The initial orienting response during human REM sleep as revealed by the N1 component of auditory event-related potentials

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Abstract

The large N1 wave of the auditory event-related potentials (ERPs) typically occurring to the first stimulus after a long silent interval seems to be associated with the involuntary initial-orienting response. Since the mechanisms involved in the generation of this brain response are assumed to be activated automatically, the present study aims at determining whether this electrophysiological response can also be elicited during human REM sleep, the sleep stage considered most sensitive to external stimuli. To achieve this goal, the auditory N1 wave was analyzed in wakefulness and REM sleep for frequency deviant tones delivered in several positions (1, 2, 4 and 6) within homogenous stimulus trains separated by different intervals of silence (3, 6 and 9 s), the intra-train stimulus interval being 600 ms. A significant increment in the amplitude of the N1 component for the first deviant tone, as compared with deviants delivered in remaining positions, was observed in both brain states, independently of the inter-train interval length. This result cannot be explained by a release-from-refractoriness effect, since only one deviant was presented in each train and the inter-deviant interval hardly changed from one train to another. The increase in N1 to the first stimulus of the train, probably due to the contribution of the neuronal elements responsible for the supratemporal and non-specific components, may be explained by changes in the silent interval, rather than by variations in the stimulus frequency. The enhanced N1 could be reflecting a general increase in sensory sensitivity associated with the arousal factor of the orienting response. These findings suggest that the brain maintains the potential ability to trigger the brain events responsible for the OR elicitation, even during REM sleep. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Orienting response; N1; Auditory event-related potentials; Sleep; REM sleep

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1. Introduction

Psychophysiological evidence suggests that the N1 wave of the auditory event-related potentials (ERPs) reflects the outcome of spatial and temporal overlapping of, at least, five different components, depending on the physical and temporal characteristics of stimulation and the general state of the subject. Three of these components were proposed by Näätänen and Picton (1987) to have different brain generator sources. Neuronal populations involved in generating one of them are located bilaterally in the supratemporal auditory cortices (Vaughan and Ritter, 1970; Giard et al., 1994), another component is generated in the lateral surface of the temporal lobes (Wolpaw and Penry, 1975), and the third one is the non-specific component, whose brain generator sources are probably in the frontal motor and premotor cortex (Näätänen and Picton, 1987). According to Näätänen’s model on the controlled versus automatic processing of auditory information (Näätänen, 1990, 1992), both the supratemporal and non-specific components seem to reflect the activation of a transient-detector system, especially sensitive to onsets and offsets of continuous stimulation (Loveless and Brunia, 1990), and to variations in the interstimulus interval (Hari et al., 1982; Lü et al., 1992a, b). Two additional components of N1 wave, reported by Alcaini et al. (1994), are generated in the frontal regions: the earliest is considered an obligatory component evoked independently of stimulation rate, and the later one is only elicited for interstimulus intervals longer than 4 s.

Some of the N1 components seem to be involved in the initiation of the involuntary orienting response (OR) towards a novel stimulus, specifically the supratemporal component (Escera et al., 1998), the non-specific N1 (Näätänen and Picton, 1987), and the later frontal negative wave proposed by Alcaini et al. (1994) — which could be equivalent to the non-specific component. Likewise, there is another auditory potential, independent of N1, that can be recorded in the same temporal interval when a discernible physical or temporal change is introduced in a homogeneous stimulus sequence: the mismatch negativity (MMN). MMN, which also receives contribution from generators in frontal areas (Giard et al., 1990; Alho et al., 1994; Molnár et al., 1995; Levänen et al., 1996; Alain et al., 1998; Deouell et al., 1998; Kasai et al., 1999), has also been proposed to index brain processes able to initiate — but not elicit — the orienting response to unattended auditory stimulus changes (Schröger, 1996; Escera et al., 1998; for a review, Escera et al., 2000). Thus, while neural elements generating the N1 components are more easily activated by a high degree of stimulus novelty, the neural mechanisms underlying the MMN component are mainly responsible for stimulus change detection — even for small stimulus variations — postulated by the orienting-reflex theory (Sokolov, 1963; see also Bernstein, 1979). Nevertheless, detection of a mismatch is not condition enough to elicit an OR; indeed, the level of significance seems to be an additional and necessary condition for an OR to be elicited by a change in stimulation (Gati and Ben-Shakhar, 1990). On the other hand, several investigators argue that OR is a positive function of the amount of the stimulus change (Siddle and Heron, 1976; Campbell and Haroutunian, 1983; Johnen and Schnitzler, 1989). This would explain the fact that MMN, which shows change detection, is not always accompanied by changes in the autonomic nervous system responses that indicate elicitation of OR (Lyytinen et al., 1992), or by the P3a component of the ERPs, which indicates the involuntary attention shifting to a novel stimulus (for a review, Escera et al., 2000).

Accordingly, the supratemporal and non-specific N1 components, as well as the frontal component of MMN, are assumed to index the activity of early neural mechanisms involved in the initiation of the involuntary OR. Since these brain responses are expected to be generated automatically, even in the absence of attention, they must also be elicited in other brain states different from wakefulness. MMN has been recorded in human subjects, at least for frequency-deviant stimuli, during drowsiness (Salminen and Lyytinen, 1997), stage 2 of sleep (Campbell et al., 1992; Salminen et al., 1994; Loewy et al., 1996), and REM sleep (Loewy et al., 1996;
Atienza et al., 1997, 2000) with a smaller amplitude, shorter latency and duration as compared with the waking state. As shown by results obtained in these studies, the change-detection mechanisms remain active in the wake/sleep continuum. Therefore, it can be expected that the brain mechanisms responsible for initiating OR remain active in other brain functional states.

On the basis of the fact that the large N1 wave typically occurring to the first stimulus after a long, silent interval (Näätänen and Gaillard, 1983) — due to the contribution of the supratemporal and, especially, the non-specific component (Näätänen and Picton, 1987) — is associated with the involuntary initial-orienting response (O’Gorman, 1979), the present study aims at determining whether this electrophysiological response can also be elicited during human REM sleep, the sleep stage considered most sensitive to external stimuli (Niiyama et al., 1994). To reach this goal, the auditory N1 wave was analyzed in wakefulness and REM sleep for frequency-deviant tones delivered in several positions within homogenous stimulus trains separated by intervals of silence of different lengths. Since the inter-deviant interval hardly changed from one train to another in this paradigm, an increase in the N1 amplitude associated with the deviant tone in the first position of the train could not be explained by a release-from-refractoriness phenomenon, as in the case of a repetitive stimulus (Ritter et al., 1968; Näätänen and Picton, 1987; Näätänen, 1990, 1992). Thus, the N1 increment could be considered as an electrophysiological index of the initial-orienting response in both brain states, supporting the hypothesis suggested by Näätänen and Picton (1987) that this rise in amplitude is due to a general increase in sensory sensitivity, independently of brain state.

2. Materials and methods

2.1. Subjects

Polysomnographic recordings were obtained from 27 student volunteers (13 women) ranging between 18 and 27 years. All subjects were screened for health status with a structured medical interview, and sleep questionnaires were used to confirm the absence of sleep disorders. They were instructed to abstain from alcohol and caffeine during the 24 h prior to the experimental session. In addition, the subjects were asked to fill in a sleep diary for the 2 weeks previous to the experiment in order to assure a regular and normal sleep–wake schedule. Previously, every subject gave informed consent to participate after a full explanation of the experimental procedure.

2.2. Experimental procedure

Sleep recordings were conducted in an acoustically and electrically shielded room during 2 consecutive nights, first for adaptation, for those subjects who had not previously participated in sleep studies (9 subjects). Stimulation was presented during REM sleep — only during the second night — and the following morning. In the latter case, subjects read a book and were asked to ignore the auditory stimuli.

Train bursts of nine tones of 1000 Hz (standard) and one tone of 2000 Hz (deviant) lasting 60 ms (including a rise–fall time of 5 ms) were presented binaurally via insert earphones (Etymotic Research®, Model ER-3A) at an intensity of 80 dB SPL. The deviant tone could appear in position 1, 2, 4 or 6 within the train. The interstimulus interval (600 ms) was kept constant within the stimulus train, and three silent intervals of 3, 6 and 9 s were examined in three separate groups of subjects (nine subjects per group). Auditory stimulation during sleep started just after the first ocular movements that occurred in the REM stage, and was stopped after a change in the arousal level (presence of K-complexes, continuous alpha activity, increasing EMG level), bodily movements, and/or signals indicating a sleep stage change. Stimulation delivered during the first REM sleep period was always rejected because of the frequent fluctuations in the arousal level. The first stimulus train of each block, as well as the first one after an interruption of stimulation, was also rejected from the analyses.
2.3. Recording and data analysis

Electroencephalographic (EEG) activity was recorded along the midline at Fz, Cz, Pz and Oz. In addition, six lateral electrodes were placed on the two hemispheres connecting the mastoids through Fz. These electrodes will be referred to as L1, R1 (1/3 of the distance from Fz to each mastoid), L2, R2 (2/3 of the distance from Fz to each mastoid), and L3, R3 (left and right mastoids), respectively. An electrode placed on the tip of the nose was used as reference. Electrooculographic (EOG) activity was recorded from the upper and lower canthi of the left and right eyes, and the submental electromyography (EMG) from a bipolar chin montage. All electrophysiological parameters were amplified and recorded on a Medicid 4 system (Neuronic*) and digitized online at 250 Hz. Both EEG and EOG were bandpass-filtered at 0.1 and 100 Hz, whereas EMG was filtered at 5 and 70 Hz. Impedance of electrode/skin was kept below 5000 Ω in all cases. All-night sleep recordings were independently scored by three different sleep technologists according to standard criteria (Rechtschaffen and Kales, 1968).

Artifact-free epochs of 600 ms, including a 100-ms pre-stimulus baseline, were selected in each trial. Trials with an EEG- or EOG-amplitude change exceeding ±75 µV were rejected. After averaging, the signals were digitally filtered with a cutoff frequency of 30 Hz (3 dB down). ERPs to deviant stimuli (at least 50 trials) were averaged for each experimental condition and subject.

The N1 amplitude was measured for standard and deviant tones as both the maximum peak relative to pre-stimulus baseline and the P1–N1 peak-to-peak amplitude at Cz, where the supratemporal component of N1 shows a similar amplitude to that recorded at Fz and the non-specific component is supposed to be larger (Hari et al., 1982; Scherg and von Cramon, 1985). N1 latency was defined as the delay time from stimulus onset to maximum peak. Differences in amplitude and latency for each type of stimulus were assessed using a mixed-model analysis of variance (ANOVA) with the inter-stimulus interval (ITI) (3, 6 and 9 s) as the between-subject factor, and brain state (waking and REM sleep) and position of deviant (1, 2, 4 and 6) as the within-subject factors. Significance levels of the $F$ ratios were adjusted with the Greenhouse–Geisser correction where appropriate.

3. Results

3.1. Standard stimuli

Fig. 1 shows superimposed grand average ERPs to standard tones occurring in position 1, 2, 4 and 6 within the train at Cz for each ITI condition (3, 6 and 9 s), both in wakefulness and REM sleep.

The three-way ANOVA with repeated measurements (brain state × position × ITI) showed significant main effects of the brain state [$F(1,24) = 44.9, P < 0.001$] and position factors [$F(3,72) = 13.46, P < 0.001, \varepsilon = 0.926$], as well as a signifi-
cant interaction between these two factors \[ F(3,72) = 2.68, P < 0.045, \varepsilon = 0.813 \]. The examination of the interaction effect yielded that the N1 amplitude was dependent on the stimulus position within the train during both brain states [waking: \( F(3,72) = 15.91, P < 0.001, \varepsilon = 0.829; \) REM: \( F(3,72) = 3.49, P < 0.022, \varepsilon = 0.977 \)]. However, N1 reached a larger amplitude to the first standard tone as compared with remaining standard tones during wakefulness [\( F(3,32) = 13.47, P < 0.0001 \)], but in REM sleep, there were differences only between the N1 response elicited by the standard tone in position 1 and 6 [\( F(3,32) = 2.81, P < 0.05 \)]. Therefore, the increment of the N1 to first stimulus was observed in both brain states, but the magnitude of the effect was much larger in wakefulness. Such an increase associated with the standard tone at the beginning of the train, after a silent interval, was expected to be found, since a silence of 3, 6 or 9 s is enough time for the neuronal population underlying the supratemporal N1 component to restore, partially or fully, its excitability before stimulation Hari et al., 1982, 1989; Lu et al., 1992a,b.

N1 reached its maximum with a longer latency during REM sleep as compared with wakefulness [\( F(1,24) = 28.34, P < 0.001 \)]. The differences found after comparing the four positions of the standard tone within the train [\( F(3,72) = 10.61, P < 0.001, \varepsilon = 0.496 \)] were due, according to post hoc analyses, to a shorter latency for those stimuli delivered in position 4 and 6 [\( F(3,32) = 5.93, P < 0.0025 \)]. These differences were dependent on the brain state [\( F(3,72) = 5.51, P < 0.004, \varepsilon = 0.643 \)]. Thus, the N1 latency was longer for tones in position 1 as compared with the remaining stimulus positions only during wakefulness [\( F(3,32) = 12.12, P < 0.0001 \)].

3.2. Deviant stimuli

Fig. 2 illustrates superimposed grand average ERPs to deviant tones delivered in position 1, 2, 4 and 6, for 3-, 6- and 9-s ITIs from various electrodes during wakefulness. Fz, Cz, and Pz were those of 10–20 system. R3 was at the right mastoid, while R1 and R2 were 1/3 and 2/3 from Fz to R3, respectively. L1, L2 and L3 were the homologous positions at the left side. Note the larger amplitude of the N1 component to deviants in position 1, especially at Cz, and the absence of this effect at mastoids.

Both figures, frequency deviants elicited a complex P1–N1–P2 that showed its maximum amplitude at Cz and tended to invert in polarity at mastoids, especially during wakefulness. As previously reported in the literature, the N1 potential was larger in waking, while the two positive waves showed an enhanced amplitude during REM sleep (for a review, Campbell et al., 1992). Statistical analyses confirmed that N1 reached a larger amplitude in wakefulness than in REM sleep [\( F(1,24) = 23.38, P < 0.001 \)], in spite of the volt-
age values included in the ANOVA being defined as P1–N1 peak-to-peak, which were proved to be less dependent on the brain state (Lugt et al., 1996).

The N1 wave showed an increased amplitude for the deviant tones occurring at the beginning of the train in comparison with the rest of deviant stimuli in both brain states. This increment was especially evident at Cz (Figs. 2 and 3). A main effect of deviant position factor on the N1 amplitude was later confirmed by the three-way ANOVA \(F(3,72) = 31.42, P < 0.001, \varepsilon = 0.728\), and the post hoc analyses proved that N1 to first deviant was significantly larger than N1 to deviants in any other position \(F(3,32) = 13.04, P < 0.0001\). This effect of the deviant position within the train on the N1 amplitude was equally noticeable when the amplitude was defined as the maximum peak deflection relative to baseline \(F(3,72) = 4.93, P < 0.001, \varepsilon = 0.827\). Table 1 includes the two measurements of the N1 amplitude to deviant stimuli (maximum peak relative to pre-stimulus baseline and P1–N1 peak-to-peak) and standard errors at Cz for all experimental conditions. The increased amplitude shown by N1 potential to the first deviant after the three silent intervals was similar in wakefulness and REM sleep, since no interaction between position and brain state, and/or ITI factors, was found.

Table 2 presents the mean peak latency at Cz in the different experimental conditions (only for deviant tones). It was modulated by the brain state, mean latency being approximately 12 ms longer during REM sleep \(F(1,24) = 19.04, P < 0.001\). The ANOVA also yielded a significant effect of the deviant position factor \(F(3,72) = 14.59, P < 0.001, \varepsilon = 0.976\). This effect was due to N1 elicited by the first deviant tone, reaching the maximum amplitude with a delay time of approximately 6–8 ms with regard to the other deviant positions, as confirmed by the post hoc analyses \(F(3,32) = 4.22, P < 0.007\). No differences in the N1 latency were found as the ITI increased. Neither did the ANOVA show significant interaction effects.

4. Discussion

The present results support the hypothesis of O’Gorman (1979), that neural mechanisms responsible for the OR to the first stimulus of a train and to a stimulus change within the train are not necessarily identical. Thus, the first deviant tone presented after different silent intervals resulted in an increment in the N1 amplitude as compared with deviant stimuli delivered in other positions within the train. This increase cannot be explained by different refractory periods of neural populations involved in the N1 generation, as would be in the case of repetitive stimuli, since only one frequency deviant stimulus was delivered in each train and the inter-deviant interval hardly changed from one train to an-
Table 1
Mean amplitude and standard error (in parentheses) defined as both the maximum peak deflection relative to prestimulus baseline and P1–N1 peak-to-peak for N1 component to deviant tones at Cz, during wakefulness and REM sleep, for positions 1, 2, 4, 6 and ITI conditions (3, 6, 9 s)

<table>
<thead>
<tr>
<th>Experimental conditions</th>
<th>Waking</th>
<th>REM sleep</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Maximum peak (µV)</td>
<td>P1–N1 (µV)</td>
</tr>
<tr>
<td><strong>3-s ITI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p1</td>
<td>−5.59 (2.82)</td>
<td>6.59 (3.03)</td>
</tr>
<tr>
<td>p2</td>
<td>−2.97 (2.24)</td>
<td>4.76 (1.86)</td>
</tr>
<tr>
<td>p4</td>
<td>−2.57 (3.03)</td>
<td>4.29 (2.69)</td>
</tr>
<tr>
<td>p6</td>
<td>−2.94 (2.45)</td>
<td>4.53 (2.23)</td>
</tr>
<tr>
<td><strong>6-s ITI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p1</td>
<td>−5.44 (2.76)</td>
<td>6.87 (3.18)</td>
</tr>
<tr>
<td>p2</td>
<td>−3.84 (2.00)</td>
<td>4.46 (1.81)</td>
</tr>
<tr>
<td>p4</td>
<td>−2.79 (0.91)</td>
<td>4.59 (2.14)</td>
</tr>
<tr>
<td>p6</td>
<td>−2.62 (1.25)</td>
<td>4.32 (1.77)</td>
</tr>
<tr>
<td><strong>9-s ITI</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p1</td>
<td>−4.98 (2.17)</td>
<td>6.53 (2.11)</td>
</tr>
<tr>
<td>p2</td>
<td>−3.57 (2.83)</td>
<td>4.20 (1.63)</td>
</tr>
<tr>
<td>p4</td>
<td>−2.44 (1.41)</td>
<td>3.34 (1.47)</td>
</tr>
<tr>
<td>p6</td>
<td>−2.47 (1.88)</td>
<td>3.72 (1.72)</td>
</tr>
</tbody>
</table>

Other. This result may be attributed to the two simultaneous changes associated with the deviant in the first stimulus position of the stimulus train. On the one hand, the interval changed from regular 0.6 s to a much longer 3, 6 or 9 s, and, on the other, tone frequency changed from 1000 to 2000 Hz. However, variation in the silence length seems to be mainly responsible for the enhanced N1, since changes in the ITI were only associated with the deviant in position 1, whereas changes in frequency would have affected all deviant tones independently of the position within the train.

Furthermore, N1 in response to standard tones in position 1 showed a similar increment in all ITI conditions in the wakefulness state (Fig. 1). Therefore, the rise in the N1 amplitude, probably due to the contribution of neural elements involved in generation of the non-specific component, may be indexing the automatic initial OR that typically appears associated with the first stimulus after a long interval of silence. However, the most interesting result was the elicitation of this brain response even during REM sleep. This finding suggests that the increased N1 component

Table 2
Mean latency and standard errors (in parentheses) of N1 component to deviant tones at Cz, defined as the delay time to peak deflection from stimulus onset during wakefulness and REM sleep, for positions 1, 2, 4, 6 and ITI conditions (3, 6, 9 s)

<table>
<thead>
<tr>
<th>Position of the deviant within the stimulus train</th>
<th>Waking</th>
<th>REM sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p1 (ms)</td>
<td>p2 (ms)</td>
</tr>
<tr>
<td><strong>Waking</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 s</td>
<td>116.67 (13.72)</td>
<td>112.72 (11.10)</td>
</tr>
<tr>
<td>6 s</td>
<td>121.36 (9.74)</td>
<td>116.41 (7.50)</td>
</tr>
<tr>
<td>9 s</td>
<td>111.50 (15.84)</td>
<td>109.74 (13.82)</td>
</tr>
<tr>
<td><strong>REM sleep</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 s</td>
<td>135.94 (7.50)</td>
<td>122.40 (15.74)</td>
</tr>
<tr>
<td>6 s</td>
<td>133.85 (12.93)</td>
<td>123.18 (10.73)</td>
</tr>
<tr>
<td>9 s</td>
<td>126.49 (14.24)</td>
<td>126.30 (16.45)</td>
</tr>
</tbody>
</table>
to first stimulus could then reflect the *arousal factor* of OR proposed by Näätänen (1992), which is assumed to be independent of the arousal level and to facilitate a general increase in sensory sensitivity (Näätänen and Picton, 1987).

A possible explanation for the increase in the N1 amplitude to the first deviant as compared with the remaining deviant tones could be the overlapping with an MMN component, which indexes the automatic change detection. However, in a previous study, using the same experimental paradigm, the MMN component was elicited by the frequency-deviant tones during human REM sleep only after a silence of 3 s, as confirmed by a similar topographic distribution of this component in waking and REM sleep (Atienza et al., 2000). While no differences in the MMN amplitude were found in the previous experiment between different positions in which deviant tones took place, the present results showed highly significant differences in the N1 amplitude in comparing deviants in position 1 with deviants in the remaining positions. In addition, in contrast to the decrease in the MMN amplitude as the silent interval was longer, the N1 amplitude to first deviant tone in the present study showed no variations for the different conditions of the ITI variable (Figs. 2 and 3). According to these findings, the overlapping of N1 with MMN to the first deviant tone of the train during REM sleep may be possible for the 3-s ITI, but not for the longer ITIs.

Taking together the results obtained with the previous and the present study, recording of the N1 and MMN components suggests the activation of two independent neural mechanisms. According to the model of Näätänen (1990, 1992), the brain response to the first stimulus of the tone train would reflect the outcome of the transient-detector system, which is independent of memory processes, while the mechanisms involved in the MMN generation would be activated by the stimulus-change detector system, which is dependent on information being retained for a period of several seconds in sensory memory system. It can be inferred from the topographical distribution of the N1 potential to frequency deviant tones in both brain states (Figs. 2 and 3) that a physical change at the beginning of the stimulus train after a long silent interval would likely activate the non-specific N1 generators associated with the involuntary initial OR, while the introduction of this change within the stimulus train would probably activate MMN generator mechanisms, provided that there is an activated neuronal representation of repetitive stimulation, which does not always initiate the OR. In agreement with this, the negative wave recorded during REM sleep at approximately 300 ms showed an increment for deviant tones in position 2, 4 and 6, suggesting that the auditory change detection had most likely already happened. In two other studies, a similar negativity was reported to be elicited by the deviant stimulus (Winter et al., 1995; Nordby et al., 1996). Although these late negative waves were recorded under different conditions, and hence, could be interpreted in different ways, all of them indicate that the deviant stimulus receives a high and prolonged processing level, even during sleep.

The N1 amplitude was smaller during REM sleep as compared with wakefulness, in spite of the P1–N1 peak-to-peak amplitude being reported to be less influenced by the brain state (Lugt et al., 1996). N1 tended to invert its polarity at mastoids in waking and REM sleep, probably due to our reference at the nose tip being slightly more negative than the mastoid sites, but the N1 amplitude in these electrodes was not affected by the position of the deviant tone within the train. The absence of such an effect could be explained by the fact that the signal-to-noise ratio at the mastoid sites was too low to demonstrate the effect of the deviant stimulus position. Nevertheless, differences in amplitude between the N1 to first deviant and the deviant stimuli in other positions were independent of the brain state, supporting the hypothesis postulated by Näätänen and Picton (1987) that the *energetic or arousal factor* of OR is not affected by a different arousal state. In contrast, the *attentional factor* of OR, which consists of an attention shift to a novel stimulus as revealed by the P3a component of ERPs, is likely to be more dependent on the arousal level, as was suggested by studies that found a modulation of this component by atten-
tion (Woods, 1992). In this sense, a larger increment of the positive wave in the 350–400 ms range with a frontocentral topographic distribution can be observed during the wakefulness state for the longest ITI (Fig. 2), suggesting the presence of a P3a. However, the positive potential obtained during REM sleep showed a maximum amplitude over parietal regions (Fig. 3), which could be equivalent to P3b, as previously shown when the deviant tone in wakefulness was both a relevant (Niiyama et al., 1994) and irrelevant stimulus (Bastuji et al., 1995; Pratt et al., 1999). Therefore, the present results suggest that the early neural mechanisms involved in the initiation of OR (independent of brain state) do not always lead to an OR elicitation (dependent on brain state).

To date, no previous study to our knowledge has found either electrophysiological or autonomic changes that index the brain events leading to initiation of an OR towards neutral stimuli in sleeping humans. The larger amplitude for the first deviant N1 obtained in the present study, both in wakefulness and REM sleep after a long silent interval, was probably caused by the different degree of novelty associated with this stimulus, as compared with the frequency change occurring within the train. According to the model proposed by Gati and Ben-Shakhar (1990) to explain and predict the effects of novelty and significance of psychophysiological responsivity, the degree of novelty is interpreted in terms of the degree to which the stimulus input matches the stimulus set that preceded it in a given context. Stimulation by train bursts allowed us to assess the auditory sensory processing of the same stimulus in two different contexts, when preceded by a set of tones that only differ in one physical feature, and by a long interval of silence. As shown by the present results, the degree of novelty seems to be larger in the latter case. Different studies provided evidence that novelty is a sufficient requirement to produce an OR (Siddle et al., 1979; Ben-Shakhar and Lieblich, 1982; Ben-Shakhar et al., 1982, 1989), but not the only one. According to the present results, the increment in the N1 amplitude to deviants at the start of the stimulus train, as a result of a contribution of the non-specific component, may index the activation of early neural mechanisms initiating the OR. This activation probably facilitates the later processing of eliciting stimulus, both in wakefulness and REM sleep, but does not necessarily lead to OR elicitation.

The experimental paradigm used seems to be appropriate for the study of the early neural mechanisms involved in the OR, and for demonstrating that these mechanisms can also be activated during REM sleep. This finding suggests that the dreaming brain maintains the potential ability to trigger the brain events responsible for the OR elicitation, provided that the external stimulation is highly meaningful for the organism. Since the impossibility of dissociating the habituation phenomenon from a release-from-refractoriness effect after a long interval of silence by using ERPs (e.g. Barry et al., 1992), future experiments are necessary to study the relationship between the N1 potential associated with the first stimulus after a silence and changes in autonomic responses. Results from these studies would permit us to test the viability of using this brain response as an index of early OR neural mechanisms. Such a response could then be utilized successfully in coma patients, better than the N1 to standard and deviant tones in a classical oddball paradigm, which has been demonstrated to be less specific than MMN in predicting return to consciousness (Fischer et al., 2000). It might be expected to find larger differences between the N1 amplitude to first deviant as compared with the others within the train in those patients with a major probability of leaving the coma state.

References


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