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Changes in mismatch negativity across pre-hypnosis, hypnosis and post-hypnosis conditions distinguish high from low hypnotic susceptibility groups

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Abstract

The role of alterations in mismatch negativity (MMN) in hypnosis was examined by recording MMN of the auditory ERP at frontal (F3, Fz, and F4) and mastoid (M1 and M2) placements. Frontal MMN is believed to reflect activity in right anterior cortical generators, whereas MMN at mastoid leads reflects generators located bilaterally in the temporal auditory cortex. MMN recordings were obtained in 11 low and 12 high hypnotically susceptible participants in three successive blocks; pre-hypnosis, hypnosis and post-hypnosis. Frontal (but not temporal) MMN showed a significant quadratic trend across testing conditions. It increased during hypnosis and then dropped post-hypnosis for both susceptibility groups. Linear trends for frontal and temporal MMN showed directly opposite patterns of change in the interaction between hypnotic susceptibility and testing blocks. Frontal MMN built up linearly over the test blocks in high relative to low susceptibility participants. Temporal MMN showed the reverse pattern and increased linearly across test conditions in those with low relative to high hypnotic susceptibility.

Keywords: Hypnosis; Hypnotic susceptibility; MMN; Roving standard; Frontal MMN; Temporal MMN

1. Introduction

Kallio and Revonsuo have proposed non-conscious neurophysiological precursors of veridical environmental perceptions as likely candidates for neurophysiological processes underpinning possible state-like changes in hypnosis [16]. To assist such identification they have advocated the use of single case studies with virtuoso hypnotic subjects [16,17]. MMN is a well-known auditory event-related potential paradigm with an established topographical maximum over frontal electrodes. MMN is elicited to auditory stimuli by a sudden stimulus change (deviant) in a series of predictable (standard) stimuli and is calculated by subtracting the ERP to the standard stimulus from the ERP to the deviant stimulus. Each new auditory stimulus is compared to a representation in very short-term auditory memory built up from the preceding similar stimuli. The MMN corresponds to the detection of a discrepancy between the neural representation of the novel stimulus and the pre-existing neural template [19]. The MMN is preconscious and occurs even in sleep or while attention is diverted to another task. Therefore it well fits the criterion of a non-conscious neurophysiological precursor of veridical environmental perceptions.

Source localization studies indicate that the principal generators of the MMN (and its magnetic equivalent) are located bilaterally in the superior temporal gyrus, i.e. in the auditory cortex [14,21,24,26]. However, another important generator has also been identified in the right frontal cortex [1,2,5,22]. According to Näätänen [19] the generators in the auditory cortex correspond to an automatic, pre-attentive, change detection mechanism, while the right frontal generator is likely to correspond to a process that recruits attentional resources to the detected change. Kallio et al. [17]

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hypothesised that if hypnosis, in highly susceptible participants, results in a state of anterior inhibition, then the MMN (over frontal electrodes) should be diminished in hypnosis. Contrary to these predictions, in a single case study with a virtuoso hypnotic subject, they reported a significant increase in MMN in the hypnotised compared to the non-hypnotised condition at the fronto-centrally located electrode Fz. They concluded that this result failed to support the theory of frontal inhibition as a core feature of any state of hypnosis.

Furthermore the exclusive reliance on single case studies of hypnotic virtuosos, though useful in themselves, has important limitations and needs to be supplemented by additional research strategies. Electro-physiological measures demonstrate a marked degree of inter-individual variability. It cannot be reliably inferred that because one individual shows a particular pattern of performance that this response will be generally shared. The generalisability of results to other highly susceptible subjects requires demonstration. It also appears to be assumed that the electro-physiological changes found in hypnosis by a virtuoso subject will not be matched by a subject with low susceptibility. It is presumed that because the participant with low susceptibility does not become hypnotised that they show no EEG changes in hypnosis, but this does not allow for neurophysiological sequelae such as adaptation to the test situation, anxiety reduction, familiarity with the task, etc. [7]. It is dangerous to presume that simply because a highly susceptible subject shows a particular neurophysiological change in hypnosis that this is a feature of a hypnotic state [20,23,27]. Rather the identification of such differences is only one step in the process of specifying state-like transitions in some hypnotised individuals [13].

In light of these considerations the present study seeks to replicate and extend the findings of Kallio et al. [17] by studying MMN in groups of participants with low and high hypnotic susceptibility. Both frontal and temporal MMN components are tracked across pre-hypnosis, hypnosis, and post-hypnosis conditions. A roving standard paradigm [3] is adopted to maximize the magnitude of the (otherwise often weak) temporal MMN component measured at the mastoid electrodes. Alternative explanations for the original MMN finding [17] predict either a linear or quadratic pattern of change across the three successive testing conditions of the present experiment which may be directly tested by the use of linear or quadratic polynomial trend analysis.

1.1. Hypotheses

1. The effect of situational factors associated with the hypnosis condition (but not unique to those with high hypnotic susceptibility) is predicted to produce a quadratic trend across the experimental conditions in all subjects.
2. However, the effect of factors uniquely engaged in those with high hypnotic susceptibility when in the hypnosis condition (i.e. the hypnotic state) is predicted to produce a quadratic trend in the interaction between experimental condition and susceptibility.
3. An increase in the strength of auditory memory template building (a non-hypnotic cortical process) with task repetition is predicted to produce a linear trend across the experimental conditions in all subjects.
4. Alternatively the effect of hypnotic susceptibility (independent of processes specifically engaged by hypnosis) on the temporal development of MMN is predicted to produce a linear trend in the interaction between experimental condition and susceptibility.

2. Method

2.1. Participants

All participants were doubly screened for hypnotic susceptibility. Firstly by the Harvard Group Scale [25] and then individually on the SHSS: C [28]. Low susceptibility was categorised as a score of 0–3 on both occasions and high susceptibility as a score of 9–12 on both occasions. There were 11 low susceptibility and 12 high susceptibility participants in all. One left-handed participant was included in each of the high and low groups. Participants were recruited from among staff and students at the Imperial College Faculty of Medicine. The Riverside Research Ethics Committee gave ethical approval for the study. All participants provided signed consent after experimental procedures had been fully explained.

2.2. Procedure

2.2.1. Stimulation protocol

MMN was measured using duration deviants occurring after either three or six standard tones. Within each stimulus sequence all standards were of the same frequency, intensity and duration. A deviant differing only in duration followed each sequence of standards. The number of standards in each stimulus sequence varied randomly from one sequence to the next. However, stimulus frequency was always varied on the succeeding stimulus sequence (the roving standard paradigm) [1–3]. During EEG recording participants viewed a Necker cube and pressed a response button whenever they experienced a reversal in the appearance of the figure. This served to divert attention from the tones and to reduce eye movement artefact.

2.2.2. Design

This procedure was administered three times to each participant in an ABA repeated measures design. The first was immediately before hypnosis in a pre-hypnosis baseline. The second was after a hypnotic induction procedure (specifically designed to exclude relaxation suggestions) and arm levitation suggestion. The third was post-hypnosis. The hypnotic induction procedure was worded so as not to include either a relaxation procedure or suggestions of relaxation. Post-hypnosis testing occurred after both de-induction and

several minutes of deliberately alerting conversation fostered by the hypnotist. A similar design had been used previously [29] where it disclosed changes in electrocortical oscillations in highly hypnotisable subjects that were sustained beyond hypnosis to the post-hypnosis condition.

2.2.3. Stimuli

Pure sinusoidal tones (70 dB SPL, 5 ms rise/fall) were administered binaurally via headphones. Twelve different frequencies were utilised ranging in 50 Hz steps from 700 to 1250 Hz. Standard tones were of 25 ms duration whereas deviants were of 50 ms in length. A total of 1100 stimuli were presented in each condition with 100 deviants following each of the three and six standard sequences, respectively. All stimuli were presented with a stimulus onset asynchrony of 0.3 s.

2.2.4. EEG recording

EEG was recorded continuously throughout the task from tin electrodes placed frontally at F3, Fz and F4, and on both the left and right mastoids (M1 and M2) in accordance with the international 10–20 system. Impedance was kept below 5 kΩ for all participants except one in the high and one in the low group for whom all impedances remained below 9 kΩ. Electrodes placed above and below the right eye measured EOG. The system band pass was 0–100 Hz, with a digital sampling rate of 500 Hz. The ground electrode was placed 1.5 cm anterior to Fz with a reference on the nose.

2.2.5. ERP processing

Data were first corrected for eye blink artefact offline using the Neuroscan 4.1 OAR algorithm. EEG data epochs were 500 ms in total length including a pre-stimulus baseline of 100 ms. Data epochs were filtered with a band pass of 0.5–20 Hz. Epochs with amplitudes exceeding ±100 μV were further excluded. MMN was obtained by subtracting the ERP to the immediately preceding standard from the ERP for deviants. This was obtained separately for deviants following each of three or six standard sequences. Mean amplitudes were then calculated in the difference waveforms between 100 and 200 ms post-stimulus.

2.3. Data analysis

In order to discriminate between the contributions of the predicted effects to frontal and temporal MMN components a series of planned polynomial contrasts were carried out separately on the means of the frontal (FZ, F4 and F3) and mastoid (M1 and M2) derivations, respectively. Unlike pair wise comparisons, polynomial contrasts analyse predicted patterns of change across an ordered sequence of testing conditions. Hypothesised patterns in the total data may be significant even when no pair wise comparison reaches significance. Thus polynomial contrasts provide a useful alternative to more common pair wise contrasts when hypotheses can be formulated in terms of such patterns.

In the present case of three successive tests only two patterns are possible, a linear or a quadratic trend (pair wise comparisons by definition may only reveal local linear trends). Linear or quadratic trends in the interaction between susceptibility and experimental condition refer to the total pattern of differences between high and low hypnotically susceptible groups across all three successive experimental conditions and are not equivalent to the interaction effects in an omnibus *F*-test.

3. Results

MMN waveforms for high and low susceptibility groups, at each electrode (F3, Fz, F4, M1 and M2), are presented in Figs. 1–3 for each of the pre-hypnosis, hypnosis and post-hypnosis testing conditions, respectively. The mean values (and standard errors) for MMN averaged across frontal electrodes F3, Fz, F4 between 100 and 200 ms post-stimulus are presented in Fig. 4 for high and low susceptibility groups for each of the pre-hypnosis, hypnosis and post-hypnosis testing conditions. The values for MMN averaged across temporal electrodes M1 and M2 between 100 and 200 ms post-stimulus

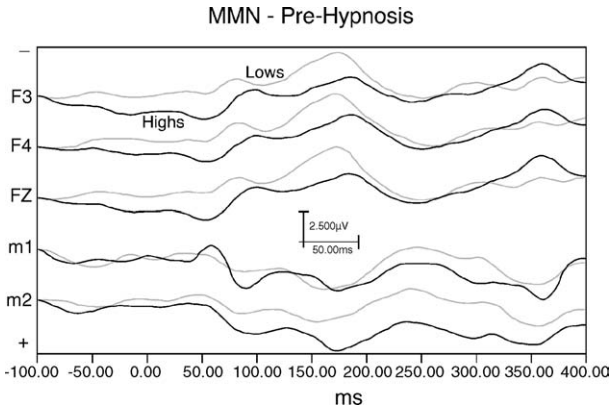

Fig. 1. Pre-hypnosis MMN difference waves in high and low susceptible groups at frontal (F3, F4 and Fz) and mastoid (Ml and M2) electrodes.

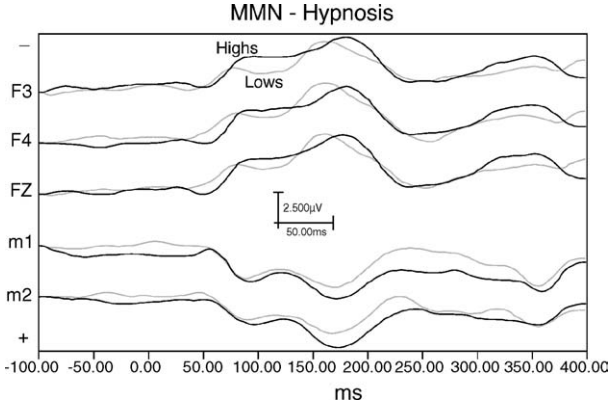

Fig. 2. Hypnosis MMN difference waves in high and low susceptible groups at frontal (F3, F4 and Fz) and mastoid (Ml and M2) electrodes.

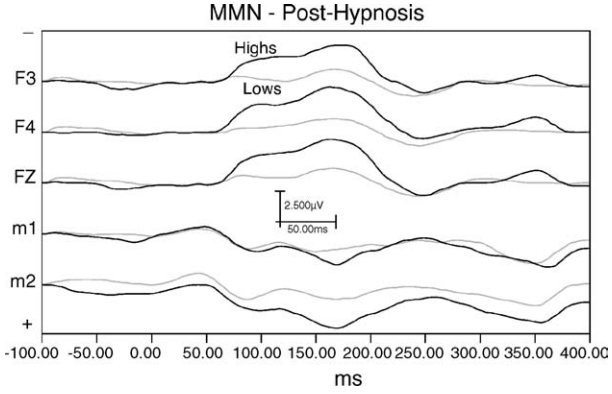

Fig. 3. Post-hypnosis MMN difference waves in high and low susceptible groups at frontal (F3, F4 and Fz) and mastoid (Ml and M2) electrodes.

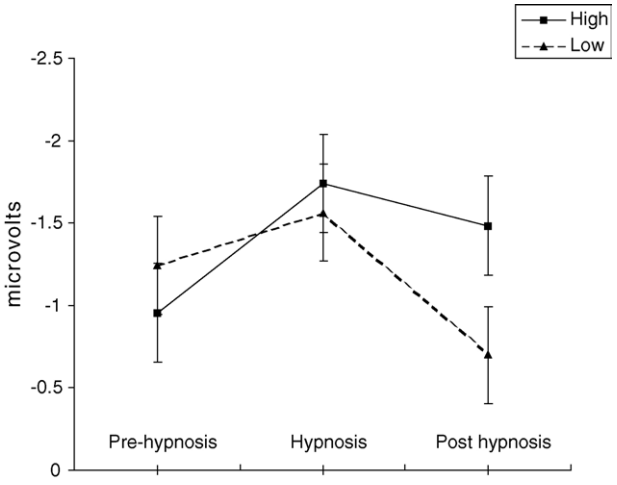

Fig. 4. Mean frontal Mismatch Negativity (Fz, F4 and F3) and standard error: Hypnosis Condition × Hypnotic Susceptibility.

are presented in Fig. 5 (for high and low susceptibility groups across each of the pre-hypnosis, hypnosis and post-hypnosis testing conditions).

The sign of MMN reverses from negative to positive below the temporal plane; consequently the sign of values at M1 and M2 was reversed to allow for a direct comparison of the analyses of frontal and temporal MMN. Results for linear and

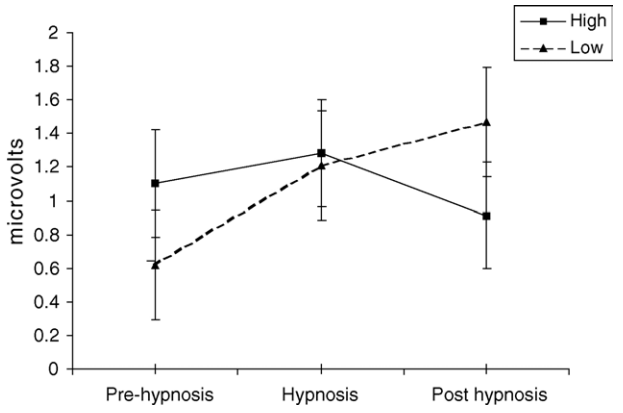

Fig. 5. Mean temporal Mismatch negativity (M1 and M2) and standard error: Hypnosis Condition × Hypnotic Susceptibility.

quadratic polynomial contrasts for hypnosis condition and hypnotic susceptibility by hypnosis condition are presented in Table 1 for frontal and temporal MMN averages, respectively.

3.1. Frontal MMN

A significant quadratic trend was evident for hypnosis instruction in the frontal MMN. There was no evidence for a linear trend (these are independent but not mutually exclusive polynomial contrasts) (see Table 1).

For the interaction between hypnotic susceptibility and hypnosis condition a significant linear trend was obtained. That is the difference between high and low susceptible groups changed linearly across the successive hypnosis conditions. Fig. 4 shows that pre-hypnosis frontal MMN is greater in the low susceptible group than the high susceptible group. This difference switches direction in the hypnosis condition and then further expands in that (reversed) direction in the post-hypnosis condition. There is no evidence for a quadratic trend in this interaction.

3.2. Temporal MMN

Neither a significant quadratic trend nor a linear trend was evident for hypnosis instruction in the temporal MMN (see Table 1).

Table 1
Planned polynomial contrasts

	Source	Contrast	df	*F*	Sig
MMN frontal	Hypnosis Condition (Pre, Hyp, Post)	Linear	1, 21	0.000	0.994
		Quadratic	1, 21	8.344	0.009**
	Hypnosis condition × susceptibility	Linear	2, 42	4.675	0.042*
		Quadratic	2, 42	0.031	0.861
MMN temporal	Hypnosis Condition (Pre, Hyp, Post)	Linear	1, 21	2.174	0.155
		Quadratic	1, 21	1.688	0.208
	Hypnosis condition × susceptibility	Linear	2, 42	5.417	0.030*
		Quadratic	2, 42	0.097	0.758

* $p < 0.05$.
** $p < 0.01$.

A significant linear trend was again obtained for the interaction between hypnotic susceptibility and hypnosis condition. However, the direction of change in the difference between high and low susceptible groups across successive hypnosis conditions is completely opposite to that displayed by frontal MMN above.

In this case Fig. 5 shows that pre-hypnosis temporal MMN is greater in the high susceptible than the low susceptible group. This difference dwindles greatly in the hypnosis condition and then expands in the reversed direction ('lows' greater than 'highs') in the post-hypnosis condition. There is again no evidence for a quadratic trend in this interaction.

4. Discussion

Our study set out to replicate, with a group of highly hypnotisable subjects, the frontal MMN increment reported in a single virtuoso hypnotic subject [17]. With the inclusion of a low hypnotically susceptible group we also sought to determine the contribution of four specific explanations of the reported effect. They were: situational hypnosis factors (a quadratic trend for condition); hypnotic state factors (a quadratic trend for condition by susceptibility interaction); a build up of MMN response over testing blocks (a linear trend for condition); or susceptibility related differences in the build up of MMN responses across testing blocks (a linear trend for condition by susceptibility interaction). We further sought to determine whether these patterns occurred in temporal as opposed to frontal MMN.

Our results did provide a replication of the increment in frontal MMN, extending the generality of previous findings [17] to a group of highly hypnotisable participants who were not in the hypnotic virtuoso range. For the highly susceptible participants frontal MMN did rise and fall with the induction and termination of hypnosis (showing a significant quadratic trend). However, the group of subjects with low hypnotisability, who were manifestly not hypnotised by the procedure, also demonstrated the same effect. Hence, the frontal increase in MMN, though related to the hypnosis condition, could not be attributed to distinctive hypnotic processes per se.

Additionally our inclusion of an analysis of temporal MMN disclosed important differences in the relationship between hypnosis condition and susceptibility at the frontal and temporal MMN components. Frontal MMN grew linearly in the high susceptibility group relative to the low susceptibility group across successive testing blocks (a significant linear trend for condition by susceptibility). In contrast, temporal MMN increased linearly in the low susceptibility group relative to the high group across successive testing conditions (a significant linear trend for condition by susceptibility but in the reverse direction). Thus frontal and temporal MMN responses built very differently over time in the two groups. These differences would not be possible if the components simply reflected activity in identical functional and neurophysiological networks, a possibility already excluded by Baldeweg et al. [1–3]. However, to properly disentangle the effects of the distinct generators contributing to temporal and frontal MMN, it will be necessary to move (in future studies) beyond scalp electrodes to a dipole source analysis and directly investigate changes in activity levels in the dipoles themselves.

The difference between high and low susceptibility groups taking the form of a linear increase across the three conditions may signify facilitation in frontal MMN processing and a possible call for the allocation of attentional resources [19] with continued exposure to the auditory stimuli in subjects with high rather than low hypnotisability; a similar effect was reported previously in the N100 difference wave recorded from central and frontal placements [11]. The contrasting linear increase, between groups, across the three conditions in temporal MMN may signify the construction of a stronger neural template of the standard stimulus in the auditory cortex, with continued exposure to the auditory stimuli, in subjects with low rather than high hypnotisability [3].

It may be worth noting in this context that hypnotic susceptibility has been reported to correlate with aspects of schizotypy [10,15] a construct which has been independently associated with alterations in MMN [2]. Whatever the explanation, the results of the present study (see also Williams and Gruzelier [29]) suggest that future investigations should also explore the immediate post-hypnotic period in relation to differences in neurophysiological functioning with high and low hypnotisability. These results also demonstrate the necessity of following up single case studies of hypnotic virtuosos [16,17] with designs allowing statistical comparisons of participants with high and low hypnotic susceptibility.

The current results (and those of Kallio et al. [17]) also raise possible issues for accounts of anterior functions in hypnosis. Both findings may suggest that the right frontal generator of the MMN is not diminished in activity during hypnosis, as it would be if hypnosis was accompanied by a global alteration of anterior cortical activity. The maintenance of right frontal functions is consistent with a model of altered frontal functions which posits that frontal alterations of function in hypnosis are largely left-sided [6,8].

Other results may also suggest this. For example highly susceptible subjects fluency for words designated by letter categories, which requires left dorsolateral pre-frontal activity, declines in hypnosis while fluency for words designated by semantic categories, which requires left temporal involvement, remains unimpaired [12]. This neuropsychological pattern was not observed in the group with low susceptibility [12,18]. Furthermore fluency for designs, which requires the integrity of the right frontal lobe, was unimpaired [12]. Other experiments have shown that haptic sorting times have declined with hypnosis in highly hypnotisable participants, and the decline was specific to the left hemisphere, within one experiment the left hemispheric decline correlated positively with the depth of hypnosis [4,9]. This possibility is being actively explored by current research within our laboratory.

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