickard, N., & Knight, R. T. (2006). Spatial location is accurately tracked by human auditory sensory memory: evidence from the mismatch negativity. *European Journal of Neuroscience*, 24(5), 1488-1494.
- Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proceedings of the National Academy of Sciences*, 93(24), 13494-13499.
- Devine, P. G. (1989). Stereotypes and prejudice: Their automatic and controlled components. *Journal of personality and social psychology*, 56(1), 5.
- Dittmann-Balcar, A., Thienel, R., & Schall, U. (1999). Attention-dependent allocation of auditory processing resources as measured by mismatch negativity. *Neuroreport*, 10(18), 3749-3753.
- Doeller, C. F., Opitz, B., Mecklinger, A., Krick, C., Reith, W., & Schröger, E. (2003). Prefrontal cortex involvement in preattentive auditory deviance

REFERENCES

- detection: neuroimaging and electrophysiological evidence. *Neuroimage*, 20(2), 1270-1282.
- Doll, B. B., Jacobs, W. J., Sanfey, A. G., & Frank, M. J. (2009). Instructional control of reinforcement learning: a behavioral and neurocomputational investigation. *Brain research*, 1299, 74-94.
- Doya, K. (2002). Metalearning and neuromodulation. *Neural Networks*, 15(4), 495-506.
- Draganova, R., Eswaran, H., Murphy, P., Huotilainen, M., Lowery, C., & Preissl, H. (2005). Sound frequency change detection in fetuses and newborns, a magnetoencephalographic study. *Neuroimage*, 28(2), 354-361.
- Draganova, R., Eswaran, H., Murphy, P., Lowery, C., & Preissl, H. (2007). Serial magnetoencephalographic study of fetal and newborn auditory discriminative evoked responses. *Early human development*, 83(3), 199-207.
- Escera, C., & Corral, M. J. (2007). Role of mismatch negativity and novelty-P3 in involuntary auditory attention. *Journal of Psychophysiology*, 21(3-4), 251-264.
- Escera, C., Alho, K., Winkler, I., & Näätänen, R. (1998). Neural mechanisms of involuntary attention to acoustic novelty and change. *Journal of cognitive neuroscience*, 10(5), 590-604.
- Escera, C., & Malmierca, M. S. (2014). The auditory novelty system: an attempt to integrate human and animal research. *Psychophysiology*, 51(2), 111-123.
- Escera, C., Yago, E., Corral, M. J., Corbera, S., & Nuñez, M. I. (2003). Attention capture by auditory significant stimuli: semantic analysis follows attention switching. *European Journal of Neuroscience*, 18(8), 2408-2412.

REFERENCES

- Feldman, H., & Friston, K. (2010). Attention, uncertainty, and free-energy. *Frontiers in human neuroscience*, 4, 215.
- Felleman, D. J., & Van Essen, D. C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral cortex*, 1(1), 1-47.
- Fischer, C., Morlet, D., Bouchet, P., Luaute, J., Jourdan, C., & Salord, F. (1999). Mismatch negativity and late auditory evoked potentials in comatose patients. *Clinical neurophysiology*, 110(9), 1601-1610.
- Fischer, C., Morlet, D., & Giard, M. H. (2000). Mismatch negativity and N100 in comatose patients. *Audiology and Neurotology*, 5(3-4), 192-197.
- Fitzgerald, K., Provost, A., & Todd, J. (2017). First-impression bias effects on mismatch negativity to auditory spatial deviants. *Psychophysiology*.
- Friedman, D., Cycowicz, Y. M., & Gaeta, H. (2001). The novelty P3: an event-related brain potential (ERP) sign of the brain's evaluation of novelty. *Neuroscience & Biobehavioral Reviews*, 25(4), 355-373.
- Friston, K. (2003). Learning and inference in the brain. *Neural Networks*, 16(9), 1325-1352.
- Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 360(1456), 815-836.
- Friston, K. (2008). Hierarchical models in the brain. *PLoS computational biology*, 4(11), e1000211.
- Friston, K. (2009). The free-energy principle: a rough guide to the brain?. *Trends in cognitive sciences*, 13(7), 293-301.
- Friston, K., (2012). The history of the future of the Bayesian brain. *Neuroimage*, 62(2), 1230-1233.

REFERENCES

- Friston, K., & Kiebel, S. (2009). Predictive coding under the free-energy principle. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *364*(1521), 1211-1221.
- Friston, K., Kilner, J., & Harrison, L. (2006). A free energy principle for the brain. *Journal of Physiology-Paris*, *100*(1), 70-87.
- Fritz, J. B., David, S. V., Radtke-Schuller, S., Yin, P., & Shamma, S. A. (2010). Adaptive, behaviorally gated, persistent encoding of task-relevant auditory information in ferret frontal cortex. *Nature neuroscience*, *13*(8), 1011-1019.
- Frost, J. D., Winkler, I., Provost, A., & Todd, J. (2016). Surprising sequential effects on MMN. *Biological psychology*, *116*, 47-56.
- Fuster, J. M. (1988). Prefrontal cortex. In *Comparative neuroscience and neurobiology* (pp. 107-109). Birkhäuser Boston.
- Galizio, M. (1979). Contingency-shaped and rule-governed behavior: Instructional control of human loss avoidance. *Journal of the Experimental Analysis of Behavior*, *31*(1), 53-70.
- Garrido, M. I., Friston, K. J., Kiebel, S. J., Stephan, K. E., Baldeweg, T., & Kilner, J. M. (2008). The functional anatomy of the MMN: a DCM study of the roving paradigm. *Neuroimage*, *42*(2), 936-944.
- Garrido, M. I., Kilner, J. M., Kiebel, S. J., Stephan, K. E., & Friston, K. J. (2007). Dynamic causal modelling of evoked potentials: a reproducibility study. *Neuroimage*, *36*(3), 571-580.
- Garrido, M. I., Kilner, J. M., Stephan, K. E., & Friston, K. J. (2009). The mismatch negativity: a review of underlying mechanisms. *Clinical neurophysiology*, *120*(3), 453-463.

REFERENCES

- Giard MH, Perrin F, Pernier J, Bouchet P. (1990) Brain generators implicated in processing of auditory stimulus deviance: a topographic event-related potential study. *Psychophysiology*, 27, 627–40.
- Gibson, J. J. (1962). The survival value of sensory perception. In *Biological prototypes and synthetic systems* (pp. 230-232). Springer US.
- Gibson, E. J. (1963). Perceptual learning. *Annual review of psychology*, 14(1), 29-56.
- Gomes, H., Bernstein, R., Ritter, W., Vaughan, H. G., & Miller, J. (1997). Storage of feature conjunction in transient auditory memory. *Psychophysiology*, 34(6), 712-716.
- Gil-da-Costa, R., Stoner, G. R., Fung, R., & Albright, T. D. (2013). Nonhuman primate model of schizophrenia using a noninvasive EEG method. *Proceedings of the National Academy of Sciences*, 110, 15425-15430.
- Gregory, R. L. (1980). Perceptions as hypotheses. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, 290(1038), 181-197.
- Griffiths, T. L., Kemp, C., & Tenenbaum, J. B. (2008). Bayesian models of cognition.
- Grimm, S., Widmann, A., & Schröger, E. (2004). Differential processing of duration changes within short and long sounds in humans. *Neuroscience Letters*, 356(2), 83-86
- Haenschel, C., Vernon, D. J., Dwivedi, P., Gruzelier, J. H., & Baldeweg, T. (2005). Event-related brain potential correlates of human auditory sensory memory-trace formation. *The journal of Neuroscience*, 25, 10494-10501.
- Halgren, E., Sherfey, J., Irimia, A., Dale, A. M., & Marinkovic, K. (2011). Sequential temporo-fronto-temporal activation during monitoring of the

REFERENCES

- auditory environment for temporal patterns. *Human brain mapping*, 32(8), 1260-1276.
- Hayes, S. C. (1993). Rule governance: basic behavioral research and applied implications. *Current Directions in Psychological Science*, 2(6), 193-197.
- Hayes, S. C. (1989). Rule-governed Behavior: Cognition, Contingencies, and Instructional Control. Plenum Press.
- Hayes, S. C., Brownstein, A. J., Zettle, R. D., Rosenfarb, I., & Korn, Z. (1986). Rule-governed behavior and sensitivity to changing consequences of responding. *Journal of the Experimental Analysis of behavior*, 45(3), 237-256.
- Hamilton, D. L. (1979). A Cognitive-Attributional Analysis of Stereotyping. *Advances in experimental social psychology*, 12, 53-84.
- Hamilton, D. L., Katz, L. B., & Leirer, V. O. (1980). Cognitive representation of personality impressions: Organizational processes in first impression formation. *Journal of Personality and Social Psychology*, 39(6), 1050.
- Hari, R., Hämäläinen, M., Ilmoniemi, R., Kaukoranta, E., Reinikainen, K., Salminen, J., ... & Sams, M. (1984). Responses of the primary auditory cortex to pitch changes in a sequence of tone pips: neuromagnetic recordings in man. *Neuroscience letters*, 50(1-3), 127-132.
- Helmholtz, H. V. (1867). *Handbuch der physiologischen Optik* (transl. in English by JPC Southhall as *Treatise on Physiological Optics*). Leipzig, Germany: L. Voss.
- Hertwig, R., Barron, G., Weber, E. U., & Erev, I. (2004). Decisions from experience and the effect of rare events in risky choice. *Psychological science*, 15(8), 534-539.

REFERENCES

- Hochstein, S., & Ahissar, M. (2002). View from the top: Hierarchies and reverse hierarchies in the visual system. *Neuron*, *36*(5), 791-804.
- Hogarth, R. M., & Einhorn, H. J. (1992). Order effects in belief updating: The belief-adjustment model. *Cognitive psychology*, *24*(1), 1-55.
- Horváth, J., Sussman, E., Winkler, I., & Schröger, E. (2011). Preventing distraction: assessing stimulus-specific and general effects of the predictive cueing of deviant auditory events. *Biological Psychology*, *87*, 35-48.
- Hughes, H. C., Darcey, T. M., Barkan, H. I., Williamson, P. D., Roberts, D. W., & Aslin, C. H. (2001). Responses of human auditory association cortex to the omission of an expected acoustic event. *Neuroimage*, *13*(6), 1073-1089.
- Huotilainen, M., Kujala, A., Hotakainen, M., Parkkonen, L., Taulu, S., Simola, J., ... & Näätänen, R. (2005). Short-term memory functions of the human fetus recorded with magnetoencephalography. *Neuroreport*, *16*(1), 81-84.
- Iglesias, S., Mathys, C., Brodersen, K. H., Kasper, L., Piccirelli, M., den Ouden, H. E., & Stephan, K. E. (2013). Hierarchical prediction errors in midbrain and basal forebrain during sensory learning. *Neuron*, *80*(2), 519-530.
- Jääskeläinen, I. P., Ahveninen, J., Bonmassar, G., Dale, A. M., Ilmoniemi, R. J., Levänen, S., ... & Tiitinen, H. (2004). Human posterior auditory cortex gates novel sounds to consciousness. *Proceedings of the National Academy of Sciences of the United States of America*, *101*(17), 6809-6814.
- Jacobsen, T., Horváth, J., Schröger, E., Lattner, S., Widmann, A., & Winkler, I. (2004). Pre-attentive auditory processing of lexicality. *Brain and Language*, *88*, 54-67.
- Jacobsen, T., & Schröger, E. (2001). Is there pre-attentive memory-based comparison of pitch?. *Psychophysiology*, *38*(4), 723-727.

REFERENCES

- Jacobsen, T., & Schröger, E. (2003). Measuring duration mismatch negativity. *Clinical Neurophysiology, 114*(6), 1133-1143
- Jacobsen, T., Schröger, E., Winkler, I., & Horváth, J. (2005). Familiarity affects the processing of task-irrelevant auditory deviance. *Journal of Cognitive Neuroscience, 17*(11), 170.
- Jacoby, L. L., Wahlheim, C. N., Rhodes, M. G., Daniels, K. A., & Rogers, C. S. (2010). Learning to diminish the effects of proactive interference: Reducing false memory for young and older adults. *Memory & Cognition, 38*(6), 820-829.
- Jaramillo, M., Paavilainen, P., & Näätänen, R. (2000). Mismatch negativity and behavioural discrimination in humans as a function of the magnitude of change in sound duration. *Neuroscience Letters, 290*(2), 101-104.
- Javitt, D. C., Grochowski, S., Shelley, A. M., & Ritter, W. (1998). Impaired mismatch negativity (MMN) generation in schizophrenia as a function of stimulus deviance, probability, and interstimulus/interdeviant interval. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 108*, 143-153.
- Javitt, D. C., Zukin, S. R., Heresco-Levy, U., & Umbricht, D. (2012). Has an angel shown the way? Etiological and therapeutic implications of the PCP/NMDA model of schizophrenia. *Schizophrenia bulletin, 38*, 958-966.
- Kane, N. M., Curry, S. H., Butler, S. R., & Cummins, B. H. (1993). Electrophysiological indicator of awakening from coma. *The Lancet, 341*(8846), 688.
- Kane, N. M., Curry, S. H., Rowlands, C. A., Manara, A. R., Lewis, T., Moss, T., ... & Butler, S. R. (1996). Event-related potentials—neurophysiological tools

REFERENCES

- for predicting emergence and early outcome from traumatic coma. *Intensive care medicine*, 22(1), 39-46.
- Kekoni, J., Hämäläinen, H., Saarinen, M., Gröhn, J., Reinikainen, K., Lehtokoski, A., & Näätänen, R. (1997). Rate effect and mismatch responses in the somatosensory system: ERP-recordings in humans. *Biological psychology*, 46(2), 125-142.
- Kersten, D., Mamassian, P., & Yuille, A. (2004). Object perception as Bayesian inference. *Annu. Rev. Psychol.*, 55, 271-304.
- Kiebel, S. J., Daunizeau, J., & Friston, K. J. (2008). A hierarchy of time-scales and the brain. *PLoS Comput Biol*, 4(11), e1000209.
- Knight, R. T. (1984). Decreased response to novel stimuli after prefrontal lesions in man. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 59(1), 9-20.
- Knight, R. T., & Scabini, D. (1998). Anatomic bases of event-related potentials and their relationship to novelty detection in humans. *Journal of Clinical Neurophysiology*, 15(1), 3-13.
- Knill, D. C., & Pouget, A. (2004). The Bayesian brain: the role of uncertainty in neural coding and computation. *TRENDS in Neurosciences*, 27(12), 712-719.
- Kok, P., & de Lange, F. P. (2015). Predictive coding in sensory cortex. In *An introduction to model-based cognitive neuroscience* (pp. 221-244). Springer New York.
- Krauel, K., Schott, P., Sojka, B., Pause, B. M., & Ferstl, R. (1999). Is there a mismatch negativity analogue in the olfactory event-related potential?. *Journal of Psychophysiology*, 13(1), 49.

REFERENCES

- Kujala, T., Tervaniemi, M., & Schröger, E. (2007). The mismatch negativity in cognitive and clinical neuroscience: theoretical and methodological considerations. *Biological psychology*, *74*(1), 1-19.
- Lee, T. S., & Mumford, D. (2003). Hierarchical Bayesian inference in the visual cortex. *JOSA A*, *20*(7), 1434-1448.
- Lieder, F., Stephan, K. E., Daunizeau, J., Garrido, M. I., & Friston, K. J. (2013). A neurocomputational model of the mismatch negativity. *PLoS computational biology*, *9*, e1003288.
- Light, G. A., Swerdlow, N. R., Rissling, A. J., Radant, A., Sugar, C. A., Sprock, J., ... & Braff, D. L. (2012). Characterization of neurophysiologic and neurocognitive biomarkers for use in genomic and clinical outcome studies of schizophrenia. *PLoS One*, *7*(7), e39434.
- Lim, K. H., Benbasat, I., & Ward, L. M. (2000). The role of multimedia in changing first impression bias. *Information Systems Research*, *11*(2), 115-136.
- Maekawa, T., Goto, Y., Kinukawa, N., Taniwaki, T., Kanba, S., & Tobimatsu, S. (2005). Functional characterization of mismatch negativity to a visual stimulus. *Clinical Neurophysiology*, *116*(10), 2392-2402.
- Mantonakis, A., Rodero, P., Lesschaeve, I., & Hastie, R. (2009). Order in choice: Effects of serial position on preferences. *Psychological Science*, *20*(11), 1309-1312.
- Mathys, C., Daunizeau, J., Friston, K. J., & Stephan, K. E. (2011). A Bayesian foundation for individual learning under uncertainty. *Frontiers in human neuroscience*, *5*, 39.

REFERENCES

- Mathys, C. D., Lomakina, E. I., Daunizeau, J., Iglesias, S., Brodersen, K. H., Friston, K. J., & Stephan, K. E. (2014). Uncertainty in perception and the Hierarchical Gaussian Filter. *Frontiers in human neuroscience*, *8*.
- Maunsell, J. H., & Treue, S. (2006). Feature-based attention in visual cortex. *Trends in neurosciences*, *29*(6), 317-322.
- May, P. J., & Tiitinen, H. (2010). Mismatch negativity (MMN), the deviance-elicited auditory deflection, explained. *Psychophysiology*, *47*(1), 66-122.
- May, P. J., Tiitinen, H., Ilmoniemi, R.J., Nyman, G., Taylor, J.G., & Näätänen, R. (1999). Frequency change detection in human auditory cortex. *Journal of Computational Neuroscience*, *6*, 99–120.
- Mesulam, M. M. (1998). From sensation to cognition. *Brain*, *121*(6), 1013-1052.
- Mittag, M., Takegata, R., & Winkler, I. (2016). Transitional probabilities are prioritized over stimulus/pattern probabilities in auditory deviance detection: memory basis for predictive sound processing. *Journal of Neuroscience*, *36*(37), 9572-9579.
- Mullens, D., Winkler, I., Damaso, K., Heathcote, A., Whitson, L., Provost, A., & Todd, J. (2016). Biased relevance filtering in the auditory system: A test of certainty-weighted first-impressions. *Biological psychology*, *115*, 101-111.
- Mullens, D., Woodley, J., Whitson, L., Provost, A., Heathcote, A., Winkler, I., & Todd, J. (2014). Altering the primacy bias - How does a prior task affect mismatch negativity? *Psychophysiology*, *51*(5), 437-445.
- Müller, B. W., Jüptner, M., Jentzen, W., & Müller, S. P. (2002). Cortical activation to auditory mismatch elicited by frequency deviant and complex novel sounds: a PET study. *Neuroimage*, *17*(1), 231-239.

REFERENCES

- Müller, D., Widmann, A., & Schröger, E. (2013). Object-related regularities are processed automatically: evidence from the visual mismatch negativity. *Frontiers in human neuroscience*, 7.
- Muller-Gass, A., Stelmack, R. M., & Campbell, K. B. (2005). "... and were instructed to read a self-selected book while ignoring the auditory stimuli": the effects of task demands on the mismatch negativity. *Clinical Neurophysiology*, 116(9), 2142-2152.
- Mumford, D. (1992). On the computational architecture of the neocortex. *Biological cybernetics*, 66(3), 241-251.
- Näätänen, R. (1984). In search of a short-duration memory trace of a stimulus in the human brain. *Perspectives to human action and personality: Essays in honour of Martti Takala. Jyväskylä studies in education, psychology and social science*, 22-36.
- Näätänen, R. (1990). The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. *Behavioral and Brain Sciences*, 13(02), 201-233.
- Näätänen, R. (1992) *In Attention and Brain Function*. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Näätänen, R. (2001). The perception of speech sounds by the human brain as reflected by the mismatch negativity (MMN) and its magnetic equivalent (MMNm). *Psychophysiology*, 38(1), 1-21.
- Näätänen, R., & Alho, K. (1997). Higher-order processes in auditory-change detection. *Trends in Cognitive Sciences*, 1(2), 44-45.
- Näätänen, R. Gaillard, & Mäntysalo, (1978). Early selective-attention effect on evoked potential reinterpreted. *Acta Psychol*, 42, 313–29.

REFERENCES

- Näätänen, R., & Michie, P. T. (1979). Early selective-attention effects on the evoked potential: a critical review and reinterpretation. *Biological psychology*, 8(2), 81-136.
- Näätänen R., Jacobsen, T., & Winkler, I. (2005). Memory-based or afferent processes in mismatch negativity (MMN): a review of the evidence. *Psychophysiology*, 42, 25-32.
- Näätänen, R., Kujala, T., & Winkler, I. (2011). Auditory processing that leads to conscious perception: a unique window to central auditory processing opened by the mismatch negativity and related responses. *Psychophysiology*, 48, 4-22.
- Näätänen, R., Lehtokoski, A., Lennes, M., Cheour, M., Huotilainen, M., Iivonen, A., ... & Allik, J. (1997). Language-specific phoneme representations revealed by electric and magnetic brain responses. *Nature*, 385(6615), 432.
- Näätänen, R., Paavilainen, P., Alho, K., Reinikainen, K., & Sams, M. (1987). The mismatch negativity to intensity changes in an auditory stimulus sequence. *Electroencephalography and clinical neurophysiology. Supplement*, 40, 125.
- Näätänen, R., Paavilainen, P., & Reinikainen, K. (1989). Do event-related potentials to infrequent decrements in duration of auditory stimuli demonstrate a memory trace in man?. *Neuroscience letters*, 107(1), 347-352.
- Näätänen, R., Paavilainen, P., Rinne, T., & Alho, K. (2007). The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clinical Neurophysiology*, 118(12), 2544-2590.
- Näätänen, R., Paavilainen, P., Titinen, H., Jiang, D., & Alho, K. (1993). Attention and mismatch negativity. *Psychophysiology*, 30(5), 436-450.

REFERENCES

- Näätänen, R., Pakarinen, S., Rinne, T., & Takegata, R. (2004). The mismatch negativity (MMN): towards the optimal paradigm. *Clinical Neurophysiology, 115*(1), 140-144.
- Näätänen, R., Simpson, M., & Loveless, N. E. (1982). Stimulus deviance and evoked potentials. *Biological psychology, 14*(1), 53-98.
- Näätänen, R., & Winkler, I. (1999). The concept of auditory stimulus representation in cognitive neuroscience. *Psychological bulletin, 125*(6), 826.
- Nakayama, Y., Yamagata, T., Tanji, J., & Hoshi, E. (2008). Transformation of a virtual action plan into a motor plan in the premotor cortex. *Journal of Neuroscience, 28*(41), 10287-10297.
- Nashida, T., Yabe, H., Sato, Y., Hiruma, T., Sutoh, T., Shinozaki, N., & Kaneko, S. (2000). Automatic auditory information processing in sleep. *Sleep, 23*(6), 821-828.
- Nisbett, R. E., & Ross, L. (1980). *Human inference: Strategies and shortcomings of social judgment*. Englewood Cliffs, NJ: Prentice Hall.
- Nittono, H., Momose, D., & Hori, T. (2001). The vanishing point of the mismatch negativity at sleep onset. *Clinical neurophysiology, 112*(5), 732-739.
- Nordby, H., Hammerborg, D., Roth, W. T., & Hugdahl, K. (1994). ERPs for infrequent omissions and inclusions of stimulus elements. *Psychophysiology, 31*(6), 544-552.
- Nordby, H., Roth, W. T., & Pfefferbaum, A. (1988). Event-Related Potentials to Time-Deviant and Pitch-Deviant Tones. *Psychophysiology, 25*(3), 249-261.
- Opitz, B., Rinne, T., Mecklinger, A., Von Cramon, D. Y., & Schröger, E. (2002). Differential contribution of frontal and temporal cortices to auditory change detection: fMRI and ERP results. *Neuroimage, 15*(1), 167-174.

REFERENCES

- Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human brain mapping, 25*(1), 46-59.
- Paavilainen, P., Karlsson, M. L., Reinikainen, K., & Näätänen, R. (1989). Mismatch negativity to change in spatial location of an auditory stimulus. *Electroencephalography and clinical neurophysiology, 73*(2), 129-141.
- Paavilainen, P., Simola, J., Jaramillo, M., Näätänen, R., & Winkler, I. (2001). Preattentive extraction of abstract feature conjunctions from auditory stimulation as reflected by the mismatch negativity (MMN). *Psychophysiology, 38*(2), 359-365.
- Paavilainen, P., Tiitinen, H., Alho, K., & Näätänen, R. (1993). Mismatch negativity to slight pitch changes outside strong attentional focus. *Biological psychology, 37*(1), 23-41.
- Pakarinen, S., Huotilainen, M., & Näätänen, R. (2010). The mismatch negativity (MMN) with no standard stimulus. *Clinical Neurophysiology, 121*(7), 1043-1050.
- Pakarinen, S., Takegata, R., Rinne, T., Huotilainen, M., & Näätänen, R. (2007). Measurement of extensive auditory discrimination profiles using the mismatch negativity (MMN) of the auditory event-related potential (ERP). *Clinical Neurophysiology, 118*(1), 177-185.
- Perdue, C. W., & Gurtman, M. B. (1990). Evidence for the automaticity of ageism. *Journal of Experimental Social Psychology, 26*(3), 199-216.
- Pratto, F., & Bargh, J. A. (1991). Stereotyping based on apparently individuating information: Trait and global components of sex stereotypes under attention overload. *Journal of Experimental Social Psychology, 27*(1), 26-47.

REFERENCES

- Pulvermüller, F., & Shtyrov, Y. (2006). Language outside the focus of attention: the mismatch negativity as a tool for studying higher cognitive processes. *Progress in neurobiology, 79*, 49-71.
- Raij, T., McEvoy, L., Mäkelä, J. P., & Hari, R. (1997). Human auditory cortex is activated by omissions of auditory stimuli. *Brain research, 745*(1), 134-143.
- Rao, R. P., & Ballard, D. H. (1999). Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects. *Nature neuroscience, 2*(1), 79-87.
- Rinne T, Alho K, Ilmoniemi RJ, Virtanen J, Näätänen R (2000). Separate time behaviors of the temporal and frontal mismatch negativity sources. *Neuroimage, 12*, 14–9.
- Rinne, T., Antila, S., & Winkler, I. (2001). Mismatch negativity is unaffected by top down predictive information. *NeuroReport, 12*, 2209-2213.
- Rinne, T., Särkkä, A., Degerman, A., Schröger, E., & Alho, K. (2006). Two separate mechanisms underlie auditory change detection and involuntary control of attention. *Brain research, 1077*(1), 135-143.
- Rosburg, T., Trautner, P., Boutros, N. N., Korzyukov, O. A., Schaller, C., Elger, C. E., & Kurthen, M. (2006). Habituation of auditory evoked potentials in intracranial and extracranial recordings. *Psychophysiology, 43*(2), 137-144.
- Rosburg, T., Zimmerer, K., & Huonker, R. (2010). Short-term habituation of auditory evoked potential and neuromagnetic field components in dependence of the interstimulus interval. *Experimental brain research, 205*(4), 559-570.
- Rothbart, M., & Park, B. (1986). On the confirmability and disconfirmability of trait concepts. *Journal of Personality and Social Psychology, 50*(1), 131.

REFERENCES

- Rozin, P., & Royzman, E. B. (2001). Negativity bias, negativity dominance, and contagion. *Personality and social psychology review*, 5(4), 296-320.
- Ruge, H., & Wolfensteller, U. (2009). Rapid formation of pragmatic rule representations in the human brain during instruction-based learning. *Cerebral Cortex*, 20(7), 1656-1667.
- Ruhnau, P., Herrmann, B., & Schröger, E. (2012). Finding the right control: the mismatch negativity under investigation. *Clinical Neurophysiology*, 123(3), 507-512.
- Rüsseler, J., Altenmüller, E., Nager, W., Kohlmetz, C., & Münte, T. F. (2001). Event-related brain potentials to sound omissions differ in musicians and non-musicians. *Neuroscience letters*, 308(1), 33-36.
- Ruusuvirta, T., Huotilainen, M., Fellman, V., & Näätänen, R. (2003). The newborn human brain binds sound features together. *Neuroreport*, 14(16), 2117-2119.
- Saarinen, J., Paavilainen, P., Schöger, E., Tervaniemi, M., & Näätänen, R. (1992). Representation of abstract attributes of auditory stimuli in the human brain. *NeuroReport*, 3(12), 1149-1151.
- Salisbury, D. F. (2012). Finding the missing stimulus mismatch negativity (MMN): emitted MMN to violations of an auditory gestalt. *Psychophysiology*, 49(4), 544-548.
- Sallinen, M., Kaartinen, J., & Lyytinen, H. (1994). Is the appearance of mismatch negativity during stage 2 sleep related to the elicitation of K-complex? *Electroencephalography and clinical neurophysiology*, 91(2), 140-148.
- Sams, M., Alho, K., & Näätänen, R. (1983). Sequential effects on the ERP in discriminating two stimuli. *Biological psychology*, 17(1), 41-58.

REFERENCES

- Sams, M., Hari, R., Rif, J., & Knuutila, J. (1993). The human auditory sensory memory trace persists about 10 sec: neuromagnetic evidence. *Journal of cognitive neuroscience*, 5(3), 363-370.
- Sams, M., Paavilainen, P., Alho, K., & Näätänen, R. (1985). Auditory frequency discrimination and event-related potentials. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 62(6), 437-448.
- Sarter, M., Bruno, J. P., & Turchi, J. (1999). Basal forebrain afferent projections modulating cortical acetylcholine, attention, and implications for neuropsychiatric disorders. *Annals of the New York Academy of Sciences*, 877(1), 368-382.
- Sarter, M., Parikh, V., & Howe, W. M. (2009). Phasic acetylcholine release and the volume transmission hypothesis: time to move on. *Nature Reviews Neuroscience*, 10(5), 383-390.
- Sato, Y., Yabe, H., Todd, J., Michie, P., Shinozaki, N., Sutoh, T., ... & Kaneko, S. (2003). Impairment in activation of a frontal attention-switch mechanism in schizophrenic patients. *Biological psychology*, 62, 49-63.
- Scharf, B. (1978). Loudness. *Handbook of Perception*. Vol. IV Hearing.
- Scherg, M., Vajsar, J., & Picton, T. W. (1989). A source analysis of the late human auditory evoked potentials. *Journal of Cognitive Neuroscience*, 1(4), 336-355.
- Schröger, E. (1996). A neural mechanism for involuntary attention shifts to changes in auditory stimulation. *J Cogn Neurosci*, 8, 527-39.
- Schröger, E. (1997). On the detection of auditory deviations: A pre-attentive activation model. *Psychophysiology*, 34(3), 245-257.

REFERENCES

- Schröger, E. (1998). Measurement and interpretation of the mismatch negativity. *Behavior Research Methods, Instruments, & Computers*, *30*(1), 131-145.
- Schröger, E. (2007). Mismatch negativity: A microphone into auditory memory. *Journal of Psychophysiology*, *21*(3-4), 138-146.
- Schröger, E., Marzecová, A., & SanMiguel, I. (2015). Attention and prediction in human audition: a lesson from cognitive psychophysiology. *European Journal of Neuroscience*, *41*(5), 641-664.
- Schröger, E., & Wolff, C. (1996). Mismatch response of the human brain to changes in sound location. *Neuroreport*, *7*(18), 3005-3008.
- Sculthorpe, L. D., Ouellet, D. R., & Campbell, K. B. (2009). MMN elicitation during natural sleep to violations of an auditory pattern. *Brain research*, *1290*, 52-62.
- Semlitsch, H. V., Anderer, P., Schuster, P., & Presslich, O. (1986). A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. *Psychophysiology*, *2*, 695-703.
- Shelley, A. M., Silipo, G., & Javitt, D. C. (1999). Diminished responsiveness of ERPs in schizophrenic subjects to changes in auditory stimulation parameters: implications for theories of cortical dysfunction. *Schizophrenia research*, *37*, 65-79.
- Shinozaki, N., Yabe, H., Sutoh, T., Hiruma, T., & Kaneko, S. (1998). Somatosensory automatic responses to deviant stimuli. *Cognitive brain research*, *7*(2), 165-171.
- Shteingart, H., Neiman, T., & Loewenstein, Y. (2013). The role of first impression in operant learning. *Journal of Experimental Psychology: General*, *142*(2), 476.

REFERENCES

- Skowronski, J. J., & Carlston, D. E. (1992). Caught in the act: When impressions based on highly diagnostic behaviours are resistant to contradiction. *European Journal of Social Psychology*, *22*(5), 435-452.
- Spratling, M. W. (2008). Reconciling predictive coding and biased competition models of cortical function. *Frontiers in computational neuroscience*, *2*.
- Stephan, K. E., Baldeweg, T., & Friston, K. J. (2006). Synaptic plasticity and dysconnection in schizophrenia. *Biological psychiatry*, *59*, 929-939.
- Stuss, D. T., & Benson, D. F. (1984). Neuropsychological studies of the frontal lobes. *Psychological bulletin*, *95*(1), 3.
- Sussman, E. S. (2007). A new view on the MMN and attention debate: the role of context in processing auditory events. *Journal of Psychophysiology*, *21*, 164-175.
- Sussman, E. S. (2013). Attention matters: pitch vs. pattern processing in adolescence. *Frontiers in psychology*, *4*, 333.
- Sussman, E., Gomes, H., Nousak, J. M. K., Ritter, W., & Vaughan, H. G. (1998). Feature conjunctions and auditory sensory memory. *Brain Research*, *793*(1), 95-102.
- Sussman, E. S., & Gumenyuk, V. (2005). Organization of sequential sounds in auditory memory. *Neuroreport*, *16*(13), 1519-1523.
- Sussman, E., & Steinschneider, M. (2006). Neurophysiological evidence for context-dependent encoding of sensory input in human auditory cortex. *Brain research*, *1075*(1), 165-174.
- Sussman, E., & Winkler, I. (2001). Dynamic sensory updating in the auditory system. *Cognitive Brain Research*, *12*(3), 431-439.

REFERENCES

- Sussman, E., Winkler, I., Huoutilainen, M., Ritter, W., & Näätänen, R. (2002). Top-down effects on the initially stimulus-driven auditory organization. *Cognitive Brain Research, 13*, 393–405.
- Sussman, E., Winkler, I., & Wang, W. (2003). MMN and attention: competition for deviance detection. *Psychophysiology, 40*(3), 430-435.
- Szymanski, M. D., Yund, E. W., & Woods, D. L. (1999). Phonemes, intensity and attention: differential effects on the mismatch negativity (MMN). *The Journal of the Acoustical Society of America, 106*(6), 3492-3505.
- Takegata, R., Paavilainen, P., Näätänen, R., & Winkler, I. (1999). Independent processing of changes in auditory single features and feature conjunctions in humans as indexed by the mismatch negativity. *Neuroscience Letters, 266*(2), 109-112.
- Tervaniemi, M., Lehtokoski, A., Sinkkonen, J., Virtanen, J., Ilmoniemi, R. J., & Näätänen, R. (1999). Test–retest reliability of mismatch negativity for duration, frequency and intensity changes. *Clinical Neurophysiology, 110*(8), 1388-1393.
- Tervaniemi, M., Maury, S., & Näätänen, R. (1994a). Neural representations of abstract stimulus features in the human brain as reflected by the mismatch negativity. *Neuroreport, 5*(7), 844-846.
- Tetlock, P. E. (1983). Accountability and the perseverance of first impressions. *Social Psychology Quarterly, 285-292*.
- Todd, J., Harms, L., Schall, U., & Michie, P. T. (2013). Mismatch negativity: translating the potential. *Frontiers in psychiatry, 4*,

REFERENCES

- Todd, J., Heathcote, A., Mullens, D., Whitson, L. R., Provost, A., & Winkler, I. (2014a). What controls gain in gain control? Mismatch negativity (MMN), priors and system biases. *Brain topography*, 1-12, 578- 589.
- Todd, J., Heathcote, A., Whitson, L. R., Mullens, D., Provost, A., & Winkler, I. (2014b). Mismatch negativity (MMN) to pitch change is susceptible to order-dependent bias. *Frontiers in Neuroscience*.
- Todd, J., Michie, P. T., Schall, U., Karayanidis, F., Yabe, H., & Näätänen, R. (2008). Deviant matters: duration, frequency, and intensity deviants reveal different patterns of mismatch negativity reduction in early and late schizophrenia. *Biological psychiatry*, 63(1), 58-64.
- Todd, J., Michie, P. T., Schall, U., Ward, P. B., & Catts, S. V. (2012). Mismatch negativity (MMN) reduction in schizophrenia—Impaired prediction-error generation, estimation or salience? *International Journal of Psychophysiology*, 83, 222-231.
- Todd, J., Provost, A., Cooper, G. (2011). Lasting first impressions: A conservative bias in automatic filters of the acoustic environment. *Neuropsychologia*, 49, 3399-3405.
- Todd, J., Provost, A., Whitson, L.R., Cooper, G., Heathcote, A. (2013). Not so primitive: Context sensitive meta-learning about unattended sound sequences. *Journal of Neurophysiology*, 109, 99-105.
- Todd, J., Provost, A., Whitson, L., & Mullens, D. (2017). Initial uncertainty impacts statistical learning in sound sequence processing. *Journal of Physiology-Paris*.

REFERENCES

- Trejo, L. J., Ryan-Jones, D. L., & Kramer, A. F. (1995). Attentional modulation of the mismatch negativity elicited by frequency differences between binaurally presented tone bursts. *Psychophysiology*, *32*(4), 319-328.
- Ulanovsky, N., Las, L., Farkas, D., & Nelken, I. (2004). Multiple time scales of adaptation in auditory cortex neurons. *The Journal of Neuroscience*, *24*, 10440-10453.
- Van Zuijen, T. L., Sussman, E., Winkler, I., Näätänen, R., & Tervaniemi, M. (2004). Grouping of sequential sounds – an event-related potential study comparing musicians and non-musicians. *Journal of Cognitive Neuroscience*, *16*, 331-338.
- Vapnik, V. N., & Vapnik, V. (1998). *Statistical learning theory* (Vol. 1). New York: Wiley.
- Vuust, P., Pallesen, K. J., Bailey, C., van Zuijen, T. L., Gjedde, A., Roepstorff, A., et al., (2005). To musicians, the message is in the meter pre-attentive neuronal responses to incongruent rhythm are left-lateralized in musicians. *Neuroimage*, *24*, 560-564.
- Waiter, G. D., Deary, I. J., Staff, R. T., Murray, A. D., Fox, H. C., Starr, J. M., & Whalley, L. J. (2009). Exploring possible neural mechanisms of intelligence differences using processing speed and working memory tasks: An fMRI study. *Intelligence*, *37*(2), 199-206.
- Waiter, G. D., Fox, H. C., Murray, A. D., Starr, J. M., Staff, R. T., Bourne, V. J., ... & Deary, I. J. (2008). Is retaining the youthful functional anatomy underlying speed of information processing a signature of successful cognitive ageing? An event-related fMRI study of inspection time performance. *Neuroimage*, *41*(2), 581-595.

REFERENCES

- Walker, L. J., Carpenter, M., Downs, C. R., Cranford, J. L., Stuart, A., & Pravica, D. (2001). Possible neuronal refractory or recovery artifacts associated with recording the mismatch negativity response. *Journal of the American Academy of Audiology, 12*(7).
- Wacongne, C., Changeux, J. P., & Dehaene, S. (2012). A neuronal model of predictive coding accounting for the mismatch negativity. *The Journal of neuroscience, 32*, 3665-3678.
- Wiens, S., Szychowska, M., & Nilsson, M. E. (2016). Visual task demands and the auditory mismatch negativity: an empirical study and a meta-analysis. *PloS one, 11*(1), e0146567.
- Winkler, I., (2007) Interpreting the mismatch negativity. *Journal of Psychophysiology, 21*, 147-163.
- Winkler, I., & Cowan, N. (2005). From sensory to long-term memory: evidence from auditory memory reactivation studies. *Experimental psychology, 52*(1), 3-20.
- Winkler, I., & Czigler, I. (2012). Evidence from auditory and visual event-related potential (ERP) studies of deviance detection (MMN and vMMN) linking predictive coding theories and perceptual object representations. *International Journal of Psychophysiology, 83*(2), 132-143.
- Winkler, I., Denham, S. L., & Nelken, I. (2009). Modeling the auditory scene: predictive regularity representations and perceptual objects. *Trends in cognitive sciences, 13*(12), 532-540.
- Winkler, I., Karmos, G., & Näätänen, R. (1996). Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. *Brain research, 742*(1), 239-252.

REFERENCES

- Winkler, I., Korzyukov, O., Gumenyuk, V., Cowan, N., Linkenkaer-Hansen, K., Ilmoniemi, R. J., ... & Näätänen, R. (2002). Temporary and longer term retention of acoustic information. *Psychophysiology*, *39* (4), 530-534.
- Winkler, I., Reinikainen, K., & Näätänen, R. (1993). Event-related brain potentials reflect traces of echoic memory in humans. *Perception & Psychophysics*, *53*(4), 443-449.
- Winkler, I., & Schröger, E., (2015). Auditory perceptual objects as generative models: Setting the stage for communication by sound. *Brain & Language*, *148*, 1-22
- Winkler, I., Schröger, E., & Cowan, N. (2001). The role of large-scale memory organization in the mismatch negativity event-related brain potential. *Journal of Cognitive Neuroscience*, *13*(1), 59-71.
- Winkler, I., Sussman, E., Tervaniemi, M., Horváth, J., Ritter, W., & Näätänen, R. (2003). Preattentive auditory context effects. *Cognitive, Affective, & Behavioral Neuroscience*, *3*(1), 57-77.
- Woldorff, M. G., Hackley, S. A., & Hillyard, S. A. (1991). The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. *Psychophysiology*, *28*(1), 30-42.
- Woldorff, M. G., & Hillyard, S. A. (1991). Modulation of early auditory processing during selective listening to rapidly presented tones. *Electroencephalography and clinical neurophysiology*, *79*(3), 170-191.
- Woldorff, M. G., Hillyard, S. A., Gallen, C. C., Hampson, S. R., & Bloom, F. E. (1998). Magnetoencephalographic recordings demonstrate attentional modulation of mismatch-related neural activity in human auditory cortex. *Psychophysiology*, *35*(3), 283-292.

REFERENCES

- Woods, D. L. (1992). Auditory selective attention in middle-aged and elderly subjects: an event-related brain potential study. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 84(5), 456-468.
- Wyer, R. S. (1973). Category ratings as "subjective expected values": Implications for attitude formation and change. *Psychological Review*, 80(6), 446.
- Yabe, H., Tervaniemi, M., & Reinikainen, K. (1997). Temporal window of integration revealed by MMN to sound omission. *Neuroreport*, 8(8), 1971-1974.
- Yabe, H., Tervaniemi, M., Sinkkonen, J., Huotilainen, M., Ilmoniemi, R. J., & Näätänen, R. (1998). Temporal window of integration of auditory information in the human brain. *Psychophysiology*, 35(5), 615-619.
- Ylinen, S., Shestakova, A., Huotilainen, M., Alku, P., & Näätänen, R. (2006). Mismatch negativity (MMN) elicited by changes in phoneme length: A cross-linguistic study. *Brain Research*, 1072(1), 175-185.
- Zeki, S., & Shipp, S. (1988). The functional logic of cortical connections. *Nature*, 335(6188), 311-317.
- Yu, A. J., & Dayan, P. (2002). Acetylcholine in cortical inference. *Neural Networks*, 15(4), 719-730.
- Yu, A. J., & Dayan, P. (2005). Uncertainty, neuromodulation, and attention. *Neuron*, 46(4), 681-692.
- Zatorre, R. J. (2001). Neural specializations for tonal processing. *Annals of the New York Academy of Sciences*, 930(1), 193-210.
- Zwislocki, J. J. (1969). Temporal summation of loudness: An analysis. *The Journal of the Acoustical Society of America*, 46(2B), 431-441.

Appendices

APPENDICES

Appendix 1: Acknowledgement of acceptance of Chapter 2 for publication

From: [Juanita Todd](#)
To: [Jade Frost](#)
Subject: FW: Your Submission
Date: Friday, 27 October 2017 4:25:24 PM

Amazingly it turns out than I can!

On 14/10/2015 6:34 pm, "ees.biopsy.0.349909.2bf13e84@eesmail.elsevier.com on behalf of Biological Psychology" <ees.biopsy.0.349909.2bf13e84@eesmail.elsevier.com on behalf of ottmar.lipp@curtin.edu.au> wrote:

Ms. Ref. No.: BIOPSY-D-15-00167R1
Title: Surprising sequential effects on mismatch negativity (MMN)
Biological Psychology

Dear Juanita,

I am pleased to confirm that your paper "Surprising sequential effects on mismatch negativity (MMN)" has been accepted for publication in Biological Psychology for the special issue on MMN in schizophrenia.

When your paper is published on ScienceDirect, you want to make sure it gets the attention it deserves. To help you get your message across, Elsevier has developed a new, free service called AudioSlides: brief, webcast-style presentations that are shown (publicly available) next to your published article. This format gives you the opportunity to explain your research in your own words and attract interest. You will receive an invitation email to create an AudioSlides presentation shortly. For more information and examples, please visit <http://www.elsevier.com/audioslides>.

Your accepted manuscript will now be transferred to our production department and work will begin on creation of the proof. If we need any additional information to create the proof, we will let you know. If not, you will be contacted again in the next few days with a request to approve the proof and to complete a number of online forms that are required for publication.

Thank you for submitting your work to this journal.

With kind regards,

Patricia T. Michie, PhD
Special Issue Guest Editor
Biological Psychology

Appendix 2: Standard/Deviant Analyses for Chapter 2

Replication Study 1.

Standard and deviant ERPs. The ERP to each sound as a standard and as a deviant are plotted in supplementary Figure 5.1. Additional analyses were performed separately on the standard waveforms to elucidate the basis of the amplitude effects in the MMN difference waveform. In Figure 5.1, the differential responsiveness to each tone depends on their role (standard vs. deviant). In prior studies (Mullens et al., 2014; Todd et al., 2013) have seen repetition effects evident in the standard ERPs. Analysis over the P2 period (140 to 170ms) revealed significantly less negative ERPs to standards elicited over the second-half of sequence blocks (*Half* main effect, $F(1, 34) = 16.89, p < .001, \eta^2 = .332$), compared to the first-half of blocks. A significant main effect of *Sequence* was also revealed ($F(1, 28) = 4.58, p < .05, \eta^2 = .119$) with standard ERPs being less negative over this period in the stable sequences when compared with unstable sequences. A *Sequence x Half* interaction ($F(1, 34) = 5.27, p < .05, \eta^2 = .134$) was found to be significant and due to standard ERPs being less negative in the fast- compared to slow- sequences. This interaction was driven by less negative standards ERPs in the unstable ($M = .94$) compared to stable ($M = 1.28$) sequences in the second but not first ($M = .74$ and $.78$ for unstable and stable sequences, respectively) half of blocks (simple contrast, $F(1, 34) = 5.27, p < .05$).

Analysis confirmed that significant effects revealed for deviant ERPs are equivalent to those generated for MMN waveforms reported in the manuscript. A significant main effect of *Deviant* ($F(1, 34) = 4.88, p < .05, \eta^2 = .126$) and *Sequence* ($F(1, 34) = 13.32, p < .01, \eta^2 = .281$) as well as a *Half x Deviant x Sequence* ($F(1, 34) = 5.25, p < .05, \eta^2 = .134$) interaction was observed. Analysis revealed that this

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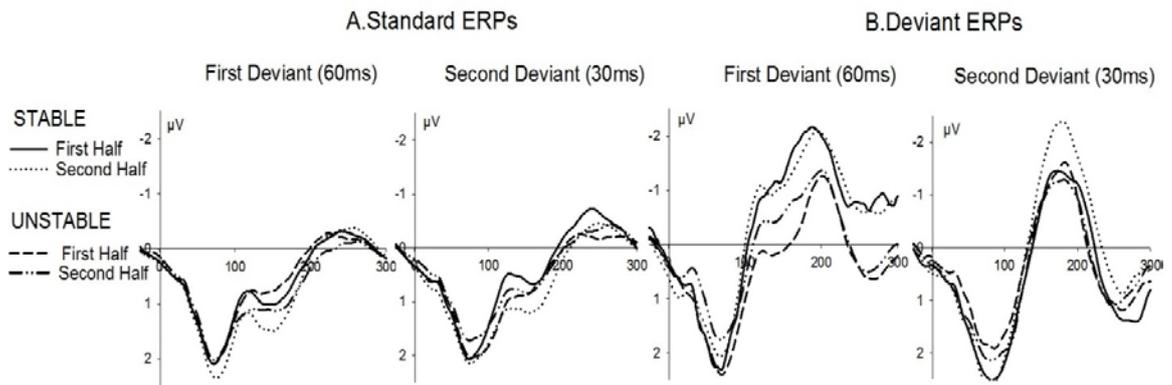


Figure 5.1. Standard and deviant ERP waveforms for replication study A. Standard and B. deviant ERPs to presentation of the sound first encountered as a deviant (60 ms) and the sound encountered as the second deviant (30 ms) in stable and unstable sequences for data obtained from the first and second half of blocks.

interaction was due to a *Deviant x Sequence* effect present in first half data only ($F(1, 34) = 5.51, p < .05, \eta^2 = .139$) that was driven by a significantly smaller MMN in the fast compared to slow sequences for the first ($p < .01$) but not second deviant ($p = .81$; see Figure 5.1). It is clear from Figure 5.1 that when tone-roles change, MMN to the sound first presented as a deviant is highly modulated by sequence stability. Comparatively, there is no difference in MMN amplitude between stable and unstable sequence for the second deviant indicating that this sound is modulated less, if at all, by the stability of tone roles within sequences. Therefore, comparison on standard and deviant ERP effects confirms that evidence of bias effects exposed in primary MMN analyses are being driven by the response to deviant tones.

Repeated Sequence Exposure Study 2

Standard and deviant ERPs. The ERP to each sound as a standard and as a deviant are plotted in supplementary Figures 5.2 and 5.3, respectively. Additional analyses were performed separately on the standard and deviant waveforms in order to

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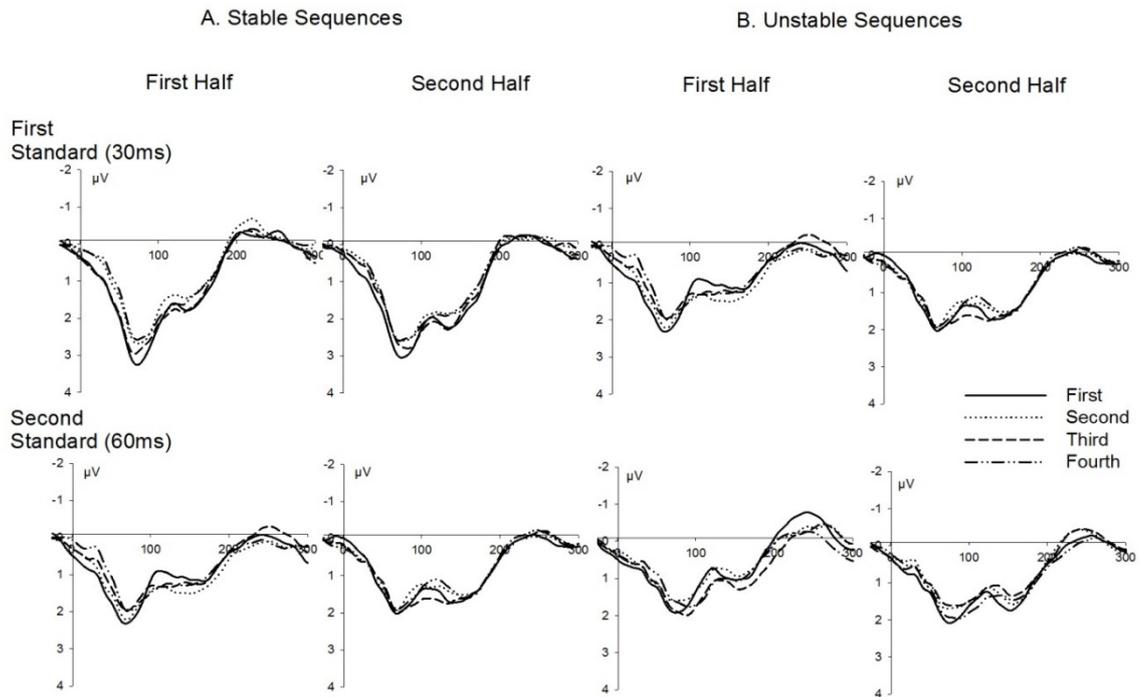


Figure 5.2. Standard ERP waveforms for repeated sequence design. The ERP responses for the first (30ms) and second (60ms) repetitive standard sounds in the 1st and 2nd half of A. Stable condition and B. Unstable sequences. The ERPs to standard sounds for data acquired in the first, second, third and fourth sequence occurrence are not differentially modulated by stability of tone roles.

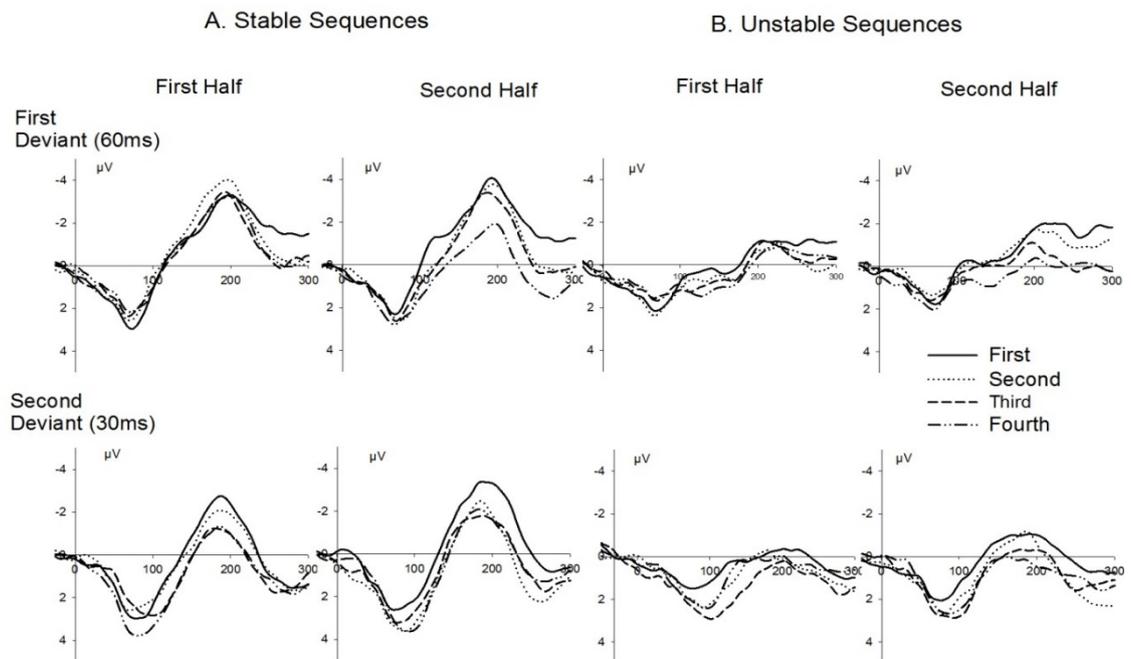


Figure 5.3. Deviant ERP waveforms for repeated sequence study. The ERP responses for the first (60ms) and second (30ms) rare deviant sounds in the 1st and 2nd half of A. Stable condition and B. Unstable sequences. It is clear that the ERPs to deviant sounds for data acquired in the first sequence presentation are differentially affected by tone roles. Remarkably, evidence of primacy bias effects is not only sustained across second, third and fourth sequence occurrences but intensify with repetition.

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confirm the basis of the amplitude effects underlying the MMN difference waveforms, across sequence repetitions. These figures emphasise that responsiveness to sounds are linked to role (standard vs. deviant) at sequence onset. In prior studies (Mullens et al., 2014; Todd et al., 2013) repetition effects evident in the standard ERPs over the P2 period from 140 to 170ms have been observed. Analysis of this period showed that standard ERPs were less negative over the second- compared to the first-half of recording blocks ($F(1, 28)_{Half} = 72.13, p < .001 \eta^2 = .720$). An effect of *Deviant* was also observed ($F(1, 28) = 8.17, p < .05 \eta^2 = .226$) with ERPs for the 60ms standard being less negative than those to the 30ms standard for both conditions. No effect of presentation was revealed for mean amplitudes of standard ERPs extracted over this period ($p = 1.72$).

Analysis of deviant ERPs revealed that effects were equivalent to those observed for MMN difference waveforms. This confirmed significant main effects of *Half* ($F(1, 28) = 4.57, p < .05 \eta^2 = .140$), *Deviant* ($F(1, 28) = 22.88, p < .001 \eta^2 = .450$) and *Presentation* ($F(3, 84) = 13.43, p < .001 \eta^2 = .324$) and a *Deviant* x *Half* ($F(1, 28) = 5.54, p < .05 \eta^2 = .165$) interaction. The interaction was due to a larger MMN to the first- relative to second-deviant regardless of condition or presentation type. From Figure 2 it is apparent that this interaction occurs due to MMN being smaller in the first-half than the second-half of sequence blocks for the second-deviant but not the first, and that MMN amplitude differs most markedly between tones for the first-half data. The breakdown of interactions mirrored the results for the MMN analysis in the manuscript confirming that the bias effects act on the MMN generated to the deviant tones.

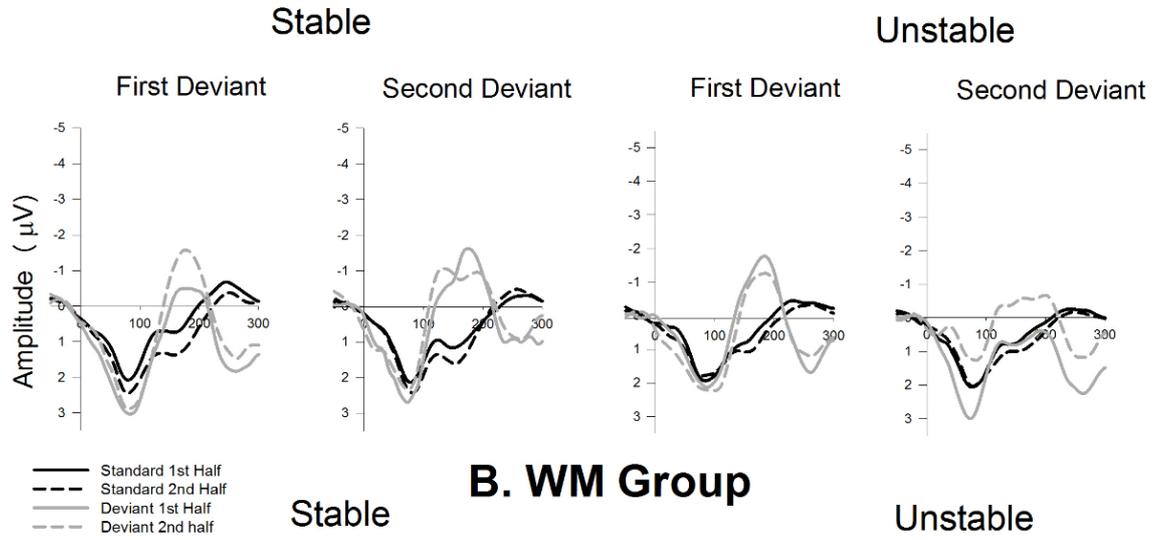
Appendix 3: Standard/Deviant Analyses for Chapter 3

Standard and Deviant ERPs. A total of eight ERP values for each tone type were compared at the F4 electrode site in a mixed measures ANOVA with sequence (stable, unstable), deviant (first deviant, second deviant) and half (1st, 2nd) as within-subject factors and condition (WM, PT, DVD) as a between-subject variable. ERPs to standard and deviant sounds were analysed separately. to determine whether main effects on MMN were evident in deviant responses, standard responses or both with significance values set at .05.

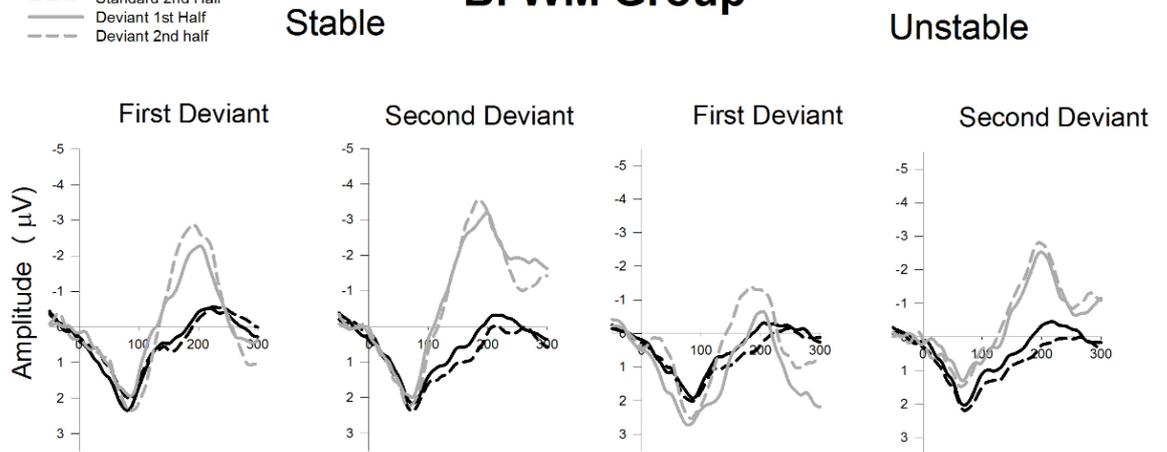
The ERPs generated to the first (30ms) and second (60ms) standard tones across the first and second half of blocks for stable and unstable sequences for the DVD, WM and PT task condition are presented in Figure 5.4.A, B, and C, respectively. Analysis of the RP period (50-150ms) revealed a significant sequence by half by sequence interaction that was further modified by group ($F(1, 43) = 3.91, p = .05, \eta^2 = .154$). Data for each group were then analysed separately. This revealed a marginal sequence by half interaction for those who completed an undemanding DVD task ($F(1, 13) = 4.62, p = .05, \eta^2 = .262$). Here standard ERPs were significantly more positive in the second relative to first half of block-contexts for the stable sequence only ($F(1, 13) = 8.00, p < .05, \eta^2 = .381$) with no differences observed for unstable sequence ($p = .40$). A significant effect of sequence stability for those who completed the PT task was also found where ERPs to deviant in the stable sequence were larger relative to the unstable sequence ($F(1, 14) = 8.33, p < .05, \eta^2 = .373$). No effects were observed for the WM group.

Analysis of the P2 period revealed a significant main effect of half ($F(1, 43) = 41.47, p < .001, \eta^2 = .53$) with the amplitude of the ERP over the 140-170ms P2

A. DVD Group



B. WM Group



C. PT Group

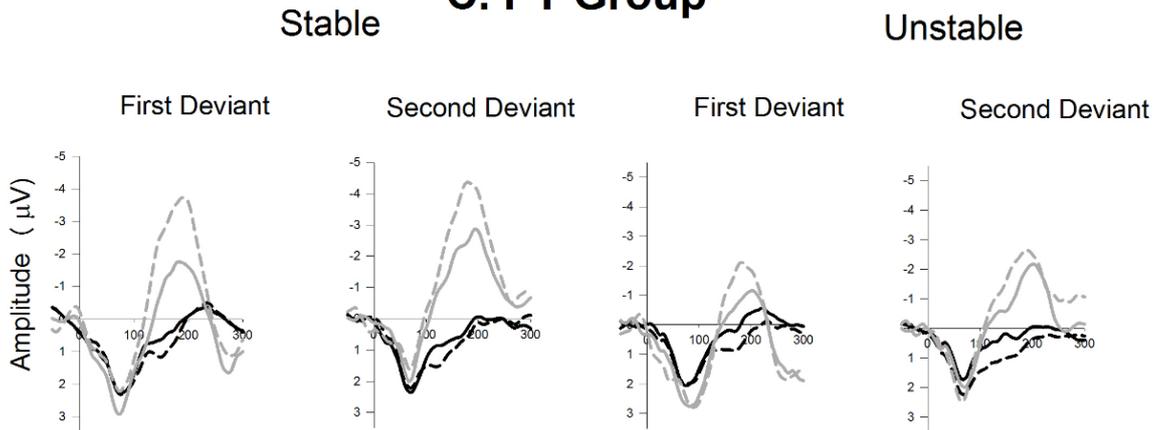


Figure 5.4. Group-averaged deviant and standard ERPs by group in the A. DVD group (undemanding condition), B. WM group, and C. PT group

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period being less negative for the second relative to first half data. A significant effect of sequence was also observed with standard ERPs less negative in the stable relative to unstable sequence type ($F(1, 43) = 8.92, p < .01, \eta^2 = .17$).

Figure 5.4A, B and C also presents each groups ERPs to deviant tones for the first and second halves of stable and unstable sequences for both the 60ms (first) and 30ms (second) deviant. These figures emphasize differences in responsiveness to sounds as a function of their role for each group task. The analysis of deviant ERPs revealed main effects of sequence (stable > unstable, $F(1, 43) = 33.94, p < .001, \eta^2 = .44$), block-context half (second half > first half, $F(1, 43) = 13.69, p < .01, \eta^2 = .24$) and deviant (first > second, $F(1, 43) = 9.28, p < .01, \eta^2 = .18$). These were further modified by a significant four-way interaction between group, sequence, half and tone ($F(2, 43) = 3.56, p < .05, \eta^2 = .14$) owed to more negative ERPs in stable sequences compared with unstable sequences.

Analysis restricted to the DVD group showed a significant sequence by half by tone interaction ($F(1, 13) = 17.43, p < .01, \eta^2 = .57$). In data generated for the stable sequence only, deviant ERPs were modulated differently by half for the two tones ($F(1, 13) = 19.70, p < .01, \eta^2 = .60$). ERPs to the first deviant sound significantly decreased by the second-half of block-contexts ($t_{13} = 3.10, p < .05$) whereas those to the second deviant showed a tendency to increase across block-context halves with marginal effects observed ($t_{13} = 1.98, p = .07$). An opposite pattern of effects was observed for the unstable sequence ($F(1, 13) = 4.91, p < .05, \eta^2 = .27$) with ERPs to the first deviant significantly increasing across halves ($t_{13} = 2.85, p < .05$) but not for the second ($p = .37$).

A comparison between WM and DVD groups revealed a sequence x deviant x half interaction that was significantly modified by group ($F(1, 29) = 10.72, p <$

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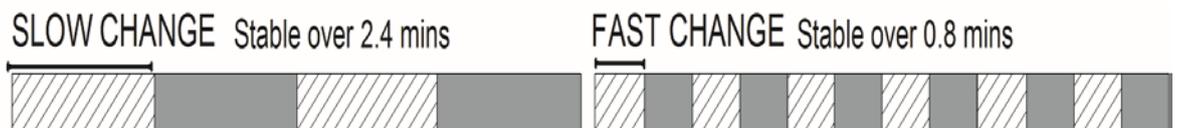
.01, $\eta^2 = .27$). A trend toward this same interaction type was found in a WM/PT comparison ($F(1, 27) = 3.01, p = .09, \eta^2 = .10$). This pattern of deviant ERP differentiation was not observed when the WM and PT groups were compared. A mixed model ANOVA revealed basic stability effects only irrespective of demanding task performed. That is, ERPs in the stable sequence were larger overall relative to the unstable sequence ($F(1, 13) = 34.43, p < .001, \eta^2 = .53$) and increased over block-context halves (second half > first half, $F(1, 29) = 18.50, p < .001, \eta^2 = .38$). An effect of tone was also observed (first deviant > second deviant, $F(1, 29) = 10.83, p < .01, \eta^2 = .26$) but no significant interactions.

Analysis limited to the WM group showed significant main effects of sequence, half and deviant (stable > unstable, $F(1, 16) = 23.90, p < .001, \eta^2 = .60$, second half > first half, $F(1, 16) = 5.31, p < .05, \eta^2 = .25$, & first deviant > second deviant, $F(1, 16) = 11.31, p < .01, \eta^2 = .41$, respectively). Significant effects of sequence (stable > unstable, $F(1, 14) = 12.36, p < .01, \eta^2 = .47$) and half (second half > first half, $F(1, 14) = 13.74, p < .01, \eta^2 = .50$) were also observed in data generated for those who completed a PT task. Notably, there were no significant interactions present in either the WM or PT group.

Appendix 4: Foreknowledge script/diagram for Chapter 4

1. You will hear two types of sounds that will vary in length. One will be a short 30ms sound, and the other will be a longer 60ms sound.
2. One of these sounds will occur frequently whereas the other will be rare.
3. At times, these sounds will change roles so that the rare tone will become frequent, and the frequent tone will become rare (refer to diagram- this is represented by the diagonal-shaded box changing to the grey-shaded box, and then repeating until the sequence is finished).
4. It is also important to know that the roles of these tones will change at different speeds.
5. First, you will hear the slow changing sequence (as shown on the left-hand side of this diagram). In this sequence the roles will change every 2.4 minutes.
6. Next, you will hear the fast changing sequence (as shown on the right-hand side of this diagram). In this sequence the roles will change every 0.8 minutes.

The following diagram was shown to participants as verbal description was provided:



Appendix 5: Standard/Deviant Analyses for Chapter 4

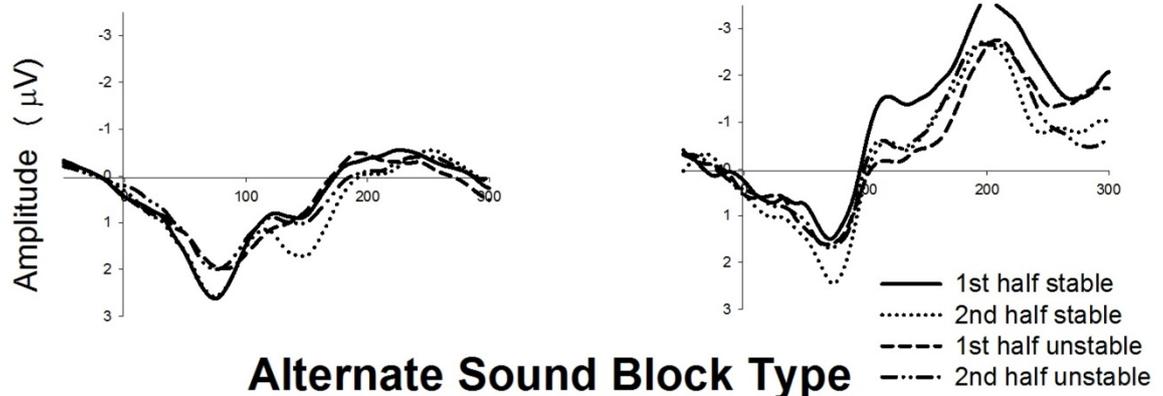
Standard and Deviant ERPS. Figure 5.5 is an illustration of the ERPs generated to standard and deviant tones across the first and second halves of stable and unstable sequences. Analysis of the P2 period (140-170 ms) revealed a significant main effect of half ($F(1, 14) = 30.56, p < .001, \eta = .686$) due to less negative ERPs in the second relative to first half of sound blocks. Standard ERPs were significantly less negative in the stable sound sequences relative to unstable sequences ($F(1, 14) = 10.21, p < .01, \eta = .422$). Similarly, analysis of the RP period (50-150ms) yielded a significant main effect of sequence type ($F(1, 14) = 19.22, p = .001, \eta = .579$) which was due to less negative ERPs in the stable compared with unstable sound sequences.

Analysis of ERPs to deviant sounds revealed that MMN to the first (60ms) deviant sound was significantly more negative than that to the second deviant ($F(1, 14) = 8.31, p < .05, \eta = .372$). A significant half x sequence interaction ($F(1, 14) = 6.05, p < .05, \eta = .302$) was also observed. Appropriate follow-up contrasts were performed revealing that ERPs to deviant tones were significantly smaller by the second half of block-contexts, relative to the first half, for stable sequences only.

Initial Sound Block Type

A. First Standard (30ms)

B. First Deviant (60ms)



Alternate Sound Block Type

C. Second Standard (60ms)

D. Second Deviant (30ms)

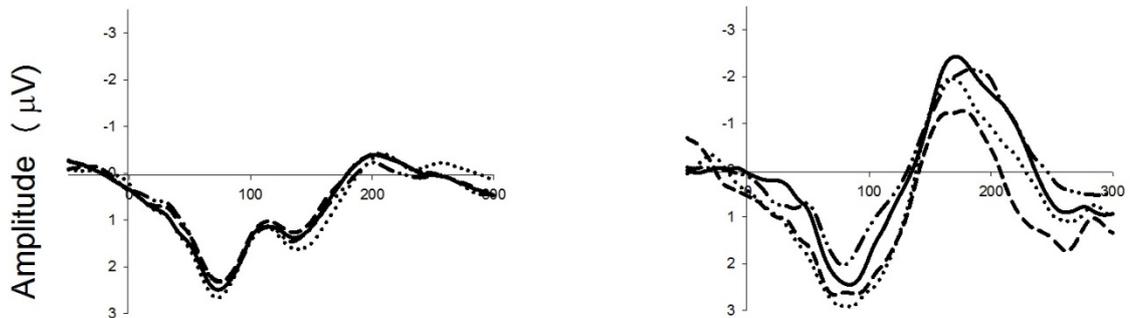


Figure 5.5. Group averaged ERPs to each tone as a function of role (standard versus deviant) within sound blocks that match those presented at sequence onset (initial sound blocks; upper half of figure) and those that do not match blocks presented at sequence onset (later sound blocks; lower half of figure). In initial sound blocks, the 30ms and 60ms tones signified A. First Standard and B. First Deviant roles, respectively. In alternate blocks, the role of each tone switched so that the first deviant signified the C. Second Standard (60ms) and the first standard signified the D. Second Deviant (30ms). NOTE: Figure legend denotes 1st and 2nd half of sound blocks within stable and unstable sequence types.

Appendix 6: Funding Sources for Chapters 2 to 4



MEMO

TO Doctor Juanita Todd
 CC
 FROM Research Grants Administration, Research Services
 DATE 17-Mar-2015
 SUBJECT G1400035 - The impact of faulty relevance filtering in schizophrenia.

Your grant (as detailed below) is ready to be established and the file has been forwarded to your Financial Services Research Accountant to create a cost collector for the Project.

Chief investigator: Juanita Todd
 Project title: The impact of faulty relevance filtering in schizophrenia.
 Institution number: G1400035
 RMO reference: 2014/3354
 Sponsor reference: APP1080938
 Sponsor/scheme: NHMRC (National Health & Medical Research Council)/Project Grant

Special Conditions (if any):

Sponsor Conditions: Any conditions relevant to receiving the funding are set out in the Schedule to the Funding Agreement and, where applicable, the associated Funding Rules. All expenditure must be in accordance with the requirements of the Funding Agreement.

All Chief Investigators, Fellows and Scholars working on NHMRC Funded Research Activities are obligated to contribute to the peer review process, as set out in clause 23.1 of the Funding Agreement. As such, please ensure your CV/Profile information is up to date in RGMS to assist in the identification of appropriate peer reviewers.

Funding may be expended as necessary to perform the Research Activity provided that:

1. The Funding is applied only to achieve the objectives and outcomes of the Research Activity as described in Item C of Schedule APP1080938
2. Funding may only be spent on the Research Activity's 'direct research costs' as described in the Guidelines for Direct Research Costs (available from the NHMRC website as modified from time to time at www.nhmrc.gov.au/grants/administering-grants/nhmrc-funding-agreement).

Legal Agreement details (if any):

Agreement type: NHMRC Schedule
 Primary Party: NHMRC
 Fully Executed: 14-Nov-2014
 Agreement type: Multi-Institutional Agreement
 Primary Party: UoN
 Fully Executed: 10-Mar-2015

Ethics or Safety Clearances (if any):

Human Ethics: Approved

In exceptional circumstances approval for early release of funding may have been granted. You must ensure that all clearances are obtained before any work on this project commences.

For forms and information on seeking clearances for Ethics or Safety, please see the Research website <http://www.newcastle.edu.au/service/grants-and-contracts/forms-and-codes/>

Reporting Requirements (if any):

Type of Report	Due Date
Progress	30-Apr-2016
Progress	30-Apr-2017
Progress	30-Apr-2018
Final	31-Aug-2018

Please see your letter of offer or agreement for details of reporting requirements. If financial reports are requested by the Sponsor, please liaise with your Financial Services Officer.

Please insert these dates in your diary now. You may also receive a reminder which will be automatically generated from RIMS (Research Services database) one month before the report is due. Please send the report's directly to the sponsor and send a copy to Research Services for the grant file. If an Institutional signature is required please send the report to Research Services and we will obtain the required signature and submit the report on your behalf.

Scholarship Funding:

If this grant will be funding a research degree scholarship, please ensure that a Research Scholarship Establishment Proposal is completed and lodged with the Office of Graduate Studies. This form can be located on the web at: <http://www.newcastle.edu.au/research-and-innovation/resources/this-supervision/research-scholarship-establishment/establishment>

If you have any questions or need further information, please contact Research Services on 4921 7733.

Regards

Research Grants Administration
 Research Services
 The University of Newcastle

T: +61 2 4921 7733
 E: research-grants@newcastle.edu.au

Research grants and ethics information is available in the Research Information Management System (RIMS). Follow this link: <https://rims.newcastle.edu.au/login.asp> and use your university number plate and password for access.

Appendix 7: Information Statement and Consent Form for Chapters 2 – 4



THE UNIVERSITY OF
NEWCASTLE
AUSTRALIA

Associate Professor Juanita Todd
School of Psychology
University of Newcastle,
Callaghan NSW 2308
AUSTRALIA
Phone: (02) 4921 5977
Email: Juanita.Todd@newcastle.edu.au



Information Statement for the Research Project:

Does that matter? How the brain decides what period of time is relevant.

You are invited to participate in the research project identified above which is being conducted by Associate Professor Juanita Todd from the School of Psychology at the University of Newcastle. The team of staff and students involved in this research is listed below. All are students are completing their undergraduate degree at the University of Newcastle under the supervision of Dr Juanita Todd. Your appointment will be conducted by one of these team members. Data generated from your appointment will be used by one or more of the students in the completion of the research component of their degree.

Why is the research being done?

Important theories about how the brain works suggest that it maintains “optimal function” by learning to ignore irrelevant events so that attention can be focused on important events that provide us with new learning. We are studying how this process operates in the auditory system, that is, in the parts of the brain that process sound.

The brain automatically uses information about the likelihood of sounds in the environment to decide what is important. When the brain encounters repetitive sounds it reduces the size of the response to these sounds because it learns to predict them and learns that they do not carry important information. When the brain then encounters a different sound it responds more strongly to these rare events and this is called a mismatch negativity or MMN response. This process happens outside your awareness, even during sleep. In this study we are going to ask you to watch a DVD movie or complete a simple visual perceptual or cognitive task and ignore the sounds that we present to you over headphones. Our sound sequences have been designed to determine the time frame over which your brain is extracting probability information in order to determine whether a sound is important or not. From this information we will also begin to understand which areas of the brain are involved in this process.

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Who can participate in the research?

We require participants to complete this study who meet the following criteria:

- (1) Aged 18-35 years.
- (2) No treatment for mental illness or diagnosis of psychosis in a first degree relative.
- (3) No known hearing loss.
- (4) No history of injury to the brain or neurological condition (e.g., stroke, epilepsy).
- (5) No excessive alcohol or drug use.

What choice do you have?

Participation in this research is entirely your choice. Only those people who give their informed consent will be included in the project. Whether or not you decide to participate, your decision will not disadvantage you in any way.

If you do decide to participate, you may withdraw from the project at any time without giving a reason and you have the option of withdrawing any information which identifies you. If you do choose to withdraw you have the option of withdrawing your data from the project also.

What would you be asked to do and how long will it take?

If you agree to participate, you will be asked to attend an appointment at the University of Newcastle. This appointment will last about 2.0 hours and will involve:

- A hearing test to ensure no significant hearing loss is present (5 minutes).
- A set-up with cap for the recording of electrical brain potentials produced in response to sounds. An elastic cap that contains small sensors will be placed on your head and a small amount of conductive gel will be inserted into the sensors so that we can record the electrical activity in the brain that occurs in response to the sound sequences. During the recording you will be asked to ignore the sounds whilst you view a self-selected DVD movie or complete a simple visual perceptual, or 2-back working memory task (40 minutes set-up and 60 minutes recording time).

You will be offered a reimbursement of \$30 in Coles Corporate vouchers for your time and inconvenience. If you are a student enrolled in PSYC1010, PSYC1020, PSYC2500 or PSYC3000 you can instead choose to receive 4 course credit points for your participation.

What are the risks and benefits of participating?

We cannot promise you any direct benefit from participating in this research. However, as noted above, increasing our knowledge of auditory system and higher-order brain area function enables us to develop better tests to understand individual differences and how problems in brain function arise. It is possible that during the hearing test we could identify some hearing loss that you are not currently aware of. If this occurs, we will discuss the result with you and suggest that you contact your general practitioner for advice.

How will your privacy be protected?

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission. There are two exceptions. If you reveal present intentions to harm yourself or others, or if you reveal specific detail about any criminal activity as we are obliged to report this to relevant persons (e.g. case worker, GP or police). All files with identifying information will be kept securely stored in a locked area of the University of Newcastle for a period of five

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years after which all copies will be shredded. Any identifiable data kept electronically will be password protected. All experimental data will be kept for a period of five years after which they will be incinerated or shredded as appropriate.

How will the information collected be used?

The researchers intend to publish the results of this research in a scientific journal. However, in any publication, information will be provided in such a way that you cannot be identified. Whilst you will have the opportunity to discuss and view some of the measures taken during your appointment, the information collected is generally only meaningful in terms of group comparisons. In the consent form you are invited to request a description of the project outcome in lay terms which will be mailed to you once the study is complete. We will also ask your consent to use the data obtained here for a comparison to measures obtained in future studies conducted by the researchers. This is completely optional and you can participate in this study without providing this permission.

What do you need to do to participate?

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, contact the researcher.

If you would like to participate, please contact one of the researchers (using the details below) to (using the details below) to arrange an appointment time that suits you. When you attend you will be required to sign a consent form acknowledging that you have received the information provided above, that all of your questions regarding participation have been answered to your satisfaction.

Further information

If you would like further information please contact [Jade Frost](#)

Thank you for considering this invitation.

Juanita Todd

Personnel	Position	Email	Phone
A/Prof Juanita Todd	Associate Professor	Juanita.Todd@newcastle.edu.au	
Dr Alexander Provost	Lecturer	Alex.provost@newcastle.edu.au	49217161
Dr Bryan Paton	Lecturer	Bryan.Payton@newcastle.edu.au	
Jade Frost	PhD Student	Jade.Frost@newcastle.edu.au	

Complaints about this research

This project has been approved by the University's Human Research Ethics Committee, Approval No. H-2010-1350

Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research Office, The Chancellery, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 49216333, email Human-Ethics@newcastle.edu.au



THE UNIVERSITY OF
NEWCASTLE
AUSTRALIA

Dr Juanita Todd
School of Psychology
University of Newcastle,
Callaghan NSW 2308
AUSTRALIA
Phone: (02) 4921 5977

Email: Juanita.Todd@newcastle.edu.au



Consent Form for the Research Project:

Does that matter? How the brain decides what is period of time is relevant.

Dr Juanita Todd

I agree to participate in the above research project and give my consent freely.

I understand that the project will be conducted as described in the Information Statement, a copy of which I have retained.

I understand I can withdraw from the project at any time and do not have to give any reason for withdrawing.

I consent to

- A hearing screen.
- A recording of electrical brain potentials produced in response to sounds presented over headphones while I watch a DVD or perform a simple visual perceptual or cognitive task.

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

I would like you to send me a lay person description of the study results when available.
If so, please provide email or postal address below.

I would like to be contacted regarding participation in future research in this area.
If so, please provide email or postal address below

I consent to allow the researchers to use the data collected here for comparison to similar measures used in future studies.

Print Name: _____ **Signature:** _____ **Date:** _____

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Appendix 8: Copy of Email from Copyright Holder Indicating Permission to Copy and Communicate Work Presented in Figure 1.1.

 Jade Frost
Fri 10/11/2017, 1:47 PM

Good afternoon Dr **Garrido**,

I am a current PhD student supervised by Associate Professor Dr Juanita Todd at the University of Newcastle (School of Psychology) and am nearing thesis completion. I am almost certain we were introduced at the last MMN conference in Leipzig, Germany in 2015. I am contacting you to seek written permission to copy and communicate the following material within the electronic version of my PhD (Clinical Psychology) thesis, as part of my introduction:

Fig. 2. Grand mean ERPs, i.e., averaged over all subjects.
From your paper **Garrido**, M. I., Kilner, J. M., Kiebel, S. J., Stephan, K. E., & Friston, K. J. (2007). Dynamic causal modelling of evoked potentials: a reproducibility study. *Neuroimage*, 36(3), 571-580.

I am essentially using your figure as a visual representation of my in-text explanation of the auditory mismatch negativity signal. The thesis will be made available on the internet via the University of Newcastle's online digital repository <http://nova.newcastle.edu.au/>. Please let me know if you any questions about using your figure in my thesis.

Look forward to hearing from you

With kind regards,
Jade Frost

Garrido 1 of 5

 Marta Garrido <m.garrido@uq.edu.au>
Sat 11/11/2017, 6:11 AM
Jade Frost

Inbox

Action Items

Hi Jade,

Of course :) and best of luck for the final stages of your PhD. Please send my love to Juanita.

Cheers,
Marta
--
Dr. Marta **Garrido**, PhD
Group Leader, [Computational Cognitive Neuroscience Laboratory](#)
Queensland Brain Institute
School of Mathematics & Physics
The University of Queensland, Australia