Todd, Juanita; Provost, Alexander; Whitson, Lisa R.; Cooper, Gavin & Heathcote, Andrew. "Not so primitive: context-sensitive meta-learning about unattended sound sequences" Published in the *Journal of Neurophysiology*, Vol. 109, Issue 1, (2013).

Available from: http://dx.doi.org/10.1152/jn.00581.2012

Title: Not so primitive: Context sensitive meta-learning about unattended sound sequences.

Running Title: Context sensitive meta-learning

Author names and affiliations (in order of importance):

Juanita TODD[1-3] Alexander PROVOST [1-2], Lisa WHITSON[1-2], Gavin COOPER[1, 3], Andrew HEATHCOTE[1-2]

1. School of Psychology
   University of Newcastle
   University Drive, Callaghan, NSW, Australia, 2308.
2. Priority Research Centre Translational Neuroscience and Mental Health Research
   University of Newcastle
   University Drive, Callaghan, NSW, Australia, 2308.
3. Schizophrenia Research Institute
   Darlinghurst, 2010, NS, Australia

Corresponding author:

Juanita Todd

School of Psychology

University of Newcastle

University Drive, Callaghan, NSW, Australia, 2308.

Email: Juanita.Todd@newcastle.edu.au

Phone: +61 2 49215977

Fax: +61 2 49216980

Author Contribution

Juanita TODD

Designed the research, supervised project conduct, analysed data and took the lead role in writing the paper.

Andrew HEATHCOTE

Participated in design, data interpretation and write-up.

Alexander PROVOST

Participated in design, data interpretation and write-up.

Lisa WHITSON

Collected and processed data.

Gavin COOPER

Participated in design and programming.

ABSTRACT

Mismatch Negativity (MMN) – an evoked response potential elicited when a “deviant” sound violates a regularity in the auditory environment – is integral to auditory scene processing and has been used to demonstrate “primitive intelligence” in auditory short-term memory. Using a new multiple context and timescale protocol we show that MMN magnitude displays a context sensitive modulation depending on changes in the probability of a deviant at multiple temporal scales. We demonstrate a primacy bias causing asymmetric evidence-based modulation of predictions about the environment, and that learning how to learn about deviant probability (meta-learning) induces context-sensitive variation in the accessibility of predictive long-term memory representations that underpin the MMN. The existence of the bias and meta-learning are consistent with automatic attributions of behavioural salience governing relevance-filtering processes operating outside of awareness.

Keywords: mismatch negativity (MMN), perceptual inference, salience, learning, auditory evoked potential.

Humans are accomplished at finding patterns in event sequences, an ability that is supported by automatic novelty detection mechanisms. In audition, automatic novelty detection is indexed by Mismatch Negativity (MMN), a fronto-central event-related potential (ERP) peaking 100-200ms after a novel event. The MMN, which is primarily generated in the auditory cortex, was first described by Näätänen, Gaillard and Mäntysalo (1978) in an auditory oddball paradigm (e.g., a series of *standard* longer tones containing an occasional shorter oddball or *deviant* tone) through the use of deviant-standard difference waveforms. MMN is elicited automatically and is usually measured while participants attend to another modality (e.g., while reading or watching a silent movie), as it does not require attention but can be masked by attention-related ERPs. MMN amplitude is proportional to the difference between deviant and standard, and is inversely proportional to the probability of the deviant. Early interpretations of the MMN (e.g., Näätänen & Michie, 1979) were in terms of a mismatch between low-level auditory sensory memory traces of the standard and deviant. However, mounting evidence has implicated much more sophisticated processing, leading Näätänen, Tervaniemi, Sussman, Paavilainen and Winkler (2001) to characterize the MMN as a marker of "primitive intelligence" in the auditory cortex.

Primitive intelligence is revealed by phenomena usually associated with higher-order cognition ranging from prediction and simple concept formation to mnemonic characteristics more associated with long-term memory than short-term sensory memory. For example, MMNs indicative of a left-hemisphere specialization in extracting abstract rules, are associated with violations of contingencies embedded in sound sequences that are independent of low-level auditory features (e.g., "the higher the frequency the louder the intensity", Paavilainen, Simola, Jaramillo, Näätänen & Winkler, 2001). Horváth, Czigler, Sussman and Winkler (2001) found MMNs implicating simultaneous memory representations of more than one type of contingency (e.g., a global "every second tone is A and every other B" rule and local a local "A follows B and vice versa" rule) that are compared in parallel with incoming sounds. These results and others (e.g., Tervaniemi, Maury & Näätänen, 1994) suggest the auditory cortex automatically learns contingencies between the features of the successive events and makes predictions about forthcoming events (Winkler, Karmos & Näätänen, 1996). The use of transition statistics (the statistical temporal dependencies linking stimuli) was formalised in a recent paper incorporating empirical data with computational modelling to explain a wide range of MMN findings. The authors provide additional support for the argument that low-level sensory effects of stimulation (e.g., habituation) are not sufficient to account for MMN results that instead conform to a more active process of cortical prediction (Wacongne, Changeux & Dehaene, 2012).

This developing understanding in the role of MMN in the auditory modality complements Friston's (2003, 2005, 2008) free-energy minimization framework for perceptual inference and learning, whereby sensory cortices are arranged hierarchically, with predictions over longer time scales made by representations in higher cortical levels modulating responses in lower levels occurring on faster time scales (see also Kiebel, Daunizeau, & Friston, 2008). The prefrontal cortex is a recognized contributor to the MMN (Alho, Woods, Algazi, Knight, & Näätänen, 1994). Escera, Yago, Corral, Corbera and Nunez's (2003) specific suggestion that the prefrontal cortex provides top-down modulation of mismatch detection in the temporal cortices was tested by Garrido, Kilner, Kiebel and Friston (2009) in an auditory pitch oddball paradigm. Garrido et al. (2009) compared Dynamic Causal Models varying in the involvement of generators in primary auditory cortex (A1), superior temporal gyrus (STG) and inferior frontal gyrus (IFG). Model selection supported the influence of adaptation in the primary auditory cortex and short-term plasticity of forward and backward connections across the auditory hierarchy in the generation of MMN (see also Schmidt, Diaconescu, Komerter et al., 2012 for a recent replication and extension). The model that best accounted for data specified a right IFG – STG – A1 hierarchy and a left STG – A1 hierarchy with extrinsic (feedforward and feedback) connections between generators within each hierarchy and intrinsic (lateral) connections within each A1 generator. These findings, and Friston's general multiple-time-scale hierarchical framework, suggest the known frontal involvement in the MMN might not only be related to proposed attention switching (Näätänen, 1990, 1992, Giard, Perrin, Pernier and Bouchet, 1990) but also to modulating MMN magnitude based on predictive confidence over longer time-scales.

We used a new technique, a *multiple context and time-scale MMN protocol*, to explore the long-term memory characteristics of the context-dependent process that adjusts predictions about auditory regularity. The technique is a refined and expanded version of the protocol used by Todd, Provost and Cooper (2011). They measured learning about the probability of a tone duration deviant in an oddball paradigm similar to that illustrated in the top row of Figure 1. In each of a series of approximately 10-minute sequences separated by several minutes of silence, either a short (e.g., 30ms) or long (e.g., 60ms) tone occurred every 300ms. Over the entire sequence both durations occurred equiprobably, but in blocks within each sequence one duration, the standard, was more probable (p=0.875), with the other duration being the MMN-eliciting deviant. The attribution of durations to deviant and standard roles alternated between blocks. Different sequences varied in block length, with Figure 1 illustrating sequences with slow (2.4 minute) and fast (0.8 minute) block alternations. If MMN amplitude is dominated by the local probability within a block – consistent with an MMN developing on the scale of a few seconds in the oddball paradigm (i.e., after several standard repetitions) – it should not vary with alternation speed (block length). If, in contrast, the probability of a deviant is measured by a moving average over a larger temporal window, MMN amplitude should be larger in slow than fast block alternation sequences.

Surprisingly, Todd et al. (2011) found both patterns. For the deviant duration that occurred in the first block (which was the same for every sequence for a given participant) MMN amplitude was larger for the slow than fast sequences. In contrast, for the duration that became the deviant in the second block, sequence speed had no effect on MMN magnitude. Todd et al. described this asymmetric finding as a “primacy bias”. They suggested that it might reflect latent inhibition (Lubow & Gewirtz, 1995), a classical conditioning phenomenon whereby learning is attenuated to familiar stimuli that have previously been inconsequential. Irrespective of the cause, the data imply a long-acting, order-driven limitation on how evidence affects perceptual inference.

The experiment reported here adds multiple contexts to the multiple temporal scales in Todd et al.’s (2011) protocol in order to investigate the cases and limits of the differential probability sensitivity indicated by the primacy bias. In the previous study, tone order was a between-subjects factor whereby half the participants always experienced the long duration sounds as the standard in the first block of any sequence and half always experience the short duration as the first standard. Furthermore, the primacy bias was assessed over a 50 minute recording period including multiple block lengths. Here we presented participants with three pairs of sequences comprising only short and long block lengths (as illustrated in Figure 1, Order 1, 2 and 3). Each sequence pair was separated by a 5-minute break and the duration that was used as the standard in the first block of each sequence changed between pairs (i.e., 30ms in the first and third pairs and 60ms in the second pair). These shorter sequences allow us to determine whether a reliable index of the bias can be extracted from a 20 minute recording and how resistant the bias is to change (i.e., whether it reverses when tone order changes). Latent conditioning is well known to be context sensitive (e.g., Hall & Honey, 1989), so if the 5-minute breaks induce a sufficiently salient change of context the primacy bias should reverse between sequence pairs. Furthermore, the repeat of Order 1 in Order 3 allows us to examine whether the bias is always replicated with the same initial sequence structure or whether prior experience can alter the effect.

Method

Participants

Participants were 15 healthy adults (8 female, 18-31 years, mean = 25 years, SD = 4 years) community volunteers and first year undergraduate Psychology students at the University of Newcastle. Participants were excluded if they were diagnosed with or being treated for mental illness, had a first degree relative with schizophrenia, regularly used recreational drugs or had history of neurological disorder, head injury or surgery, hearing impairments or heavy alcohol use. Course credit was offered for participation to students and cash reimbursement to community volunteers. Written informed consent was obtained from all participants to complete the protocol as approved by the Human Research Ethics committee, University of Newcastle, Australia.

Stimuli and Sequences

Sounds were 1000 Hz pure tones presented binaurally over headphones at 75 dB SPL. Sounds were created 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 sequences comprised 1920 sounds presented at a regular 300 ms stimulus onset asynchrony (9.6 minutes per sequence). In short-standard blocks the 30 ms tone was more probable (p=0.875) than 60 ms tone; in long-standard blocks the probabilities were reversed. In the slow sequence, block type alternated after every 480 tones creating a stable-standard period of 2.4 minutes (i.e., two repeats of each 2.4 minute block). In the fast sequence block type alternated every 160 tones creating a stable-standard period of 0.8 minutes (i.e., six repeats of each 0.8 minute block). The slow alternation sequence always preceded the fast alternation sequence. In Order 1 and in its repeat in Order 3, the short standard blocks were presented first. In Order 2, the long standard blocks were presented first. A five minute break was enforced between order conditions and shorter 1-2 minute breaks occurred between sequences (total testing time approximately 1 hour, 15 minutes).

Procedure

Participants completed a screening interview prior to testing to ensure no exclusion criteria were present. Hearing thresholds (measured across 500-4000 Hz) were assessed with a pure tone audiometer to exclude those with hearing loss (thresholds >25 dB HL). Participants were fitted with a Neuroscan Quickcap with tin electrodes, that included nose and mastoid electrodes. The continuous 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). EEG data were recorded from 16 electrode locations (FZ, FCZ, CZ, PZ, F3, FC3, C3, F4, FC4, C4 in accordance with the 10–20 system plus left mastoid, right mastoid) referenced to the nose. We also measured vertical and horizontal electro-oculograms. Impedances were reduced to below 5 kΩ before recording commenced. Sequences were presented over headphones while the participant viewed a silent DVD with subtitles and were instructed to ignore the sounds and focus attention on the movie.

Data Processing

Continuous EEG was first examined offline for major artifact before eyeblink artifact correction was completed offline using Neuroscan Edit software. The method applies a regression analysis in combination with artifact averaging (Semlitsch, Anderer, Schuster, & Presslich, 1986). The average artifact response algorithm generated was assessed for adequacy (more than 30 sweeps in the average and <5% variance) and was applied to the continuous data files. The data were epoched from 50 ms prestimulus to 300 ms post-stimulus. Epochs containing variations exceeding ± 70 μV were excluded. The data were used to generate twelve ERPs to standard tones, twelve ERPs to deviant tones and twelve difference waves per participant (a 30 ms and 60 ms version for fast and slow sequences for each of the three orders). The first five standards in a block and the first standard after each deviant were excluded from averages.

ERPs were baseline corrected pre-stimulus. The standard and deviant ERPs were digitally filtered with a lowpass of 30 Hz. Difference waveforms for 30 ms and 60 ms deviants were created for each condition by subtracting the ERP to that tone as a standard from that tone as a deviant. For example, the MMN to 30 ms deviants in fast change blocks was extracted from a difference waveform created by subtracting the ERP to the 30 ms standard in fast change blocks from the ERP to the 30 ms deviant tone in fast change blocks. This approach assists in reducing the contribution of exogenous effects on the computation of MMN (Jacobsen & Schröger, 2003). The difference wave was then filtered with a low pass of 20 Hz (lower cut-off recommended for MMN, Kujala et al., 2007).

All ERPs were re-referenced to the averaged activity at the left and right mastoid sites. Individual data were then visually inspected to determine whether a MMN was present. One participants’ data were rejected on this criterion showing no evidence of a MMN to the

30 ms or 60 ms deviant for any condition. Three participants only completed Order 1 and 2 of the study and were therefore excluded from statistical analyses and results display.

The within-subjects variables of interest were order (1, 2, 3), speed of block alternation (slow, fast) and tone type (30 ms, 60 ms). Inspection of the data revealed that the speed and order effects on MMN amplitude were maximal at the front-central scalp site F4. MMN was quantified by identifying the peak latency in group averaged data and extracting mean amplitude 10 ms either side of that peak. MMNs to the 30 ms tone peaked uniformly around 170 ms and those to the 60 ms sound peaked uniformly around 150 ms (see Figure 2 below). Mean amplitude was therefore extracted over 160-180ms for 30 ms MMNs and from 140-160 ms for 60 ms MMNs. MMN amplitude was examined in an order by speed by tone repeated measures ANOVA. Greenhouse-Geisser statistics are reported where appropriate.

Results

The MMNs generated to the 30 ms and 60 ms tones as deviants are presented in Figure 2 for the site F4. The differential effect of tone order on the MMNs to 30 ms and 60 ms deviants is visibly apparent. In Order 1, only the MMNs to 60 ms tones show evidence of the expected standard stability effect (slow-larger-than-fast alternation) on MMN size. In Order 2, the pattern reverses entirely, where the slow-larger-than fast alternation effect is only visible for the MMNs to the 30 ms tone as deviant. In Order 3, however, the slow-larger-than-fast effect is clearly present for both the 30 ms and 60 ms MMN.

Analysis of MMN amplitude exposed a main effect of speed ($F(1,10) = 8.00$, $p<.05$) modified by a significant three-way interaction between order, tone and speed of block change ($\varepsilon= 0.76$, $F(2,20) = 8.58$, $p<.005$). In Order 1, there was a tone x speed interaction ($F(1,10) = 5.50$, $p<.05$), reflecting a significantly larger slow change MMN than fast change MMN for the 60 ms deviants only. In Order 2, a significant tone x speed interaction reflected the opposite pattern: a significantly larger slow than fast change MMN for the 30 ms deviant only ($F(1,10) = 26.31$, $p<.001$). In Order 3, only the speed of change main effect reached significance ($F(1,10) = 12.07$, $p<.01$), reflecting larger MMNs to deviants in the slow change than fast change conditions for both tone types. The full set of ANOVA results are presented in Table 1.

The group averaged mean amplitudes of the MMN are presented in Figure 3. The significant order effect on interactions between tone type and speed of alternation are very clear in panel C of Figure 3. The effect of order and speed of alternation on each tone type is presented separately in panels A and B. A repeated measures ANOVA within each tone type confirms a significant quadratic trend for the interaction between order and speed for both tones (30 ms $F(1,10) = 7.80$, $p<.05$, 60 ms $F(1,10) = 27.18$, $p<.001$) although the interaction only reaches significance for the 60 ms tone (see Table 1) . This is visible in Figure 3 where the impact of speed on the difference in MMN amplitudes is maximal where the tone was the first encountered deviant in that order (order 2 for the 30 ms tone and orders 1 & 3 for the 60 ms tone). The modulations, in particular those for the 60 ms tone, show how order modulates MMN amplitude in both directions, consistent with a relative rather than absolute effect.

An examination of the ERPs to the repetitive sounds in each sequence revealed no significant impact of any of the within-subject variables supporting Todd et al.'s (2011) interpretation that the origin of the effects, particularly the bias, is in response to the deviant tone.

Discussion

Since its discovery by Näätänen et al. (1978), the MMN has not only found application in an increasing number clinical and applied fields (Näätänen, Kujala, Escera et al., 2012), but has also been central to revealing an increasingly sophisticated story about auditory processing by the brain (Näätänen et al., 2001). The early conception that the MMN reflects a simple mismatch between incoming sounds and a rapidly decaying trace of low level auditory features has been replaced by the notion that it is integral to auditory scene analysis and reflects a learning process based on the success of multiple simultaneously active predictive models or "regularity representations" residing in long-term memory (Winkler & Cowan, 2005).

In this paper we have used a new multi-context, multi-timescale MMN paradigm revealing a bias in inferential processes underlying MMN. The results extend Todd et al.'s (2011) previous work by demonstrating: (1) that a reliable index of the bias can be obtained in as little as 20 minutes; (2) within-in subject evidence that the bias is anchored to the initial structure of the sequence and so reverses when tone order is reversed (results order 1 versus order 2); but (3) extraction of information about sequence structure over a much longer time course can abolish the bias (no bias when order 1 is repeated in order 3). The data show that experience with sound can affect how subsequent evidence influences automatic perceptual inferences. Although lower-level processes like stimulus-specific adaptation have demonstrated sensitivity to event-probability on multiple timescales (Ulanovsky, Lars & Nelkin, 2003), we know of no mechanism by which it could account for the observed bias and, in particular, the disappearance of the bias in order 3. Given ERP studies provide evidence that adaptation in subsets of neurons coding probability on multiple timescales can influence MMN size (e.g., Costa-Faidella, Grimm, Slabu, Diaz-Santaella & Escera, 2011), these factors must play a role in the phenomena we are measuring but seem inadequate to explain why the bias would be created, reverse and then be overwritten over the three order conditions. A recent computational modelling study suggests that the process from which MMN derives reflects stored information about the conditional probability of observing a particular second stimulus at a certain latency after the first and that “MMN reflects, in a quantitative manner, the degree of violation of such transition probabilities” (Wacongne et al., 2012). The bias in present data and that in Todd et al. (2011) indicate that such transition statistics are only part of the story and insufficient to account for these order-dependent phenomena.

Similar order-dependent biases observed in artificial grammar learning prompting the proposal that: “adult learners have a prior probability, either innately or via early experience, that structures do not undergo rapid change without a strong contextual cue” (Gebhart et al., 2009, p1110). This prospect links well with recent conceptualizations of the MMN process and raises the possibility of a more top-down implementation of acquired knowledge. Winkler (2007) and Sussman (2007) discuss how mechanisms explaining the probability sensitivity of MMN in terms of the absolute strength of a memory trace for the standard, or its strength relative to a memory trace for the deviant, have been replaced by a regularity-violation interpretation within which the MMN reflects learning about predictive confidence. Within this framework, our sequences can be conceptualised as setting up two competing models of the environment. Model A stipulates that the environment is best accounted for by the characteristics of the first standard (30ms) tone. Model B reflects the competing expectation that the environment will match the characteristics of the second standard (60 ms) tone. Evidence for model A and B change over time and at different rates in the fast and slow alternation sequences. The fact that deviations elicit larger MMN in slow than fast change sequences for model A only implies an order-dependent differential impact of experience on predictive confidence. In other words, additional stability in the slow changing sequence (and conversely instability in the fast change sequence) has an impact on MMN size for the violations of model A but not model B. It is as though the initial standard repetition in order 1 (or model A) is accepted as a global structure and the dominant model. Model B becomes a local departure from this structure insensitive to modification by longer term experience. In order 2, model B becomes the global structure/dominant model. The fact that the bias can be so readily reversed by a 5 minute silence might then be explained by the silence preceding order 2 leading to the assumption that this sequence originates from a different object to that in order 1. By order 3, both models have played a role as global/dominant models, are recognised as equally likely (possibly as separate auditory objects) and therefore the bias is abolished. In this way, the bias creates a conservative preservation of stability in initial object perception, presumably until sufficient counter-evidence is acquired.

A slightly different perspective emerges when considering the functional relevance of a prediction-error signal. Model-competition assumes that the bias occurs through preferential re-evaluation of one prediction model (linked to the first standard). In contrast, an information-value perspective assumes that the bias emerges because of the prediction-error (linked to the first deviant). Prediction-errors motivate learning by signalling when reality differs from inferences based on past experience. The goal of subsequent learning is to minimise the error (Friston, 2005). This is achieved by enlisting resources that can provide more information on how to predict the event and/or on what the event predicts. The bias we observed is linked to the presentation order of tones. The first large prediction-error signal is the MMN to the first encountered deviant (e.g., 60ms tone in order 1, 30ms tone in order 2). One perspective on the functional significance of MMN is that it signals that the environment departed significantly from the predicted state and this departure may be important. The best way to learn more about this event is to monitor its occurrence over a longer time frame. Over a longer sampling window, the 60ms sound is less rare (or likewise the transition from 30 ms standard to 60 ms deviant is less rare) in fast change sequences than in the slow change sequences, providing a probability-based explanation of why MMN amplitude to the 60ms tone is modulated by speed of change. In contrast, the initial high repetition of the first encountered standard with no linked consequence may result in learned redundancy, failing to engage higher order monitoring and in turn, explaining why longer term probability changes have no effect on MMN size.

Viewed from this information value perspective, the primacy bias is a failure to unlearn this redundancy, and so it resembles latent inhibition attenuating learning about familiar inconsequential stimuli. If this is the case it appears that the flexibility to be sensitive to variations in deviant probability at multiple temporal scales might be hampered by its implementation through a relatively simple learning mechanism. Our new finding that the primacy effect reverses after a 5-minute break might also be consistent with this simple conditioning explanation given latent inhibition is known to be context sensitive. However, the complete disappearance of the primacy bias (i.e., the fact that speed modulates MMN for both tone durations) after a further break appears to be indicative of a more sophisticated meta-learning process. In particular, why would speed modulation for MMN to the 60ms deviant, which occurs first in in order 1, fail to occur when it subsequently occurs second in order 2, yet the speed modulation observed on the MMN to the 30ms deviant that occurs first in order 2 is also seen when it appears second in order 3? The disappearance of primacy bias suggests that by the time the third sequence pair occurs, higher-order learning promotes longer term monitoring of all sounds to minimise prediction error in an environment with changing sound relevance (and/or multiple auditory objects).

Predictive-confidence and information-value based accounts have slightly different implications for learning. According to the former, the bias reflects how evidence is used to evaluate predictions about the environment. The later implies that even outside our awareness, the automatically determined information-value of a sound will influence the level of engagement in monitoring its occurrence. In either case, it appears that with sufficient experience, the MMN, and early auditory processing of unattended sequences, can reflect influences from brain processes with a hierarchy of temporal scales that enable quite sophisticated adaptation of learning processes to utilise higher-order patterning in predictions (Kiebel, Daunizeau & Friston, 2008). At face value the bias appears to have methodological implications for studies that employ reversed-oddball control designs (e.g., Jacobsen & Schröger, 2003). However, such designs generally hold standard probability stable for longer periods than that used here and do not alternate back-and-forth. Furthermore, it would appear from the outcomes of the present study that a period of silence between two opposing blocks is sufficient to “re-set” or remove the former bias. At present we consider the implications minor unless a study runs the reverse-oddball sequences contiguously. The extent to which this is true depends on the outcomes of ongoing studies in our lab exploring the longevity of the effect in the face of countermanding evidence – that is, whether the bias holds for model A when it is followed by very long periods of stability in model B.

Our results suggest that the multi-context multi-scale MMN protocol provides a sensitive technique for probing the characteristics of perceptual learning about prediction at multiple temporal scales. For example, new studies could examine whether the primacy we demonstrated – one induced by an order-dependent consequential history in the current context – is also found with other types of prior bias (e.g., pre-existing differences in stimulus salience). The way in which context change modulates learning also seems particularly suited to studying the role of long-term memory in the storage and retrieval of regularity representations in mismatch detection. Finally, all of these possibilities can be explored when deviance is defined relative to recently acquired (e.g., Atienza & Cantero, 2001) or long-term (e.g., Pulvermuller et al., 2001) knowledge, or potentially by higher order relationships, such as various stimulus contingencies (e.g., Paavilainen et al., 2001; Tervaniemi et al., 1994), or when multiple simultaneous regularities are active (e.g., Horváth et al., 2001).

Acknowledgements

This research was supported by a Project grant 1002995 from the National Health and Medical Research Council of Australia.

Author Contribution

Juanita TODD

Designed the research, supervised project conduct, analysed data and took the lead role in writing the paper.

Andrew HEATHCOTE

Participated in design, data interpretation and write-up.

Alexander PROVOST

Participated in design, data interpretation and write-up.

Lisa WHITSON

Collected and processed data.

Gavin COOPER

Participated in design and programming.

References

Alho K, Woods DL, Algazi A, Knight RT, Näätänen, R. Lesions of frontal cortex diminish the auditory mismatch negativity. *Electroencephalography and Clinical Neurophysiology, 91,* 353-362*,* 1994**.**

Atienza M, Cantero JL. Complex sound processing during human REM sleep by recovering information from long-term memory as revealed by the mismatch negativity (MMN). *Brain Research*, *901*, 151-160, 2001.

Costa-Faidella J, Grimm S, Slabu L, Diaz -Santaella F, Escera C. Multiple time scales of adaptation in the auditory system as revealed by human evoked potentials. *Psychophysiology*, *48*, 774–783, 2011.

Escera C, Yago E, Corral MJ, Corbera S, Nunez MI. Attention capture by auditory significant stimuli: semantic analysis follows attention switching. *European Journal of Neuroscience*, *18*, 2408–2412, 2003.

Friston K. Learning and inference in the brain. *Neural Networks*, *16*, 1325–1352, 2003.

Friston K. A theory of cortical responses. *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences, 360*, 815-836, 2005.

Friston K. Hierarchical models in the brain. *PLoS Computational Biology*, *4*: e1000211, 2008.

Garrido MI, Kilner JM, Kiebel SJ, Friston KJ. Dynamic causal modeling of the response to frequency deviants, *Journal of Neurophysiology*, *101*, 2620–2631, 2009.

Giard MH, Perrin F, Pernier J, Bouchet P. Brain generators implicated in the processing of auditory stimulus deviance; a topographic event-related potential study. *Psychophysiology*, *27*, 627–640, 1990.

Gebhardt AL, Aslin RN, Newport EL. Changing structures in midstream: Learning along the statistical garden path. *Cognitive Science, 33*, 1087-1116, 2009.

Horváth, J, Czigler I, Sussman E, Winkler I. Simultaneously active pre-attentive representations of local and global rules for sound sequences. *Cognitive Brain Research*, *12*, 131-144, 2001.

Jacobsen T, Schröger E. Measuring duration mismatch negativity. *Clinical Neurophysiology, 114*, 1133-1143, 2003.

Kiebel SJ, Daunizeau J, Friston KJ. A hierarchy of time-scales and the brain. *PLoS Computational Biology, 4*(11), e1000209, 2008.

Kujala T, Tervaniemi M, Schröger E. "The mismatch negativity in cognitive and clinical neuroscience: theoretical and methodological considerations." *Biological Psychology 74*, 1-19, 2007.

Lubow RE, Gewirtz,JC. Latent inhibition in humans: data, theory, and implications for schizophrenia. *Psychol Bull, 117*, 87-103, 1995.

Morey RD. Confidence Intervals from Normalized Data: A correction to Cousineau (2005). Tutorials in Quantitative Methods in Psychology, 4, 61-64, 2008.

Näätänen R, Tervaniemi M, Sussman E, Paavilainen P, Winkler I. "Primitive intelligence" in the auditory cortex. *Trends in Neurosciences, 24*, 283-288, 2001.

Näätänen R, Gaillard AWK, Mäntysalo S. Early selective attention effect on evoked potential reinterpreted. *Acta Psychologica*, 42, 313–329, 1978.

Näätänen R, Kujala T, Escera C, Baldeweg T, Kreegipuu K, Carlsen S, Ponton C. The mismatch negativity (MMN)--a unique window to disturbed central auditory processing in ageing and different clinical conditions. *Clinical Neurophysiology 123*, 424-458, 2012.

Näätänen R, Michie PT. Early selective attention effects on the evoked potential: A critical review and reinterpretation. *Biological Psychology*, *8*, 81–136, 1979.

Näätänen R, Tervaniemi M, Sussman E, Paavilainen P, Winkler I. “Primitive intelligence” in the auditory cortex. *Trends in Neurosciences*, *24*, 283–288, 2001.

Näätänen R. 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*, 201–288, 1990.

Näätänen R. Attention and brain function. Hillsdale, NJ:Erlbaum, 1992.

Paavilainen P, Simola J, Jaramillo M. Näätänen R., Winkler I. Preattentive extraction of abstract feature conjunctions from auditory stimulation as reflected by the mismatch negativity (MMN). *Psychophysiology*, *38*, 359–365, 2001.

Pulvermuller F, Kujala T, Shtyrov Y, Simola J, Tiitinen H, Alku P, Alho K, Martinkauppi S, Ilmoniemi RJ, Näätänen R. Memory traces for words as revealed by the mismatch negativity. *NeuroImage*, *14*, 607–616, 2001.

Schmidt A. Diaconescu AO, Kometer M, Friston KJ, Stephan KE, Vollenweider, FX. Modeling ketamine effects on synaptic plasticity during the mismatch negativity. *Cerebral Cortex*, doi:10.1093/cercor/bhs238.

Semlitsch HV, Anderer P, Schuster P, Presslich O. A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. *Psychophysiology, 23*, 695-703, 1986.

Sussman ES. A new view on the MMN and attention debate: The role of context in processing auditory events. *Journal of Psychophysiology*, *21*, 164–175, 2007.

Tervaniemi M, Maury S, Näätänen R. Neural representations of abstract stimulus features in the human brain as reflected by the mismatch negativity. *NeuroReport*, *5*, 844–846, 1994.

Todd J, Provost A, Cooper G. Lasting first impressions: A conservative bias in automatic filters of the acoustic environment. *Neuropsychologia, 49*, 3399-3405, 2011.

Ulanovsky N, Las L, Nelken I. Processing of low probability sounds by cortical neurons. *Nature Neuroscience*, 6, 391–398, 2003.

Wacongne C, Changeux JP, Dehaene S. A neural model of predictive coding accounting for the mismatch negativity. *Journal of Neuroscience*, *32*, 3665-78, 2012.

Winkler I, Karmos G, Näätänen R. Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. *Brain Research, 742*, 239-252, 1996.

Winkler I. Interpreting the mismatch negativity. *Journal of Psychophysiology*, *21*, 147–163, 2007.

Winkler I, Cowan N. From sensory to long–term memory: Evidence from auditory memory reactivation studies. *Experimental Psychology, 52*, 3–20, 2005.

Figure Legends

Figure 1. Example structure of tone sequences used by Todd et al.'s (2011, first row only) and the present study. Cross-hatched rectangles represent blocks with a 30ms standard and 60ms deviant tone and grey rectangles represent blocks with reversed tone probabilities; in both Pr(standard)=0.875 and Pr(deviant)=0.125. Note that Todd et al. also used several intermediate speeds and found no difference between results when the different speeds occurred in different orders, and so only the slow then fast order was used in the present study.

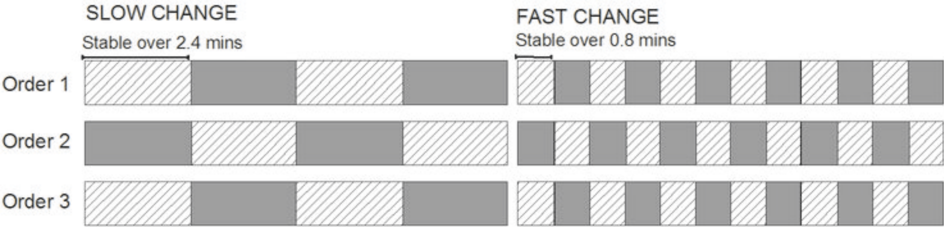
Figure 2. The group average mastoid re-referenced MMN waveforms at F4 to 30 ms (grey line) and 60 ms (black line) deviant tones in the fast and slow change sequences for orders 1-3.

Figure 3. The group averaged mean amplitudes for MMN to 30 ms and 60 ms deviant sounds as a function of change speed and block order. A: Fast and slow speed effects in the MMN to the 30 ms deviant across orders 1-3. B: Fast and slow speed effects in the MMN to the 60 ms deviant across orders 1-3. C: Interactions effects on MMN size

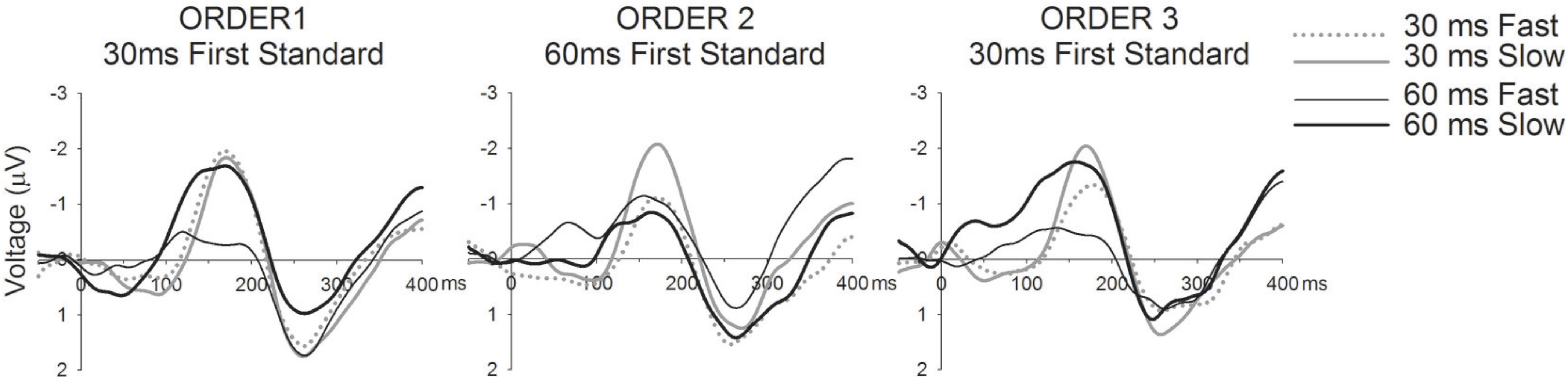
between speed effects and tone type across orders 1-3. Error bars = Morey's (2008) corrected normalized within-subject standard errors.

Table 1. Results for repeated measures analysis of variance exploring main effects and interaction on mean mismatch negativity (MMN) amplitude to 30ms and 60 ms tones in the fast and slow change conditions for sequences orders 1, 2 and 3.

EFFECT	ε	F-STATISTIC	P-VALUE	Mean Square	Error Mean Square
OVERALL					
ORDER	0.96	F(2,20) = 0.72	0.50	0.72	1.08
SPEED	1.00	F(1,10) = 8.00	0.02	16.89	2.11
TONE	1.00	F(1,10) = 1.76	0.21	16.39	9.23
ORDER x SPEED	0.86	F(2,20) = 1.71	0.21	1.24	0.73
ORDER X TONE	1.00	F(2,20) = 1.02	0.38	0.60	0.59
SPEED X TONE	1.00	F(1,10) = 0.61	0.45	0.61	0.35
ORDER X SPEED X TONE	0.76	F(2,20) = 8.58	0.01	9.91	1.16
ORDER 1					
SPEED	1.00	F(1,10) = 2.78	0.13	4.73	1.70
TONE	1.00	F(1,10) = 3.70	0.08	10.45	2.82
SPEED X TONE	1.00	F(1,10) = 5.50	0.04	6.80	1.24
ORDER 2					
SPEED	1.00	F(1,10) = 3.19	0.10	2.10	0.66
TONE	1.00	F(1,10) = 1.43	0.26	3.56	2.50
SPEED X TONE	1.00	F(1,10) = 26.31	0.01	7.57	0.29
ORDER 3					
SPEED	1.00	F(1,10) = 12.07	0.01	12.12	1.01
TONE	1.00	F(1,10) = 0.70	0.42	3.59	5.09
SPEED X TONE	1.00	F(1,10) = 1.54	0.24	0.89	0.58
30 ms					
ORDER	0.91	F(1,10) = 1.18	0.32	1.20	1.01
SPEED	1.00	F(1,10) = 8.66	0.01	6.65	0.77
SPEED X ORDER	0.65	F(2,20) = 2.96	0.10	4.21	0.92
60 MS					
ORDER	0.89	F(1,10) = 0.37	0.67	0.29	0.79
TONE	1.00	F(1,10) = 6.18	0.03	10.45	1.69
SPEED X ORDER	0.91	F(2,20) = 10.10	0.01	6.42	0.58


SLOW CHANGE
Stable over 2.4 mins
FAST CHANGE
Stable over 0.8 mins
Order 1
Order 2
Order 3

MMN to 30 ms and 60 ms sounds as deviants in fast and slow change sequences.



MMN mean amplitude to 30 ms and 60 ms deviants in fast and slow change sequences.