



## Effects of sleep deprivation on auditory change detection: a N1-Mismatch Negativity study

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### ABSTRACT

The effects of sleep deprivation on neural activity underlying stimulus change detection are still debated. The aim of this study was to investigate the effects of sleep deprivation on the relationship between N1 refractoriness and Mismatch Negativity (MMN) as indexes of different stages of change detection. Respectively, N1 represents the sensory feature trace creation with stimulus repetition and MMN represents the memory-based detection of deviance in a new incoming stimulus. Event-related potentials (ERPs) were recorded from 22 healthy participants during a passive auditory oddball task after a night of normal sleep and after a night of total sleep deprivation (TSD). Importantly, stimulus presentation was organized as a train of 10 stimuli, so that N1 refractoriness could be measured as amplitude decrease with stimulus repetition within each train. Results showed that N1 refractoriness and MMN were not affected by TSD suggesting that the change detection process was preserved in our paradigm. However, the overall N1 amplitude increased after TSD, an effect that may be related to an enhancement of cortical excitability.

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### 1. Introduction

Sleep deprivation is associated with many sleep disruptive disorders and, more generally, with poor sleep hygiene. It has been associated with a decrease in performance involving several cognitive functions (Pilcher and Huffcutt, 1996; Banks and Dinges, 2007), such as attention (Drummond et al., 2001) and memory (Harrison and Horne, 2000).

Change detection processes are believed to be pre-attentive in nature, and therefore can be performed even when attention is reduced (Näätänen, 1990; Sussman, 2007). Moreover, they may be responsible for involuntary shifts of attention toward potentially dangerous stimuli (Näätänen, 1990; Schröger, 1996). In this context, the effects of sleep deprivation on change detection have captured the interest of many researchers. However, changes in the neural activity associated with stimulus processing and change detection after sleep deprivation are still debated.

Stimulus change detection is usually studied by means of the auditory oddball task. In this paradigm, a “standard” stimulus is repeatedly presented in a sequence and is occasionally replaced by a “deviant” stimulus differing from the standard stimulus along one physical feature (e.g. frequency, duration, etc.). According to the model developed by Näätänen and coworkers (Näätänen, 1990; Näätänen and Winkler, 1999; Näätänen et al., 2005), during the

repetition of the standard tone, a representation of the standard stimulus feature is created. When a deviant stimulus is presented, the deviant stimulus features are compared with the representation of the previously presented standard stimuli, leading to the detection of change.

This process is reflected in two components of electroencephalographic event-related potentials (ERPs): the N1 generated by the repeatedly presented standard stimulus and by the deviant stimulus, and the Mismatch Negativity (MMN) generated by the deviant stimulus presentation.

N1 is a negative wave peaking at about 50–150 ms after sound presentation with peak amplitude at the vertex and polarity inversion over inferior lateral regions (Peronnet et al., 1974). When an auditory stimulus is repeatedly presented with a short inter-stimulus interval (ISI) of a few seconds, N1 amplitude decreases at every repetition (Davis et al., 1966). The shorter the ISI, the stronger the decrease becomes (Mäntysalo and Näätänen, 1987; Ritter et al., 1968). This effect, called refractoriness, reflects a decrease of stimulus-specific responsiveness of N1 generators (Näätänen, 1988) and is thought to index the formation of the sensory feature trace of the standard stimulus (Näätänen and Picton, 1987).

MMN is a negative deflection elicited 100–250 ms after stimulus onset, in response to a change in one or more attributes of repetitive auditory stimulation (Näätänen and Winkler, 1999). MMN is usually calculated by subtracting the ERPs elicited by the standard stimulus from the ERPs elicited by the deviant stimulus, although it has been shown that this difference wave is a compound of a “genuine” MMN component and a N1 increase to the deviant sound (Jacobsen and

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Schröger, 2001; Jacobsen et al., 2003). MMN is believed to provide a physiological measure of memory-based stimulus discrimination. Along this line, MMN may be generated by a conflict of the current deviant sensory input with the active memory representation of previous stimulation (Watson et al., 2007) possibly through predictive models encoding stimulus regularity (Winkler, 2007). Therefore, the MMN can be elicited as long as the memory representation of standard stimulation is available for the matching process (Näätänen, 1992; Korzyukov et al., 1999; Schröger, 2007). Accordingly, several studies have shown that MMN decreases in amplitude with longer ISI and is generated for intervals up to 10–20 s (Mäntysalo and Näätänen, 1987; Sams et al., 1993; Sabri and Campbell, 2001).

Previous studies investigating the effects of sleep deprivation on change detection have found inconsistent results (Dikaya et al., 1992; Raz et al., 2001; Lee et al., 2004). Several studies have shown that MMN is unaffected by sleep quality in healthy subjects and patients (Salmi et al., 2005; Gosselin et al., 2006; Naumann et al., 2001), during wake–sleep transition (Ruby, et al., 2008; Winter et al., 1995), and after one night of sleep deprivation (Dikaya et al., 1992). On the other hand, a decrement in the MMN amplitude has been reported after short total sleep deprivation (Raz et al., 2001; Sallinen and Lyytinen, 1997) and during wake–sleep transition (Nashida et al., 2000; Sabri et al., 2000; Nittono et al., 2001; Sabri et al., 2003).

Whereas most studies have focused only on the MMN, some have also investigated the effects of sleep deprivation on the N1 amplitude. Raz et al. (2001), for example, showed that the N1 amplitude increases after one night of sleep deprivation, suggesting an association between a decrease in N1 refractoriness and MMN amplitude decrease. In fact, a lack of decrease in N1 amplitude over repeated stimulations would result in increased N1 amplitude averaged across all standards. Although plausible as a mechanism, this issue has never been approached in a thorough way. Moreover, at odds with the results of Raz and colleagues, a later study reported no changes in N1 amplitude after sleep deprivation in an oddball paradigm (Lee et al., 2004).

The aim of the present study was to investigate the effects of total sleep deprivation on change detection *separately* on the N1 elicited by repeated standard stimulation and on the MMN generated by the deviant stimulus presentation. In particular, we investigated the creation of a sensory feature trace with standard repetition and the fading of the stimulus discrimination process with increasing ISIs. We developed a new auditory oddball paradigm based on the study of Cowan et al. (1993), in which stimuli were presented in trains with specific ISIs. We measured the N1 refractoriness with the repetition of the standard tone as an index of the sensory features trace creation, and the modulation of MMN amplitude with different ISI as an index of change detection.

## 2. Methods

### 2.1. Participants

Twenty-two undergraduate students (11 males, aged 20 to 29) participated in this experiment. Data from two participants was subsequently rejected due to excessive artefacts in the EEG signal. All participants reported no medical or psychiatric disease, or ongoing pharmacological treatment. All participants gave written consent, and were told that they were free to leave the experiment at any time. Moreover, to increase compliance to the experimental schedule, they received 75 euros once they completed both the experimental sessions. The study was approved by the Ethics Committee of Psychology Research of the University of Padova.

### 2.2. Task

The task was a passive auditory oddball paradigm during which participants read a book without paying attention to the sounds. Participants were monitored through a video camera and were

engaged in conversation about the book at the end of the experiment, to make sure that they were compliant with the experiment requirements.

Acoustic stimuli were pure tones of 50 ms duration and 5 ms rise/fall time, generated by Cool Edit Pro 1.2 (Syntrillium Software Corporation) and delivered binaurally through an electrically shielded headphone (Sony DJ MDR-V150). The automated delivery of stimuli was controlled by a PC provided with E-Prime software (Psychology Software Tools, Inc.).

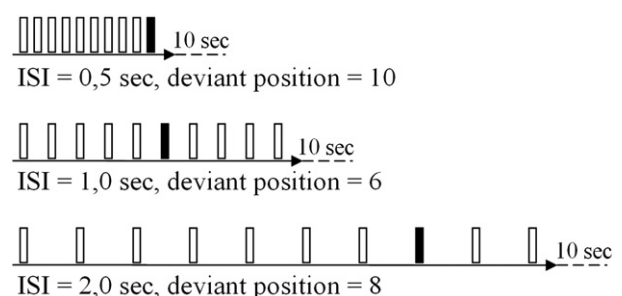
Auditory stimuli were delivered in trains of ten tones (9 standard and 1 deviant) separated by 10 s inter-sequence intervals. Each train was uniquely characterized by its own specific standard/deviant pair, ISI and position of the deviant stimulus within the sequence. Standard and deviant stimuli were different in frequency. Five of the nine different pairs of standard and deviant stimuli used by Cowan et al. (1993) were chosen: 420–490 Hz, 510–595 Hz, 600–700 Hz, 690–805 Hz, 780–910 Hz. The deviant/standard frequency ratio was 7:6 in half of the trains (high pitch deviant and low pitch standard), and 6:7 in the other half (low pitch deviant and high pitch standard). In each train the ISI was 0.5 s, 1 s or 2 s. The deviant stimulus could occur in position 6, 8 or 10 of the sequence (see Fig. 1 for a schematic representation of trains of stimuli at different ISIs in which the deviant stimulus occurred in different positions). In order to avoid long-term memory effects, the trains had a quasi-random distribution in which two consecutive trains could not have the same frequency values.

We chose to present several pairs of standard/deviant stimuli so that the creation of the standard sensory trace took place independently for each stimulus train and without involving long term consolidation of the standard representation from previous presentation. Moreover, consecutive trains never had the same ISI in order to minimize the effect of temporal probability of the deviant presentation (Sabri and Campbell, 2001). 1800 stimuli in 180 trains (1620 standards and 180 deviants) were delivered for each recording session.

### 2.3. Procedure

The experiment consisted of four sessions. The first two sessions were recorded in the morning and in the evening after a normal night of sleep (control condition). Two weeks later, the same two sessions were recorded after a night of total sleep deprivation (sleep deprivation condition). Half of participants performed the control condition first, while the other half performed the sleep deprivation condition first. Participants completed a sleep diary during the week prior to the first experimental condition and during 2 weeks between the first and the second experimental condition in order to exclude the presence of sleep disorders or poor sleep hygiene (i.e., highly variable sleep schedules, sleep restriction, etc.).

Participants spent the night of sleep deprivation in the laboratory with a researcher monitoring their activity. They could watch movies,



**Fig. 1.** Oddball paradigm. Schematic representation of short trains of stimuli. Each train included ten stimuli (rectangles), nine standard (white) and one deviant (black). The first five stimuli of each train were always standard stimuli. The deviant stimulus could appear in position 6, 8 or 10. Stimuli within trains were separated by one out of three different ISI (0.5, 1 or 2 s). Trains of stimuli were separated by an interval of 10 s.

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