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Title

Altering the primacy bias – How does a prior task affect mismatch negativity (MMN)?

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Abstract

The role in which two tones are first encountered in an unattended oddball sequence affects how deviance detection, reflected by mismatch negativity (MMN), treats them later when the roles reverse: a “primacy bias”. We tested whether this effect is modulated by previous behavioural relevance assigned to the two tones. To this end, sequences in which the roles of the two tones alternated were preceded by a go-nogo task in which tones were presented with equal probability. Half of the participants were asked to respond to the short sounds, the other half to long sounds. Primacy bias was initially abolished but returned dependent upon the go-stimulus the participant was assigned. Results demonstrate a long-term impact of prior learning on deviance detection; and that even when prior importance/equivalence is learned, the bias ultimately returns. Results are discussed in terms of persistent go-stimulus-specific changes in responsiveness to sound.

“Primacy bias” refers to the effect of the role (frequent “standard” or infrequent “deviant”) in which sounds are first encountered in an unattended oddball sequence on how these sounds are processed later when the roles are exchanged. This effect has been demonstrated by the mismatch negativity (MMN) component of the auditory event-related potential (ERP) (Todd, Provost & Cooper, 2011). When a regular (e.g., repetitious) stream of sound contains a sound that breaks that regularity (e.g., the repeating sound is occasionally exchanged for a different sound) MMN is elicited (Näätänen, Gaillard & Mäntysalo, 1978; for recent review, see Näätänen, Kujala & Winkler, 2011). The extraction of patterns from sound sequences occurs rapidly, with MMN elicited to pattern violations after as few as three repetitions outside the focus of attention (Sams, Hari, Rif & Knuutila, 1993; Cowan, Winkler, Teder & Näätänen, 1993) and after only two repetitions when the sounds are attended (Bendixen, Roeber & Schröger, 2007). In general, the more established the repetition (and the more rare the deviation) the larger the MMN (Giese-Davis, Miller & Knight, 1993; Näätänen, Sams, Järvilehto & Soininen, 1983). However the primacy bias reveals that there are circumstances in which environmental statistics are not preserved, such that MMN amplitude to a deviation is differentially affected by probability depending upon when it occurs within the sequence. The present study was designed to test whether this bias could reflect automatic assumptions about the information-value of the sound.

Todd, Provost & Cooper (2011) reported evidence for a primacy bias using a two-tone sequence in which a short and long sound alternated roles as a highly probable standard (p=0.875) and as a rare deviant (p=0.125). The period over which roles remained stable was varied from fast-changing every 160 tones or 0.8 mins, to slow, changing every 480 tones or

2.4 mins. The system underlying MMN is highly dynamic and contextually sensitive (Sussman & Winkler, 2001), so it rapidly produces MMN to the former standard when it becomes a deviant in the new context (Winkler, Karmos & Näätänen, 1996). However, based on tone probabilities on a longer timescale, the MMN elicited in Todd et al.’s (2011) slow change condition should have been larger than that in the fast change condition if the sampling window for probability extraction exceeded 0.8 mins. That is, prolonged stability in a repetitious standard should have led to larger growth in MMN size. Surprisingly, Todd et al. observed (and Todd, Provost, Whitson, Cooper & Heathcote, 2013, replicated) the effect of role-stability to be a function of the order in which tones are presented. For the tone that was the first encountered as deviant, MMN was indeed larger in slow- than fast-changing sequences. However, for the tone that was the first standard, role-stability had no effect on MMN size when it was later encountered as a deviant. This finding was independent of tone-type as it was present in both the subgroup who always heard the sequence with the long sound as the first deviant and the subgroup who always heard the sequence with the short sound as the first deviant (Todd et al., 2011) . These data appear to violate a fundamental assumption about the MMN process – that MMN size should reflect transition statistics in the acoustic stream (Garrido et al., 2008; Wacongne, Changeux & Dehaene, 2012). Although others have drawn attention to the fact that context dependent factors can influence the MMN-generating process (e.g., Sussman, Sheridan, Kreuzer, & Winkler, 2003; for a review, see Sussman, 2007) these data revealed a profound bias of unknown origin on the deviance detection system.

Todd et al. (2011) drew an analogy between the primacy bias and the concept of “lasting first impressions” – that is, the resistance of one’s initial impression to re-evaluation. They also likened the bias to a latent-inhibition like effect suggesting that initial exposure to the first tone as a highly repetitious and uninformative sound altered subsequent learning about this sound. Todd et al. (2013) designed a study to test the latent inhibition-related explanation of bias. This study utilised a similar design to the first (short and long sounds alternating roles as standard and deviant) but, the order of the first deviant was manipulated within-subject to test the longevity (or alternately the flexibility) of the bias. In orders 1 and 3 the long sound was the first-encountered deviant and in order 2 the short sound was the first encountered deviant. The results of order 1 replicated the earlier finding where only MMN elicited to the first deviant (the long sound) was larger in the slow than fast changing sequence. In order 2, presented with only a 5 min silent break after the order 1 sequence, once again only MMN to the first encountered deviant (this time the short sound) was modulated by speed of change. These results confirm the rapid establishment of an order-dependent bias linked to initial sequence structure. However, in order 3 (repetition of order 1), the bias was abolished with MMN to both sounds larger for slow than fast changing sequences. The latent-inhibition explanation cannot account for either the reversal of the bias between order 1 and 2 or the lack of bias observed in order 3 (depending on the hypothetical duration of the inhibition effect). Instead, the complete disappearance of the primacy bias in the repeat of order 1 was interpreted as indicative of a meta-learning process. Meta-learning was proposed to account for why stability modulation for MMN to the long deviant (1st deviant in *order 1*), fails to occur when it is encountered second in *order 2*, yet the stability modulation observed on the MMN to the short deviant (1st deviant in *order 2*) reappears in *order 3*. The disappearance of primacy bias was proposed to indicate higher-order learning that may promote flexible monitoring of all sounds in an environment with changing sound relevance.

Data from both studies imply that the initial sequence structure has a profound effect on how information about the two tones is subsequently sampled. One explanation put forward by

Todd et al. (2013) is that the bias emerges due to an automatic determination of the potential information-value of the two sounds. The frequent repetition of the initial standard without any linked consequence (i.e., no behavioural relevance) may result in “stamping in” high confidence that this sound is of low importance. In contrast, the first encountered deviant has unknown and thus comparatively higher behavioural relevance. This initial impression may then alter how information about the two sounds is processed. Todd et al. (2013) further suggest that the results observed in their order 3 may reflect that once the bias has operated in both directions, both sounds are recognised as equally important and cortical responsiveness is affected similarly for both. The present study was designed to test this hypothesis by repeating the paradigm used in Todd et al. (2013), but preceded by a go-stimulus detection task comprising the same two tones used in the oddball sequences. If the primacy bias is due to a different attribution of behavioural relevance for the two sounds, completion of the go-stimulus detection task should alter the effect through the prior assignment of (different) behavioural relevance to the two sounds.

The behavioural task used was a simple go-stimulus detection task in which 50% of the sounds were identical to the long sounds participants would later hear in the oddball sequence while the other 50% were equivalent to the short sounds in the subsequent oddball sequence. Half of the participants were asked to respond as quickly as possible to the long sound (long go-stimulus group) and the other half to the short sound (short go-stimulus group). Thus both sounds had (albeit opposite) behavioural relevance for both groups: the occurrence of the designated go-stimulus cued the need to respond and the occurrence of the designated no-go-stimulus, the need to inhibit a response. We hypothesised that if the primacy bias is due to assignment of higher behavioural relevance attributed to the first deviant, then the prior task would either abolish the bias (due to both sounds having behavioural relevance in the task) or interfere with the establishment of a bias favouring the no-go-stimulus (i.e., no short-sound bias in order 2 for the long-prime group and no long sound bias in order 1 and 3 for the short-prime group).

Method

Participants

A total of 30 healthy participants (aged 18-35 years; mean=22.4; SD=4.6) were recruited. Of the total group 9 were male and all participants were recruited from the first year Undergraduate Psychology student body at the University of Newcastle or volunteers from the community. Volunteers were excluded if they were under 18 or over 35 years of age, were diagnosed with or being treated for mental illness, had a first degree relative with schizophrenia, regularly used recreational drugs, regularly consumed alcohol heavily, had a history of neurological disorder, head injury or surgery, or a hearing impairment. Course credit was offered for participation to students, and cash remuneration to community volunteers. Written informed consent was obtained from all participants.

Go-stimulus Detection Task

Participants' encountered long (60ms) and short (30ms) 1000Hz pure tones presented binaurally over headphones at 75dB SPL. Each sound was created with a 5ms rise/fall time, and either a 20ms or 50ms pedestal to produce a 30ms and 60ms sound respectively. Short and long tones were pseudorandomly presented at equal probability (50:50) with the restriction that no more than 3 of the same sounds occurred in a row. The assigned go-stimulus was either the short tone (short go-stimulus group) or long tone (long go-stimulus group), which was alternated across participants. Participants were presented with three blocks of 100 sounds presented at a 300 ms stimulus onset asynchrony, and were instructed to push a button each time the go-stimulus sound was heard (150 total go-stimulus, 50 for each block). There were 15 participants in the short go-stimulus group and 15 in the long go-stimulus group. As Todd et al. (2011) found a relationship between auditory sensory memory and bias, subgroups performance was matched on total Digit Span score (the sum of forwards and backwards scores, short go-stimulus group mean = 18.58 (SD= 3.85), long go-stimulus group mean = 18.74 (SD = 3.25), a task in which participants hear digits spoken at a rate of one per second and have to repeat them back in forwards or backwards order (Wechsler, 1997).

Oddball Sequences

The same short and long sounds were presented in two different block types characterised by different sound probabilities. These were classified as short standard blocks where the 30ms (short) sound was highly probable (p=0.875) and the 60ms (long) sound was the rare deviant (p=0.125); and long standard blocks where the probabilities were reversed (60ms presented p=0.875 and 30ms p=0.125). Figure 1 depicts the sequences. Both short and long standard blocks were presented with slow and fast alternation rates. The slow–changing sequence contained 1920 sounds in blocks alternating after every 480 tones which created a role-stability period of 2.4 minutes (two repeats of each block). The fast-changing sequence contained the same number of sounds, but the blocks alternated every 160 tones creating a role-stability period 0.8 minutes (six repeats of each block). Each sequence lasted 9.6 minutes in total.

The sequences were presented in two different orders as per Figure 1 and replicated the protocol used by Todd et al (2013). The slow sequence always preceded the fast sequence. In Order 1 and Order 3, the sequence began with the short standard blocks whilst in Order 2, the sequence began with the long standard block first. A two-minute break was enforced between order conditions and short 1-2 minute breaks occurred between sequences to allow participants to move or stretch (total testing time of approximately 1 hour and 15 minutes).

Procedure

All participants completed a screening interview to ensure inclusion criteria were met. Audiometric screening using a pure tone audiometer established hearing thresholds across 500Hz to 4000Hz to check for adequate hearing (≤20 dB HL) and exclude participants with hearing loss. Participants were then fitted with a Neuroscan Quickcap with tin electrodes, which included nose and mastoid electrodes. The continuous EEG was recorded on a Synamps 2 Neuroscience system at 1000Hz sampling rate (highpass 0.1Hz, low pass 70Hz, notch filter 50Hz and a fixed gain of 2010). EEG data was recorded from 10 scalp electrode locations (FZ, FCZ, CZ, PZ, F3, FC3, C3, F4, FC4, C4 in accordance with the 10-20 system plus left mastoid, right mastoid) and referenced to the nose. Vertical and horizontal electro-oculargrams were monitored by electrodes above and below the left eye, and 1cm from the outer canthi of each eye to monitor blinks and unnecessary eye movements. Impedances were reduced to below 5 kΩ before recording commenced.

Participants completed the go-stimulus detection task first and the oddball sequences followed with the break between the task and sequences no longer than 5 minutes. Oddball sequences were presented over headphones while the participant viewed a silent DVD with subtitles and was asked to remain as still as possible (to minimise movement artifact in the ERP) and to ignore the sounds and focus attention on the movie.

Data Analysis

Go-stimulus detection performance was quantified in terms of hits rate (correct go-stimulus identification), false alarm rate (go-stimulus response to no-go-stimulus sounds) and sensitivity (Snodgrass & Corwin's, 1988, logistic discrimination index). Results for the sensitivity index were compared in a mixed model ANOVA with block (1,2,3) as the within-subjects factor and group (Short Prime, Long Prime) as the between-subjects factor.

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

Data for two participants allocated to the short go-stimulus group was rejected due to poor quality leaving 13 participants in this group.

Epochs were baseline corrected pre-stimulus and then averaged according to stimulus type. The standard and deviant ERPs were digitally filtered with a low pass of 30Hz. Difference waves were computed by subtracting the averaged response to each standard from the averaged response to each deviant in each sequence. For example, the difference wave to a 30ms deviant in fast change blocks was created by subtracting the ERP to the 30ms standard in fast change blocks from the ERP to the 30ms deviant tone in the fast change blocks. This reduces contribution of exogenous component differences in the computation of MMN (Jacobsen & Schröger, 2003). The difference waves were then filtered with a low pass of 20Hz (lower cut-off recommended for MMN, Kujala, Tervaniemi & Schröger, 2007). All ERPs were re-referenced to the averaged activity at the left and right mastoid sites to maximise signal to noise ratio (Joutsiniemi et al., 1998).

MMN was quantified in difference waveforms by finding the latency of the negative peak within 100-250ms post-stimulus and measuring the mean voltage within a window with 10ms on either side of the peak (a mean-peak measure). Mean-peak amplitudes at F4 were analysed in a mixed model ANOVA using within-subjects factors of order (1,2,3), speed of change (Fast, Slow) and tone (short, long) and a between-subjects factor of group (short go-stimulus, long go-stimulus). Within-subjects contrasts were analysed to identify significant linear and quadratic trends. ERPs to standard tones were overlaid for identification of periods of apparent difference. Mean amplitude was extracted from 100-150ms and the same mixed model ANOVA design was used to investigate effects. All significant results are reported together with the η^2 effect size and the ε Greenhouse-Geisser corrections for sphericity where appropriate.

Results

Go-stimulus Detection Task

A repeated measures ANOVA confirmed a main effect of block on sensitivity (ε = 0.72, F(2, 54) = 18.48, p<.001). As groups did not differ significantly on any index of go-stimulus detection performance results are presented collapsed over group. Go-stimulus detection on block 1 was low on average (hit rate m = 0.54, sd = 0.07, false alarm rate m = 0.19, sd = 0.07, sensitivity m = 2.93, sd = 0.52). Performance improved dramatically for block 2 (hit rate m = 0.82, sd = 0.03, false alarm rate m = 0.07, sd = 0.03, sensitivity m = 5.34, sd = 0.36) and remained stable for block 3 (hit rate m = 0.86 sd = 0.03, false alarm rate m = 0.08 sd = 0.03, sensitivity m = 5.64 sd = 0.41). Given the rapid delivery rate of sounds the improvement in sensitivity may in part reflect adjusting to the short stimulus onset asynchrony.

MMN Results

Difference waves at F4 for short and long tones for the fast- and slow-changing sequences are presented in Figure 2 for each of the three sequence orders and both go-stimulus groups. The mean-peak amplitudes of each of the MMNs at F4 are presented in Figure 3. The omnibus repeated measures ANOVA produced a significant main effect of *speed* (F(1,26) = 16.80,

$p<.001$, $\eta^2 = 0.39$) and an *order* × *tone* ($\varepsilon = 0.97$, $F(2,26) = 8.25$, $p<.001$, $\eta^2 = 0.24$) as well as an *order* x *tone* x *speed* interactions ($\varepsilon = 0.87$, $F(2,54) = 3.22$, $p<.05$, $\eta^2 = 0.11$). Analysis of trends additionally revealed that the three-way interaction was further modified by *grou*p in a quadratic trend (*order* × *speed* × *tone* × *group*, $F(1,26) = 4.55$, $p<.05$, $\eta^2 = 0.15$). To explore interactions the results analysed separately within *orders*, *groups*, and *speed* are reported below.

Analysis restricted to order 1 revealed a main effect of *speed* only ($F(1,26) = 5.70$, $p<0.05$, $\eta^2 = 0.18$) with MMNs in the slow-changing sequences generally larger than in the fast-changing sequences for both tones (see Figure 3). Analysis of order 2 data revealed a main effect of *speed* ($F(1,26) = 14.90$, $p<0.001$ $\eta^2 = 0.36$) further modified by *tone* and *group* (*speed* × *tone* × *group* interaction, $F(1,26) = 5.40$ $p<0.05$, $\eta^2 = 0.17$). This interaction is apparent in Figure 3, where the short- but not the long-go-stimulus group showed a much larger *speed* effect on the short than the long tone MMN amplitudes. Finally in order 3, the analysis revealed a main effect of *tone* only ($F(1, 26) = 5.05$, $p<0.05$ $\eta^2 = 0.16$) due to the MMN to the long tones being larger overall in both groups. In general, it is clear that the two groups produced similar data for orders 1 & 3 (where the sequence begins with the long deviant) but differ substantially in their responses for order 2 (where the sequence begins with the short deviant).

Analysis restricted to the short-go-stimulus group revealed a significant main effect of *speed* ($F(1,12) = 8.26$, $p<0.05$, $\eta^2 = 0.41$) and an *order* × *tone* interaction ($\varepsilon = 0.98$, $F(2,24) = 4.61$, $p<0.05$, $\eta^2 = 0.40$). Analysis of trends revealed the former to be characterised by a linear pattern (slow-changing larger than fast-changing MMN amplitudes) with the order × tone interaction defined by a quadratic trend ($F(1,12) = 6.58$, $p<0.025$, $\eta^2 = 0.35$) that was further modified by *speed* (*order* × *tone* × *speed* interaction, $F(1,12) = 6.76$, $p<0.05$, $\eta^2 = 0.36$).

The trends in the data are best visualised in Figure 4, where the MMN amplitudes for each tone are plotted as a function of *order*, separately for the fast- and the slow-changing sequences. In Figure 4, it is clear that the effect of *order* differs for the two tones as a function of *speed* – the difference between slow- and fast-changing sequence MMNs to the short tone clearly increases in order 2 (a quadratic trend in an *order* × *speed* interaction ($F(1,12) = 15.30$, $p<.005$, $\eta^2=0.56$), whereas the MMN to the long tone remains unchanged (no significant effects or interactions for the long tone MMNs).

Analysis within the long-go-stimulus group revealed a main effect of *speed* ($F(1,14) = 8.57$, $p<0.05$, $\eta^2=0.38$) and an *order* × *tone* interaction ($F(1,14) = 4.08$, $p<0.05$, $\eta^2=0.23$). Unlike the short-go-stimulus group, the long-go-stimulus group did not show any increase in MMN amplitude to the 30-ms tone in the slow sequences for order 2 and the *order* × *tone* interaction for this group was defined by a linear trend, only ($F(1,14) = 6.90$, $p<.02$, $\eta^2=0.33$). For the 30-ms tone MMN amplitude, there was a significant linear trend for *order* ($F(1,14) = 6.83$, $p<.05$, $\eta^2=0.33$) with the MMN declining over orders 1 to 3 (see Figure 4). In contrast, for the long tone, there was a linear trend for *speed* ($F(1,14) = 6.84$, $p<.05$, $\eta^2=0.33$) with slow-changing MMN amplitudes larger than fast-changing ones across the three orders.

Analyses within the fast-changing sequence data revealed no main effects or interactions. In contrast, the slow-changing sequence data was characterised by an *order* × *tone* interaction ($\varepsilon=0.77$, $F(2,52) = 12.11$, $p<0.001$, $\eta^2=0.32$) which was further modified by *group* in quadratic trends (*order* × *tone* × *group* interaction, $F(1,26) = 4.50$, $p<0.05$, $\eta^2=0.15$). Although both short- and long-go-stimulus groups exhibited an *order* × *tone* interaction in slow-changing sequence data (ε =0.67, F(2,11) = 18.88, $p<.005$, η^2 =0.43, and ε =0.84, F(2,13) = 4.85, $p<0.05$, η^2 =0.26, respectively), the former was characterised by a quadratic trend (marked by a prominent difference between the MMNs elicited by the two tones in order 2, F(1,12) = 20.21, $p<0.001$, η^2 =0.63,), whereas the latter a linear trend (the difference between MMN amplitudes to the two tones increasing across the orders with the MMN amplitude for long tones increasing and that for the 30-ms tones decreasing, F(1,14) = 7.69, $p<0.05$, η^2 =0.38). The difference in trends is visible in Figure 4.

Analysis of the ERP Responses Elicited by the Standards

The right frontal (F4) ERP responses to the standard tones for each order and speed are presented in Figure 5, separately for the short- and long-go-stimulus groups. Differences apparent in the ERP responses appeared maximal between 100 and 150 ms. Therefore, mean amplitudes for this interval were computed. A repeated measures ANOVA revealed a *tone* × *speed* interaction (F(1,27) = 25,88, $p<.001$ η^2 =0.49). For the long tone, there was a clear main effect of *speed* (MMN amplitudes larger for slow than for fast-changing sequences, F(1,27) = 14.41, $p<.001$ η^2 =0.35) which was not modified by group. In contrast, for the 30-ms tone, there were no significant effects or interactions, only a significant linear trend in *order* × *speed* (F(1,27) = 4.42, $p<.05$ η^2 =0.14). Specifying this interaction revealed that *speed* only impacted significantly on the amplitude of the positivity in order 3 where it is in fact larger for the fast- than for the slow-changing sequence (paired t_{28}= 2.83, $p<.01$).

Discussion

The primacy bias (Todd et al., 2011, 2013) is not explained by existing theories about how MMN amplitude should change with environmental sound statistics. Given that MMN amplitude can lead to orienting responses (Näätänen & Gaillard, 1983; Näätänen, Kujala & Winkler, 2011), understanding influences on the MMN amplitude can provide insights into the processes that determine resource allocation in the brain. This study was designed to assess the primacy bias when the two tones are assigned roles prior to encountering them in the oddball sequences. In the current study, the long and short tones were first encountered in a go-nogo task where they had equal probability. So the first difference from previous studies in which the bias has occurred is that neither tone is first encountered as rare. Further, participants were divided into two groups differing only in terms of whether they were asked to respond to occurrences of the short tone (short go-stimulus group) or to the long tone (long go-stimulus group) in the initial task. Thus the other difference between the current and previous studies was that both tones had behavioural relevance prior to being presented within the oddball sequences: one tone required a response whereas the other that a response should be withheld. Performance on the task indicated that both groups achieved equivalent (and high) sensitivity in differentially responding to the tones.

The MMN data acquired in this study reveal a complex pattern of results that are only partially consistent with the hypothesis that the prior task would either abolish the bias (due to both sounds having behavioural relevance in the task) or interfere with the establishment of a bias favouring the no-go-stimulus (i.e., no short-sound bias in order 2 for the long-prime group and no long sound bias in order 1 and 3 for the short-prime group). The MMN data definitely differ from that observed in Todd et al. (2013). Firstly, the typical pattern of the bias characterised by a *tone* x *speed* interaction is absent in order 1. Instead, order 1 data were characterised by MMN to both tonal deviants being larger in slow- than in fast-changing sequences as reflected in a main effect of the *speed* factor. As reviewed in the introduction, the primacy bias is characterised by the absence of significant modulation of the MMN amplitude to a deviant that was first encountered as a standard. In order 1, this would have appeared as a null-effect of speed of alternation on the MMN to the short tone (as observed in Todd et al., 2013). This is clearly not the case in the present study. The data are consistent with the notion that the way the tones have been processed was altered by either: (a) first encountering tones with equal probability (a necessary feature of the prior task); or (b) task-related effects occurring prior to encountering the tones in the oddball sequences (a predicted consequence of the prior task).

Group differences in how MMN was affected across the sequence orders provides evidence supporting the interpretation that the nature of the task itself altered how the tones were processed in the oddball sequences. Although short- and long-go-stimulus groups demonstrated very similar data for orders 1 & 3, they responded distinctly differently in order 2 – that is, they differed significantly only in the order that has previously been observed to promote a bias favouring MMN to the short tone. Those assigned the short sound as a go-stimulus actually demonstrate a pattern of data consistent with the bias observed in previous studies (Todd et al (2011, 2013). In the short-go-stimulus group, the effect of speed was significant for the short tone only, which was the first encountered deviant in this experimental order. This pattern is absent in the long go-stimulus group consistent with the hypothesis that the nature of the prior task could interfere with establishing a bias favouring the no-go stimulus. Since both groups had equivalent exposure to the two sounds, the only manipulation distinguishing the two groups is how participants were asked to respond to tones in the task. Those who were instructed to respond to the short tones exhibited the primacy bias when sequence order favoured growth in MMN amplitude for this tone. Those, who were instructed to respond to the long tones, did not show the bias. In summary, the data support an effect of go-stimulus type on the MMN recorded in the subsequent oddball sequences.

An observation germane to this issue is that MMN has been demonstrated to reflect perceptual aspects of deviance rather than being tied specifically to the physical parameters of standards and deviants (Ross, Tervaniemi & Näätänen, 1996; Winkler et al., 1995). When considering the process of perceptual inference more broadly, we are reminded that generative models in the brain shape our perception: “what we perceive is that part of our model of the world that best fits current inputs and expectations, rather than simply an accumulation of sensory evidence” (den Ouden, Kok & de Lange, 2012, p6). Considered in this way, the primacy bias may indicate that the generative models underlying perception can distort sensory evidence through expectations about the sequence and/or the tones. The key question is why the order of presentation (or rather the first role assigned to the tones) distorts expectations.

By what mechanisms does go-stimulus allocation affect the deviance detection process reflected by MMN? Todd et al (2013) raise the possibility that the initial role assigned to tones (standard versus deviant) induces the bias by allocating a differential value/relevance to tones that has a lasting influence on sequence processing. Specifically, the initial standard is a predictable sound that is redundant – it requires no action and does not cue anything of relevance in the environment. The first encountered deviant, in contrast, elicits a prediction-error signalling an event that the current model could not account for. Thus this sound is a violation of the expectations, carries information previously not known by the system and, therefore, it might be important. A prediction-error signal should engage resources that evaluate the potential need for 'action', changing the current model and/or responding to the stimulus (Friston, 2005). The prior go-nogo task was expected to disrupt this automatic allocation of differential value by explicitly assigning behavioural relevance. The absence of bias in order 1 data is certainly consistent with prior relevance preventing a bias. The group difference in response to order 2 is evidence that prior relevance has a more specific effect on subsequent processing – its absence in the long-go stimulus group being consistent with a problem establishing bias favouring a no-go stimulus. However, if this can explain the order 2 differences, it is unclear why the groups do not also show different MMN response patterns in orders 1 & 3 for which the direction of the bias should conflict with the no-go stimulus for the short-go-stimulus group.

Research from attentive target detection paradigms in animals indicates that assigning behavioural relevance to a sound can produce long lasting alterations in prefrontal neuronal responses that are linked to alterations in auditory cortical receptive fields (Fritz, David, Radtke-Schuller, Yin & Shamma, 2010). In ferrets it has been shown that, although many neurons revert back to pre-training responsiveness after behavioural training, a number of neurons in prefrontal cortex (40%) actually show persistent target-specific changes in responsiveness to sounds that can last for minutes to hours (Fritz, et al., 2010). Authors attribute particular importance to this persistent activity noting that top-down signals from this area can dynamically reshape receptive fields in auditory cortex in a way that reflects the task-relevant feature's salience, both for frequency (Elhilali et al., 2006, Fritz et al, 2005, 2010) and temporal discrimination (Fritz, et al., 2007) tasks. In particular, the receptive field changes observed tend to enhance responsiveness to the relevant (target) feature and inhibit response to adjacent features. It is possible that in the current study, similar task-induced changes in responsiveness could have interacted with those induced by the oddball sequences, creating the complex pattern that differentiates the short- and long-go-stimulus groups.

In Todd et al. (2011) role-stability also had an impact on the ERP to standard tones. The impact was consistent with small changes (increased positivity) in response to the standards in slow versus fast changing sequences. However, this effect was not modified by tone type leading to the conclusion that the bias primarily reflected changes in the deviant ERP. In Todd et al. (2013) there were no significant differences observed in the ERP to standard tones. In the present study data for the long tone resemble Todd et al. (2011) with the general trend being a larger positivity in the standard ERP for slow than fast sequences regardless of sequence order or go-stimulus identity. Results differ for the short tone for which the positivity observed for the standard-tone response in the slow-changing sequences is definitely not larger than that in fast-changing sequences; in fact it is smaller in the slow- than in the fast-changing sequence in order 3. The period of difference in the standard ERP precedes the period over which MMN reaches maximum amplitude (after 150ms) but could certainly contribute to the early peak evident in the double-peak morphology often visible in the long-tone MMN (see Figure 2). This result highlights the importance of considering change in the standard ERPs as well as in the computed difference waveforms used to measure the MMN. The interaction observed reflects the positivity incrementing in the slow versus the fast sequences, for the long tone only. Although this could indicate a tone effect (i.e., a feature of repeating longer sounds) a similar trend (larger growth in positivity in more stable sequences for the sound that was the first deviant) is visible but not significant in Todd et al (2011) Figure 3C. It is present both in the group who heard all sequences beginning with the short sound as the first deviant as well as in those who heard the same sequences with the long sound as the first deviant. It is therefore possible that the primacy bias does indeed affect response to both standards and deviants with the latter dominating the effect.

In the present study, main effects and interactions were restricted to the slow-sequence data. Precision in error estimation is a factor influencing predictive inferences and will have an impact on the degree to which model adjustments are made. One interpretation of the selective effect on slow-sequence data is that the instability in faster changing sequences limits MMN amplitude due to overall lower precision in a less stable (noisy) environment (Friston, 2005). The power to demonstrate differential impact of group membership or order on fast sequence MMN may therefore be limited. It is noteworthy that significant order effects have been demonstrated on fast-sequence MMNs previously (Todd et al., 2013). However, in the current data there are clearly no significant effects of this type.

There are a number of limitations to consider in interpreting the present data. Firstly, the duration of the tones was not symmetrically varied with group and order. Although the bias has clearly been shown to exist when sequence speeds are counterbalanced (Todd et al., 2011) and when tone orders are reversed (Todd et al, 2013), it remains unclear whether the properties of the tones are rendered then differentially sensitive to the effects induced by the prior task. Secondly, we have attributed the absence of bias in order 1 to performing a prior task but it is of course possible that the bias observed previously was simply absent in this sample. Although the effect size of the bias observed in Todd et al. (2013) was reasonably large (Cohen's 1992, *d* = 1.4), this finding is new and though it has replicated the results of a prior study (Todd et al. 2011) it should still be considered cautiously. Thirdly, we suggest that animal research showing enduring effects of the behavioural relevance of sound may translate to the task performed by human participants in the present study. There is no direct measure of such effects in the current study. Finally, a *tone* × *speed* interaction was observed on the standard-stimulus ERPs in the present study raising caution about computing differences waveforms. The practice of balancing the physical features in computing the difference waveform risks confounding effects that are taking place in one block (where the sound is a standard) with those in another block (where it is the deviant). This highlights the importance of inspecting change in the original ERPs rather than only examining MMNs in insolation.

In conclusion, the primacy bias modulation of MMN amplitude was abolished in this sample where the unattended sound sequence had been preceded by a go-nogo task featuring the same sounds. The data are partially consistent with the possibility that the prior task primes the response to auditory stimuli in a way that interacts with the mechanisms that give rise to the bias. Although it is possible that the initial disruption of the bias in order 1 could be attributed to equivalent prior exposure to the two sounds (hence no go-stimulus group differences), the group differentiation in order 2 indicates that the nature of the task performed (the assigned go-stimulus) has a lasting effect on how sound sequences are processed. These data imply a relatively long-term impact of prior learning about relevance on responsiveness to subsequent sound.

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Figure Captions

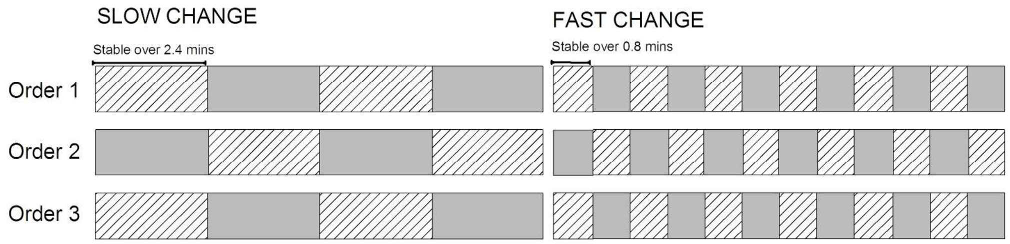
Figure 1. Example structure of tone sequences used by Todd et al.’s (2011, first row only) and the present study. Cross-hatched rectangles represent blocks with a short standard and long deviant tone and grey rectangles represent blocks with reversed tone probabilities; in both Pr(standard)=0.875 and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

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

Figure 3. The group averaged peak amplitudes for MMN to short and long deviant sounds as a function of change speed and block order. Results are presented separately for the Short and Long Go-stimulus groups at F4. Error bars = Morey's (2008) corrected normalized within-subject standard errors.

Figure 4. The group averaged peak amplitudes for MMN to short and long deviant sounds emphasizing how block order effects on speed of change differ between groups. Error bars = Morey's (2008) corrected normalized within-subject standard errors.

Figure 5. The group averaged ERPs to standard tones F4 to short (grey line) and long (black line) tones in the fast and slow change sequences for orders 1-3.



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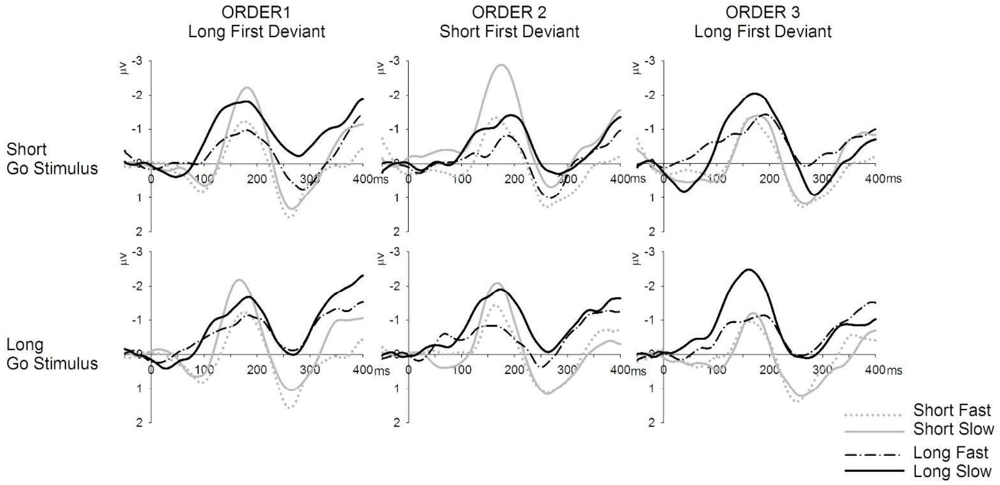
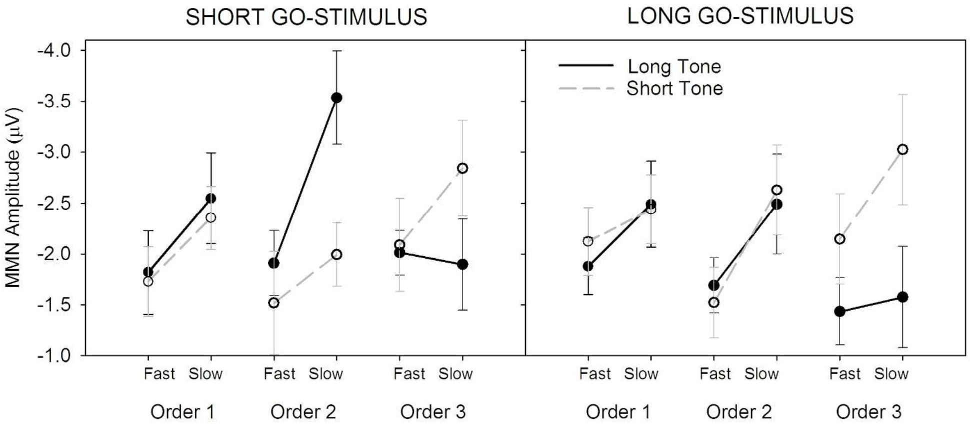


The group averaged mastoid re-referenced MMN waveforms at F4 to short (grey line) and long (black line) deviant tones in the fast and slow change sequences for orders 1-3.
290x140mm (300 x 300 DPI)



The group averaged peak amplitudes for MMN to short and long deviant sounds as a function of change speed and block order. Results are presented separately for the Short and Long Go-stimulus groups at F4. Error bars = Morey's (2008) corrected normalized within-subject standard errors.
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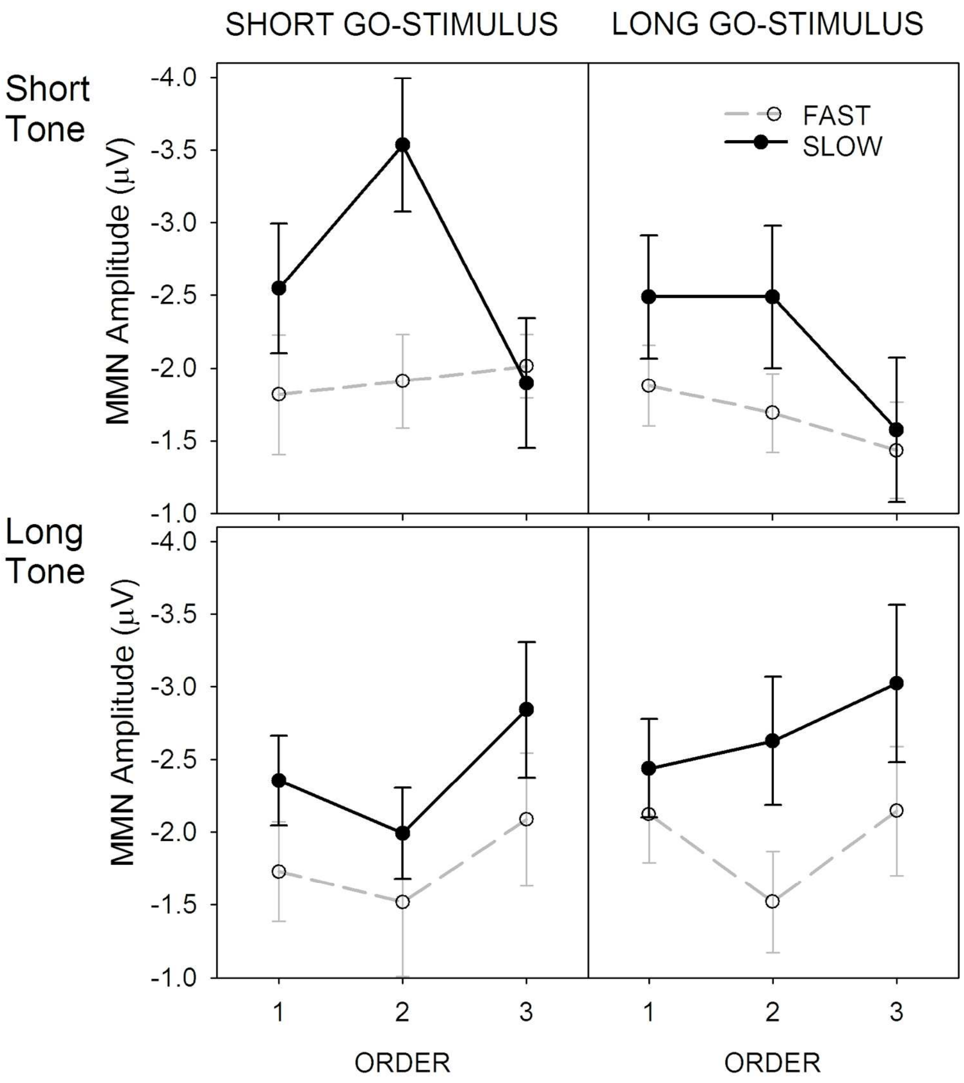

The group averaged peak amplitudes for MMN to short and long deviant sounds emphasizing how block order effects on speed of change differ between groups. Error bars = Morey's (2008) corrected normalized within-subject standard errors.
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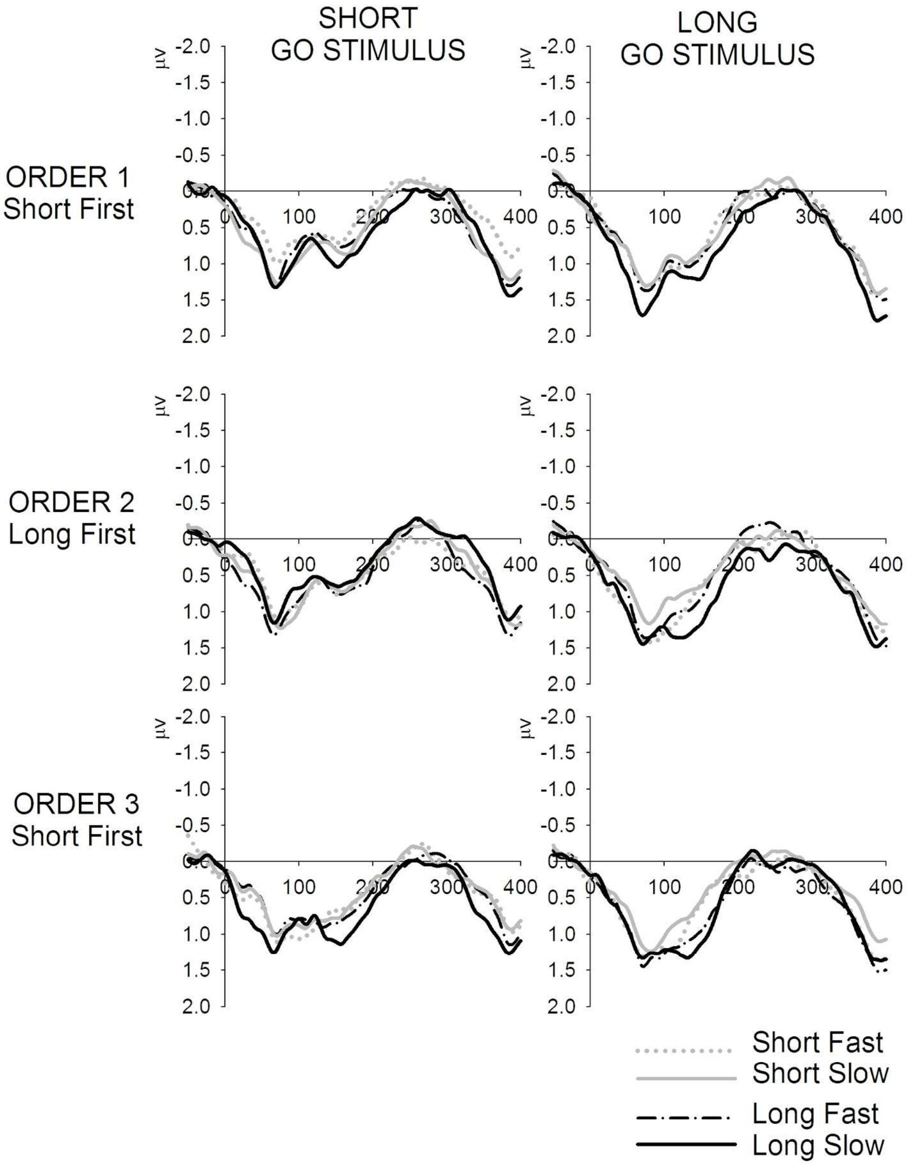

The group averaged ERPs to standard tones F4 to short (grey line) and long (black line) tones in the fast and slow change sequences for orders 1-3.
159x206mm (300 x 300 DPI)