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Todd, Juanita, Provost, Alexander, Whitson, Lisa & Mullens, Daniel. "Initial uncertainty impacts statistical learning in sound sequence processing" Published in *Journal of Physiology*, Vol. 110, Issue 4, p. 497-507, (2016).

Available from: <http://dx.doi.org/10.1016/j.jphysparis.2017.01.001>

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Accessed from: <http://hdl.handle.net/1959.13/1392026>

Initial uncertainty impacts statistical learning in sound sequence processing

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Abstract

This paper features two studies confirming a lasting impact of first learning on how subsequent experience is weighted in early relevance-filtering processes. In both studies participants were exposed to sequences of sound that contained a regular pattern on two different timescales. Regular patterning in sound is readily detected by the auditory system and used to form “prediction models” that define the most likely properties of sound to be encountered in a given context. The presence and strength of these prediction models is inferred from changes in automatically elicited components of auditory evoked potentials. Both studies employed sound sequences that contained both a local and longer-term pattern. The local pattern was defined by a regular repeating pure tone occasionally interrupted by a rare deviating tone ($p=0.125$) that was physically different (a 30ms vs. 60ms duration difference in one condition and a 1000Hz vs. 1500Hz frequency difference in the other). The longer-term pattern was defined by the rate at which the two tones alternated probabilities (i.e., the tone that was first rare became common and the tone that was first common became rare). There was no task related to the tones and participants were asked to ignore them while focussing attention on a movie with subtitles. Auditory-evoked potentials revealed long lasting modulatory influences based on whether the tone was initially encountered as rare and unpredictable or common and predictable. The results are interpreted as evidence that probability (or indeed predictability) assigns a differential information-value to the two tones that in turn affects the extent to which prediction models are updated and imposed. These effects are exposed for both common and rare occurrences of the tones. The studies contribute to a body of work that reveals that probabilistic information is not faithfully represented in these early evoked potentials and instead exposes that predictability (or conversely uncertainty) may trigger value-based learning modulations even in task-irrelevant incidental learning.

Keywords: Auditory evoked potentials, sequential learning, predictive coding, mismatch negativity, primacy bias.

1. Introduction

Our auditory system is incredibly adept at learning any patterning within a sequence of sound (Cowan, Winkler, Teder & Näätänen, 1993; Bendixen, Roeber & Schröger, 2007). Any form of regularity within a sequence is readily extrapolated into an inferred repetition, even without focused attention, and also during early stages of sleep (Loewy, Campbell & Bastien, 1996; Sculthorpe, Ouellet & Campbell, 2009). In the auditory evoked potential literature this inference has been referred to as the formation of a “prediction model” referencing a memory-based anticipation of the most likely properties of sound to be encountered in a given context (Näätänen, Tervaniemi, Sussman et al., 2001; Winkler, 2007). This inference is further weighted by an estimate of “certainty” in the underlying prediction (Winkler, 2009; Pouget, Drugomitsch, & Kepecs, 2016). In computational biology it has been presented in the Bayesian framework of predictive coding as an “internal model” referencing a “belief” about the most likely next-state of brain activation, with this belief weighted by the “precision” afforded by prior evidence (Friston, 2005; Garrido, Kilner, Stephan & Friston, 2009; Lieder, Daunizeau, Garrido, Friston & Stephan, 2013). The existence and updating of an internal model is indexed in measures of auditory evoked potentials.

When a sound matches the content of a currently active internal model the model precision estimate increments (Friston, 2005). This can be observed in changes in the evoked potential; principally in reduced negativity in the waveform recorded at fronto-centrally located scalp electrodes within 200ms of sound onset and, at least in some cases, the emergence of an early positive component (Baldeweg, 2006). Both of these effects are amplified in the presence of further matches between model predictions and brain activation (in response to sensory input), and this progression is considered a quantification of model precision (for the term precision see Baldeweg, 2006; Garrido et al., 2008; Lieder et al., 2013 and for terms strength or confidence see Schröger, 2007; Näätänen, Kujala, & Winkler, 2011; Winkler, 2007; Winkler, 2009). If there is a mismatch between the internal state caused by the incoming sound (often called a “sensory buffer”, Winkler and Cowan, 2005) and model prediction, the evoked potential is characterised by a large negativity peaking 100-200ms from the deviation. This additional negativity (commonly known as mismatch negativity or MMN, see Näätänen, Kujala, & Winkler, 2011 for review) has been suggested to reflect a prediction-error

being signalled (Friston, 2005). Prediction-errors are large if the internal model is associated with high precision, which occurs when there is low variance in the underlying repetition. For example, MMN to deviations from a repetitive pattern will be large when there are a large number of repetitions of the pattern between two successive deviations (e.g., Shelley et al., 1999, Sato et al. 2000), and when the repetition is exact (as opposed to repetition with some variance, Winkler et al., 1990; Daikhin & Ahissar, 2012; Garrido, Sahani & Dolan, 2013). However, we have previously observed that the sound probabilities at sequence onset appear to exhibit a disproportionately strong influence over precision estimates (Todd, Provost and Cooper, 2011). In analogy to other similar phenomena, we termed this effect “first-impression bias”. In psychology, “first impression” refers to the way in which future learning and memory can be anchored to the earliest experience in a given context. It is perhaps best known and documented in literature pertaining to how our beliefs about a person are heavily influenced by the first encounter (e.g., Willis & Todorov, 2006), but in the present study we demonstrate how first impressions affect many aspects of early automatic relevance-filtering processes.

The first impression bias has been observed in protocols that include a simple sound sequence that contains patterns that alternate on different timescales (the “multi-timescale paradigm”, Frost, Winkler, Provost & Todd, 2016; Todd, Provost & Cooper, 2011; Todd et al., 2013, 2014a, 2014b; Mullens et al., 2014, 2016). In these experiments there are only two sounds in the sequence and these sounds exchange roles as a common repeating “standard” defining the local pattern ($p=0.875$), and rare pattern deviation or “deviant” ($p=0.125$) that differs physically from the other tone (hereafter referred to as *context A*). The local pattern alters at regular intervals when the roles of the sounds exchange (probabilities invert, *context B*), and these exchanges happen at regularly timed intervals creating a second-order (or superordinate) pattern embodied in the length of sequence blocks. The context change from A to B is abrupt and the former deviant starts repeating, generating a sequence of prediction-errors. These error signals are rapidly suppressed (within as few as 2-3 repetitions) as a new internal model is formed (Bendixen, Prinz, Horvath, Trujillo-Barreto & Schroger, 2008; Sams, Alho, & Näätänen, 1983). This reflects a locally dynamic predictive system keeping the auditory system adaptive and current. However, it has long been known that local

probabilities are not the only influence on MMN amplitude to the deviant sounds (e.g., Horvath et al, 2001). One of the key findings in the multi-timescale paradigm is that the amplitude of MMN to the rare sounds is differently affected by local stability in the underlying pattern in context A and B (Todd et al., 2014). MMN to the sound-type that is rare in context A (the “first-deviant”) is large at the beginning of sequence blocks and stays large into the second-half of blocks. In contrast, MMN to the sound that becomes deviant in context B (the “second-deviant”) is very small at the beginning of blocks and increases in amplitude into the second-half of blocks.

In previous papers we have suggested that the different pattern of MMN amplitude in context A and B reflects a lasting first impression based on the initial sound probabilities (e.g., Todd et al., 2014, Mullens et al., 2016). We have proposed that high precision is assigned to the internal model for the repetitious sound in context A, specifying the behaviour of the sound that is first encountered as common and predictable. There is little value in updating this model, as its precision is already high (i.e., it is akin to a strong belief that is resistant to counter-evidence). In contrast, the auditory system has little information about the deviant in context A (the first-deviant) because this tone is rare (improbable in the context) and the timing of its occurrence cannot be accurately anticipated. MMN evoked in context A to this rare sound is large throughout blocks because the active internal model for context A is held with high precision producing large error signals when predictions are violated. When context B begins, the high precision for the internal model of context A may explain why the MMN evoked to the deviant in context B is small initially, but then later increases as evidence accumulates that the roles of the two sounds are reversed in the new context.

Although first-impression biases have been replicated a number of times, the analysis of effects on ERP responses has only produced significant order effects on the evoked potential to the rare deviant. However, the hypothesis put forward to explain the bias would predict that we might also see order effects on the responses to the repetitious sounds if we examine the data most likely to show the effects. Models of learning predict that with higher uncertainty about an event, learning about this event becomes fast (for confirmation in an animal model, see Dayan & Yu, 2003; Pearce & Hall, 1980). In the multi-timescale paradigm, uncertainty about an event should be associated with

more readiness to update the internal model in the face of new evidence. As noted above, at the point of role reversal, there is higher uncertainty associated with the sound that has been rare before, because the brain cannot anticipate when it will occur. Before the role reversal (in context A), the sound elicits a prediction-error signal, and when the context shifts from A to B, there is a sudden increase in the frequency of prediction errors as this sound starts to repeat and a new model needs to be built. The mechanisms of new model formation have been studied in depth by Moran et al., (2013) in pharmacological studies employing the “roving paradigm” (e.g., Baldeweg et al., 2002) where the repeating sound changes each time a deviation occurs (i.e., the deviant starts to repeat).

Moran and colleagues (2013) provided evidence that the cholinergic system performs a critical role in establishing the precision associated with internal models of the auditory environment. The authors demonstrated that administering galantamine (a cholinesterase inhibitor that increases the availability of acetylcholine) enhanced the amplitude of responses to prediction errors and slowed model updating when a deviant started to repeat (akin to the change between context A and B). The slowed model updating was inferred from less suppression of the response to the new repeating sound. The authors further explain that when a stimulus is repeated in a highly predictable way, cholinergic neurotransmission is ordinarily suppressed after encountering an unpredicted or surprising event. If the surprising event then repeats, the concurrent drop in acetylcholine levels enables rapid suppression of the response to the repeating sound as a new internal model is formed. This process is disrupted in the presence of galantamine because the boosted levels of acetylcholine interfere with the normal control over cholinergic levels, thus creating a state that can be regarded as prolonging high precision in the old model, resulting in high-amplitude error signals to the sound that is turning from deviant to standard. This interferes with the normal dynamics of model updating in the event of environmental change.

We propose that the higher uncertainty associated with the sound that is rare in context A may play a role in the above described process. More specifically, we propose that we may see accelerated learning about this sound when it becomes a repetitious event. Prediction errors are learning signals because they signify that the current internal

model does not accurately account for some events and thus may require updating (Shultz & Dickinson, 2000). When prediction errors are elicited with respect to a high-precision model, the organism can be confident that the error is informative. Therefore when the error starts to repeat we predict that we may see accelerated learning or model updating. This should result in more prominent “suppression” in amplitude of the ERP to sound repetitions, particularly around the P2 period, which has been shown to be very sensitive to repetition effects and model stability (Baldeweg, 2006; Bendixen, Roeber & Schröger, 2007). To test this hypothesis we examined data acquired within two independent studies using the same temporal/sequential design: one using two sounds of different duration, and the other using two sounds of different frequency/pitch (delivered to a separate group of participants). Both groups of participants heard sequences that began with context A (and then alternated between context A and B). Then after a break, they heard the same alternating-context sequences now beginning with context B. Finally, after a second break, they heard the sequences beginning with context A again. We examined the responses to deviant and repetitious standard tones for these sequences to determine whether any order modulations of the response were present.

2. Method

2.1 Participants

The data presented in this paper are derived from two separate studies using the multi-timescale protocol with identical temporal and sequential parameters, but different sound properties. Twenty-four participants (18-45 years, 13 female) heard sequences that comprised two pure tones of different duration (see *Duration Protocol* below) and sixteen participants (18-25 years, 10 female) heard sequences comprising two pure tones of two different frequencies (see *Frequency Protocol*). All participants were recruited from a pool of undergraduate Psychology students at the University of Newcastle and community participants from a volunteer research register and all provided written informed consent. To be included in the study all participants had to pass screening for the following exclusion criteria: regularly consumed alcohol heavily or used recreational drugs, had a first degree relative with schizophrenia, had a history of neurological disorder, head injury or surgery or a hearing impairment (see *Hearing Assessment* below). The study was approved by the Human Research Ethics Committee of the University of Newcastle, Australia.

2.2 Stimuli and Sequences

2.2.1 Duration Protocol

A pictorial depiction of the sequences used in this study is presented in Figure 1. The *Duration Protocol* sequences contained a short 30ms sound and a longer 60 ms sound that were both presented at 1000 Hz, 75 dB SPL binaurally over headphones (Sennheiser HD280pro) at a regular 300ms onset-to-onset interval with 5 ms rise/fall times. There were an equal number of both sounds (980 each) in all sequences and they were organised into two block types. In *context A* blocks the 30ms sound was the highly probable standard ($p=0.875$) and the 60m sound was the rare deviant ($p=0.125$). In *context B* blocks the probabilities were reversed. In all cases the tones occurred in a pseudorandom order such that all blocks began with 5 repetitions of the standard tone and there were always a minimum of three standards between successive deviants.

In slow-change sequences the context inverted every 480 tones (2.4 minutes) and in the fast-change sequences the context inverted more frequently, every 180 tones (0.8

minutes). Thus the two context blocks alternated in both type of sequences. These two sequences were presented in pairs (referred to as orders in Figure 1) where the slow changing sequence always preceded the fast changing sequence, with a 40-second period of silence between the sequences within a pair, and a 2-minute silent period between orders. The first and third order began with *context A* blocks and the second order began with *context B* blocks.

2.2.2 Frequency Protocol

The *Frequency Protocol* sequences also contained only two sounds: a higher frequency 1500 Hz sound and a lower frequency 1000 Hz sound that were both presented at 60 ms, 75 dB SPL, with all other parameters being identical to those of the Duration Protocol. *Context A* blocks contained the 1000 Hz tone as the repetitive standard and the 1500Hz tone as the rare deviant and in *context B* blocks the probabilities were reversed.

< Figure 1 about here >

2.3 Procedure

Participants completed the screening interview followed by the *Hearing Assessment* that involved ensuring that hearing thresholds were below 20dB HL in both ears using a pure tone audiometer (Earscan ES3S) across 500-4000 Hz.

EEG data for those who heard the *Duration Protocol* was collected using a 64 Channel ActiveTwo Biosemi system (2048Hz, Bandpass filter of DC-400Hz) with bilateral mastoid, outer canthi, supra-orbital, and infraorbital sites. Common mode sense (CMS) and driven right leg (DRL) electrodes for the biosemi active system were positioned inferior to P1 and P2, respectively. EEG data were recorded relative to an amplifier reference voltage, and then re-referenced to the common average. Biosemi data were converted to a Neuroscan compatible file type and down-sampled to 410Hz in EEGDisplay 6.4.6 (Fulham, 2015).

EEG data for those who heard the *Frequency Protocol* was collected using a Synamps 2 Neuroscan system at 1000Hz sampling rate (highpass 0.1Hz, lowpass 70Hz, notch filter

50Hz and a fixed gain of 2010). EEG data was recorded from a reduced montage of 15 electrode locations: including FZ, FCZ, CZ, PZ, F3, FC3, C3, F4, FC4, C4 in accordance with the 10–20 system plus left mastoid, right mastoid and nose reference. Vertical and horizontal electro-oculograms were also acquired from above and below the left eye and 1cm lateral to the outer cantus of each eye, respectively. Electrode impedances were reduced to below 5 k Ω for each electrode before recording commenced.

For both protocols, the participant was told they would hear sounds over the headphones, but that the brain responses we were studying were automatic and best recorded if they ignored the sounds, and focussed their attention on a self-selected muted DVD delivered with subtitles.

2.4 Data Analysis

Continuous data from both experiments was analysed in Neuroscan. Data was first marked for extreme amplitudes and eyeblink corrected using Neuroscan's in-built procedure (Semlitsch et al., 1986). The continuous data were epoched from -50 to 300ms around stimulus onset and then baseline corrected over the whole epoch. Trials exceeding $\pm 70 \mu\text{V}$ were rejected and the remaining trials were averaged, low-pass filtered (30Hz, 12dB/Octave, zerophase), re-baseline corrected over the pre-stimulus period and re-referenced to the average of the mastoid channels to increase signal-to-noise ratio (Joutsiniemi et al., 1998).

ERPs to sounds encountered as repeating "standards" and rare "deviants" were averaged separately resulting in a standard and deviant ERP for each tone, for each order and for each sequence (see Table 1 for how ERPs were averaged). In addition, previous work by our group has demonstrated that order effects are sometimes confined to the period in which a new regularity has just been established. Therefore, data from each sequence block was divided into a first and second half period (0-1.2mins, 1.2-2.4 minutes respectively for slow changing sequences and 0-0.4 mins, 0.4-0.8 mins respectively for the fast changing sequences). Two data sets were excluded from the frequency condition due to excessive noise during some of the fast sequence

blocks. The sweeps contributing to half periods for each block were then combined to create a measure of the ERP to first and second halves, averaged across block occurrences, in order to assess whether pronounced order effects were confined to the first-half periods in these data sets also. Division of blocks into halves necessarily meant that a maximum of 60 sweeps could contribute to any deviant ERP. This low number risks a reduction in signal-to-noise ratio but because the signal is changing differentially over halves for the two tones, this has proven a reliable measure of significant half effects and interactions in previous studies. To protect against inclusion of noisy data in averages we set a minimum of 40 sweeps for any individual averages. In the frequency condition, all participants met the inclusion criterion of minimum 40 sweeps contributing to averages with over 90% of the individual averages containing 50 sweeps or more. In the duration condition, five participants had less than 40 sweeps contributing to one or more of their averages with 85% of the individual averages containing 50 or more sweeps. Averages for these five participants were visually inspected for quality (i.e., a clear ERP present in the average). Two participants failed to meet these criteria for one condition only, and in these cases the mean value for the group was substituted for their individual data. The statistical analyses were run with and without these participants. As exclusion of these participants did not impact the major findings, their data was included in the analyses reported.

<Table 1 about here>

A mean peak amplitude measure was extracted for each deviant ERP (that is, a mean value of data points 5ms on either side of the negative maximum) using a search window of 100-250 ms for the duration data and 80-230 ms for the frequency data. A mean peak amplitude was extracted for the positive maximum in the standard ERP with search windows of 120-180 ms for both data. This window was chosen partly by visual inspection of the period of maximal condition effects on group averaged ERPs and partly based on our prior work showing maximal effects during the P2 period where expectation effects are often seen (Baldeweg, 2006; Todd et al., 2014). The amplitude measures were analysed at F4 (where effects have previously been observed to be maximal; e.g., Todd et al., 2011, Todd et al., 2014).

To determine whether order effects were present in the data, a repeated measures ANOVA with within-subjects factors of sequence order (3 levels – 1, 2 and 3), sound (2 levels - 1000Hz and 1500Hz for the frequency group and 30ms and 60ms for the duration group) and block half (first-half, second-half) was conducted for each sequence type and response type (deviant versus standard).

3. Results

Deviant ERPs – Slow-Changing Sequences

Order effects are clearly evident in the ERP responses to the sounds when encountered as contextually rare deviants. Repeated measures ANOVA confirmed a significant three-way interaction between sound, order and half for both the duration condition ($F(2,44) = 4.84, p < 0.05, \eta^2 = 0.18, \epsilon = .82$) and the frequency condition ($F(2,28) = 3.57, p < 0.05, \eta^2 = 0.20, \epsilon = .87$). The deviant ERPs for both first-half and second-half of sequence blocks are therefore presented separately in Figure 2.

Inspection of the deviant ERPs for both the duration and frequency condition revealed order effects to be more pronounced over the first-half than second-half periods of the slow changing sequence blocks (see Figure 2 left panels versus Figure 2 right panels). It is clearly evident from Figure 2 that the ERP to the first deviant tone tends to be more negative (larger) than to the second deviant during the first-half of the blocks (that is order 1 and 3 for the 60ms tone and the 1500Hz tone, and order 2 for the 30ms tone and the 1000Hz tone). The repeated measures ANOVA confirmed this differential modulation of response in a significant sound by order interaction for both the duration data ($F(2,44) = 6.28, p < 0.005, \eta^2 = 0.22, \epsilon = .92$, quadratic trend $F(1,22) = 13.68, p < 0.001, \eta^2 = 0.38$) and the frequency data ($F(2,28) = 4.91, p < 0.05, \eta^2 = .26, \epsilon = .93$, quadratic trend $F(1,14) = 11.12, p < 0.005, \eta^2 = .44$). The quadratic trends reflect the opposing direction of deviant ERP modulation for the first and second deviant tones in orders 1, 2 and 3 and this is most apparent in the mean amplitudes plotted in Figure 4 (left panels). Follow-up analyses for each sound separately revealed that the quadratic trend on the effect of order was significant for the first deviant only for the duration condition (for the 60ms sound $F(1,22) = 25.83, p < .001, \eta^2 = 0.54$) and for the second deviant only for the frequency condition (for the 1000Hz deviant $F(1,14) = 6.75, p < .05, \eta^2 = 0.32$).

There were no order interactions for the second half data (no main effects or interactions) for the duration condition. However, a sound by order interaction was evident in the second-half of slow sequence blocks for the frequency condition ($F(2,28) = 4.68, p < 0.05, \eta^2 = 0.25$) but it differed from that in the first-half data. The second-half sound by order interaction was characterised by a linear trend only ($F(1,14) = 13.94, p < 0.005, \eta^2 = 0.50$) and reflected a decline in amplitude over orders for response to the low deviant but not the high deviant.

< Figure 2 about here >

Standard ERPs – Slow-Changing Sequences

Order effects were also evident in the ERPs to the sounds when encountered as repeating standard tones. Unlike the deviant ERPs, the order effects on the standard ERPs endured throughout both the first and second half of blocks. The ERP waveforms to the sounds as repetitive standards are presented in Figure 3. In these data the ERP response to standard tones exhibits a modulation in the opposite direction to that observed for deviants, which is clearly apparent in the extracted amplitudes (Figure 4, right) and ERPs (Figure 3). The ERP is more suppressed (less negative) when the sound becomes a repetitive standard after first being heard as a rare pattern deviation. Repeated measures ANOVAs confirmed this differential modulation of response in a significant sound by order interaction for the duration condition ($F(2,44) = 7.07, p < 0.005, \eta^2 = 0.24, \epsilon = .93$, quadratic trend $F(1,22) = 7.79, p < 0.05, \eta^2 = 0.26$) and the frequency condition ($F(2,28) = 5.31, p < 0.05, \eta^2 = 0.27, \epsilon = .81$, quadratic trend $F(1,14) = 17.10, p < 0.001, \eta^2 = 0.57$). These modulations were not modified by block half. Follow-up analyses for each sound revealed that the quadratic trend on the order effect was significant for the 60ms sound only for the duration condition ($F(1,22) = 13.58, p < .001, \eta^2 = 0.38$) and for the 1500Hz sound only for the frequency condition ($F(1,14) = 9.12, p < .01, \eta^2 = 0.39$).

<Figure 3 about here>

To emphasize the similarity in the pattern modulation in ERPs to duration and frequency conditions, the mean amplitudes for the first-half of sequence blocks for both conditions are plotted in Figure 4 as a function of order.

<Figure 4 about here>

Deviant ERPs – Fast-Changing Sequences

The clear order effects observed in deviant ERPs for the slow changing sequences were not evident to the same deviant tones in the fast changing sequences. The ERPs to deviants within the fast-changing sequences are presented in Figure 5. Repeated measures ANOVAs revealed a main effect of half for the duration condition ($F(1,22) = 10.54, p < 0.005, \eta^2 = 0.32$) reflecting an increase in amplitude in the second half of blocks but no interactions. In the frequency condition the same ANOVA likewise produced a main effect of half with responses larger in the second half of blocks ($F(1,14) = 6.39, p < 0.05, \eta^2 = 0.31$) and also a main effect of tone with responses to the 1000 Hz tone being larger than the 1500Hz tone ($F(1,14) = 19.49, p < 0.001, \eta^2 = 0.58$).

<Figure 5 about here>

Standard ERPs – Fast-Changing Sequences

The responses to standard tones in the fast changing sequences are presented in Figure 6. The repeated measures ANOVAs revealed no significant main effects or interactions for the duration condition. However, there was a significant quadratic trend for the sound by order interaction ($F(1,22) = 8.32, p < 0.01, \eta^2 = 0.28$). This quadratic trend reflects a modulation in the same direction as that seen in the slow sequence for the first deviant, but a general increase in suppression in the standard for the second deviant across orders. Follow-up analyses for each sound revealed that the quadratic trend was significant for 60ms sound only for the duration condition ($F(1,22) = 7.84, p < .01, \eta^2 = 0.26$). The frequency condition standard responses were characterised by the same modulation seen in the slow changing sequence, namely a sound by order interaction with a quadratic trend ($F(2,28) = 7.17, p < 0.005, \eta^2 = 0.34, \epsilon = .70$, quadratic

trend $F(1,14) = 36.68, p < 0.001, \eta^2 = 0.72$). The ERP to standards in the frequency condition tended to be less negative or more suppressed the sound had first been heard as a rare deviant before becoming a common standard. Follow-up analyses for each sound revealed that the quadratic trend was significant for the 1000Hz sound only for the frequency condition ($F(1,14) = 19.49, p < .001, \eta^2 = 0.58$).

<Figure 6 about here>

4. Discussion

The results of these experiments show the powerful impact of first-impressions in shaping expectations about the structure of the environment. The relative status of two sounds, as either common or comparatively rare at sequence onset, can have a profound influence over the way future encounters modulate our predictions about these sounds.

The results of the present study confirmed our hypothesis that order-based modulation of the ERP responses would be most pronounced (or at least most reliably demonstrated) in the early period of the blocks within the slow changing sequences. The results observed resemble that in prior studies reporting effects of initial sequence structure on the modulation of response to rare deviant sounds (Frost, Winkler, Provost & Todd, 2016; Todd, Provost & Cooper, 2011; Todd, 2013a, 2013b, 2014a, 2014b; Mullens et al., 2014, 2016). These order effects were replicated here – namely that prediction-errors or MMN elicited to a pattern deviation is generally larger at the onset of sequence blocks when it was the first-deviant heard in blocks at sequence onset, than when the same sound is the rare pattern deviation when the roles reverse¹. However, for the first time we report results showing that the response to these same sounds as common repeating standards is also systematically modulated by the probability of the sound at sequence onset. The response to the repeating sound tended to be more suppressed in the blocks of the slow changing sequences when it occurred as a standard *after* it was first heard as a rare deviant than in sequences when it was first encountered

¹ Note that the modulation of responses to the 30ms deviant in this particular dataset is less pronounced than that seen in prior studies (e.g., Todd et al., 2014; Frost et al., 2016; Mullens et al., 2014), but is none-the-less significantly different to that seen for the 60ms deviant.

as a standard. This tendency is present even though there are 420 repetitions of these tones within a block; in other words, the response differences based on order appear to be rapidly established and enduring throughout a large number of repetitions.

The impact on both deviant and standard ERPs here exposes the importance of best practice in reporting the original ERPs in conjunction with any difference waveforms. We have indeed done so in our prior work but the patterns in MMN in those studies were clearly dominated by the effects on deviant ERPs. In the present study the amplitude of the modulatory influence on the standard ERP (up to $1\mu\text{V}$) was generally much smaller than that to the deviant ($2\mu\text{V}$ or more), which might explain why it has not been systematically observed in our prior studies. A second reason is that in prior studies we have included the data from the fast changing sequences in the same analysis (discussed further below), but more importantly, there are only a few studies in which the order of tones at sequence onset has been reversed, and reversed back, which is useful for two reasons. When only one sequence order is presented the physical properties of the tone and the order are confounded, so one cannot easily attribute any order effect to the order itself. Secondly, the rotation of order back and forth may provide greater power to observe this modulatory influence in quadratic trends.

It was hypothesized that the order effects observed in this study would be more profound in the slow changing sequences. This hypothesis is based on the understanding that the order-dependent effects seen previously are a function of a top-down modulation of responsiveness. As explained earlier, top-down modulatory influences are given priority when there is high precision or confidence in predictions about the environment (Friston, 2005). We propose that the long period of initial stability in context A of the slow changing sequence is more likely to set up this level of precision in predictions, and therefore lead to strong differences in modulation of the ERP to the two tones. The impact of this top-down influence does appear to diminish across the block duration with the differential modulation of the two deviant tones becoming non-significant by the end of blocks. In contrast, the fast changing sequences may not confer this same level of precision conducive to strong top-down modulation. In line with this prediction, the only order-dependent modulations of deviant ERPs in

the fast changing sequences were not driven by the role at sequence onset. In contrast, the differential modulation of responses to the tones as repetitious events was present in the fast changing sequences, albeit apparently weaker in the case of the duration condition.

The tendency for order to modulate both deviant and standard responses in these datasets can potentially be accounted for by combining the assumptions of the hierarchical predictive-coding framework (Friston, 2005) with observations derived from value learning (Sutton and Barto, 1998). “Value” may be determined at the onset of each sequence based purely on the initial tone probabilities: one rare and unpredictable and the other common and predictable. Of the two, the former can be considered to hold more “information value” in that we know less about the behaviour of this event and cannot yet predict when it will occur. The internal model for the first standard may be established rapidly while that to the rare deviant carries high uncertainty. The sharp increase in prediction errors when the initial deviant starts to repeat in context B for orders 1 and 3 and context A for order 2 should trigger a drop in acetylcholine release (see Moran et al., 2013 discussed in the introduction) making the system more amenable to rapid model updating. Consistent with this assertion the analyses confirm a relative enhancement in suppression of the ERP to the sound when it becomes a standard after it was first heard as a deviant. It is noteworthy that the sounds used show differential susceptibility to the order effects. In both the duration and frequency condition the deviant and standard ERPs tend to be oppositely modulated if they are the first rare sound versus the first common sound resulting in the quadratic trend for ERP differences to the two sounds over sequence orders. However, the impact is not strong enough to result in statistically significant order modulations on each sound analysed separately. In the duration condition the order-modulation of 60ms tone is consistently the strongest reaching significance for both the deviant and standard ERP response. In contrast, the order effects for the frequency condition vary for the 1000Hz and 1500Hz sounds. Nonetheless, the visible patterns of modulation evident in Figure 4 make clear that the direction of the effects is always consistent with an order-dependent modulation.

Animal research confirms that in reward-learning experiments the behavioural relevance of a sound shapes receptive fields in auditory cortex, and this reshaping is selectively based on the behaviourally relevant component of a complex sensory signal in which basic sensory attributes (e.g., sound location and sound intensity) co-vary (Polley, Steinberg & Merzenich, 2006). These changes are argued to be top-down in origin as they are specific to the task-relevance of the sound properties. Mullens et al., (2015) demonstrated that the order-modulations in the multi-timescale sound sequences are also affected by prior experience inducing different levels of behavioural relevance of the sound properties. When the same two sounds used in the multi-timescale paradigm are used in a prior task, behavioural relevance of the sounds (which sound the participant was asked to respond to) determined whether the first impression bias was seen. Taken together these observations are consistent with the notion that the initial sound probabilities in a sequence create a perceived information-value differential that generates a long lasting modulatory influence over learning in response to those sounds.

In conclusion the results of the present study, in combination with prior work, build a convincing case that incidental (task independent) learning of patterns in sound sequences engages complex learning mechanisms. It exposes how active inferences about the value of events to future learning can distort the effects of simple probabilistic learning at very early stages of sensory processing. The results support hierarchical models of sensory inference that suggest patterns can be extracted on multiple timescales simultaneously (Kiebel, Daunizeau and Friston, 2008), and exact long lasting modulatory influences over lower level sensory relevance filters. We acknowledge that some of the hypotheses we have offered about underlying mechanisms, and the potential neurochemistry, remain theoretical and require explicit testing in future studies. However, the implications are perhaps hardly surprising as for the sensory systems to optimally serve the well being of the organism, they should have access to how prior learning has shaped priorities. These priors have more lasting effects than many current sophisticated models of the statistical learning allow for (Wacongne, Changeux and Dehaene, 2012; Lieder et al., 2013), and appear to continue to exert their effects until a higher level of surprise is encountered (Mullens et al., 2016). These observations attest to the importance of considering contextual factors when assessing

the apparent limitations of a system (see also Cowan et al., 1993). Task-independent incidental learning studies such as these may teach us about the most endemic heuristics to which the brain is sensitive. If one assumes that the bias exists due to the advantage it confers, perhaps the first-impression reduces the computational demands of modelling all information in the environment with equal diligence (see Daw, Courville & Dayan, 2012; Vul, Goodman, Griffiths & Tenenbaum, 2014 for discussion).

Acknowledgments

DM acknowledges receipt of an Australian Postgraduate Award scholarship. We thank Gavin Cooper for his assistance in programming these experiments and Professor István Winkler for valuable comments on earlier drafts. This research was supported by funds provided by the National Health and Medical Research Council of Australia (APP1002995).

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Figure Captions

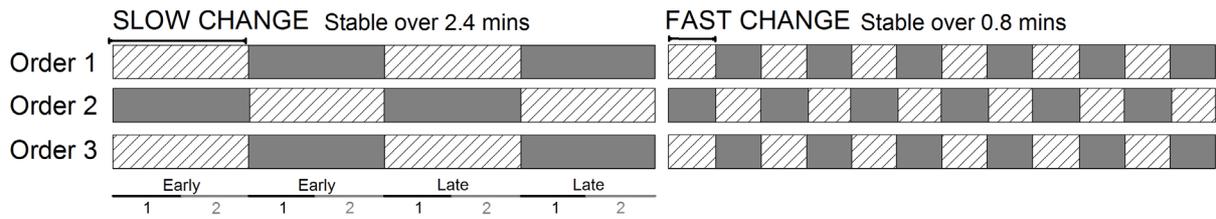
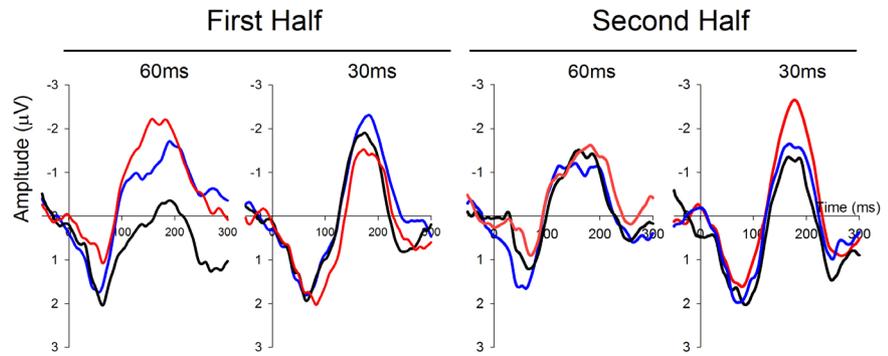


Figure 1. Pictorial depiction of the three slow changing and fast changing sequence pairs used in this study. The lined blocks versus solid blocks represent periods where the probabilities of two tones reverse between common ($p=0.875$) and rare ($p=0.125$) at regular intervals (see text for detail). There was a 40sec silent rest between sequences within an order, and a 2 minute silent rest between sequence pairs. Block order reversed in order 2 and reversed back in order 3. Data analysis of ERPs distinguished between first-half block data (the first-half periods marked "1") and second half block data (second-half periods marked "2").

A. Duration Condition



B. Frequency Condition

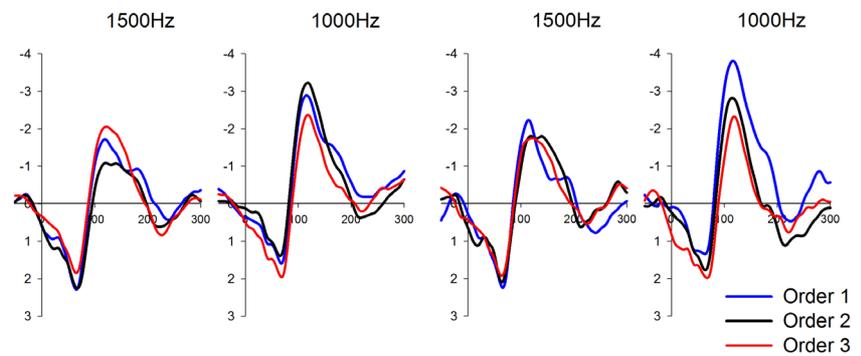


Figure 2. Group average right frontal (F4) ERP waveforms to deviant tones in the slow changing sequences for the duration condition (top) and frequency condition (bottom) for order 1 (blue), order 2 (black) and order 3 (red). In the duration condition the 60 ms tone was the first-deviant in order 1 and 3, and the second deviant in order 2. In the frequency condition the 1500 Hz tone was the first-deviant in order 1 and 3, and the second deviant in order 2.

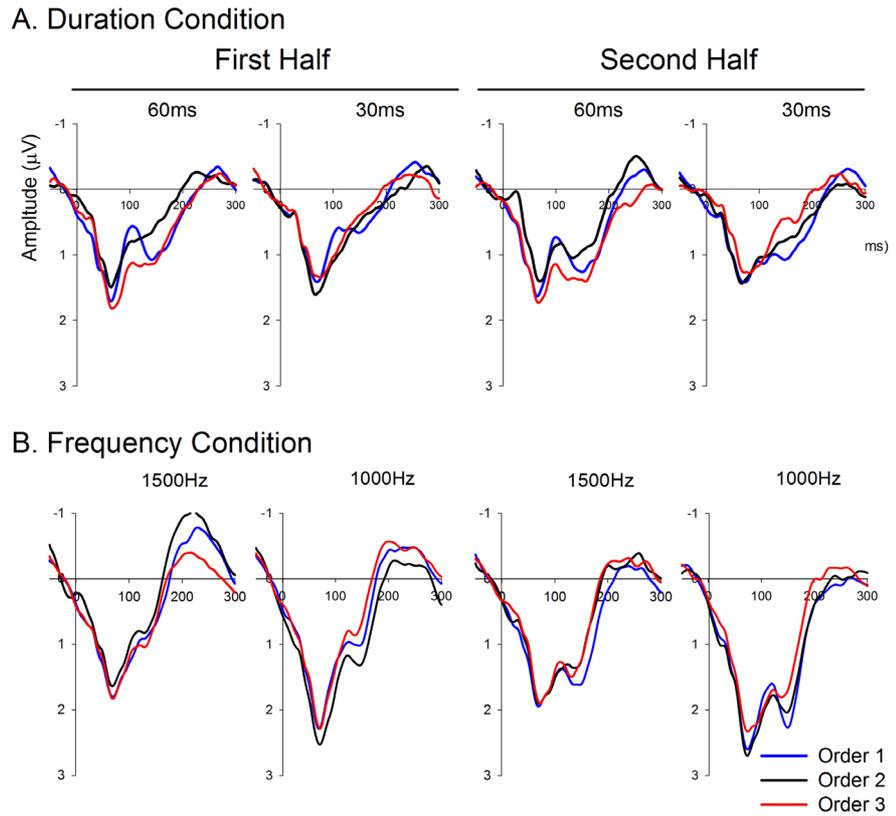


Figure 3. Group average right frontal (F4) ERP waveforms to standard tones in the slow changing sequences for the duration condition (top) and frequency condition (bottom) for order 1 (blue), order 2 (black) and order 3 (red). In the duration condition the 60 ms tone was the first-deviant in order 1 and 3, and the second deviant in order 2. In the frequency condition the 1500 Hz tone was the first-deviant in order 1 and 3, and the second deviant in order 2.

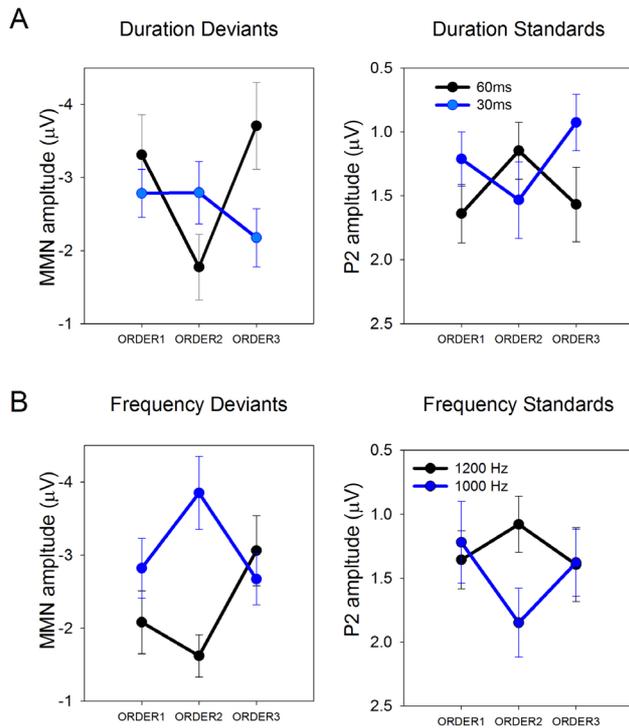
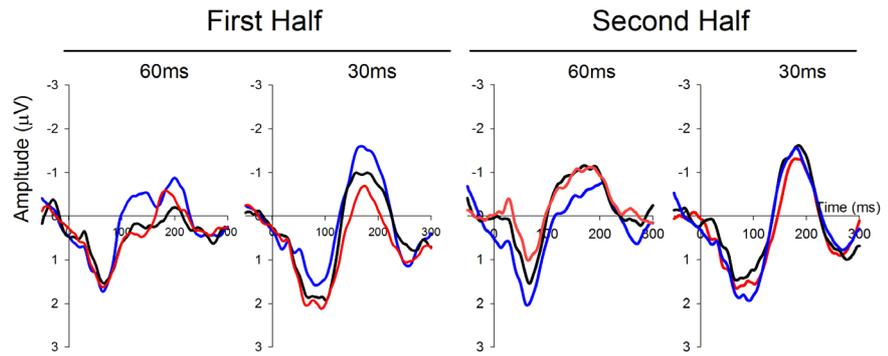


Figure 4. Group averaged right frontal (F4) ERP peak amplitudes for the duration (A top) and frequency (B bottom) deviant (left) and standard tones (right). The black lines represent the tone that was the first-deviant (second standard) in order 1 and 3, and second-deviant (first standard) in order 2. The blue lines represent the tone that was the second-deviant (first standard) in order 1 and 3, and first-deviant (second standard) in order 2. Error-bars represent standard error of the mean.

A. Duration Condition



B. Frequency Condition

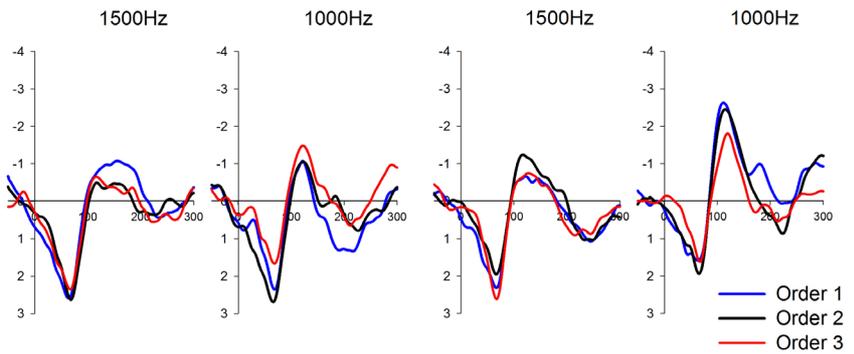


Figure 5. Group average right frontal (F4) ERP waveforms to deviant tones in the fast changing sequences for the duration condition (top) and frequency condition (bottom) for order 1 (blue), order 2 (black) and order 3 (red). In the duration condition the 60 ms tone was the first-deviant in order 1 and 3, and the second deviant in order 2. In the frequency condition the 1500 Hz tone was the first-deviant in order 1 and 3, and the second deviant in order 2.

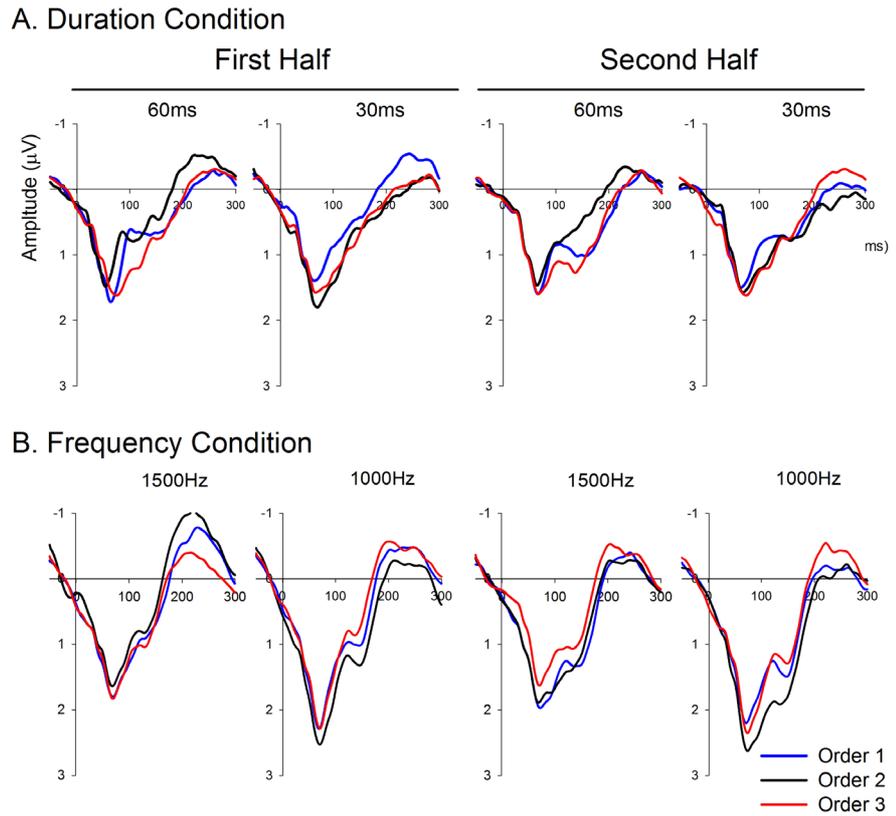


Figure 6. Group average right frontal (F4) ERP waveforms to standard tones in the fast changing sequences for the duration condition (top) and frequency condition (bottom) for order 1 (blue), order 2 (black) and order 3 (red). In the duration condition the 60 ms tone was the first-deviant in order 1 and 3, and the second deviant in order 2. In the frequency condition the 1500 Hz tone was the first-deviant in order 1 and 3, and the second deviant in order 2.