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Title

Setting precedent: Initial feature variability affects the subsequent precision of regularly varying sound contexts.

Short Title: Primacy bias expanded.

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The task of making sense of the world around us is supported by brain processes that simplify the environment. For example, repetitive patterns of sensory input help us to predict future events. This study builds on work suggesting that sensory predictions are heavily influenced by first impressions. We presented healthy adults with a sequence comprising three sounds each differing from the other two on three dimensions; for simplicity A, B and C. These three sounds were arranged in blocks where two were equally common and one was rare, and the probabilities rotated creating three different block types (i.e., probabilities, A<B=C, B<A=C, C<A=B). Sequences included two of each block type with three versions – one starting with A<B=C, one with B<A=C and one with C<A=B. The common tone evoked responses in any given block were highly suppressed consistent with the auditory system predicting regular events, while the rare tone in each block elicited a larger response signaling a prediction-error. However, results indicated that the auditory system assessed the configurations in which the two common tones were adjacent in space (within the three locations used) as less volatile compared to when they were highly separate. When the more volatile environment was encountered at the beginning of the sequence, all deviance-related responses were significantly lower in amplitude. Results suggest that the representation of a stimulus configuration is affected by the estimate drawn from the initial context, expanding our notion of the nature of primacy bias to include powerful effects of initial feature variance.

Key words: Mismatch negativity, auditory evoked potentials, perceptual inference, predictive coding, anchoring.

1. Introduction

Perception is supported by computational algorithms that assist us to anticipate the most likely state of the world around us based on prior experience (Friston, 2010; Seung & Lee, 2000). Such processes are proposed to weight the response to sensory input in line with the degree to which it conforms to predicted states, based on our internal model of the world, thus contributing to our sense of relevance of the incoming sensory information. Consider, for example the use of sound regularities in an intensive care unit. Oxygen monitors and mechanical respirators are two pieces of equipment common to this setting, with each emiting a regular pattern of sounds. The regularity in these sounds enables very precise internal models to be formed and the stability of the source means that they do not interfere with staff abilities to concentrate on a given task. The sensory stimulus response to this familiar and regular sound can be down weighted, enabling staff to control and optimise the allocation of cognitive resources to goal-directed activity. However, it is critical in intensive care settings that staff remain sensitive to any change in these regular patterns. If the pattern of regularity changes, the brain response will be much larger and alert the health professional to a possible need for action. Indeed, any sensory input that defies predictions associated with an established internal model of a regularity elicits larger evoked brain responses indicating that the event might carry information important to new learning, and the existing model might need to be updated to better predict the environment (Naatanen, Tervaniemi, Sussman, Paavilainen, & Winkler, 2001; Winkler, 2007).

Internal models reflect predictions arising out of information gleaned from experience over different timeframes, such that the model weighting of sensory response can reflect not only predictions about the nature of the next state, but also the likelihood of that state, the likelihood that that state will continue to be the most likely state, and so on (Mathys, Daunizeau, Friston, & Stephan, 2011b; Mathys et al., 2014). This sensitivity to more than the current experience has been demonstrated in many ways, such as larger sound evoked responses to a violation caused by a familiar (or previously behaviourally relevant) sound than a less familiar or relevant sound even when the physical difference between the pattern and pattern violation is the same (e.g., familiar tones (Jacobsen, Schroger, Winkler, & Horvath, 2005; Mullens et al., 2014), familiar ringtones (Roye, Schroger, Jacobsen, & Gruber, 2010) and words will elicit a larger response than equivalent pseudo words (Pulvermuller et al., 2001). One can imagine in the intensive care unit example that different pattern changes will be more salient based on how likely they are to occur. For example, a change in blood oxygenation level can be a serious warning sign so when a tone pitch change occurs it could be highly salient. However, oxygen monitors can become dislodged from a patient's finger quite easily so extended experience will lead to the expectation that tone changes associated with this occurrence are not overly rare and not always cause for immediate action. In contrast, the regular pattern of sound generated by a mechanical ventilator should never change so a spontaneous interruption to this pattern would be highly salient. In other words, our basic sensory level models of the world efficiently use information about regularity in the world, integrated with information learned over multiple timescales, to inform our behaviour.

In a laboratory setting the process of internal model formation and updating can be observed through scalp recordings of evoked brain potentials with a substantive literature exploring this ability within an auditory inferential network (Winkler, Denham, & Nelken, 2009; Winkler &

Schroger, 2015). By structuring sound sequences to contain reliable patterns and rare unpredictable pattern violations, auditory evoked potentials (AEPs) readily demonstrate the dynamic learning taking place when the brain attempts to minimise errors in anticipating the next state of the acoustic environment. Sounds that conform to patterns extracted from these sequences elicit small evoked potentials relative to sounds that violate these patterns with the mismatch or error between predicted and actual input typically indexed by the amplitude of an AEP component known as mismatch negativity (MMN). MMN elicitation signals that an event is a mismatch to model predictions, and it can trigger an update to the nature of the prediction (Winkler, Karmos, & Naatanen, 1996) and/or an update to estimates of the precision associated with the internal model (where precision can be considered an estimate of the goodness of fit of an internal model given discrepancy between actual versus expected pattern stability (Friston, 2005; Lieder, Stephan, Daunizeau, Garrido, & Friston, 2013). Studies of this kind are very useful for exploring when, how and why prior experience influences the weighting of brain responses to sound.

The present study has been designed to explore how prior experience over time is variously weighted through order effects on AEPs. More specifically, it features an exploration of how the organisation of sounds at the beginning of a sound sequence can have a long-lasting impact on how we respond to those sounds throughout subsequent experience. When a sound pattern is reliable, precision in a given model is expected to accumulate over time in line with the model's success in predicting the environment (Baldeweg, 2007; Lieder et al., 2013; Winkler, 2007). Deviations that occur in the context of a highly precise model should elicit large MMN and in this way MMN is proposed to be a "precision-weighted error signal" with the amplitude of this component being used to index how much the event departs from predictions as well as how strong those predictions are. Studies incorporating patterning on multiple timescales have revealed order-effects on the amplitude modulation of MMN consistent with a system that applies different model precision estimates (and consequently different model-update or learning rates) based on the organisation of sound when the sequence began (Fitzgerald, Provost, & Todd, 2018; Frost, Haasnoot, McDonnell, Winkler, & Todd, 2018; Frost, Winkler, Provost, & Todd, 2016a; Mullens et al., 2016b; Todd, Provost, Whitson, & Mullens, 2018; Todd, Provost, Whitson, Cooper, & Heathcote, 2013; Todd, Provost, & Cooper, 2011). These order-effects suggest very long-lasting influences that indicate that internal models do not accurately represent current environmental statistics per se, but rather reflect our assumptions about those environment statistics which are informed by what we hear first.

A schematic depiction of the typical sequence structure used to reveal order effects is presented in Figure 1. These sequences contain two sounds that alternate probabilities as common and rare in the two different blocks with the probabilities remaining stable for different periods of time (longer, 2.4 mins and shorter, 0.8 mins). The sound that is rare in a given block always elicits MMN, signaling that the rare sound deviates from the predicted state associated with the locally common tone. If model precision accumulated based on local sound probabilities and stability alone, we could expect a general effect of larger MMN amplitudes in the longer blocks. Instead, the amplitude modulation of MMN varies depending on both whether or not the stimulus probabilities match the configuration encountered at the beginning of the sequence (“initial configuration”, marked with grey on the figure), and also on the longer-term structure of the sequence. For the sequence structure in Figure 1A, MMN to rare sounds in the “initial configuration” blocks is significantly larger for the longer than the shorter blocks, but MMN amplitude to the rare sound in the “subsequent configuration” blocks (marked with a striped pattern on the figure) is approximately equal in longer and shorter blocks (Fitzgerald et al., 2018; Frost et al., 2016a; Mullens et al., 2016b; Todd, Heathcote, Whitson, et al., 2014; Todd et al., 2013; Todd et al., 2011). For the sequence structure in Figure 1B, MMN amplitude is equivalent in longer and shorter blocks for both block types (Fitzgerald & Todd, 2018; Mullens et al., 2016b). Finally, in the Figure 1C sequence structure the MMN is larger in the longer blocks than shorter blocks for both block types (Todd, Petherbridge, Speirs, Provost, & Paton, 2018).

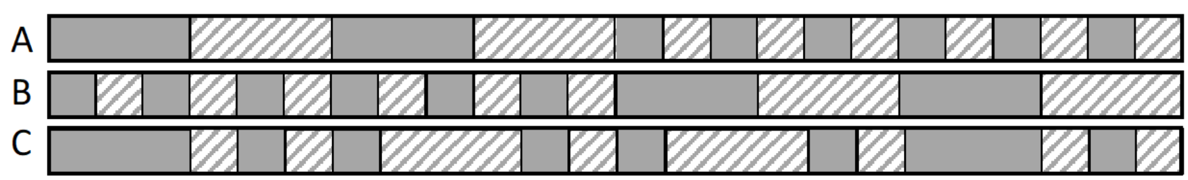

Figure 1. A schematic depiction of binary state alternating block sequences used in three prior studies. In each, the blocks contain two sounds: one common and one rare defined by a change in a single tone property. In the alternate block the common and rare tone properties invert. Grey shading marks the blocks with the initial configuration of probabilities, while the blocks with inverted probabilities is marked by a striped pattern. The different block durations reflect different periods of time over which a tone arrangement is held constant.

Over a series of studies, it has been revealed that these different patterns of MMN amplitude modulation are due to the influence of a first-impression effect creating a type of primacy bias or anchoring. When the sequence starts the participant hears a binary state defined by a common repetitive sound that is regular and predictable, and a second rare sound whose occurrence cannot be predicted. This environment remains stable for a period of time before suddenly the sound probabilities invert such that the initial rare tone starts repeating and a series of prediction-errors are encountered. This series of errors should result in a drop in the precision of the pre-existing model, and a new model associated with this second block composition must be built (Baldeweg, 2006; Lieder et al., 2013; Sussman & Winkler, 2001). A simple effect of longer-larger-than-shorter block MMN would be expected if the auditory system continued to rebuild models and accumulate model precision based on local information only as blocks remained stable. This is precisely what happens in sequences like Figure 1C where there is no consistency in block lengths over time and it was shown that indeed, MMN always starts smaller and increases in amplitude over time within the blocks irrespective of their probability configurations as well as whether they are shorter or longer blocks (Todd, Provost, et al., 2018). However, this is not the case for Figures 1A and B where the sequence starts with a regular, repeating block length (Fitzgerald et al., 2018; Frost et al., 2016a; Mullens et al., 2016b; Todd, Heathcote, Whitson, et al., 2014; Todd et al., 2013; Todd et al., 2011).

A hierarchical Gaussian filter model of learning would suggest that when hearing these sequences, we form predictions about the patterning on multiple time scales simultaneously (Mathys, Daunizeau, Friston, & Stephan, 2011). For example, we might expect the auditory system to form predictions about repeating patterns visible in 1A and B for both time-scales: the local sound probabilities inside a block on a shorter timescale and the period of stability (or block length) on a longer timescale. This model of learning further assumes that the amplitude of a given prediction error will depend not only on the precision of the predictions in the regularity it violated, but also on the precision of the predictions at the level above (i.e., those related to longer timescale patterning). Examination of MMN amplitude patterns in these studies could be explained by this style of multi-timescale modelling. Differences in MMN amplitudes to deviant sounds suggest different levels of precision for the initial and subsequent configuration blocks in the sequences depicted in Figures 1A and B. MMN amplitude inside the initial configuration blocks has been shown to be equivalently large throughout earlier and later parts of blocks representing a relatively higher precision being maintained for this model compared to the subsequent configuration blocks where MMN starts small and increases over the duration of the block (Frost, Winkler, Provost, & Todd, 2016b; Todd, Heathcote, et al., 2014a). The higher precision for the initial configuration block seems to continue until the block length changes (becomes shorter in 1A or longer in 1B), at which point the precision drops and MMN starts out smaller and then builds up over time within the blocks that occur after the change. The higher precision for models of the initial configuration block type, therefore appears to be tied to the precision in predictions based on the higher order model that specifies block length, as it drops only when this higher order predictability is violated in a manner consistent with hierarchical models of learning (Fitzgerald & Todd, 2018; Mullens et al., 2016b).

This observation of order effects is analogous to findings in aritificial language acquisition where participants can learn two artificial languages equally well if learned separately, yet are impaired in learning the second of two languages if presented contiguously (Gebhart, Aslin & Newport, 2009). Remarkably, this limitation disappears if the changeover between languages is cued by a period of silence and if participants receive explicit instruction on the existence of a second structure. This is precisely what happened in Frost et al., (2018) when participants heard the sequence depicted in Figure 1A and were told beforehand about the sequence structure. Although participants were asked to watch a movie and ignore the sounds just as in the version of the task with no explicit knowledge of the sequence, but in this case the MMN elicited by deviants was large across the entire period of both block types, therefore not showing the pattern of lower precision for the alternate block. In a subsequent study on the artificial language learning task, participants most susceptible to this type of order effect displayed a pattern of functional brain connectivity consistent with decreased sampling from the environment (Karuza, Li, Weiss, & Bulgarelli, 2016). The authors propose that learners may reduce their attention to the input once the determined estimate of uncertainty is sufficiently low . Interestingly, the strength of this order effect appears contingent on what has been referred to as initial "overlearning". The order effect can be eliminated if the second language is presented much sooner: more specifically, there is no order effect if the second language begins once robust learning of the first language has been demonstrated (Bulgarelli & Weiss, 2016). The multi-timescale sound sequences used in our studies present an interesting parallel to this work in which similar order effects emerge despite the fact that there is no explicit task and the two learning contexts alternate multiple times.

The present study was designed to determine whether first impression effects in the AEPS to multi-timescale sound sequences are confined to the type of binary state described above, or whether they might also apply to more complex sequences. More specifically, we explored whether models of the auditory environment would show these same first-impression patterns of MMN amplitude modulation if the sequence contained not two, but three tones that alternated probabilities as common and rare events. To examine this possibility tones denoted A, B and C alternated probabilities in blocks such that each was encountered as a rare event relative to the higher equally probable occurrence of the other two sounds. If the MMN amplitude to a given deviant was impacted by the order-effects described above, precision associated with the first sound arrangement would be higher than the second and third. We would therefore expect MMN to always be largest to a sound when it was the deviant in the first block heard (initial configuration block). That is, MMN to A would be larger if the sequence was heard ABCABC (where the letter A depicts that A is rare among equal numbers of B and C and likewise, B depicts where B is rare among equal numbers of C and A, and so on) than in a sequence heard BCABCA or CABCAB. Confirmation of this result would provide support that multiple timescale pattern sensitivity is not constrained to binary states but can be extended to more complex sound sequences.

2. Method

2.1 Participants

Participants were 42 healthy adults (8 male, 18 – 35 years, mean = 22.7 years) consisting of community volunteers and undergraduate students from the University of Newcastle, Australia. All participants completed a screening interview and were excluded for diagnosis and/or treatment of a mental illness, having a first-degree relative with schizophrenia, regular use of recreational drugs, history of a neurological disorder/head injury or surgery, excessive alcohol consumption or hearing impairments. Students received course credit for participation and cash reimbursement was offered to volunteers from the community. All participants provided written informed consent as approved by the Human Research Ethics Committee at the University of Newcastle.

2.2 Stimuli and Sequences

Although an ABC tone structure might seem a rather minor extension to the sequence design, it necessitated an important additional control. MMN amplitude has been shown to be modulated by the degree to which a deviant sound differs from the mean of other more common sounds (Winkler et al., 1990). If A, B and C were to differ on a single dimension (e.g., if sound duration were 30 ms, 60 ms and 90 ms, respectively), we might expect MMN to B might always be smaller than that to A or C given that it falls between A and C in value and, therefore closer to the mean of the regularity. In an attempt to balance the impact of this factor, the tones chosen for A, B and C each differed from each other in three sound features: frequency, duration, and spatial location (see Table 1 for full description of tone features and Figure 3c for a graphical representation). In other words, the A, B and C tones differed on three dimensions concurrently with each being at the mid-point of the three tones on one dimension, the upper extreme on another dimension, and the lower extreme on the third dimension. Sound stimuli were pure tones presented binaurally over headphones (Sennheiser HD 280) at a regular 300 ms stimulus onset asynchrony and at 75 db SPL and were generated with 5 ms rise/fall times.

INSERT TABLE 1 ABOUT HERE

Participants heard three sound sequences containing three block types differing in the configuration of tone probabilities. Each block contained 405 tones delivered over ca. 2 minutes.

One tone was always a rare deviant (n = 57, within-block p = .141) and there were equal numbers of the two remaining tones within the block, denoted as repetitive standards (n = 174, p = .430 for each). The role of the deviant and standards (i.e. tone probability) rotated between the tones across the three block types: block "A" in which tone A was the deviant with respect to the equally higher probability B and C tones (grey blocks Figure 2); "B" where tone B was the rare deviant (striped blocks Figure 2); and "C" where tone C became the deviant (white blocks Figure 2). The earliest position at which a deviant could occur within a block was 6. From the three block types, three types of sequences were constructed the block type changing ca. every 2 minutes and each block type appearing exactly twice (ca. 12 minutes overall duration): ABCABC, BCABCA, and CABCAB (Figure 2). Each participant heard each of these sequence compositions with the order of sequences semi-counterbalanced using a partial Latin square design. This design resulted in six sound sequence orders (123, 321, 213, 312, 132, and 231, where 1 denotes block order ABC, 2 is BCA, and 3 is CAB). A 1 min break was inserted between consecutive sequences.

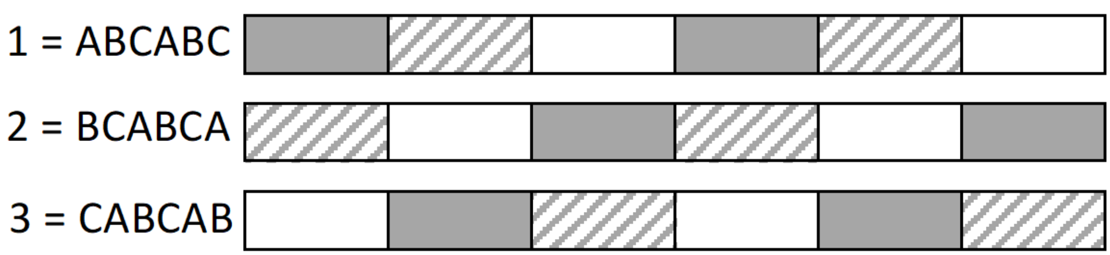

Figure 2. Sequence structure showing the ABCABC, BCABCA, and CABCAB stimulus block arrangements. In grey blocks, tone A was deviant and tones B and C were equally probable standards. In striped blocks, tone B was deviant A and C were standards. In white blocks, tone C

was deviant and tones A and B were standards. All participants heard all three types of sequences.

2.3 Procedure

The screening interview was first conducted to ensure that each participant met inclusion criteria as stated above. A pure tone audiometer (Earscan ES3S) was then used to assess that all participants met hearing threshold criteria (threshold < 25 bd HL) for the frequency range of 500-4000 Hz. Eligible participants were fitted with a Neuroscan Quikcap with Ag/AgCl electrodes. Continuous EEG was recorded on a Synamps 2 Neuroscan system at 1000Hz sampling rate (highpass 0.1Hz, lowpass 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. In order to monitor eye-blinks and movements, vertical and horizontal electro-oculograms were also recorded by placing electrodes above and below the left eye and approximately 1cm lateral to the outermost canthus of each eye, respectively. All impedances were reduced to below 5 kΩ before recording commenced.

Participants received the stimuli through stereo headphones whilst viewing a silent film with subtitles. Participants were instructed to ignore all sounds, focus on the film and remain as still as possible. During the 1 min break between sequences, participants were permitted to move and reposition themselves.

2.4 Data Analysis

Continuous EEG recording was initially examined offline to correct for major artefact and eye blinks using procedures outlined in Neuroscan (4.5) edit software. To correct for eye blinks, artefact averaging combined with regression analysis was applied (see Semlitsch, Anderer, Schuster & Presslich, 1986). The subsequent output values produced were then assessed for adequacy against model parameters (frontal maximum weight and < 5% variance) before being applied to each data set. Data were epoched from 50 ms pre-stimulus to 300 ms post-stimulus and baseline corrected over the entire interval. Epochs containing voltage variations over any electrode (excluding vertical and horizontal electrooculograms) exceeding ± 70 µV were removed. Epochs were then averaged depending on stimulus type, block type, and sequence type, baseline corrected to the pre-stimulus period and a low pass zerophase 30 Hz filter applied (12 dB roll off). Four participants were removed from the final dataset because of poor data quality due to movement or other artifacts.

Trials were averaged in specific ways to answer key questions. Firstly, it was important to determine whether the auditory system could detect a given sound as deviant relative to the other two more probable sounds. An overall deviant and an overall standard average were created for each tone type by separately averaging all instances of the same tone when it was rare (deviant AEP), and whet it was common (standard AEP). This resulted in 6 averaged ERPs per participant (3 tone types [A, B, C] × 2 tone roles [standard, deviant]). Deviant-minus-standard difference waveforms were then calculated separately for each tone type. These averages were used to assess topography and define periods of significant difference between common and rare occurrences of each tone type.

Secondly, separate deviant averages were generated for each tone type when it had been the deviant in the first, second or third block of the sequence (termed first-, second-, and third-deviant; e.g., on Figure 2, tone A is first-deviant in sequence 1, second-deviant in sequence 2, and third-deviant in sequence 3). Corresponding averages were generated for each tone as a standard, separately for the sequences in which the given tone was first-, second, or third-standard (e.g., tone A as standard from sequence 1, 2, and 3). This procedure resulted in 18 averages (3 tone types [A, B, C] × 3 sequence types [1,2,3] × 2 tone roles [standard, deviant]). Finally, 9 differences waveforms per participant (3 tone types [A, B, C] × 3 sequence types [1,2,3]) were computed. The order in which the three sequence combinations was heard was not a variable in the analysis given the small number of cases per order (5-7) and the fact that our goal was to test whether there was a first-deviant order effects that would survive any sequence order effects as per prior studies (Fitzgerald et al., 2018; Frost et al., 2018; Frost et al., 2016a; Mullens et al., 2016b; Todd, Provost, et al., 2018; Todd et al., 2013; Todd et al., 2011). Statistical analyses and component amplitude extractions are described in the results section. In prior studies, the order effects on MMN were demonstrated to be due to the deviant response amplitudes so these were the focus of the analyses in the present study.

3. Results

3.1 Question 1: Did the auditory system detect the deviants?

The common-averaged scalp topography maps for the overall response to A, B and C deviant tones at the peak amplitude point in difference waveforms are presented in Figure 3b. It is clear from Figure 3a that all three types of deviant tones elicited a mismatch-response with a frontal negativity that inverted polarity at posterior sites as is typical for MMN (Baldeweg, Williams, & Gruzelier, 1999; Kujala, Tervaniemi, & Schroger, 2007). For the C tone, the source distribution appears to include bilateral sources in auditory cortex and a fronto-centrally maximum distribution of negativity. For the A and B tones, the posterior source is clearly dominant over the right hemisphere with the A tone eliciting a fronto-right and the B tone a fronto-left maximum distribution of negativity. Figure 3a provides a reminder of the three tone properties which highlights that the laterality of the frontal source for tones A and B emerges contralateral to the ear of monaural sound delivery. In order to improve signal to noise ratio and to capture a "whole of MMN" amplitude (Kujala et al., 2007), in line with common practice, the AEP to each tone was subsequently re-referenced to the average of the left and right mastoid electrode. Although a small tendency for the laterality effects remains after re-reference to the average mastoid activity (Figure 3c), Fz was considered a reasonably parsimonious choice for quantifying peak amplitude.

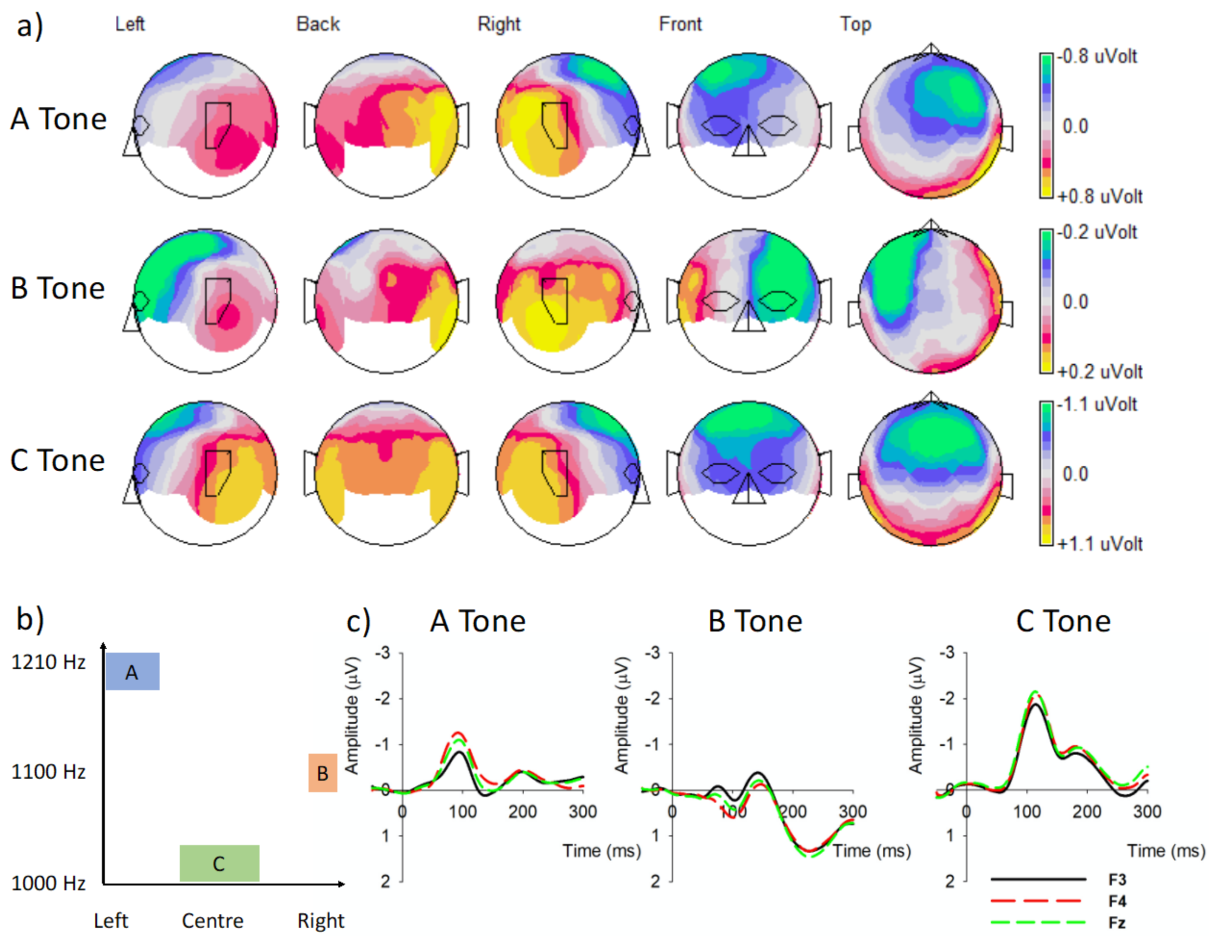

Figure 3. a) A schematic depiction of the dimensions on which the three tones vary. b) The topography of common-average referenced deviant-minus-standard difference wave response to the A, B, and C tones at the visible point of peak latency (A= 95 ms, B = 145 ms, and C = 115 ms). C) The associated average difference wave for the A, B, and C tone at sites F3, Fz, and F4 (mastoid-referenced data) where arrows reflect topography point latencies.

The averaged response to the A, B and C tones as standard repeating tones and as rare deviants at Fz are presented in Figure 4 along with the resultant subtraction difference waveforms. Separate lines denote the response to the A, B and C tones as first-, second-, and third-deviants within their sequence. Each tone type elicits a clear P1, N1, P2, N2 AEP morphology and there are visible standard versus deviant differences for all tones over the N1 period, and for the A and C tones, also over the N2 period.

Paired t-tests were used to assess for the presence of significantly larger responses to the deviant as opposed to the standard tones, as reported in Table 2. The presence of a significantly larger negativity in deviant than standard responses at Fz was supported for A and C tones for all three deviant-positions over the N1 period (see Table 2), but only when the sound was second-deviant for the B tone. A significantly larger negative response for deviants than standards was also present over the N2 period for all three deviant positions for the C tone only. These results match the visible differences evident in the difference waves in Figure 4, and are consistent with the presence of a MMN-like response to each rare tone, albeit in a context-dependent way for tone B.

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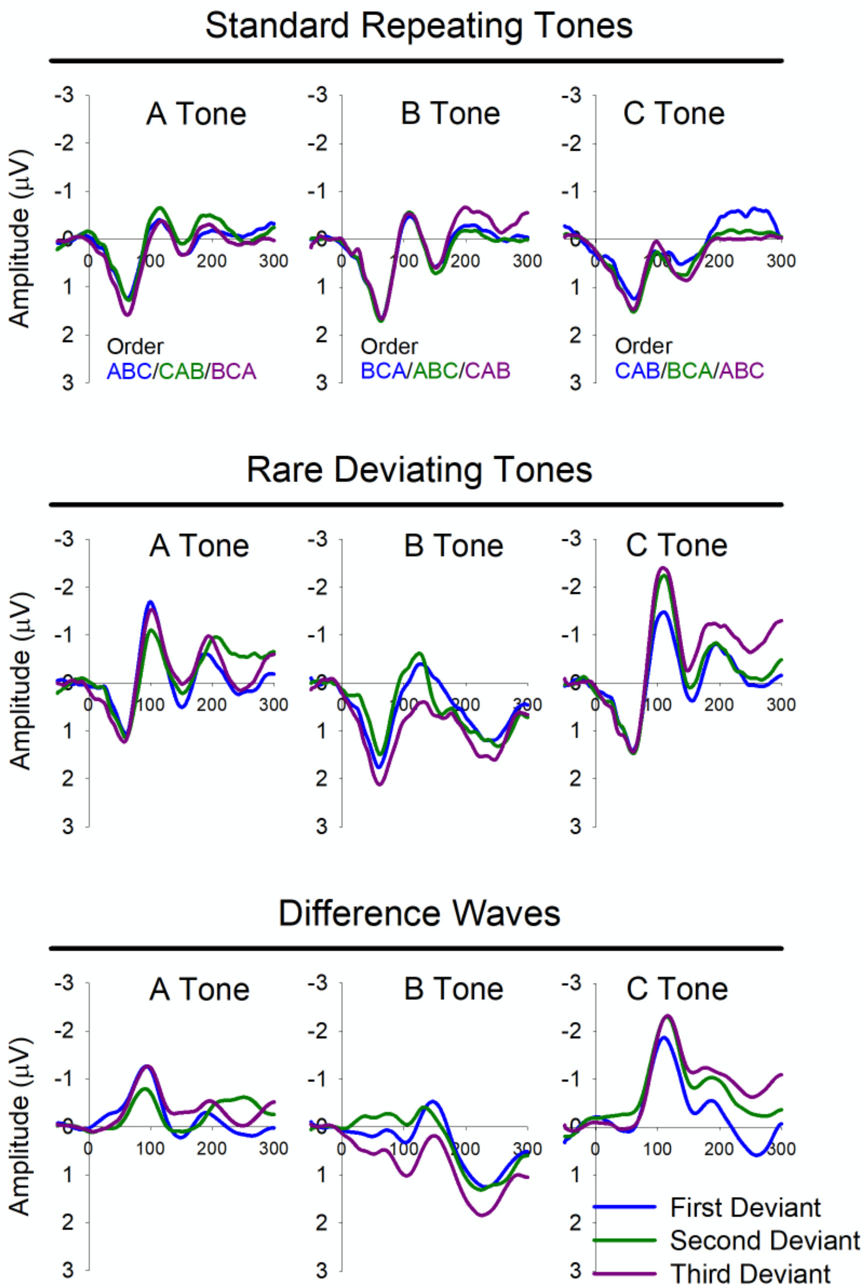

Figure 4. The average response to the A, B, and C tones as common standard tones (top), rare deviating tones (middle) and the deviant-minus-standard difference waves (bottom). Different coloured lines represent situations in which the tone was the first- (blue), second- (green) or

third-deviant (purple) heard in the sequence. The orders of each plot are given underneath the standard-tone plots (for example, the A tone was first-deviant in the ABC order, the B tone in the BCA order, and so on).

The deviant response (and consequently the difference waveform) appeared to peak later for the B tone than tones A and C (Figure 4). The topography patterns and the N1/N2 difference patterns between standards and devants can be used to infer the sound properties most likely to have elicited the MMN response. Duration MMN typically peaks at approximately 150 – 200 ms after deviance (Jacobsen & Schroger, 2003; Todd et al., 2011) so it would appear that the later MMN-like response to the C tone may indicate detection of the longer than expected tone in the context of the 30 ms and 60 ms standards. The A and B tone responses, however, do not produce significant additional negativity to the deviant occurrences over this period. Spatial deviance would have been the earliest detectable deviant feature and typically elicits an early MMN response (Deouell, Parnes, Pickard, & Knight, 2006; Fitzgerald et al., 2018) peaking at around 100 ms. This latency is a good match to the early latency of the A tone and C tone MMN responses and possibly the B tone. The slightly later response to the B tone could be indicative of one of two things. Firstly, it is possible that the deviant feature eliciting MMN is the difference in tone frequency which does typically peak later than spatial MMN around 120-150 ms for deviance magnitudes of this size (Todd, Heathcote, Whitson, et al., 2014). The B tone was in fact the middle value of this feature which may also act to limit the MMN amplitude to this feature. However, peak latency is also typically prolonged when a discrimination is more difficult (Naatanen & Alho, 1997), so it is also possible that the B tone MMN occurs in response to spatial location but is delayed. The B tone also elicits a very early difference in the P1 latency range (larger to deviants) and in the P3 latency range (larger to deviants) that is not evident for the A and the C tone. The results could therefore indicate that a system primed to expect sounds to the centre left (when A and C are common) has impaired detection of a rare monaural right tone deviance. It is certainly the case that spatial processing is a right-hemisphere dominant process so the contralateral dominance of response to sounds presented monaurally may create a relative disadvantage for the detection of the right-ear B tone (earlier and predominant activation of the left hemisphere) compared to the A and C tones, which both include input directly to the left-ear (comparatively earlier and predominant activation of the right-hemisphere).

In summary, it would appear that the auditory system could, in almost all cases, detect the rare violations of the most common combination of tone attributes in a sequence of sounds differing from each other on three dimensions. The difference wave amplitudes indicate that the B-tone deviance among common A and C tones was the most difficult discrimination. Although it is not possible to identify with certainty that the early negativity in the differences waves to the A, B and C tones reflects a spatial MMN, we consider this the most likely explanation for the present results.

3.2 Question 2: Were order effects present in the response to tones?

3.2.1 Standard Tones

To assess for order effects, we examined the responses to tones as both common standard events and rare deviating tones. A pattern visibly apparent in Figure 4a is the tendency for the repetitive response to be most suppressed to the C tone over the N1 period. Standard-tone N1 response amplitudes were compared in a repeated measures ANOVA with within-subjects factors of Tone (A, C, B) and Order (first, second, and third), with Greenhouse-Geisser corrections applied. Smaller N1 amplitude to the C tone was confirmed in a significant main effect of Tone ($\varepsilon = 0.87$, $F(2,74) = 12.50$, $p < .001$, $\eta^2 = .25$, A mean = -0.96 µV , B mean = -0.79 µV , C mean = -0.39 µV). The C tone was the lowest frequency, longest duration and it was the only sound presented binaurally. Of these attributes, it is likely to be the binaural presentation that is causal in the more pronounced suppression of the AEP for the C tone over the N1 period (see (Fitzgerald et al., 2018) for monaural/binaural examples). There was no main effect or interaction with Order.

In summary, there were no clear order effects on the response to sounds encountered as repetitive standard events. There was however a general trend for the N1 response to be more suppressed for binaurally delivered (C) compares to monaurally delivered tones (A and B).

3.2.2 Deviant Tones

In Figure 4 it is clear from the response to tones as deviant events, tone C elicits the largest N1 then the A tone followed by the B tone. This was confirmed in repeated measures ANOVA with within-subjects factors of Tone (A, C, B) and Order (first, second, and third), where there was a significant main effect of tone ($\varepsilon = 0.88$, $F(2,74) = 17.91$, $p < .001$, $\eta^2 = .33$, A mean = -2.14 µV, B mean = -1.36 µV , C mean = -2.92 µV). The main effect of tone was also significantly modified by deviant order ($\varepsilon = 0.88$, $F(4,74) = 2.94$ $p < .05$, $\eta^2 = .07$). Although the B-tone MMN tended to be smaller than the A- and C-tone MMNs for all orders, the effect of deviant order was significant for the B tone, only ($\varepsilon = 0.95$, $F(2,74) = 3.72$, $p < .050$, $\eta^2 = .09$): N1 to the B-tone deviant was largest when the B-tone was heard as deviant in the second block configuration and smallest when it was heard as deviant in the third block configuration of the sequence (B-first mean = -1.39 μV, B-second mean = -1.80 μV, B-third mean = -0.88 μV, B second versus third $t_{37} = 2.28$, $p < .05$). This order effect is clearly apparent in Figure 4. However, it is noteworthy that these differences for the B tone appear to reflect a more general pattern, where the smallest visible N1 response to deviant tones always occurred when the C tone was the first deviant. This effect is more pronounced for the B and C tones, but it is visible for all tones in Figure 4. An analysis of N1 response based on C order confirmed smaller N1 responses to all tones when the C tone was the first deviant compared to the other two type of sequences: a repeated-measures ANOVA with within subjects factors of Tone (A, B, C) and C-tone order (C-first, C-second, C-third) produced a significant main effect of C-tone order ($\varepsilon = 0.96$, $F(2,74) = 3.93$, $p < .050$, $\eta^2 = .10$; C-first mean = -1.90 μV , C-second mean = -2.11 μV , and C-third mean = -2.41 μV). Due to the unexpected nature of this effect we also conducted a mixed model ANOVA by adding Sequence-order group (six levels 123, 321, 213, 312, 132, and 231) as the between subjects factor in case the results were distorted by a certain listening order. However, sequence-order grouping yielded no significant main effect or interaction with the other two factors.

The analysis of deviant N2 peak amplitude in repeated measures ANOVA with within-subjects factors of Tone (A, C, B) and Order (first, second and third) confirmed the very visible main effect of Tone evident in Figure 4 ($\varepsilon = 0.72$, $F(2,74) = 18.99$, $p < .001$, $\eta^2 = .34$) with N2 largest for the C tone (A mean = -1.33 μV , B mean = -0.82 μV , C mean = -2.48 μV). There was also a significant Tone by Order interaction ($\varepsilon = 0.82$, $F(4,148) = 3.76$, $p < .010$, $\eta^2 = .10$) that was due to an order effect for the C tone only, with the amplitude largest when the C tone was the third deviant ($\varepsilon = 0.99$, $F(2,74) = 4.57$, $p < .050$, $\eta^2 = .11$; C-first mean = -2.34 µV , C-second mean = -2.03 µV , and C-third mean = -3.08 µV; C-first versus C-third $t_{37} = 2.05$, $p = .05$ and C-second C-versus third $t_{37} = 2.81$ $p < .010$).

In summary, order effects were evident in the deviant tone responses. The consistent order effect present in the data was the tendency for the deviant response for all tones to be smallest when the C tone was the first deviant type within the sequence. For the C tone, this obviously occurs when the C tone is the first-deviant in the sequence (blue line Figure 4), for the B tone it occurs when the B tone is the third-deviant in the sequence (purple line in Figure 4), and for the A tone it is when the A tone is the second-deviant in the sequence (green line in Figure 4). In other words, the order effects do not reflect the position of the deviant tone within the sequence – only the effect of the position of the block in which the given tone was first encountered as deviant within the sequence.

4. Discussion

This study was designed to assess whether order effects on deviant tone response amplitudes (MMN) seen in two-tone sequences with regular rotating probabilities would extend to a three-tone sequence design. As noted at the beginning of Methods, establishing a rotating design with three tones was complicated by the tendency of MMN amplitude to be modulated by a type of regression to the mean of the properties of the repeating tones (Winkler et al., 2009; Winkler & Schroger, 2015). In the effort to prevent this being a dominant factor in this study, each tone varied on three dimensions with each occupying the "highest", "lowest" and "middle" value on one of the dimensions. The resultant sequences therefore contained considerable variability and yet, remarkably, a significant MMN-like response was observed to all deviant tone types.

As discussed in the results section, it is difficult to ascertain which of the three deviating properties triggered or dominated the prediction-error (i.e., as determined by additional negativity in the deviant response). It is evident that only the C tone elicited consistently a significant prediction-error with respect to expected tone duration violation and it is also clear that this became more prominent with more experience with the tones given that this response over the N2 period was largest when the C tone was first encountered as deviant in the latest block position within the sequence (i.e., in ABC). This can be taken as evidence that in complex sequences such as those used here, it takes time for the auditory system to extract the all regularities and build internal models with precision.

Sequences were structured into three 6-block versions with first-deviant order characteristics of: ABCABC, BCABCA, or CABCAB. If the factors thought causal in previously observed order effects were also influential in the three-tone sequence, the deviant responses should have been systematically larger when a given deviant sound was the first deviant type encountered in the sequence (e.g., the A tone response would be larger in the ABCABC sequence than the BCABCA or CABCAB and so on). This simple order effect was not present in the three-tone sequence results. This suggests that, unlike for the previously studied two-tone sequences, there was no systematically significant difference in precision set up within blocks as a function of the order in which they were encountered. It is difficult to know whether this is due to the design breaking the binary state used previously or whether it represents the greater complexity in the sequence generally with three properties varying instead of one. However, the robust MMN responses elicited tend to argue against a complexity argument as do the other order effects that are indeed present in this study. Rather, we argue that the non-binary state is likely to have interfered with first-impression effects and block length learning.

Although first-deviant order-based effects were not evident in this dataset, another form of order-based modulation was apparent. The amplitude of the response to any deviant sound was consistently smaller when heard within the CABCAB sequence than in the BCABCA or ABCABC sequences (that is, green plots for tone A, purple plots for tone B and blue for tone C in Figure 4). Given that the composition of the A-deviant, B-deviant and C-deviant blocks were identical within every sequence, this effect must be attributable to the lasting impact of the environment created when the sequence started. We suggest that this result could be due to the nature of the predictability created at the sequence onset. MMN amplitudes are modulated by precision of the internal models generated which reflects the inverse of pattern volatility (Friston, 2005; Lieder et al., 2013). The order effect could be caused by the regular alternation between two common monaural sounds (left and right location) being experienced as a significantly more volatile environment than when the two common sounds were located to the centre right (when B and C are common) or to the centre left (when A and C are common). Remarkably, this first impression of a comparatively lower precision/high volatility environment has apparently endured throughout the sequence because the effect applies to all blocks that are contained within the CABCAB structure. In contrast, it is clear that the results associated with the A, B, and C tones are very similar when encountered within the ABCABC or BCABCA structure.

We are not aware of any similar order effects on AEPs generated by volatility at sequence onset. However, when the two effects are considered together (the first-deviant effects in binary state multi-timescale sequences and the volatility first impression here), both could be indicative of the lasting influence of a first-impression that is not updated unless significant counter-evidence or surprise is generated. In the case of the present study, shifting from two monaural alternating common tones (a C-deviant block) to a centre-left or centre-right common tone pattern (A deviant and B deviant blocks, respectively) does not appear to be sufficient to shift the initial sequence precision-weighting. However, if the sequence starts with centre-left or centre-right common tones, the precision-weighing associated with the MMN response to all deviant sounds is significantly higher (inferred from larger deviant response). In the binary state sequences, the key first surprise element is the sudden occurrence of repeats of the former rare tone generating a continuous sequence of errors providing a strong signal that a highly significant change has occurred, and the prevailing model no-longer applies. In the present study this shift in probabilities that occurs with the block change would not be as clearly marked. Although the first deviant never repeats in block one of a sequence, the shift to block two is characterised by two events: repeats of the first deviant but also a continuation of repeats of one of the first common standards. The "message" in this case is less stark in that an aspect of the model may need to be updated but the prevailing model does not entirely fail. As noted in the introduction, in binary state sequences, the first learning that leads to higher precision for the first block arrangement appears to endure until a higher order assumption is broken (e.g., a violation of the expected block length, (Fitzgerald & Todd, 2018; Mullens et al., 2016b). The results of the present study could therefore be taken as an indicator that the different first-impressions of precision evident in comparing MMNs between the sequence types (CABCAB versus the ABCABC and BCABCA) are never dropped, and therefore insufficient surprise is experienced to prompt a re-evaluation of the first impression.

Thus our previous notion of the nature of the first-impression bias is expanded by the current results. Whereas the previous two-tone sequence studies (Fitzgerald et al., 2018; Frost et al., 2018; Frost et al., 2016a; Mullens et al., 2016b; Todd, Provost, et al., 2018; Todd et al., 2013; Todd et al., 2011) showed an effect of the initial stimulus probability on processing the same sounds later in the sequence even after their probabilities have changed, the results obtained from the current three-tone sequences suggest that also the initial variability of the sound features can impact on how the same sounds are processed later in the sequence, even after their probabilities have varied. This means that primacy bias effects rely on a representation encoding more than just the initial probabilities; this representation also includes some estimate of featural variabilities. Although this is a post-hoc explanation of the data, it provides testable hypotheses for future research. Extrapolating from the assumption that the order effects termed primacy bias may also be caused (or influenced by) the observed initial featural variability, future research could focus on describing what kind of information is assessed quickly at the beginning of a new stimulus context, which is then used to guide sound processing as long as the same general context holds.

What we have called higher volatility in C-deviant blocks can be considered in relation to how the monaural tone spatial locations might be encoded. Auditory neurons are observed to show tuning to one or the other hemifield of space (Magezi & Krumbholz, 2010; Phillips, 2008;

Salminen, May, Alku, & Tiitinen, 2009; Salminen, Tiitinen, Yrttiaho, & May, 2010). For example, the auditory system of rats comprises neurons on the left tuned only the right hemispace and vice versa (Yao, Bremen, & Middlebrooks, 2013), while in humans, both hemispheres have representation of both hemifields (Salminen, Tiitinen, & May, 2012). When the C-tone is deviant, the equal probability of the monaural A and B tones will therefore predominantly activate different populations of neurons which contrasts the situation created when the A-tone or B-tone are deviants where the "standards" will all activate at least partially overlapping populations (overlapping on the right and left, respectively). Internal models could therefore be expected to be more accurately able to predict the activation pattern within a C/B and C/A tone regularity than an A/B tone regularity. However, this does not appear in the data as a block-based effect but rather a sequence-based effect consistent with an enduring influence of early precision estimates.

Order effects in learning are well known in tasks requiring a behavioural response but we are not aware of other observations in task-independent or "unsupervised learning" as reported here. We propose that multi-timescale sequences create a learning environment where estimates of precision are set early and they prevail unless some substantive signal of significant change is encountered. Predictions themselves clearly update as prediction-errors are generated to sounds encountered as locally rare and unpredictable events, but the amplitude of these signals are heavily influenced, if not dominated by, parameters set early in sequence learning. This proposed expansion of order effects to include initial featural variability may have implications for models of the mechanisms of statistical learning. For example, a recent review (Thiessen, 2017) distinguishes between studies of conditional and transition-based statistical learning, and those involving distributional based statistical learning. However the review argues that both might be accounted for by pursuing an understanding of key underlying memory processes; namely, activation (of similar memories), decay, integration, and abstraction.

Models of memory invoke concepts of categorisation and/or protoype formation in considering how exemplars are gleaned from experience over time (e.g., see Thiessen & Pavlik, 2012). In Frost et al., (2018) we offer a parallel between the order-effects in multi-timescale sequences learning and categorical errors made by the Adaptive Resonance Theory (ART) neural network and its biased variant (Carpenter & Gaddam, 2011). In attempting to model cognition, the ART neural networks implement a pre-processing step called complement coding. Complement coding is am implementation of antagonistic states that enable systems to act on relative rather than absolute quantities, making them tolerant to some variability in actual values (Hurvich & Jameson, 1957). A parameter called vigilance determines the current state, with low vigilance favouring abstract prototype learning, and high vigilance more specific exemplar learning. Vigilance rises after prediction errors and as vigilance rises, more attention is paid to the fit between top-down and bottom-up information. Interestingly, the learning rules implemented in ART created errors leading to overreliance on features that were critical to categorical decisions early in learning making the system prone to paying 'too much' attention to these features. This differential attention distorted memory representations later, which in turn led to errors in categorical judgements when the input changed. This issue could be overcome in ART if a bias was introduced into the system that ensured that attention would be drawn to previously unattended information after prediction errors occurred.

The comparison to the ART neural network raises the possibility that the removal of order effects on learning when participants have explicit knowledge about the likelihood (or rather certainty) that a future change will occur, could operate via a release from such attentional biases (implicit in the absence of a task in Frost et al.'s [2018] binary state multi-timescale sequences, and explicit through a task in Gebhart, Aslin & Newport's [2009] artificial language learning setup). In the present study, the three-tone/three-block sequences appear to anchor precision estimates to the featural variability present at sequence onset, which is arguably a distributional property. What remains unclear is whether featural variability could also encourage a categorical-like memory storage where a commonality extracted from "right hemispace" or "left hemispace" lends itself to a stronger memory encoding than a "right+left hemispace" commonality, which would then result in enduring differences in the response to all rare pattern deviations. The present study was not designed to address this question but it nonetheless highlights the potential for mechanistic hypotheses to be tested in future.

In conclusion, the order-effects evident in the series of multi-timescale studies suggest that sensory systems are not always Bayes optimal observers (Knill & Pouget, 2004). Local models are always updated when value predictions should change, however the constraints over precision estimates are affected by an initial precedent. We propose that when early learning provides a sufficiently precise and accurate account of the environment, learning rates decline to create energy/effort efficiencies (Friston, 2010) and these declines distort or set limits on the effects of actual event probabilities subsequently encountered. Our prior studies suggest that this only applies when the longer term environment is predictable but also not yet known (Todd, Petherbridge, et al., 2018), and updates only when a signal of significant change is encountered

(Fitzgerald & Todd, 2018; Mullens et al., 2016b). The results of the present study suggest that first-impressions of feature variability can create similar primacy biases where the estimates of initial variability become a kind of hyperparameter constraining the parameters that are applied to subsequent predictions and prediction-errors related to the sounds.

An open question arising from this work is whether the initial precedent reaches a set point criterion via sufficient accuracy of the model, via a temporal limit (i.e., a fixed sampling window) or a sampling limit (i.e., sufficient samples), or whether it is perhaps determined by the availability of cognitive resources. Studies exploring the ability of MMN to capture cognitive resources via triggering orienting responses certainly show that this system is highly dependent on concurrent task demand, but that it is generally not evident when the concurrent task is highly demanding (Bendixen et al.; Escera, Alho, Schroger, & Winkler, 2000; Muller-Gass & Schröger, 2007; Roeber, Widmann, & Schroger, 2003; Schroger, Giard, & Wolff, 2000; Schroger & Wolff, 1998; Wetzel & Schroger, 2007). We have observed that when naïve listeners hear the binary state multi-timescale sequences while performing an attentionally demanding task the AEP results are very different. Under these circumstances the learning rates in the two blocks do not differ (MMN amplitude increasing over time within both blocks) but MMN amplitude remains larger to the first-deviant than second-deviant throughout (Frost et al., 2018). Naïve listeners must structure models based on initial experience and task-based difference across studies may indicate that availability of attentional resources determines the period of time over which the "first impression" will be set. This period would be very short when attention is required in the visual modality for a demanding concurrent task, perhaps only allowing only a brief auditory sampling window capturing which sound is common and which rare with this first-impression setting different precisions for future encounters of the two tones throughout (Frost et al., 2018). In comparison, when hearing the sequences under low concurrent task demand (watching a movie) the first impression might instead extend for as long as the duration of the first block of sound explaining why block differences in learning rates occur and become re-set when block length is violated (Fitzgerald & Todd, 2018; Mullens et al., 2016a; Todd, Heathcote, et al., 2014b). While theories regarding what sets the first-impression require further testing, the present study adds to a body of work supporting the existence of influential fist-impression effects on sound sequence processing that determine the weighting given to future sensory events.

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Figure Captions

Figure 1. A schematic depiction of binary state alternating block sequences used in three prior studies. In each, the blocks contain two sounds: one common and one rare defined by a change in a single tone property. In the alternate block the common and rare tone properties invert. Grey shading marks the blocks with the initial configuration of probabilities, while the blocks with inverted probabilities is marked by a striped pattern. The different block durations reflect different periods of time over which a tone arrangement is held constant.

Figure 2. Sequence structure showing the ABCABC, BCABCA, and CABCAB stimulus block arrangements. In grey blocks, tone A was deviant and tones B and C were equally probable standards. In striped blocks, tone B was deviant A and C were standards. In white blocks, tone C was deviant and tones A and B were standards. All participants heard all three types of sequences.

Figure 3. a) A schematic depiction of the dimensions on which the three tones vary. b) The topography of common-average referenced deviant-minus-standard difference wave response to the A, B, and C tones at the visible point of peak latency (A= 95 ms, B = 145 ms, and C = 115 ms). C) The associated average difference wave for the A, B, and C tone at sites F3, Fz, and F4 (mastoid-referenced data) where arrows reflect topography point latencies.

Figure 4. The average response to the A, B, and C tones as common standard tones (top), rare deviating tones (middle) and the deviant-minus-standard difference waves (bottom). Different coloured lines represent situations in which the tone was the first- (blue), second- (green) or

third-deviant (purple) heard in the sequence. The orders of each plot are given underneath the standard-tone plots (for example, the A tone was first-deviant in the ABC order, the B tone in the BCA order, and so on).

Tables

Table 1

Frequency, Duration and Spatial Orientation Dimensions of Tones A, B and C.

Tone	Frequency (Hz)	Duration (ms)	Location
A	1210Hz	60ms	Left ear - Monaural
B	1110Hz	30ms	Right ear - Monaural
C	1000Hz	90ms	Central - Binaural

Table 2. The t values for a paired t-test between the deviant and the corresponding standard response for each tone type and the block position in which the given tone first appeared as deviant within the sequence over the N1 and N2 latency range at the Fz scalp location.

	N1 range over Deviant Order			N2 range over Deviant Order		
	First	Second	Third	First	Second	Third
A tone	-3.61*	-3.38*	-3.33*	-1.49	-1.69	-1.02
B tone	-1.56	-2.62*	-.31	.52	-.88	.01
C tone	-5.29*	-6.08*	-7.08*	-3.91*	-3.16*	-5.55*

* uncorrected t-test p value <.05.