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Original research article

The Magnetic Acoustic Change Complex and Mismatch Field: A Comparison of Neurophysiological Measures of Auditory Discrimination

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Abstract: The Acoustic Change Complex (ACC), a P1-N1-P2-like event-related response to changes in a continuous sound, has been suggested as a reliable, objective, and efficient test of auditory discrimination. We used magnetoencephalography to compare the magnetic ACC (mACC) to the more widely used mismatch field (MMF). Brain responses of 14 adults were recorded during mACC and MMF paradigms involving the same pitch and vowel changes in a synthetic vowel sound. Analyses of peak amplitudes revealed a significant interaction between stimulus and paradigm: for the MMF, the response was greater for vowel changes than for pitch changes, whereas, for the mACC, the pattern was reversed. A similar interaction was observed for the signal to noise ratio and single-trial analysis of individual participants' responses showed that the MMF to Pitch changes was elicited less consistently than the other three responses. Results support the view that the ACC/mACC is a robust and efficient measure of simple auditory discrimination, particularly when researchers or clinicians are interested in the responses of individual listeners. However, the differential sensitivity of the two paradigms to the same acoustic changes indicates that the mACC and MMF are indices of different aspects of auditory processing and should, therefore, be seen as

complementary rather than competing neurophysiological measures.

Keywords: Acoustic change complex; auditory discrimination; magnetoencephalography; mismatch field; mismatch negativity

1. Introduction

The ability to discriminate between different sounds is a basic prerequisite for spoken language perception [1]. However, poor performance on behavioural tests of auditory discrimination need not necessarily indicate a perceptual impairment. This is especially true in populations such as young children, or individuals with neurodevelopmental or degenerative conditions, for whom poor attention or task understanding might impact adversely upon performance. For this reason, researchers have increasingly made use of electroencephalography (EEG) and magnetoencephalography (MEG) to passively measure event-related cortical responses to changes in auditory stimuli, taking the presence and magnitude of the elicited brain response as an index of perceptual discrimination.

The majority of these studies have employed an oddball paradigm, in which participants hear a sequence of discrete sounds composed of frequent “standards” and rare “deviants” that differ along a single stimulus dimension. The Mismatch Negativity (MMN) or its magnetic counterpart, the Mismatch Field (MMF), is calculated by subtracting the brain response to the standard from the response to the deviant sound [2,3]. The amplitude of the MMN has been found to correlate with performance on behavioural discrimination tasks [4–7]. However, a number of researchers have questioned the reliability of the paradigm, noting that the MMN response is not always elicited, even for easily discriminable stimuli [6,8–12]. A less commonly used alternative is the acoustic change paradigm in which participants hear a continuous auditory stimulus containing a discrete change in, for example, pitch. This elicits a P1-N1-P2 evoked potential referred to as the Acoustic Change Complex (ACC) [13–15]. Like the MMN, the ACC is correlated with behavioural measures of intensity and frequency change [13,16,17] and has good test-retest reliability [15,16].

Surprisingly, only one study to date has directly compared the MMN and the ACC. Using EEG, Martin and Boothroyd [14] elicited an ACC response by presenting participants with 790 ms stimuli that transitioned at their midpoint from a complex tone to spectrally matched noise (or back again). The MMN was elicited using 150 ms tones and noise bursts as standards and deviants. Martin and Boothroyd reported that the ACC response was 2.5 times larger than the equivalent MMN. Moreover, every participant produced an ACC response that was clearly visible and identifiable.

The current investigation extended Martin and Boothroyd’s study in two directions. First, rather than tones and noises, we employed linguistically relevant stimuli. Specifically, participants heard

semi-synthesized vowel sounds with changes in either pitch (fundamental frequency) or vowel identity (formant frequencies). Second, rather than EEG, we used MEG to measure the MMF and the magnetic ACC (henceforth mACC). As a research tool, MEG has a number of advantages over EEG, particularly for studies of child and clinical populations. Set-up is quick and straightforward and does not involve scalp-scratching or physical contact with the sensors [18,19]. Moreover, MEG has higher spatial resolution, allowing for more accurate source reconstruction and clearer resolution of hemispheric differences [20,21]. However, because MEG is mostly sensitive to cortical sources oriented tangentially to the surface, it does not always provide a superior signal to EEG.

Participants were tested in two 15-minute sessions, once with an MMF paradigm using pitch- and vowel-changes in semi-synthesized speech, and once using a mACC paradigm with the same stimulus changes. We compared the amplitude and signal to noise ratio (SNR) of the MMF and mACC, and objectively determined whether a reliable response could be obtained for each individual participant. In this way, we aimed to determine whether the ACC advantage identified by Martin and Boothroyd extended to MEG and to linguistically-relevant acoustic changes.

2. Materials and Method

2.1. Subjects

Seventeen participants were tested, but three were excluded due to (a) movement of the head-position cap during recording; (b) missing event triggers; and (c) excessive noise in the source waveforms. The final sample included 14 participants, aged 19–40 years (mean = 29.02, SD = 8.71). Thirteen of the fourteen participants were right-handed according to the Edinburgh Handedness Inventory [22]. Participants had a mean score of 11.9 (SD = 2.9) on the Matrices subtest of the Wechsler Adult Intelligence Scale [23]—a measure of nonverbal IQ (population mean = 10, SD = 3). None of the participants reported any history of neurological abnormalities or hearing impairment and hearing threshold was in normal range (<20 dB HL) at frequencies 0.25, 0.5, 1, 2, 4, 8 kHz for all subjects. Written consent was obtained from all participants and procedures were approved by the Macquarie University Human Research Ethics Committee. Participants received monetary compensation for taking part in the study.

2.2. Stimuli

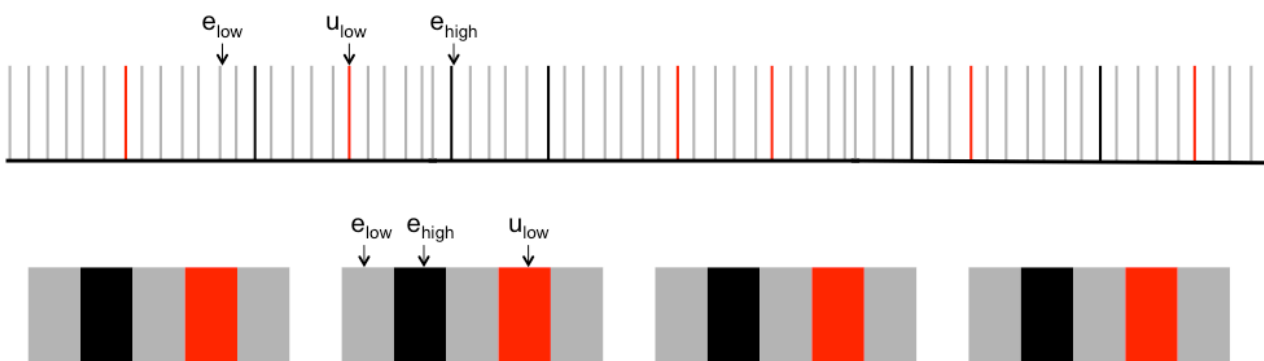
Three synthesized speech vowels were generated in Praat [24] based on source-filter theory. The standard sound (e_{low}) was a synthesized /e/ vowel sound. The pitch deviant (e_{high}) differed from the standard in its fundamental frequency, whereas the vowel deviant (u_{low}) had the same fundamental frequency as e_{low} , but differed in the second and third formants, making an /u/ sound. Table 1 shows the frequency composition of the three sounds.

Table 1. Formant Frequencies (in Hertz) for the three stimuli.

	e_{high}	e_{low}	u_{low}
F0	138	125	125
F1	280	280	280
F2	2620	2620	920
F3	3380	3380	2200

For the MMF paradigm (Figure 1, upper panel), the stimuli were each 75 ms in duration (including 10 ms ramp on and off). Each sequence contained 86% standards (e_{low}), 7% pitch deviants (e_{high}) and 7% vowel deviants (u_{low}) in a pseudo-random order. Within each sequence, at least the first ten sounds were standard sounds in order to create a memory trace and at least two standard sounds were presented between deviants. Stimulus onset asynchrony (SOA) was jittered uniformly between 450–550 ms. Stimuli were presented in three blocks, each lasting 5 minutes, resulting in 1600 trials including 112 pitch deviants and 112 vowel deviants.

For the mACC paradigm (Figure 1, lower panel), a single continuous sound sequence was created, consisting of five units of sound, each of 1500 ms. To prevent audible clicks whilst maintaining as much as possible a constant stimulus amplitude, each stimulus was windowed with a 10 ms rise-fall ramp and the stimuli were concatenated with 5 ms of overlap. Each sound sequence (total duration 7500 ms) was separated by a 1500 ms silence. The order of the sounds in each sequence was: e_{low} , e_{high} , e_{low} , u_{low} , e_{low} . A total of 96 sequences were presented across three 5 minute blocks, so participants heard 96 onset responses, 96 pitch changes (e_{low} to e_{high}), and 96 vowel changes (e_{low} to u_{low}). mACC responses were also elicited by the e_{high} to e_{low} and u_{low} to e_{low} changes but these were not analysed as corresponding changes were not present in the MMF paradigm.

**Figure 1. Schematic representation of the MMF (above) and mACC (below) paradigms.**

2.3. MEG recording

All MEG testing was performed at the KIT-Macquarie Brain Research Laboratory. Neuromagnetic data were recorded at 1000 Hz using 160-channel whole cortex MEG (Model PQ1160R-N2, KIT, Kanazawa, Japan). The MEG system consists of 160 coaxial first-order gradiometers with a 50 mm baseline [25,26]. During the recording, participants lay on a comfortable bed inside the magnetically shielded room and watched a silent DVD of their choice projected on the ceiling to keep them occupied and awake. They were told to ignore the sounds, give their full attention to the movie, and keep still throughout.

Prior to MEG recording, five marker coils were placed on an elasticised cap on the participant's head, and their positions and the participant's head shape were measured with a pen digitiser (Polhemus Fastrack, Colchester, VT). Head position was measured with the marker coils before and after each MEG recording. Participants were monitored for head movements via a video camera placed inside the magnetically shielded room. Participants who exceeded head-movement of 5 mm (pre- and post-marker coil measurement, as pre-processed in MEG160) were excluded from further analyses.

The mACC and MMF were acquired in two separate acquisition blocks, each with 3 blocks of sounds. Order of testing was randomized across participants. All sound sequences were presented binaurally using MATLAB software at 75dB SPL via pneumatic tubes and custom insert earphones. The stimulus delivery system has a relatively flat frequency response between 500 and 8 kHz and an approximate 10 dB/octave roll-off for frequencies below 500 Hz [27].

2.4. MEG data analysis

MEG data were analysed using the SPM12 M/EEG analysis suite [28] and custom MATLAB scripts. The initial processing steps were as follows: (i) downsample to 250 Hz; (ii) high pass filter at 0.1 Hz; (iii) bandstop filter between 49 and 51 Hz; (iv) low pass filter at 30 Hz; (v) epoch between -100 and 400 ms (from either the onset of the response or the change in the stimulus); (vi) baseline correct between -100 and 0 ms. At this point, we computed the "single trial" MMF by subtracting the response to the preceding standard (predeviant) from the deviant response [29]. Next, for all conditions, we performed robust averaging [30], which down-weights extreme values, thereby minimizing the influence of artefacts. We then re-applied the 30Hz low pass filter to remove any high frequency noise introduced by robust averaging and calculated the global field power (see Figure 2) which provides an overall measure of scalp field strength at each time point [31].

The mACC and MMF responses were extracted from virtual sensors placed in the vicinity of bilateral auditory cortex using a single sphere forward model. Bilateral dipoles were fitted to the M100 response to the onset of the sequence (mACC) or the standard stimulus (MMF), operationalized as the peak in the global field power between 52 and 152 milliseconds. Dipoles were placed in left and right auditory cortex (MNI coordinates: [40 -21 9]; [-40 -21 9]) then fitted by

allowing them to orient freely and move within a gaussian centred at this location with standard deviation 10 mm. Next we used the dipole solution as a spatial filter to extract single-trial epoched “virtual sensor” data from the bilateral auditory cortices. Source waveforms for each hemisphere and condition were calculated by robust averaging of the single-trial waveforms followed by 30 Hz low-pass filtering (see Figure 3).

Statistical analyses of the waveforms were performed in R (R Markdown detailing each step of the analyses is available at <http://rpubs.com/JonBrock/242837>). From each hemisphere, paradigm, and condition, we determined the peak amplitude (maximum for the mACC and minimum for the MMF as these have opposite polarities) within a 100 ms window centred on the peak in the corresponding grand mean global field power. We calculated the SNR by dividing the root mean square of the response post stimulus onset (i.e., 0 to 400 ms) by the root mean square of the response during the baseline period (−100 to 0 ms). Amplitude and SNR measures were subjected to analysis of variance (ANOVA) with Paradigm (mACC vs MMF), Stimulus (Pitch vs Vowel) and Hemisphere (Left vs Right) as repeated measures.

We also performed single-trial analysis of each waveform to determine whether there was a statistically reliable response for each participant. We conducted a one-sample (mACC or MMF vs zero) non-parametric test implemented using the “std_stat” function of the EEGLab toolbox [32] applied to the single trial data for the epoch100 −400 ms. We ran 1000 permutations and set statistical significance at a p -value of 0.01, false discovery rate corrected.

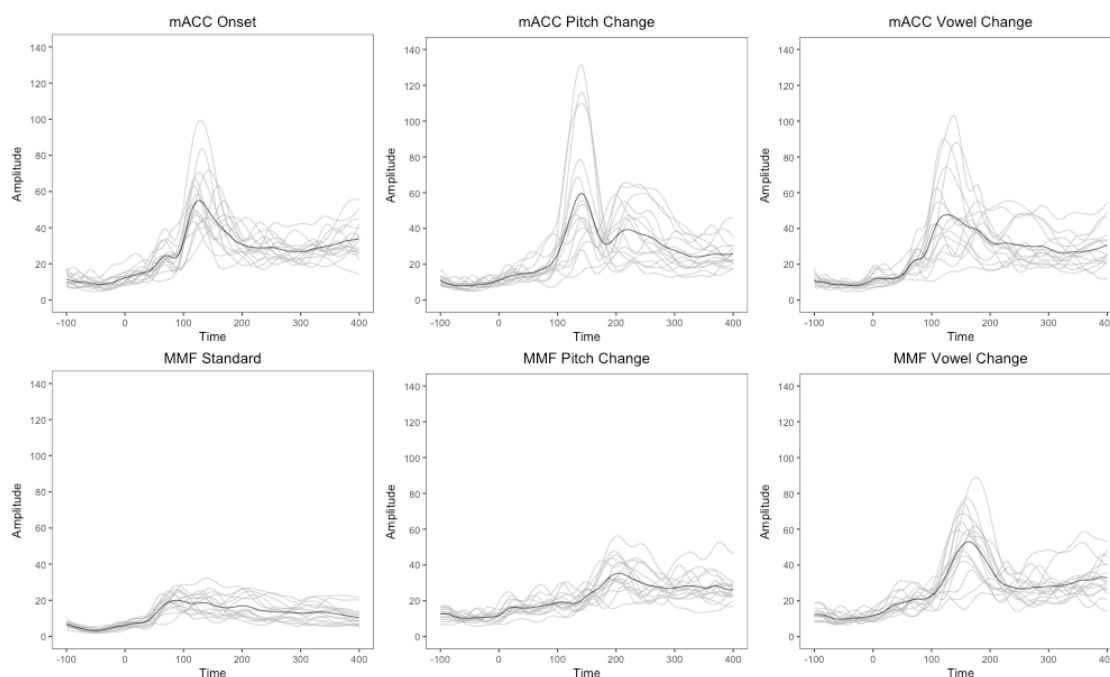


Figure 2. Global field power waveforms for the mACC and MMF paradigms. Grey lines show the responses for individual subjects. Black lines show the mean of all subjects.

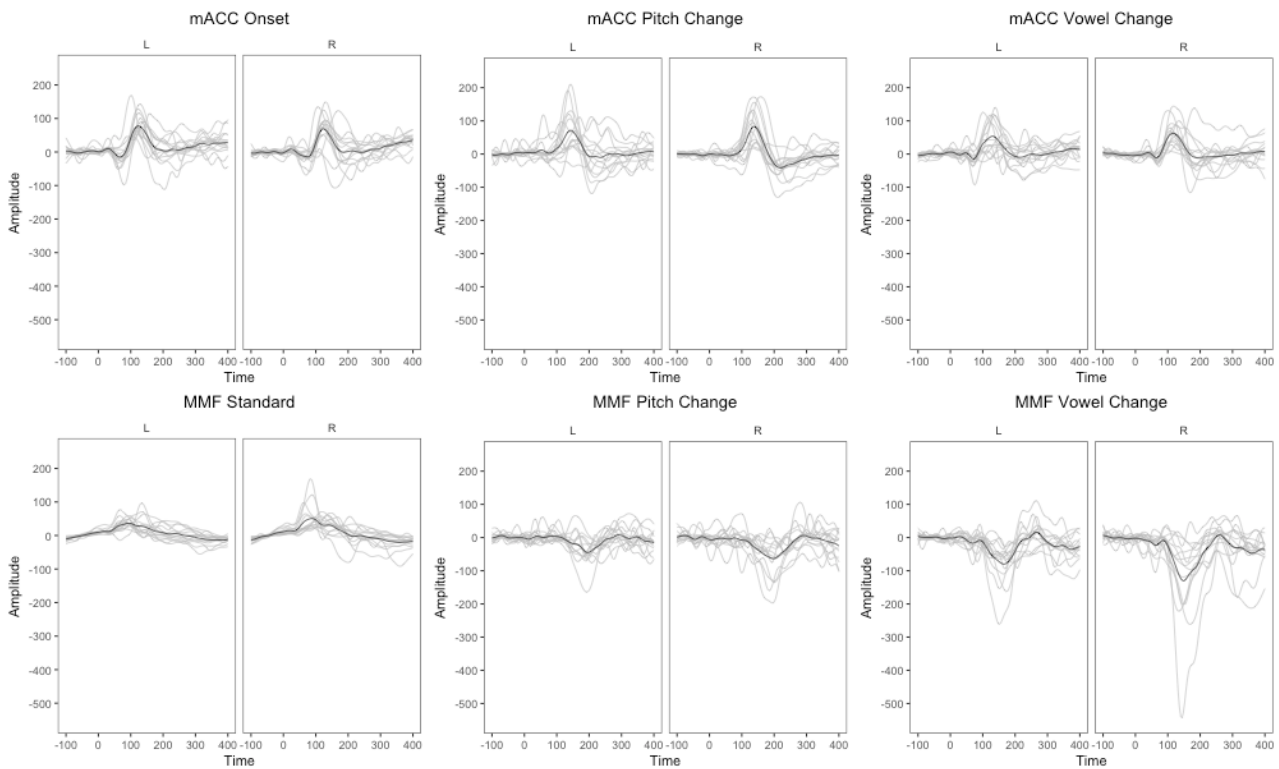


Figure 3. Left (L) and right (R) source waveforms for the mACC and MMF paradigms. Grey lines show the responses for individual subjects. Black lines show the mean of all subjects.

3. Results

Figure 4 shows the peak amplitude and SNR of the mACC and MMF responses. Consistent with the global field power and source waveforms (Figures 2 and 3), it suggests differential sensitivity of the two responses to the Pitch and Vowel stimuli—an impression confirmed by the analyses of variance.

ANOVA on the Peak Amplitude showed no overall effect of Paradigm ($F[1,13] = 0.54, p = 0.474, \eta_G^2 = 0.008$), but we did find a significant effect of Stimulus ($F[1,13] = 6.10, p = 0.028, \eta_G^2 = 0.017$), which was qualified by a Paradigm by Stimulus interaction ($F[1,13] = 23.03, p < 0.001, \eta_G^2 = 0.061$). ANOVAs conducted for each Paradigm separately both showed a main effect of Stimulus, but in opposite directions. For the MMF, the Vowel response was larger than the Pitch response ($F[1,13] = 15.87, p = 0.002, \eta_G^2 = 0.094$). For the mACC, the Pitch response was larger than the Vowel response ($F[1,13] = 8.30, p = 0.013, \eta_G^2 = 0.027$). No effects or interactions involving Hemisphere were significant.

For SNR, the results were similar. We again found no significant effect of Paradigm ($F[1,13] = 2.64, p = 0.128, \eta_G^2 = 0.048$), a significant effect of Stimulus ($F[1,13] = 4.71, p = 0.049, \eta_G^2 = 0.036$), and a significant Paradigm by Stimulus interaction ($F[1,13] = 7.82, p = 0.015, \eta_G^2 = 0.039$). Again, no effects of Hemisphere and no interactions involving Hemisphere were found to be significant. The Vowel MMF was larger than the Pitch MMF ($F[1,13] = 9.39, p = 0.009, \eta_G^2 = 0.192$). However, in

contrast to the Peak Amplitude analysis, we found no difference between the Pitch and Vowel mACCs ($F[1,13] = 0.01$, $p = 0.937$, $\eta_G^2 = 0.000$). For Pitch stimuli, the SNR was higher for the mACC than for the MMF ($F[1,13] = 9.45$, $p = 0.009$, $\eta_G^2 = 0.209$), but there was no Paradigm effect for Vowel stimuli ($F[1,13] = 0.02$, $p = 0.894$, $\eta_G^2 = 0.000$).

Figure 4 shows one participant with a particularly large MMF response. We re-analyzed the Peak Amplitude and SNR data excluding this outlier. In both cases, the interaction between Paradigm and Stimulus remained significant, indicating that it could not be attributed to that outlying participant.

Finally, we determined whether each source waveform for each participant was reliably different to a null response (see Table 2). For the mACC, the Pitch and Vowel changes both elicited a significant response in at least one hemisphere for 12/14 and 13/14 of the participants respectively. The vowel-change MMF was present for 11/14 participants, but only 8/14 produced a reliable pitch-change MMF.

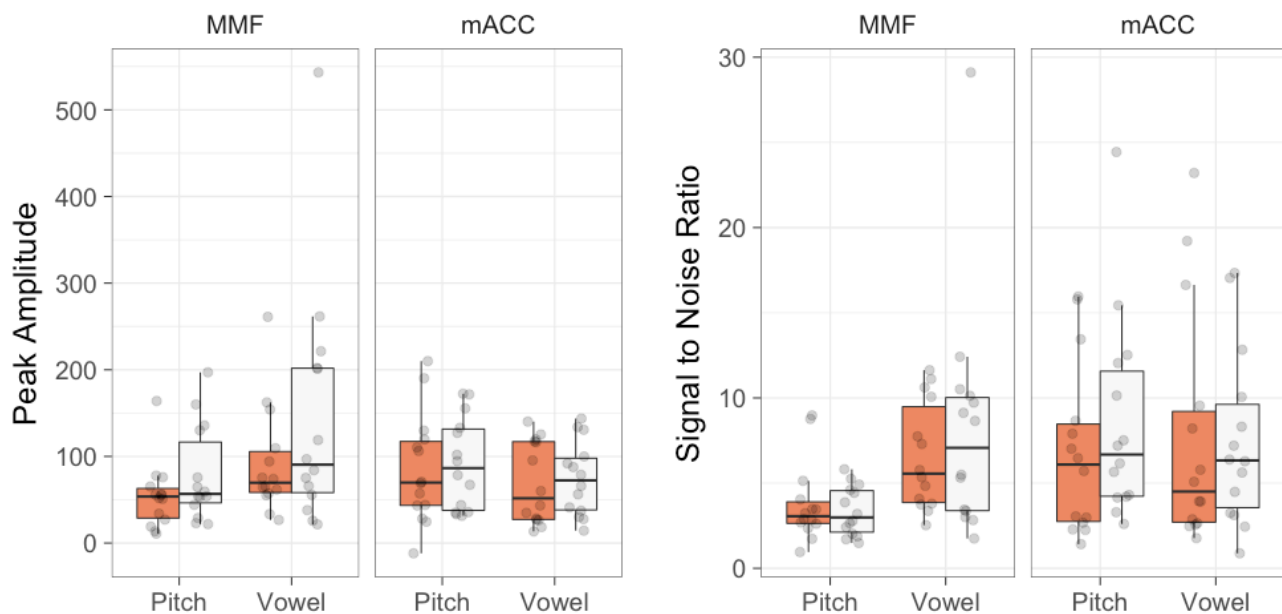


Figure 4. Boxplots showing peak amplitude (left panel) and signal-to-noise ratio (right panel) for mACC and MMF. Dots represent individual participants. Left and right hemisphere sources are in orange and white respectively.

Table 2. Presence of mACC and MMF for individual subjects in the left (L) and right (R) hemisphere. X indicates that the waveform contains at least one cluster of time points that was significantly different to zero (cluster-corrected).

Subject	mACC				MMF			
	Pitch		Vowel		Pitch		Vowel	
	L	R	L	R	L	R	L	R
1	X	X	X	X		X	X	X
2	X		X		X			
3	X	X	X	X	X	X	X	X
4		X		X		X	X	X
5	X	X						
6	X	X	X	X			X	
7	X	X	X	X	X	X	X	X
8	X	X	X	X				X
9		X		X			X	X
10		X		X		X		X
11				X			X	X
12		X	X	X		X	X	X
13	X	X	X	X	X	X	X	X
14				X				
Total	8	11	8	12	4	7	9	10

4. Discussion

The current study directly contrasted two complementary MEG paradigms for investigating auditory change detection, the MMF and the less commonly employed mACC. Although the MMN/MMF is much more widely used, the only previous study directly comparing the two responses found that the ACC is a larger and more robust response than the MMN elicited by the same auditory change [14]. The results of the current study indicate that the relative merits of the two paradigms may in fact be contingent on the stimuli used. For pitch changes, the mACC had a significantly higher SNR than the MMF and reliable responses were obtained more consistently. However, for vowel changes, the MMF had similar SNR to the mACC, and similar reliability at the individual subject level. Importantly, this interaction between Paradigm and Stimuli was also apparent in the global field power, which provides an assumption-free measure of brain responses across the sensors. As such, it would appear to reflect genuine differences in the relative sensitivity of the MMF and mACC to pitch and vowel changes, as opposed to differences in the quality of source model fit across conditions.

In seeking an explanation for this interaction, it is worth considering the putative mechanisms responsible for the mACC and MMF. The ACC/mACC is thought to arise due to the activation and deactivation of neural populations within the tonotopically organised auditory cortex [14,33,34]. The MMN/MMF on the other hand has sources in prefrontal areas [2,35–37] as well as auditory cortex [38–40] and, in addition to change detection, is thought to index processes of memory, attention switching, and the adjustment of internal models of the auditory environment [41–47]. The differential MMF response to vowel and pitch changes (in the presence of similar mACC responses) may, therefore, reflect the influence of one or more of these higher order functions, perhaps involving differences in frontal activation or fronto-temporal connectivity.

Whatever the precise explanation, the current results provide partial support for Martin and Boothroyd's contention that the ACC paradigm is the more efficient measure of auditory change detection. The mACC/ACC has now been found to have superior SNR for both pitch changes and complex tone to noise changes, with equivalent SNR for vowel changes. For the MMF procedure, there appears little scope to improve SNR without making the testing session considerably longer. In contrast, the efficiency of our mACC procedure could be further increased by eliminating the redundant e_{low} at the end of the stimulus, decreasing the duration preceding acoustic changes that are not of interest (e_{high} to e_{low} and u_{low} to e_{low}), and potentially, decreasing all durations and using deconvolution techniques to separate overlapping responses [48].

This is not to say, however, that MMN/MMF should be abandoned. The ACC paradigm is restricted to the study of discrete changes in steady state stimuli such as tones and vowel sounds. In contrast, the MMN can be used to index discrimination of consonant sounds (e.g., /ba/ vs /da/) and is also sensitive to more abstract representations of complex rules such as the conjunction of two different acoustic features [44,49–52]. Moreover, studies that use *both* paradigms may prove particularly informative. For example, in clinical populations, the profile of response across the mACC/ACC and the MMF/MMN may allow a distinction to be made between individuals with basic auditory discrimination deficits, and those with higher-order auditory processing difficulties. Ultimately, the choice of paradigm depends on the question at hand and, as the current results indicate, the precise nature of the acoustic change under investigation.

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Conflict of Interest

The authors report no conflict of interest.

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