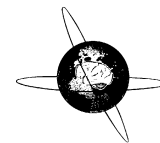


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## Clinical Neurophysiology

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## Evidence for a dual versus single origin of the MMNs evoked by cued versus cueless deviants

I. Hoonhorst<sup>a,b</sup>, P. Deltenre<sup>a,b</sup>, E. Markessis<sup>b,c</sup>, G. Collet<sup>a,d,e</sup>, X. Pablos Martin<sup>a,b</sup>, C. Colin<sup>a,b,\*</sup><sup>a</sup> Unité de Recherches en Neurosciences Cognitives, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium<sup>b</sup> Laboratoire de Neurophysiologie Sensorielle et Cognitive, Université Libre de Bruxelles (U.L.B.), CHU Brugmann, Brussels, Belgium<sup>c</sup> Institut Libre Marie Haps & Faculté de Médecine de l'Université Libre de Bruxelles (U.L.B.), Brussels, Belgium<sup>d</sup> FNRS, Brussels, Belgium<sup>e</sup> Laboratoire Cognition, Langage et Développement, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium

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## HIGHLIGHTS

- The mismatch negativity (MMN) evoked by cued deviants containing a frequency sweep within a tone is much larger than the one evoked by cueless deviants.
- A cued–cueless asymmetry between behavioural discrimination and neurophysiological data was demonstrated.
- The respective contributions of the memory-based and adaptation/fresh-afferent models of MMN generation are discussed on the basis of the present results.

## ABSTRACT

**Objective:** This study was designed to separately test the effect of the cued/cueless nature of deviant stimuli and that of temporal distance between sound and deviance onsets on the mismatch negativity (MMN) as well as to look for discrepancies between behavioural discrimination performances and MMN amplitude when deviants are cueless.

**Methods:** Ten healthy adults passively listened to stimuli that were contrasted by the presence or absence of a frequency sweep starting early or late within the sound. Discrimination performances were collected after the electrophysiological sessions.

**Results:** MMNs were much larger for cued than for cueless deviants. The temporal distance between sound and deviance onsets affected MMNs evoked by both cued and cueless deviants, even to the point of abolishing the MMN when cueless deviance occurred late in the stimulus. Behavioural data were at ceiling levels for all conditions, contrasting with the absence of MMN evoked by cueless deviants with late onset.

**Conclusions:** Two mechanisms contribute to the MMN evoked by cued deviants: the memory comparison process and the adaptation/fresh-afferent one. Within the temporal window of integration, the delay at which each component disappears is different.

**Significance:** Comparing waveforms evoked by cued versus cueless deviants provides a fairly simple way of isolating the MMN memory-based component.

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## 1. Introduction

Among auditory event-related potentials (ERPs), the mismatch negativity (MMN) has been, and still is, the subject of many investigations because of its unique characteristics allowing objective assessment of neural correlates of percepts (Picton et al., 2000).

The MMN is considered to be an attention-independent process indexing the automatic detection of deviance of a rarely occurring stimulus with respect to frequent standard background stimuli (for reviews, see Näätänen, 1992; Lang et al., 1995; Ritter et al., 1995; Näätänen and Alho, 1997; Schröger, 1997; Picton et al., 2000; Näätänen et al., 2007; May and Tiitinen, 2010).

The MMN can be elicited by many types of acoustic deviances (e.g., frequency contrast: Alho et al., 1990, intensity contrast: Näätänen et al., 1987, spatial localisation contrast: Paavilainen et al., 1989, duration contrast: Näätänen et al., 1989) as well as by contrasts in abstract features of complex stimuli such as in

\* Corresponding author at: Research Unit in Cognitive Neuroscience, CP191, Free University of Brussels, 50, Roosevelt Avenue, 1050 Brussels, Belgium. Tel.: +32 2 650 25 39; fax: +32 2 650 22 09.

E-mail address: [ccolin@ulb.ac.be](mailto:ccolin@ulb.ac.be) (C. Colin).

music (e.g., Tervaniemi et al., 1993), speech (e.g., Kraus et al., 1992) or even spatial (Colin et al., 2002b; Stekelenburg et al., 2004) and phonetic (Colin et al., 2002a, 2004) illusory percepts.

The prevailing view about the process eliciting the MMN is that it is the outcome of an automatic comparison performed between a new, deviant stimulus and the memory trace formed by the sensory representation of the standard stimulus within short-term memory (Novak et al., 1990; Näätänen, 1990, 1992; Cowan et al., 1993; Cowan, 1995; Näätänen and Alho, 1995; Näätänen et al., 2007). However, this view is challenged by several authors who argue that the MMN is generated by fresh-afferent neuronal activity and is an expression of the auditory N1 component modulated in latency and amplitude by differential adaptation effects (Jääskeläinen et al., 2004; May and Tiitinen, 2010 for a comprehensive review). In a recent review, Näätänen et al. (2011) argue that such an N1 effect elicited by an oddball paradigm can be dissociated from the genuine MMN, conceived as reflecting the memory-based detection of a violation of auditory regularities.

Another classical description of the MMN properties is that its amplitude is highly correlated to behavioural discrimination measures in healthy (e.g., Lang et al., 1995) and clinical (e.g., Kraus and McGee, 1996) populations.

In a previous study (Colin et al., 2009), we analysed the latencies and amplitudes of the MMNs evoked by duration contrasts, each of which was built by opposing a fixed duration standard with duration increments or decrements of identical relative deviance magnitude. For each duration of the standard stimulus, the increment and decrement duration deviants differed from the standard ones by a fixed proportion (50%). The same stimuli were also used in psychophysical measurements in order to correlate the MMN results with behavioural discrimination performances across all duration contrasts.

We found that for a given duration contrast, duration decrements gave rise to significantly larger MMNs than increments did, a result that agreed with another recent study by Takegata et al. (2008). By contrast, hit rates were at ceiling levels and reaction times were similar for every contrast, irrespective of the relative length of the deviants. This major discrepancy does not fit with the classical correlation between MMN and behavioural parameters. This calls for an explanation of the neurophysiological mechanisms responsible for the MMN drastic reduction, whereas behavioural performances remained at a maximum.

Other even more striking asymmetries brought about by exchanging the roles of standard and deviant within a single contrast pair have been demonstrated in the literature. For example, Bishop et al. (2005) found that, whether participants attended or ignored the stimuli, significant MMNs were elicited by frequency-modulated deviants presented among unmodulated standards, but no MMN was evoked when an unmodulated deviant was presented among frequency-modulated standards. No behavioural data were recorded in this latter study. The asymmetric effect of deviance direction on MMN elicitation was interpreted by Bishop et al. (2005) as reflecting the activation of low-level feature detectors activated when the deviant stimulus was a modulated sound (i.e., contained a specific cue). Such an interpretation might also hold for the amplitude asymmetry between the MMN evoked by duration increments and decrements: when a long deviant is presented among shorter duration standards, the deviant can be regarded as a cueless stimulus because there is no physical marker making deviance quantification possible until the end of the sound.

However, another possible explanation for the MMN amplitude asymmetry between duration increments and decrements rests on the different temporal distance between sound and deviance onsets across the two conditions. Using frequency-modulated deviants, Grimm and Schröger (2005) showed that the later the deviation occurred within the sound, the smaller the MMN ampli-

tude was, suggesting that the temporal distance between stimulus onset and deviance onset is relevant for MMN elicitation. In Colin et al. (2009), it was impossible to disentangle the cued/cueless effect from the deviance onset one, since the temporal distance between sound and deviance onsets was always shorter for duration decrements than for increments.

We therefore formulate the hypothesis that the temporal distance between sound onset and deviance onset on the one hand and the presence or absence of a specific cue within the deviant sound on the other hand will modulate MMN parameters independently of behavioural performances. To test this hypothesis, we used stimuli that all had the same duration and were contrasted by the presence or absence of a frequency sweep with an onset positioned early or late within the sound. With such a design, we were able to test the cued/cueless effect by comparing MMNs evoked by deviants containing a frequency sweep against fixed frequency standards and MMNs evoked by deviants containing a fixed frequency against frequency sweep standards. We were also able to test the temporal distance effect by comparing MMNs evoked by an early deviance onset within the sound (100 ms after sound onset) to MMN evoked by a later deviance onset (280 ms after sound onset). Behavioural data were collected after the electrophysiological sessions in order to assess the level of correlation between perceptual performances and MMN parameters.

## 2. Methods

### 2.1. Subjects

Ten healthy right-handed subjects (eight women) aged 21–36 years (mean: 26.1) participated in the experiment. They gave their informed consent to participate after the details of the procedure had been explained to them. The experimental protocol has been approved by the ethical committee of the Brugmann Hospital, where the neurophysiological recordings took place.

### 2.2. Stimuli

All stimuli had an overall duration of 500 ms. The MMN-eliciting contrast was obtained by opposing stimuli with a fixed frequency (1000 Hz) to ones containing a frequency sweep. To test the temporal distance hypothesis, the frequency sweep started at either 100 or 280 ms after sound onset. To test the cued/cueless hypothesis, two oddball sequences were built for each contrast: one with the stimulus containing the frequency sweep as deviant and one containing the fixed frequency stimulus as deviant.

The stimuli containing the frequency sweeps were made of three successive segments. The first segment was a 1000-Hz fixed frequency sound and lasted either 100 ms (for the stimuli with the frequency sweep onset at 100 ms) or 280 ms (for the stimuli with the frequency sweep onset at 280 ms). The second segment was the frequency sweep (sweep rate = 1 Hz ms<sup>-1</sup>) and always lasted 100 ms. The third segment was a 1100-Hz fixed frequency sound that lasted either 300 ms (for the stimuli with the frequency sweep onset at 100 ms) or 120 ms (for the stimuli with the frequency sweep onset at 280 ms). The starting phases of the second and third segments were adjusted to the instantaneous phase value of the last point of the preceding segment so that there was no discontinuity in the sinusoidal pattern of the signal. Stimuli were Blackman-windowed with a rise and fall time of 20 ms.

### 2.3. Procedure

The stimuli were binaurally delivered at 60 dB SL with Etymotic earphones (model ER-3A) connected through a 25-cm-long silicon

tube ending into a hollowed foam cylinder inserted into the entrance of the ear canals.

Subjects were comfortably seated in an armchair fitted with a back headrest. They were instructed to ignore the auditory stimuli while watching a digital versatile disc (DVD) with subtitles, so as to minimise the risk of contaminating the data by attention-related ERP components such as N2b and P300 (Näätänen, 1991; Picton et al., 2000).

TDT hardware (System II) and software (SigGen 3.51 and Sig-Play 3.3) generated the stimuli and controlled their duration and intensity. The TDT was interfaced with an InstEP stimulation system (software ver. 3.3) that controlled the presentation order and timing of the stimuli.

To minimise the risk of MMN habituation reported to occur when sessions are too long (McGee et al., 2001), stimuli were presented in short sequences of about 10 min. In each short sequence, 450 standard stimuli and 75 deviant stimuli were randomly delivered with a stimulus onset asynchrony (SOA) of 1100 ms.

A complete MMN data bank for each condition was made up of four short sequences, to include 300 deviant stimuli of each kind before data analysis. Moreover, for each type of deviant, one deviant-alone series comprising 300 single tones was recorded with the same SOA (1100 ms) as in the oddball sequences (e.g., Kraus et al., 1995).

The presentation order of the short sequences was pseudo-randomised so that the same sequence was never presented more than once in immediate succession. The deviant-alone sequences were randomly interspersed among the oddball sequences.

Subjects were free to take any type of break they wished between sequences.

#### 2.4. Electrical activity recording

Brain electrical activity was recorded with Ag–AgCl electrodes from  $F_z$ ,  $F_3$ ,  $F_4$ ,  $C_3$ ,  $C_4$  (10–20 system) as well as from left and right mastoids ( $M_1$ ,  $M_2$ ), all referred to the tip of the nose. Horizontal and vertical eye movements were monitored using two bipolar recordings: one between each outer eye canthus and one between a supraorbital electrode and an electrode positioned just below the lower eyelid on the right side. After amplification (10,000 times for brain activity channels and 5000 times for eye movement channels) and filtering (0.1–70 Hz), the input signals were digitised with a sampling rate of 512 Hz and stored on the computer disc for off-line averaging.

#### 2.5. MMN computation and measurement

Data averaging was performed with an InstEP system (software version 3.3). Recording epochs with a total duration of 1024 ms were averaged separately for the deviant alone and the deviant in oddball sequences stimuli. The pre-stimulus baseline was 332 ms.

Rejection of artefacted sweeps from the final averages was performed on the basis of a  $\pm 100 \mu\text{V}$  criterion for all channels. Averaged waveforms were digitally filtered (0.1–30 Hz) and baseline-corrected before being converted into ASCII format and exported to a spreadsheet program for further analysis and plotting. The MMN was computed as the differential waveform obtained by subtracting the tracings evoked by deviant stimuli presented alone from the ones evoked by deviant stimuli embedded in the oddball sequences (Kraus et al., 1995).

To maximise signal-to-noise ratio and take the entire MMN equivalent dipole into consideration, we re-referenced the waveforms recorded at  $F_z$  to the average of the mastoids (Näätänen et al., 2004; Pettigrew et al., 2004a,b; Pakarinen et al., 2007; Pablos Martin et al., 2007; Takegata et al., 2008). For each contrast, the

presence of a significant MMN was objectively ascertained by submitting these re-referenced differential waveforms to the  $t$ -test computation proposed by Kraus et al. (1993). This method performs a point-to-point comparison of the amplitudes of the waveforms evoked by the standard and deviant stimuli (or by the deviant alone and deviant in oddball sequences stimuli in the present case), to determine the latency period over which the grand averages are significantly different from zero. For each contrast,  $t$ -tests were computed within a 300-ms time period symmetrically centred on the visually identified MMN latency peak on the grand average waveforms. Significance level was set at  $p < 0.05$ .

Peak latency and mean amplitude values were gathered, on the re-referenced differential waveform, for each subject and each contrast. The MMN peak latency was determined as the most negative point occurring during the period of consecutive significant  $t$ -tests on the grand averages. It was measured from the theoretical point in time at which deviance could be detected (i.e., from sweep onset for the deviants containing the frequency sweep and from the moment at which sweep onset should have occurred for the fixed frequency deviants).

Mean amplitudes were measured within 40-ms duration time windows centred on the grand average MMN peak latency. Resorting to mean rather than to peak amplitudes avoided the presence of missing data in the analysis of variance (ANOVA) computation, despite the absence of a significant MMN for one of the four contrast types (see Section 3). For this contrast type (late onset/cueless), we used the same temporal windows to determine peak latencies and mean amplitudes as for the late onset/cued condition.

#### 2.6. Psychophysical experiment

To avoid carry-over effects of attention that could have spoilt the inattentive condition requested for recording MMNs uncontaminated by N2b and P300 components (Näätänen, 1991; Picton et al., 2000), the behavioural discrimination data were collected after the electrophysiological session. The stimuli were the same as in the electrophysiological experiment and were delivered in the same way. Only one oddball sequence of 525 trials was presented for each condition. The subjects were informed that they would hear deviant sounds among standard ones and that their task was to press the left mouse button when they perceived a deviant sound. Reaction times were collected from the moment at which deviance occurred.

For each subject and each standard-deviant contrast, discrimination performances were assessed by computing  $d'$  values according to the signal detection theory (Green and Swets, 1966). In the present study, perfect detection (100% of hits and 0% of false alarms) should give a  $d'$  value of 5.03 after correction for ceiling and floor effects, whereas chance responses (50% of hits and 50% of false alarms) should give a  $d'$  value of 0.

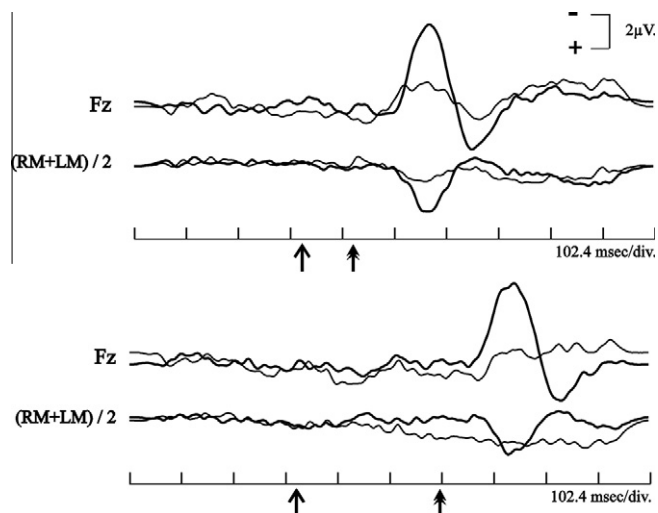
#### 2.7. Statistical analysis

ANOVAs were conducted to assess whether deviance onset (early versus late) and deviance type (cued versus cueless deviants) affected MMN latencies and mean amplitudes as well as behavioural hit rates and reaction times.

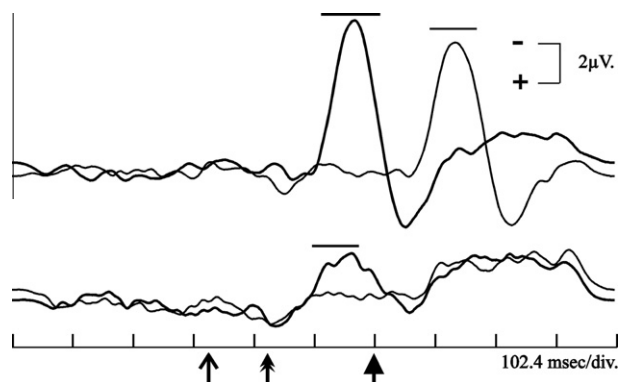
### 3. Results

#### 3.1. MMN assessment

Fig. 1 illustrates differential waveforms grand-averaged across all subjects and evoked by the two kinds of deviant stimuli for each



**Fig. 1.** Differential waveforms referred to the tip of the nose and grand averaged across all subjects for  $F_z$  and the average of both mastoids, evoked by the two kinds of deviant stimuli (thin lines: fixed frequency deviants versus thick lines: deviants containing the frequency sweeps) against the 100 ms deviance onset (upper panel) and against the 280 ms deviance onset (lower panel). The single arrow indicates sound onset and the double arrow indicates deviance onset.



**Fig. 2.** Differential re-referenced waveforms evoked by the two kinds of deviant stimuli (cued deviants: upper tracings; cueless deviants: lower tracings) against the 100 ms (thick lines) and 280 ms (thin lines) deviance onsets. The short horizontal lines on top of the MMN peaks indicate the periods of consecutive significant  $t$ -tests.

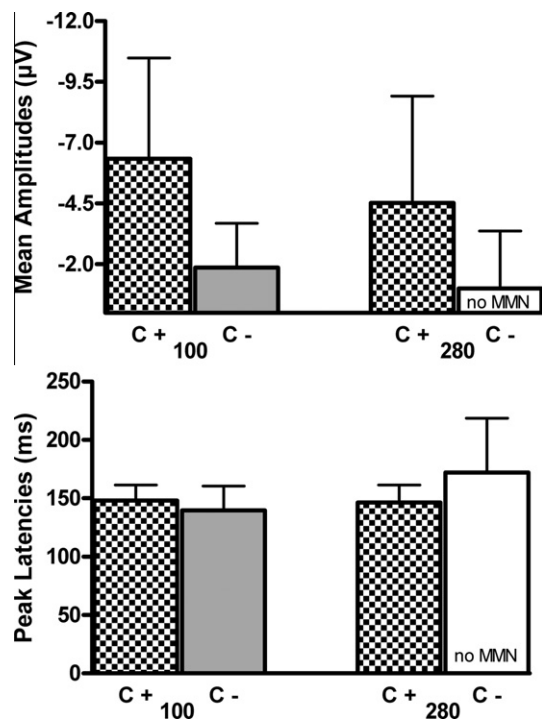
of the two deviance onsets (upper panel: 100 ms; lower panel: 280 ms).

The visual analysis of Fig. 1 shows that all deviants but the one corresponding to a fixed frequency sound played against a standard containing a frequency sweep with late onset (280 ms) elicited clear-cut MMNs inverted in polarity between scalp convexity and mastoids. As shown in Fig. 2, objective  $t$ -test analysis applied on the re-referenced enhanced waveforms confirmed this observation.

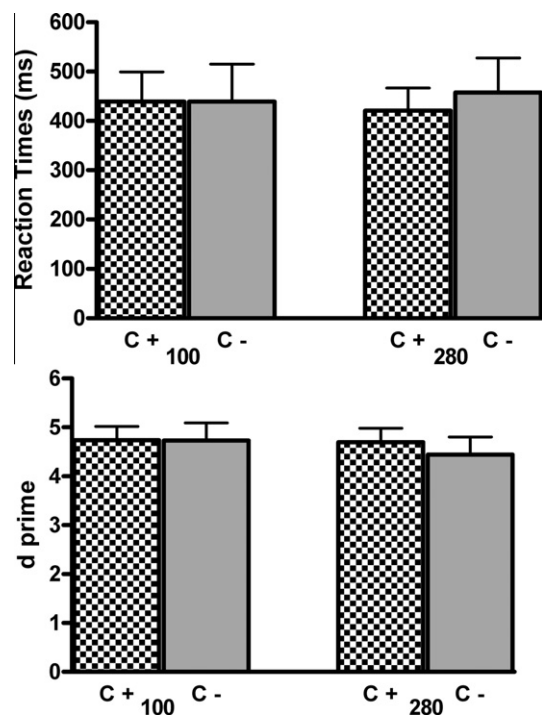
### 3.2. Statistical analysis of the MMN parameters

Fig. 3 illustrates the distributions of the MMN mean amplitudes and latencies, measured on the re-referenced waveforms in the four experimental conditions.

With regard to mean amplitudes, there was a significant effect of deviant type ( $F(1,9) = 12.30, p < 0.01$ ), the MMN mean amplitude being 242% larger when the deviant stimulus was cued than when it was cueless. The effect of deviance onset timing was significant too ( $F(1,9) = 5.52, p < 0.05$ ), the late onset giving rise to smaller



**Fig. 3.** Bar graphs illustrating the mean and standard deviations of the MMN mean amplitudes (upper panel) and peak latencies (lower panel) across all conditions. Chequered bars represent the conditions in which the deviant contained the frequency sweep (C+) whereas unpatterned bars represent the conditions in which the deviant was the fixed frequency sound (C-).



**Fig. 4.** Bar graphs illustrating the mean and standard deviations of reaction times (upper panel) and  $d'$  (lower panel) across all conditions. Chequered bars represent the conditions in which the deviant contained the frequency sweep (C+) whereas unpatterned bars represent the conditions in which the deviant was the fixed frequency sound (C-).

MMNs than the early onset. The interaction between deviant type and deviance onset was not significant ( $F < 1$ ).

For MMN latencies, there was neither deviant type effect ( $F(1,9) = 1.03$ ,  $p > 0.05$ ) nor deviance onset effect ( $F(1,9) = 4.20$ ,  $p > 0.05$ ), nor interaction ( $F(1,9) = 3.80$ ,  $p > 0.05$ ).

### 3.3. Psychophysical experiment

Results (reaction times and  $d'$ ) are displayed, for each contrast, in Fig. 4.

Two-way ANOVAs were performed on  $d'$  and reaction times (RT) with deviant type (two levels) and deviance onset (two levels) as independent variables.

For both  $d'$  and RT, there was neither deviant type effect ( $F(1,9) = 2.58$ ,  $p > 0.05$  for  $d'$  and  $F < 1$  for RT), deviance onset effect ( $F(1,9) = 4.69$ ,  $p > 0.05$  for  $d'$  and  $F < 1$  for RT) nor interaction between deviant type and deviance onset ( $F(1,9) = 1.26$ ,  $p > 0.05$  for  $d'$  and  $F(1,9) = 1.43$ ,  $p > 0.05$  for RT). Mean reaction time for the four possible contrasts was 439 ms and mean  $d'$  was 4.65 (which can be regarded as almost ceiling level, given the maximum possible  $d'$  in the present experiment).

## 4. Discussion

The present results clarify previous work on duration and frequency content contrasts which had revealed:

- major asymmetries in the amplitudes of MMNs evoked by the same amount of acoustic deviance, according to the cued/cueless nature of the deviant (Bishop et al., 2005; Colin et al., 2009);
- a detrimental effect of increasing the temporal delay between sound and deviance onset beyond 300 ms (e.g., Grimm and Schröger, 2005); and
- discrepancies between behavioural hit rates (almost at ceiling levels) and neurophysiological data (Grimm et al., 2004; Colin et al., 2009).

Such asymmetries and discrepancies were further examined in the present study, using frequency sweep contrasts. The stimuli all had the same duration but deviants could contain the frequency sweep (and were then played against a fixed frequency standard) or were fixed frequency sounds (played against standard containing the frequency sweep). Moreover, the onset of the frequency sweep contrast within the sound was either 100 or 280 ms. This configuration enabled us to separately manipulate the effect of the cued/cueless nature of the deviants and that of temporal distance between sound and deviance onset as well as to look for possible interactions between the two. Moreover, we collected behavioural performances for each experimental condition to look for a discrepancy between behavioural and neurophysiological data akin to the one found for cueless duration contrasts (Colin et al., 2009).

As stated in the Introduction, the process eliciting the MMN is explained by two models that are often considered to be mutually exclusive (Jääskeläinen et al., 2004): the memory-based (cf. Näätänen et al., 2007) and the adaptation/fresh-afferent hypotheses (cf. May and Tiitinen, 2010).

The present striking asymmetry in MMN amplitude between cued and cueless deviants does not favour one model over the other but indicates that, rather than being mutually exclusive, the two models can add their effects to contribute to MMN generation. Bishop et al. (2005) suggested that the asymmetry they found between cued and cueless deviants was due to the automatic activation of low-level feature detectors when the deviant was the frequency-modulated sound. Although they were cautious in their conclusion and avoided claiming that the MMN was solely dependent on increased activity in feature detectors, their results,

unlike to ours, did not demonstrate the presence of an MMN for cueless deviants. In the present study, the fact that cueless deviants evoked a significant MMN is best interpreted as the output of the memory comparison process since the cueless deviant did not contain any physical feature able to trigger specialised feature detectors. The enhanced MMN we found for cued deviants can then be interpreted as reflecting the addition of activity emanating from specific feature detectors for frequency sweeps to activity corresponding to the automatic memory-based comparison.

Whether the memory-based and the adaptation/fresh-afferent MMN components are separable has been discussed in numerous papers (for the most recent reviews, see May and Tiitinen, 2010, arguing that the MMN can be fully accounted for by the N1 difference between standards and deviants and Näätänen et al., 2011, arguing that N1- and MMN-related neural activities may be clearly separated). Some of the major arguments in favour of the separability are the possibility to observe MMNs under conditions in which there is no systematic N1 difference between deviants and standards (e.g., language-specific MMNs obtained in categorical perception paradigms), different generator loci for the MMN and the N1 in humans and different developmental time courses of the MMN and N1.

Using cueless deviants, as done in the present study, is another fairly simple method of isolating the MMN generated by a memory comparison from the one due to fresh afferents or feature detector activities.

Increasing the temporal distance between sound and deviance onsets from 100 to 280 ms induced a detrimental effect on the MMN evoked by cued and by cueless deviants. According to Näätänen and Winkler (1999), the integration of the different parallel feature-specific processes involved in sound analysis presumably uses a temporal window of integration (TWI) of some 200-ms duration, initiated by sound onset and during which acoustic information is integrated into a unitary percept (Näätänen, 1990). According to Grimm and Schröger (2005), the longer the temporal distance is between two sound events, the weaker the relation is between onset and offset represented in a way, allowing the pre-attentive deviance-detection system to register a change in this relation.

The failure of cueless deviants to elicit any significant MMN in the late-onset condition may indicate that the amplitude decrement associated with the deviance onset delay is faster for the genuine MMN than for the N1-related component.

Another possibility is that both MMN components have the same decay rate but that because the one evoked by cued stimuli has a higher amplitude it falls back within the background noise later than the one evoked by cueless stimuli. This scheme is illustrated in Fig. 4 of Grimm and Schröger (2005) showing the hypothetical gradual decline of stimulus encoding as a function of time, in attend and ignore conditions. The amplitude enhancement of the cued MMN could theoretically be due not only to the addition of the memory-based and fresh-afferent components but also to a kind of attentional capture triggered by the cue heralding deviance onset. This attentional capture would enhance the MMN amplitude allowing it to be detected over a longer temporal window (Grimm and Schröger, 2005). We do not, however, favour this explanation for the present results since one would expect an attentional capture to evoke an N2b in addition to the MMN, a fact that is not supported by the data: the MMN clearly inverted its polarity, during its complete time window, whereas N2b does not invert in polarity (Näätänen et al., 1993). Moreover, we did not observe two separate peaks in the differential waveform and, based on visual analysis, the MMN was larger at  $F_z$  than at  $C_z$ , whereas N2b has a more posterior location (Näätänen et al., 1993).

The striking discrepancy between behavioural and MMN data challenges another classical view of the MMN according to which

there is a correlation between MMN parameters and behavioural data (e.g., Lang et al., 1995). Several other recent studies reported similar discrepancies. In their studies on the temporal constraints on MMN elicitation, Grimm et al. (2004, Grimm et al. 2005) as well as Weise et al. (2010) observed a severe reduction of the MMN in conditions in which behavioural hit rates were around 90%. In our previous study (Colin et al., 2009), using duration contrasts, although the MMN was abolished for a long deviant played against a short standard, behavioural results remained at ceiling levels. It thus appears that, in some circumstances, the MMN can be dramatically reduced or absent, whereas behavioural discrimination results are almost at ceiling levels. Such reductions in MMN amplitude thus appear to be a purely neurophysiological phenomenon that does not impact behavioural discrimination. This observation calls for caution in clinical applications aiming at measuring discrimination performances through neurophysiological recordings only.

Given the numerous research and clinical applications of the MMN, it is of prime importance to gain a thorough understanding of the neurophysiological processes underlying amplitude asymmetries between contrast types sharing the same acoustic distance as well of the discrepancies between MMN parameters and behavioural data. Applications for which the key issue is to track the automatic discrimination abilities (e.g., use of MMN as a predictor for coma outcome, for a review see Daltozzo et al., 2007) and for which the inherently low signal-to-noise ratio of the MMN is an issue (clinical populations) would benefit from contrasts eliciting large MMNs (and more specifically contrasts in which the deviant is cued), even though such MMNs do not guarantee the presence of a genuine memory MMN and a direct link with the attentional system. On the other hand, for research applications devoted to tapping into the memory issues only, it might be important to use featureless deviants that would evoke an MMN limited to the output of the comparison mechanism in auditory sensory memory.

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## References

- Alho K, Sainio K, Sajaniemi N, Reinikainen K, Näätänen R. Event-related brain potential of human newborns to pitch changes of an acoustic stimulus. *Electroencephalogr Clin Neurophysiol* 1990;77:151–5.
- Bishop DVM, O'Reilly J, McArthur GM. Electrophysiological evidence implicates automatic low-level feature detectors in perceptual asymmetry. *Cognitive Brain Res* 2005;24:177–9.
- Colin C, Radeau M, Soquet A, Colin F, Deltenre P. Mismatch negativity evoked by the McGurk-MacDonald effect: evidence for a phonological representation within the auditory sensory short term memory. *Clin Neurophysiol* 2002a;113:495–506.
- Colin C, Radeau M, Soquet A, Dachy B, Deltenre P. Electrophysiology of spatial scene analysis: the mismatch negativity (MMN) is sensitive to the ventriloquism illusion. *Clin Neurophysiol* 2002b;113:507–18.
- Colin C, Radeau M, Soquet A, Deltenre P. Generalization of the generation of an MMN by illusory McGurk percepts: voiceless consonants. *Clin Neurophysiol* 2004;115:1989–2000.
- Colin C, Hoonhorst I, Markessis E, Radeau M, de Tourchaninoff M, Foucher A, et al. Mismatch negativity (MMN) evoked by duration contrasts: an unexpected major effect of deviance direction on amplitudes. *Clin Neurophysiol* 2009;120:51–9.
- Cowan N, Winkler I, Teder W, Näätänen R. Memory prerequisites of mismatch negativity in the auditory event-related potential (ERP). *J Exp Psychol Learn* 1993;19:909–21.
- Cowan N. Attention and memory. An integrated framework. Oxford: Oxford University Press; 1995.
- Daltozzo J, Wioland N, Mutschler V, Kotchoubey B. Predicting coma and other low responsive patients outcome using event-related brain potentials: a meta-analysis. *Clin Neurophysiol* 2007;118:606–14.
- Green DM, Swets JA. Signal detection theory and psychophysics. New York, NJ: Wiley; 1966.
- Grimm S, Widmann A, Schröger E. Differential processing of duration changes within short and long sounds in humans. *Neurosci Lett* 2004;356:83–6.
- Grimm S, Schröger E. Pre-attentive and attentive processing of temporal and frequency characteristics within long sounds. *Cognitive Brain Res* 2005;25:711–21.
- Jääskeläinen LP, Ahveninen J, Bonmassar G, Dale AM, Ilmoniemi RJ, Levänen S, et al. Human posterior auditory cortex gates novel sounds to consciousness. *Proc Natl Acad Sci USA* 2004;101:6809–14.
- Kraus N, McGee T, Sharma A, Carrell T, Nicol T. Mismatch negativity event-related potential is elicited by speech stimuli. *Ear Hear* 1992;13:158–64.
- Kraus N, McGee T, Micco A, Sharma A, Carrell T, Nicol T. Mismatch negativity in school-age children to speech stimuli that are just perceptibly different. *Electroencephalogr Clin Neurophysiol* 1993;88:123–30.
- Kraus N, McGee T, Carrell TD, Sharma A. Neurophysiologic bases of speech discrimination. *Ear Hear* 1995;16:19–37.
- Kraus N, McGee TJ. Auditory neurophysiologic responses and discrimination deficits in children with learning problems. *Science* 1996;273:971–3.
- Lang AH, Eerola O, Korpiolahti P, Holopainen I, Salo S, Aaltonen O. Practical issues in the clinical application of mismatch negativity. *Ear Hear* 1995;16:117–29.
- May PJ, Tiitinen H. Mismatch negativity (MMN), the deviance-elicited auditory deflection, explained. *Psychophysiology* 2010;47:66–122.
- McGee TJ, King C, Tremblay K, Nicol TG, Cunningham J, Kraus N. Long-term habituation of the speech-elicited mismatch negativity. *Psychophysiology* 2001;38:653–8.
- Näätänen R, Paavilainen P, Alho K, Reinikainen K, Sams M. The mismatch negativity to intensity changes in an auditory stimulus sequence. *Electroencephalogr Clin Neurophysiol* 1987;Suppl 40:125–31.
- Näätänen R, Paavilainen P, Reinikainen K. Do event-related potentials to infrequent decrements in duration of auditory stimuli demonstrate a memory trace in man? *Neurosci Lett* 1989;107:347–52.
- Näätänen R. The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. *Behav Brain Sci* 1990;13:201–88.
- Näätänen R. Mismatch negativity (MMN) outside strong attentional focus: a commentary on Woldorff et al.. *Psychophysiology* 1991;28:478–84.
- Näätänen R. Attention and brain function. Hillsdale, NJ: Lawrence Erlbaum Associates; 1992.
- Näätänen R, Paavilainen P, Tiitinen H, Jiang D, Alho K. Attention and mismatch negativity. *Psychophysiology* 1993;30:436–50.
- Näätänen R, Alho K. Mismatch negativity—a unique measure of sensory processing in audition. *Intern J Neurosci* 1995;80:317–37.
- Näätänen R, Alho K. Mismatch negativity—the measure for central sound representation accuracy. *Audiol Neuro-Otol* 1997;2:341–53.
- Näätänen R, Winkler I. The concept of auditory stimulus representation in cognitive neuroscience. *Psychol Bull* 1999;125:826–59.
- Näätänen R, Syssoeva O, Takegata R. Automatic time perception in the human brain for intervals ranging from milliseconds to seconds. *Psychophysiology* 2004;41:660–3.
- Näätänen R, Paavilainen P, Rinne T, Alho K. The mismatch negativity (MMN) in basic research of central auditory processing: a review. *Clin Neurophysiol* 2007;118:2544–90.
- Näätänen R, Kujala T, Winkler I. Auditory processing that leads to conscious perception: a unique window to central auditory processing opened by the mismatch negativity and related responses. *Psychophysiology* 2011;48:4–22.
- Novak GP, Ritter W, Vaughan Jr HG, Wizniter ML. Differentiation of negative event-related potentials in an auditory discrimination task. *Electroencephalogr Clin Neurophysiol* 1990;75:255–75.
- Paavilainen P, Karlsson ML, Reinikainen K, Näätänen R. Mismatch negativity to change in spatial location of an auditory stimulus. *Electroencephalogr Clin Neurophysiol* 1989;73:129–41.
- Pablos Martin X, Deltenre P, Hoonhorst I, Markessis E, Rossion B, Colin C. Perceptual biases for rhythm: the mismatch negativity latency indexes the privileged status of binary versus non-binary interval ratios. *Clin Neurophysiol* 2007;118:2709–15.
- Pakarinen S, Takegata R, Rinne T, Huotilainen M, Näätänen R. Measurement of extensive auditory discrimination profiles using the mismatch negativity (MMN) of the auditory event-related potential (ERP). *Clin Neurophysiol* 2007;118:177–85.
- Pettigrew CM, Murdoch BE, Kei J, Chenery HJ, Sockalingam R, Ponton CW, et al. Processing of English words with fine acoustic contrasts and simple tones: a mismatch negativity study. *J Am Acad Audiol* 2004a;15:47–66.
- Pettigrew CM, Murdoch BE, Ponton CW, Kei J, Chenery HJ, Alku P. Subtitled videos and mismatch negativity (MMN) investigations of spoken word processing. *J Am Acad Audiol* 2004b;15:469–85.
- Picton TW, Alain C, Otten L, Ritter W, Achim A. Mismatch negativity: different water in the same river. *Audiol Neuro-Otol* 2000;5:111–39.

- Ritter W, Deacon D, Gomes H, Javitt DC, Vaughan Jr HG. The mismatch negativity of event-related potentials as a probe of transient auditory memory: a review. *Ear Hear* 1995;16:52–67.
- Schröger E. On the detection of auditory deviants: a pre-attentive activation model. *Psychophysiology* 1997;34:245–57.
- Stekelenburg JJ, Vroomen J, de Gelder B. Illusory sound shifts induced by the ventriloquist illusion evoke the mismatch negativity. *Neurosci Lett* 2004;357:163–6.
- Takegata R, Tervaniemi M, Alku P, Ylinen S, Näätänen R. Parameter-specific modulation of the mismatch negativity to duration decrement and increment: evidence for asymmetric processes. *Clin Neurophysiol* 2008;119:1515–23.
- Tervaniemi M, Alho K, Paavilainen P, Sams M, Näätänen R. Absolute pitch and event-related brain potentials. *Music Percept* 1993;10:305–16.
- Weise A, Grimm S, Müller D, Schröger E. A temporal constraint for automatic deviance detection and object formation: a mismatch negativity study. *Brain Res* 2010;1331:88–95.