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Clinical Neurophysiology 112 (2001) 2031–2045

www.elsevier.com/locate/clinph

Auditory information processing during human sleep as revealed by event-related brain potentials

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Accepted 2 August 2001

Abstract

The main goal of this review is to elucidate up to what extent pre-attentive auditory information processing is affected during human sleep. Evidence from event-related brain potential (ERP) studies indicates that auditory information processing is selectively affected, even at early phases, across the different stages of sleep–wakefulness continuum. According to these studies, 3 main conclusions are drawn: (1) the sleeping brain is able to automatically detect stimulus occurrence and trigger an orienting response towards that stimulus if its degree of novelty is large; (2) auditory stimuli are represented in the auditory system and maintained for a period of time in sensory memory, making the automatic-change detection during sleep possible; and (3) there are specific brain mechanisms (sleep-specific ERP components associated with the presence of vertex waves and K-complexes) by which information processing can be improved during non-rapid eye movement sleep. However, the remarkably affected amplitude and latency of the waking-ERPs during the different stages of sleep suggests deficits in the building and maintenance of a neural representation of the stimulus as well as in the process by which neural events lead to an orienting response toward such a stimulus. The deactivation of areas in the dorsolateral pre-frontal cortex during sleep contributing to the generation of these ERP components is hypothesized to be one of the main causes for the attenuated amplitude of these ERPs during human sleep. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Auditory event-related potentials; Pre-attentive processing; Sleep; N1; Mismatch negativity; P3a; Evoked K-complexes

1. Introduction

It is well known that the sleeping brain is not fully disconnected from its environment. In fact, many external stimuli incoming during sleep can reach consciousness if they eventually lead to awakening. Conditions in which environmental events are capable of waking the sleeping organism may vary considerably, depending on the interaction of several factors, such as the nature of the external input, the ongoing brain state, the stage of cerebral development, previous experience, drug status, and mental or physical illness. Moreover, the combination of these factors will finally determine the level of analysis that a particular external stimulus will receive.

According to cognitive models of information processing, external inputs may be analyzed under pre-attentive or attentive conditions. Pre-attentive processing is considered to be a fast, parallel, and effortless processing that is not under the direct control of the subject intentions or motivations (equivalent to the 'automatic' processing, see Schneider et al., 1984). In contrast, attentive processing is slow, serial, subject-regulated, and depends on the capacity to allocate the available attentional resources to external events (equivalent to 'controlled' processing, see Schneider et al., 1984). These two types of processing may be differently modulated throughout the sleep–wakefulness continuum.

From a homeostatic perspective, wakefulness and sleep are considered as integrated states of physiological variables. The wakefulness-to-sleep transition, the well established sequence of the non-rapid eye movement (NREM) sleep (stages 2–4), and the NREM and REM sleep cycles, appear as global long-lasting brain states being defined by their characteristic fluctuations of the background electroencephalographic (EEG) activity, and determined by homeostatic demands (e.g. Borbély, 1982). However, within each of these global brain states, transient events, occurring spontaneously or elicited in response to external stimuli, can also be observed in the EEG background. The functional

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1388-2457/01/$ - see front matter © 2001 Elsevier Science Ireland Ltd. All rights reserved.
PII: S1388-2457(01)00650-2

significance of these transient events is to preserve the continuity of the global activation state and to ensure arousability in response to external/internal changes (Halász, 1998; Cantero and Atienza, 2000).

External stimuli often elicit noticeable changes in the EEG background observable to the naked eye. Usually, these changes are, however, only seen after an exhaustive analysis of the EEG signals, by means, for instance, of the averaging method to disclose event-related brain potentials (ERPs). ERPs are voltage deflections recorded from the scalp arising from summated postsynaptic potentials of large neural populations (Hillyard and Picton, 1987). The amplitude and latency of successive peaks in the ERP waveform can be used to determine the time course of information processing in the brain, whereas the distribution of voltage over the scalp can be used to estimate, with the appropriate computational analysis, the neuroanatomical loci of these processes.

In the auditory modality, ERPs generated in the brainstem within the first 10–12 ms from a stimulus onset are not affected by the different sleep–wake states (Campbell and Bartoli, 1986), but rather by body temperature variations (Bastuji et al., 1988). However, the brain state has been shown to exert a clear effect on external information processing as indicated by changes in the amplitude of middle-latency ERPs, occurring from 15 to 50 ms from stimulus onset. These brain responses, which probably reflect thalamo-cortical activity (Picton et al., 1974), suffer a progressive amplitude decrease from wakefulness to stage 4 of slow wave sleep (SWS), but they can surpass waking values during REM sleep (e.g. Deiber et al., 1989). Subsequent stages of information processing, as indexed by longer-latency ERP components, can be expected, therefore, to be selectively affected by the different states of the sleep–wakefulness continuum.

In the present review, we will focus on brain-state specific modulation of pre-attentive information processing conveyed from 50 ms after the occurrence of an acoustic event, as indicated by long-latency auditory ERPs. The extraction of stimulus features and the emergence of sensory feature traces seem to be reflected, at least in wakefulness, in the N1 component of the ERPs (Näätänen and Picton, 1987; Näätänen and Winkler, 1999), whereas the formation of the auditory stimulus representation in sensory memory is indexed by the mismatch negativity (MMN) (Näätänen, 1992; Näätänen and Winkler, 1999). Neural mechanisms underlying both the N1 and the MMN also seem to trigger a chain of brain events leading to an involuntary switching of attention, which is presumably reflected in the earliest component of the P3 deflection, the so-called P3a (Squires et al., 1975; Knight, 1984). The functional role of neural mechanisms underlying each of these ERP components will be first shortly examined; later, which of these functions are still sustained during sleep and the degree up to which they are affected will be discussed. Finally, a section will be devoted to sleep-specific ERPs. Such ERPs are mainly influenced by the presence of transient events like vertex waves and evoked K-complexes, and their brain generator mechanisms seem to be involved in arousability and pre-attentive information processing during human NREM sleep.

2. The auditory N1: a first step in the processing pathway towards the conscious perception of sound

2.1. Studies in wakefulness

The N1 is a negative deflection elicited between 75 and 150 ms from an auditory stimulus onset. N1 generator sources are mainly located bilaterally in the supratemporal auditory cortex (e.g. Giard et al., 1994; Alho et al., 1998), although it also receives a further contribution from neural elements in frontal regions (Näätänen and Picton, 1987; Alcaini et al., 1994; Giard et al., 1994; Woods, 1995). The fact that several neural populations from different locations are activated simultaneously to generate the N1 indicates a spatiotemporal overlapping of different components, which presumably reflect different functional specialization.

The N1 is particularly sensitive to transient aspects of auditory stimulation (e.g. Loveless and Brunia, 1990) and its amplitude decreases after presenting the same stimulus several times. This result has been suggested to be due to an incomplete recovering of the neural excitability from a stimulus to another (Näätänen and Picton, 1987; Näätänen, 1990, 1992). This interpretation is supported by studies showing enhanced N1 amplitudes with the increasing interstimulus interval (e.g. Hari et al., 1987; Lü et al., 1992; Loveless et al., 1996).

Magnetoencephalographic (MEG) studies have shown that different stimulus attributes are associated to N1s generated in different brain locations. These results suggest that neural mechanisms involved in N1 generation encode specific stimulus features, such as frequency, intensity, or location (Elberling et al., 1982; Pantev et al., 1989). The information provided by this type of sensory analysis reflected in N1 is preserved for a period varying from 150–200 ms (Loveless et al., 1996) to 10–15 s (Hari et al., 1987). Näätänen and Winkler (1999) used the concept of 'sensory feature traces' to refer to this memory store. Such feature traces contain information about physical but not temporal characteristics of the sound, as suggested, for instance, by the fact that stimulus duration longer than 30–50 ms did not affect the N1 amplitude (Kodera et al., 1979). Evidence suggests that information stored in auditory feature traces is not available to mechanisms responsible for voluntary discrimination (Winkler et al., 1997). However, the outcome of the processing underlying the N1 frontal component may trigger involuntary attention switching, which may lead in turn to conscious perception of the stimulus. This functional role of the neural mechanisms involved in N1 generation is supported by the relationship between behavioral distraction and N1 magnitude. Indeed, novel irrelevant auditory events, which elicited large N1 amplitudes, administered during visual task performance were found to prolong reaction times (RT) to visual target occurring 300 ms thereafter (Escera et al., 1998). These results led the authors to speculate that the N1 generator mechanisms activated by novel sounds were involved in triggering involuntary switches of attention to novel events occurring in the unattended environment.

From the studies reviewed above, it is therefore apparent that the N1 generator mechanisms are mainly involved in two different processes: (i) in the formation of auditory feature traces, which provide relevant information for subsequent stimulus integration as an unique event; and (ii) in the triggering of an automatic switch of attention to irrelevant external events which may be potentially relevant for the organism. According to Näätänen and Winkler (1999), the first process involved in N1 generation, i.e. the encoding and short-term storing of the physical but not the temporal features of a sound in the so-called feature traces, can be considered as a pre-representational phase. At this phase, an auditory stimulus will not be consciously experienced, unless N1 activation recruits its attention-trigger function. Consequently, the chain of brain processes underlying N1 seems to be a mandatory step in the route of pre-attentive processing before conscious experience.

2.2. Studies in sleep

There are several experimental findings that suggest that N1 components are brain-state dependent: (i) the N1 undergoes a decrease in amplitude and an increase in latency during human NREM sleep (e.g. Paavilainen et al., 1987), as well as a gradual decline in amplitude from wakefulness to SWS and a slight recovery during human REM sleep (e.g. Bastuji et al., 1995); and (ii) the N1 amplitude is positively correlated with task performance during alert waking (Näätänen and Gaillard, 1974) and sleep onset (Ogilvie et al., 1991). Most of these studies point out the decreased amplitude shown by the N1 during sleep. The N1 amplitude has been demonstrated to be affected even by the simultaneous presence of phasic events characteristic of a particular sleep stage. For instance, Elton et al. (1997) reported a smaller N1 during stage 2 in the presence of sleep spindles, the functional role of which seems to be associated with the inhibition of external information processing during sleep (Steriade et al., 1993). Consequently, the neural excitability responsible for N1 generation is apparently modulated by macro and microstates of the brain.

The attenuation of N1 can be accounted for by stage-dependent changes occurring before information reaches the cortex. Observations of sleep-specific changes in middle-latency auditory ERPs (MERPs) support this notion. Thus, MERP amplitude has been found to be reduced during sleep (e.g. Deiber et al., 1989), indicating that the early processing of the specific stimulus features indexed by these MERP components is also affected in sleep. Therefore, the different available information for subsequent brain processes, such as those reflected in the N1, may explain amplitude attenuation of subsequent cognitive ERPs reflecting higher stages of information processing, such as the MMN (e.g. Paavilainen et al., 1987) or the P300 (e.g. Nielsen-Bohlman et al., 1991). However, the attenuated amplitude of MERPs cannot explain the fact that N1 is differentially affected in each sleep stage (e.g. Bastuji et al., 1995), since MERPs are not sensitive to transitions across the different sleep stages.

Single-unit studies in the guinea-pig have shown that extracellular recordings of evoked responses from the cochlear nucleus (Peña et al., 1992), superior olive (Pedemonte et al., 1994), and inferior colliculus (Morales-Coba et al., 1995) are highly state-dependent. At these subthalamic levels, most of the cells showed an increase in evoked responses from waking to SWS, and a decrease from waking to paradoxical sleep (equivalent to REM sleep in humans). Paradoxically, a high percent (63%) of neurons at primary auditory cortex (A1) showed the same amount of spikes/s in SWS and paradoxical sleep (Peña et al., 1999). Taken together, these results could hardly explain changes in the N1 amplitude across the different stages of sleep. Nevertheless, recent results obtained in the thalamic neurons of unanesthetized guinea-pigs (Edeline et al., 2000) seem to provide a satisfactory explanation of the differential modulation of the N1 amplitude in wakefulness, SWS, and REM sleep. In this study, depressed evoked responses were found in SWS as compared with wakefulness. Interestingly, opposite behaviors were exhibited by different neural populations in paradoxical sleep. While one set of neurons (60% of the cells tested) exhibited strongly decreased responses compared to the wake state, another cell group (40% of the cells tested) showed responses equivalent to those in waking. As a consequence of the decreased evoked responses of thalamic cells, a decrease in the frequency receptive field size and an increase in the frequency selectivity were specially remarkable during SWS. In fact, when the evoked responses were not decreased in paradoxical sleep, the frequency selectivity and the receptive field size did not differ from those in wakefulness. Therefore, the information received by cortical neurons from thalamic cells is expected to be different in SWS and paradoxical sleep. This would explain the enhanced N1 in REM sleep as compared with SWS, as well as the differential modulation of ERPs in the subsequent stages of information processing.

According to the functional role of the N1, its elicitation during sleep suggests the formation of feature traces providing relevant information in order to make feasible the subsequent formation of a neural representation of the incoming stimulus. But results in wakefulness indicate that some of the N1 components are also involved in the initiation of the involuntary orienting response towards a novel stimulus, specifically the supratemporal component (Escera et al.,

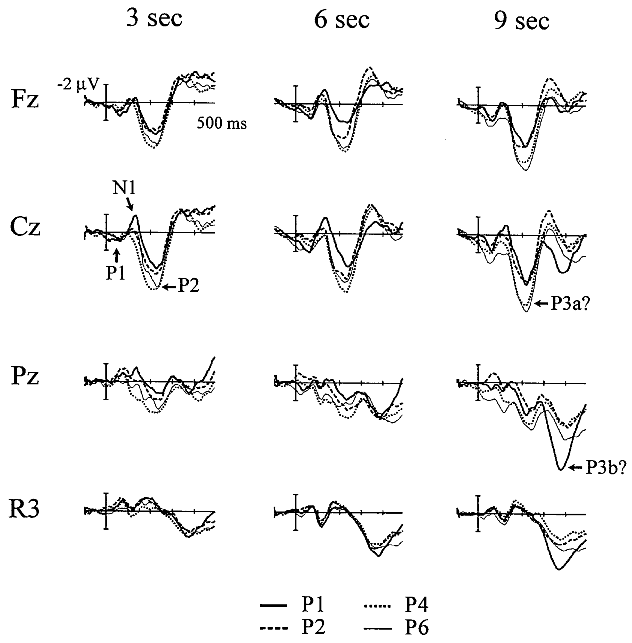

Fig. 1. Grand averages ($n = 9$) of ERPs to deviant tones presented in different positions within the stimulus train (1, 2, 4, or 6), for each intertrain interval (3, 6, and 9 s), during REM sleep. Note the enhanced N1 for the deviant tones presented in the first position of the stimulus train, independently of the length of the intertrain interval. Note also that the positive waves recorded at Cz and Pz derivations are differently affected by the position of the deviant tone within the train depending on the length of the intertrain interval. (Modified from Atienza et al., 2001.)

1998), the non-specific N1 (Näätänen and Picton, 1987), and the later subcomponent of N1 reported by Alcaini et al. (1994). Accordingly, Atienza et al. (2001) found an enhanced N1 during wakefulness and REM sleep to frequency-deviant tones presented at the beginning of a stimulus train as compared with deviant stimuli occurring in other positions within the train (Fig. 1). This increase cannot be explained by a release-from-refractoriness (period of time during which neurons have not yet recovered their full excitability), as would be in the case of repetitive stimuli (Näätänen and Picton, 1987; Näätänen, 1990, 1992), since only one frequency-deviant stimulus occurred in each train and the interdeviant interval barely changed from one train to another. According to the authors, variation of silence length may be responsible for the enhanced N1, since changes in the intertrain interval were only associated to the deviant in position 1. Changes in frequency cannot be a factor here as a similar increase was also observed to standards in the first-stimulus position. The enhanced N1 obtained during waking and REM sleep (more remarkably in wakefulness than in sleep) is probably due to the contribution of neural elements involved in generation of the non-specific component, and may be indexing the 'automatic initial orienting response' (O'Gorman, 1979) that typically appears associated with the first stimulus after a long interval of silence (Kenemans et al., 1989).

In summary, the sleeping brain is able to automatically detect stimulus occurrence and trigger an orienting response towards that stimulus if its degree of novelty is large. However, the outcome of the information processing carried out by the N1 generator mechanisms is slower and impoverished judging from the longer latency and smaller amplitude of the N1 showed during sleep as compared with waking, especially remarkable during SWS. The possibility that intrinsic changes occurring at cortical level account for the modulation of the N1 latency and amplitude across the sleep stages cannot be ruled out, but evidence in human and animal studies strongly suggests that sensory processing is modulated during the different sleep stages at subcortical level. We can conclude, therefore, that the decrease in the N1 amplitude results from the different information available in cortical neurons during sleep as result of an early modulation in the ascending sensory processing.

3. MMN: an index of stimulus representation in sensory memory

3.1. Studies in wakefulness

The MMN, a negative component of the auditory ERPs appearing 100–200 ms from stimulus onset, is elicited by any discernible variation in a repetitive stream of auditory stimulation (Näätänen, 1990). Its fronto-central scalp distribution and polarity reversal below the Sylvian fissure suggests main neural generators located in the superior temporal plane of the auditory cortex (see review by Alho, 1995). In addition to this sensory-specific supratemporal component, a frontal component involved in triggering involuntary attention switches to acoustic changes has also been corroborated by scalp current density maps (Giard et al., 1990; Escera et al., 2000), magnetic source analysis (Levänen et al., 1996; Rinne et al., 2000), and results from patients with lesions in the dorsolateral prefrontal cortex (Alho et al., 1994; Alain et al., 1998). The contribution of pre-frontal neurons to MMN generation has also been confirmed by recordings of cerebral hemodynamic activity with possitron emission tomography (PET) (Tervaniemi et al., 1999) and functional magnetic resonance imaging techniques (fMRI) techniques (Celsis et al., 1999).

Two different but not incompatible explanations for MMN generation have been proposed: (a) as a result of a memory comparison process, in such a way that MMN is elicited when the afferent auditory input, or infrequent-stimulus representation (Schröger, 1997), does not match the neural representation of the repetitive stimulus stored in sensory memory (Näätänen, 1990, 1992), or (b) as the automatic adjustment (or updating) of the acoustic neural model to a change in the auditory environment (Winkler et al., 1996). The formation of the stimulus representation as well as the updating or comparison processes are automatic processes in the sense that they are not under the direct control of attention (Rinne et al., 2001).

It has been suggested that the information provided by the change-detector system underlying MMN may be used by the mechanisms of conscious perception (Näätänen, 1992; Näätänen and Winkler, 1999). This is mainly supported by studies reporting a positive correlation between MMN peak latency and that of other endogenous ERP components such as the N2b and P3 (Novak et al., 1992), and between MMN peak latency and RT in discrimination tasks (see review by Näätänen and Alho, 1997). Moreover, it has been recently shown that the amplitude of MMN predicts the accuracy of perceptual discrimination of attended sounds (Amenedo and Escera, 2000), suggesting that conscious perception of auditory stimuli is mediated by the neural representations underlying MMN.

In summary, the auditory information provided by memory traces underlying MMN may be used at different stages of information processing. This information seems to be useful for automatically detecting discernible changes appearing in the auditory environment and for consciously perceiving auditory events. It is hard to believe that any stimulus can be consciously experienced during sleep. Nevertheless, this does not mean that the automatic stimulus-change detection is not possible during sleep states. The generation of the N1 potential during sleep suggests that physical stimulus features are analyzed up to some extent. A further requirement for change detection would be the formation of a neural representation of any repetitive stimulus during sleep.

3.2. Studies in sleep

The above-discussed studies suggest that MMN is the outcome of an automatic mismatch detection after a comparison process between the afferent input and a memory trace developed by the repetitive stimulation (Näätänen, 1992). Based on the fact that both the development of memory traces and the comparison process are pre-attentive processes (Näätänen, 1990), MMN is expected to be elicited during sleep. However, the results obtained to date suggest that these pre-attentive processes are markedly affected during sleep, especially during NREM sleep. Table 1 summarizes MMN results obtained during different sleep stages.

In children, MMN can be obtained in all brain states from wakefulness to sleep (see review by Cheour et al., 2000). However, most studies carried out during NREM sleep in human adults have failed to find a distinct MMN (e.g. Paavilainen et al., 1987; Nielsen-Bohlman et al., 1991; Winter et al., 1995; Loewy et al., 2000). MMN has been recently found to disappear at sleep onset, specifically when low-voltage theta waves emerged after alpha flattening (Nittono et al., 2001). Several reasons have been provided to explain the lack of MMN in NREM sleep, including the use of long interstimulus intervals (Winter et al., 1995), a too slight separation between the standard and deviant stimuli (Paavilainen et al., 1987), the spatiotemporal overlapping with the large slow waves typical of SWS (Paavilainen et al., 1987; Loewy et al., 1996), and the use of intensity deviants (Loewy et al., 2000), which are known to be more affected than the frequency deviants by the level of attention (Näätänen et al., 1993a). In one study, an MMN-like response was only reported in stage 2 of NREM sleep by averaging those trials containing a K-complex as a response to deviant stimuli, probably due to the higher arousal level (see Section 5.2 below) associated with this sleep phasic event (Sallinen et al., 1994; see however Sallinen et al., 1997).

In the case of REM sleep, several studies have reported a distinct MMN in response to single frequency deviancies. Loewy et al. (1996) presented deviant stimuli of 2000 or 1050 Hz, in different blocks, in a homogenous sequence of 1000 Hz tones. The MMN obtained in REM sleep had a smaller amplitude as compared with that of wakefulness for the large frequency changes and a similar amplitude in both brain-state conditions for the small deviance. In this later case, MMN latency was, however, shorter in REM sleep than in wakefulness. Similar results have been found in subsequent studies (Atienza et al., 1997, 2000; Nashida et al., 2000). However, other studies using a similar paradigm reported different findings. This is the case of the Sallinen et al. (1996) study, who found a large positivity (P210) elicited to small and large deviancies during REM sleep but no clear MMN. Lack of MMN in REM sleep was also observed by Bastuji et al. (1995), who presented frequency-deviant tones that, in a condition administered prior to sleep, served as target stimuli in an active-counting paradigm. According to Sallinen et al. (1996), the drastic attenuation of MMN during REM sleep may be due to an overlapping between the MMN and the subsequent large P210. In the Bastuji et al. (1995) study, where no MMN was observed, it is, however, difficult to disentangle whether the larger N1 to the deviant tone, as compared to the standard N1, overlapped the MMN, given the large frequency separation between the standard and deviant tones used in their study (2000 versus 1000 Hz).

In the cases in which an MMN-like response was obtained during REM sleep, its amplitude was always smaller than in wakefulness. It is possible that MMN attenuation during REM sleep might result from a reduced contribution of some of its components. For instance, neural contributions from frontal areas to MMN seem to be more affected by brain state than the supratemporal MMN component, as shown by a range of results. Indeed, Loewy et al. (1996) found that MMN underwent attenuation of its later portion to widely frequency-deviant tones during REM sleep, which was attributed by these authors to a deactivation of the frontal MMN generators. On the other hand, the polarity inversion of MMN at mastoid locations, which reflects the supratemporal MMN component when the nose is used as reference (Giard et al., 1990), is hardly affected by decrements in alertness during sleepiness in contrast with the notable attenuation observed over fronto-central regions (Sallinen and Lyytinen, 1997; see however Nittono et al., 2001). Sallinen and Lyytinen (1997) suggested, on the basis of this result, that the activation of the attention-switching mechanism associated with the frontal MMN component is probably more disturbed for waking–sleep transitions than the activation of the change-detection mechanism reflected in the supratemporal MMN component. Supporting this

Table 1
Review of MMN studies conducted during human sleep[a]

	Frequent stimuli	Infrequent stimuli	Sleep stage	Properties of MMN
Paavilainen et al. (1987)	1000 Hz (90%); 75 dB; 50 ms; ISI: 510 ms	1050 Hz (10%); 75 dB; 50 ms	Stage 1 Stage 2 Stages 3 + 4	Latency: 150–200 ms; amplitude: not significant No MMN No MMN
Nielsen-Bohlman et al. (1991)	1000 Hz (80%); 50 dB; 50 ms; ISI: 1 s	1500 Hz (10%); 50 dB; 50 ms; Novel sounds (10%); 44 dB; 300 ms	Stage 2 Stages 3 + 4	Latency: 100–150 ms; amplitude: not significant No MMN
Niiyama et al. (1994)	1000 Hz (80%); 60 dB; 100 ms; ISI: 1.5–2.5 s	2000 Hz (20%); 60 dB; 100 ms	NREM REM	No MMN No MMN
Sallinen et al. (1994)	1000 Hz (97.5%); 45 dB; 50 ms; ISI: 625 ms	1200 Hz (2%); names (0.5%); 50 ms; 45 dB	Stage 2 + KC Stages 3 + 4	Latency: 100–250 ms; amplitude: −7.67 μV at Fz No MMN
Winter et al. (1995)	1000 Hz (80%); 65 dB; 50 ms; ISI: 1 s	1050 Hz (10%); 1200 Hz (10%); 65 dB; 50 ms	Stage 2	No MMN
Loewy et al. (1996)	1000 Hz (80%); 80 dB; 55 ms; ISI: 600 ms	1050 Hz (10%); 2000 Hz (10%); 80 dB; 55 ms	Stage 2 Stage 3 + 4 REM	Latency: 100–150 ms; amplitude: not significant No MMN Latency: 100–150 ms; amplitude: −1.12 μV at Fz
Nordby et al. (1996)	800 Hz (80% or 20%); 75 dB; 50 ms; ISI: 1.5 s	1200 Hz (20% or 80%); 75 dB; 50 ms	NREM REM	No MMN No MMN
Sallinen et al. (1996)	1000 Hz (97%); 50 dB; 50 ms; ISI: 625 ms	1100 Hz (1.5%); 2000 Hz (1.5%); 50 dB; 50 ms	Tonic REM Phasic REM	Latency: 100–200 ms; amplitude: not significant Latency: 100–200 ms; amplitude: not significant
Sallinen et al. (1997)	1000 Hz (97%); 50 dB; 50 ms; ISI: 625 ms	1100 Hz (1.5%); 2000 Hz (1.5%); 50 dB; 50 ms	Stage 2 ± KC Subjective drowsiness	No MMN No MMN
Sallinen and Lyytinen, 1997	1000 Hz (90%); 55 dB; 55 ms; ISI: 450 ms	1050 Hz (10%); 1200 Hz (10%); 55 dB; 55 ms	Objective drowsiness	Latency: 100–150 ms; amplitude: −1.3 μV at Fz only for the larger deviant (1200 Hz), for the other (1050 Hz) MMN was not significant
Atienza et al. (1997)	10 stimulus trains; 1000 Hz (90%); 80 dB; 50 ms; ISI: 600 ms; ITI: 3 s	10 stimulus trains; 2000 Hz (10%); 80 dB; 50 ms	REM	Latency: 100–150 ms; amplitude: −1.48 μV at Fz
Atienza et al. (2000)	10 stimulus trains; 1000 Hz (90%); 80 dB; 50 ms; ISI: 600 ms; ITI: 3, 6, 9 s	10 stimulus trains; 2000 Hz (10%); 80 dB; 50 ms	REM	Latency: 75–150 ms; amplitude: −1.7 μV at Fz only for the intertrain interval of 3 s. MMN was not significant for longer intertrain intervals
Nashida et al. (2000)	1000 Hz (90%); 60 dB; 50 ms; ISI: 450 ms	2000 Hz (10%); 60 dB; 50 ms	Stage 1 Stages 2, 3 + 4 REM	Latency: 115–155 ms; amplitude: −1.28 μV at Fz No MMN Latency: 115–155 ms; amplitude: −1.13 μV at Fz
Loewy et al. (2000)	70 dB (80%); 1000 Hz; 55 ms; ISI: 600 ms	60 dB (10%); 80 dB (10%); 1000 Hz; 55 ms	Stage 2 REM	No MMN Latency: 100–200 ms; amplitude: not significant
Nittono et al. (2001)	1000 Hz (90%); 60 dB; 50 ms; ISI: 450 ms	1050 Hz (5%); 1200 Hz (5%); 60 dB; 50 ms	Different phases of Stage 1	MMN appeared at early phases of Stage 1 (i.e. before theta waves emerged). Latency: 150–195 ms; amplitude: −1.5 to −2 μV at Fz
Atienza and Cantero (2001)	Complex patterns: 720–500–638–1040–117–565–815–920 Hz (87%); 70 dB; 365 ms; ISI: 975 ms	Complex patterns: 720–500–638–1040–117–650–815–920 Hz (13%); 70 dB; 365 ms	REM	Latency: 150–200 ms; Amplitude: −1.05 μV at Fz

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[a] Stimulus parameters used in each study are shown in the second and third column. The fourth column contains the brain state in which the stimuli were presented. The fifth column shows the latency range in which MMN was measured and the amplitude obtained at Fz only when it was significantly different from zero. The presence of an MMN-like response that never reached statistical significance is also indicated.

interpretation, neuroimaging studies during human REM sleep have revealed a functional deactivation of the dorsolateral pre-frontal cortex (Maquet et al., 1996; Braun et al., 1997; Lövblad et al., 1999), a brain region thought to be involved in the generation of the frontal MMN component (e.g. Giard et al., 1990). However, the notion that attenuation of MMN during REM sleep is caused by the deactivation of the frontal component remains as a suggestive hypothesis, and further studies need to be conducted to clarify this issue.

From an information processing point of view, the same interpretation of diminished N1 during sleep might also explain the attenuation of MMN. According to this perspective, it is likely that the decreased MMN amplitude stems from changes at thalamic level. This would be supported by the fact that both the N1 and MMN show the same state-dependent changes, i.e. a decrease of their respective amplitudes from wakefulness to drowsiness (e.g. Paavilainen et al., 1987) and an enhanced amplitude during REM sleep as compared with the remaining sleep stages (Bastuji et al., 1995; Loewy et al., 1996). Consequently, the sound representation in sensory memory indexed by MMN would be weaker and unstable, which, in turn, may lead to the fact that such a representation remains active for less time during sleep than in wakefulness. The shorter duration of sensory memory during sleep is supported by the results recently obtained by Atienza et al. (2000). In that study, 3 groups of subjects were presented with tone-trains separated by different silent intervals (3, 6, and 9 s). Each train included 9 tones of 1000 Hz and one deviant tone of 2000 Hz appearing in different positions within the train (1, 2, 4, or 6). The MMN amplitude was smaller in REM sleep than in wakefulness, like in previous studies, and decreased faster with the prolongation of the silent interval than in wakefulness. Fig. 2 shows ERPs to deviant and standard tones in wakefulness and REM sleep for the 3 intertrain intervals and for each deviant-stimulus position of the train. No significant MMN was elicited by deviant tones at any position when the intertrain interval was 9 s in REM sleep, whereas a clear MMN was obtained in the same condition during wakefulness. These findings are in consonance with the initial assumption that the neural representation of repetitive stimuli vanishes faster in REM sleep than in wakefulness, probably as a result of an unstable representation.

Most of the results obtained during human sleep using the MMN as measure of sensory memory point out a deficit in the formation of the neural representation of the stimulus. There is growing evidence that information stored in long-term memory can be used by the MMN system to improve sensory processing (e.g. Näätänen et al., 1993b; Näätänen et al., 1997; Koelsch et al., 1999; Winkler et al., 1999). Since the activation of information in long-term memory is a pre-attentive process, it is plausible that the enhanced MMN observed in wakefulness as a result of previous experience could be also observed during sleep. For instance, Atienza and Cantero (2001) recently found an increase in MMN amplitude in waking and REM sleep after subjects learned to discriminate two complex spectrotemporal auditory patterns during wakefulness (Fig. 3). Surprisingly, the MMN amplitude obtained during REM sleep was not significantly different from that obtained during wakefulness. These results clearly demon-

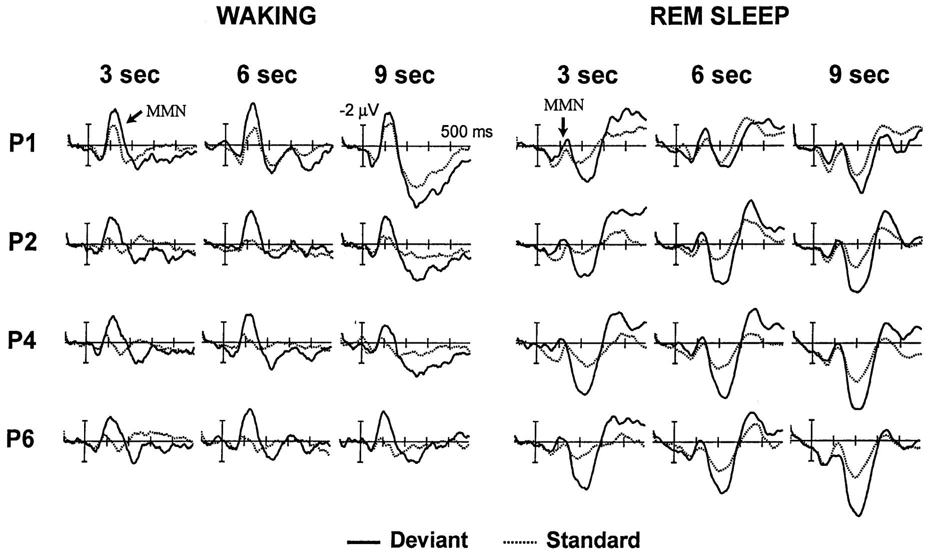

Fig. 2. Grand averages ($n = 9$) at Fz to standard tones (dashed lines) and deviant tones (solid lines) for each silent interval between tone trains (3, 6, and 9 s), during wakefulness (left) and REM sleep (right). Note that the difference in the amplitude of ERPs to standard and deviant tones within the temporal window of MMN (100–150 ms from the stimulus onset) is higher in wakefulness than in REM sleep. These differences in amplitude during REM sleep were statistically significant only for the 3 s intertrain interval. (From Atienza et al. (2000). Copyright 2000 Society for Psychophysiological Research. Reprinted with permission.)

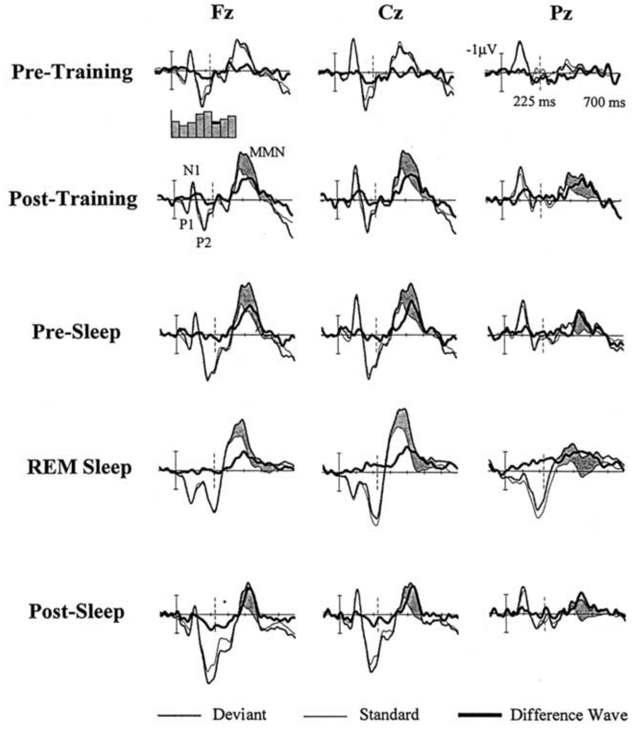

Fig. 3. Grand averages ($n = 16$) of ERPs to standard and deviant complex auditory patterns at Fz, Cz and Pz in different experimental conditions: before training on the discrimination task, just after training, and during REM sleep 2 days after training. The difference waves (deviant minus standard) are also shown superimposed in each condition. ERPs were obtained to complex patterns like shown in the first plot. The vertical dotted line indicates the frequency deviance onset within the pattern (225 ms from the stimulus onset). (Modified from Atienza and Cantero, 2001.)

strate that the automatic detection of infrequent auditory patterns can be improved in REM sleep, presumably by recruiting information from long-term memory.

The results reviewed in this section indicate that the formation of auditory stimulus representation and the maintenance of such a representation in sensory memory are still possible during human sleep. However, these two processes seem to be strikingly affected during sleep, as indicated by the reduced MMN amplitude and the faster disappearance of this ERP component during REM sleep as compared with wakefulness with the increase of the silent interval, respectively. These findings can be up to some extent expected on the basis of the N1 results (see Section 2.2). If the formation of a neural representation of an auditory event is based on the integration of temporal and physical features of the incoming input, and the information regarding the physical features of that stimulus is poor during sleep, as indicated by the reduced sleep-N1, an impoverished neural representation of the auditory stimulus in sensory memory is not surprising. However, if a neural representation of the repetitive stimulus already exists in a longer form of memory other than sensory memory, then sensory processing during sleep may be improved (as indicated by enhanced MMN) by accessing information from this long-term memory system.

4. The P3a component: an ERP index of attentional orienting

4.1. Studies in wakefulness

The P3a is a positive ERP peaking between 220 and 280 ms from the stimulus onset with a fronto-central scalp distribution (Squires et al., 1975). This component is elicited by novel stimuli, such as natural environmental sounds, occurring in an attended or unattended homogenous stimulus sequence (Woods, 1990), by widely deviant stimuli presented in ignored conditions (Näätänen, 1990), and even by small deviancies when the primary task is not very demanding (Sams et al., 1985). Intracranial and MEG recordings as well as lesion studies suggest the participation of multiple brain structures in the generation of P3a, including the dorsolateral pre-frontal, temporal, and parietal cortices, the hippocampus, and the cingulate gyrus (see reviews by Knight and Scabini, 1998; Escera et al., 2000).

P3a is thought to reflect the automatic orienting of attention to environmental changes occurring either outside (e.g. Escera et al., 1998) or inside the current focus of attention (Woods et al., 1992). Several results support this assumption. First, it has been found that an increase in P3a amplitude is followed by a delay in RT to targets preceded by a novel stimulus (Woods et al., 1992). Second, several brain regions clearly associated with the orienting response, such as the frontal and hippocampal regions, are also involved in P3a generation (e.g. Knight, 1984, 1996). Third, several factors modulate both the automatic orienting response and the P3a amplitude, such as the salience of eliciting stimulus (novel versus deviant) (Alho et al., 1998), the probability of infrequent stimulus (Katayama and Polich, 1996), the direction of attention (Woods et al., 1992), the stimulus context (Katayama and Polich, 1998), and the number of infrequent stimuli delivered previously (e.g. Knight, 1984; Polich, 1988).

Recently, Escera et al. (1998) found that P3a elicited by novel auditory stimuli was composed of two different subcomponents: an early-P3a with a peak latency of about 230 ms from stimulus onset and a centrally dominant scalp distribution with polarity reversal in posterior and inferior electrodes; and a late-P3a component peaking at about 315 ms, showing a frontal scalp distribution, particularly over the right hemisphere, with no polarity reversal over posterior areas. The different topographies shown by these two components suggest brain generators located in the temporal–parietal and pre-frontal cortices, respectively. In addition, the results obtained in that study indicated that the late P3a amplitude was modulated by attentional demands associated to the primary task. The authors concluded, according to the different scalp distribution and attentional dependence, that the early P3a might reflect violation of a polysensory model of the external world maintained in the temporal–parietal association cortex, whereas the pre-frontal generators of the late P3a probably are involved in the orienting of attention itself.

4.2. Studies in sleep

Several studies have examined the P3 response during sleep. However, to our knowledge, no study was aimed at determining the influence of sleep on P3a generation. Some of the positivities recorded during drowsiness period and stage 1 of NREM sleep, using the oddball paradigm, resembled the waking P3b, according to their latencies and posterior scalp distributions (Nielsen-Bohlman et al., 1991; Salisbury et al., 1992; Harsh et al., 1994; Niiyama et al., 1994; Bastuji et al., 1995; Winter et al., 1995; Pratt et al., 1999). In all these studies, the positive waves showed longer latencies and smaller amplitudes during sleep than in wakefulness. Bastuji et al. (1995) found that the P3 became progressively smaller, more delayed, and topographically restricted to the posterior areas from the alert wake state to drowsiness, and finally to a consolidated stage 1 of sleep. Furthermore, the brain response to the deviant stimuli was quite different in the remaining NREM sleep stages, indicating, in all these cases, the involvement of neural mechanisms different from those responsible for the waking-P3 generation. On the contrary, the positive waves recorded during wakefulness and REM sleep showed a latency (about 300 ms) and scalp topography (centro-parietal) highly alike (Bastuji et al., 1995; Cote and Campbell, 1999a,b). In spite of this similarity, it is difficult to accept that the waking P3b and REM-P3 generator mechanisms play the same functional role, because of the attentional resources required for elicitation of this component in wakefulness and the elaborated cognitive processing reflected. However, some data suggest that the P3b can also be elicited using passive paradigms (Polich, 1988), which makes its recording in sleep still possible.

There is also some evidence suggesting that a positive wave similar to the waking P3a can be obtained during sleep. Previous studies have found an early positive wave distributed over anterior cortical regions in stage 1 (Nittono et al., 2001) and stage 2 of sleep (Nielsen-Bohlman et al., 1991; Salisbury et al., 1992; Sallinen et al., 1994, 1997; Winter et al., 1995; Hull and Harsh, 2001). Nielsen-Bohlman et al. (1991) recorded a positivity at about 200 ms from stimulus onset to deviant and novel stimuli, its amplitude being larger to novel stimuli in stage 2 of sleep than in wakefulness. Since this potential was accompanied by a decrease in N1 and MMN amplitudes, the authors interpreted their results as ‘sleep-related changes’. The reduction of the N1 and MMN components together with the larger amplitude of this positivity to deviant as compared with novel stimuli makes its consideration as a sleeping P3a unlikely. The central positivity (P210) found by Winter et al. (1995) during drowsiness and stage 2 of sleep was higher for widely than for slightly frequency-deviant tones. However, these authors also considered the equivalence between this wave and the waking P3a unlikely, based on several reasons: (i) the positive wave was elicited by both standard and deviant tones; (ii) its latency was shorter than that of the waking P3a, and (iii) it was preceded by no N1 or MMN response, which is thought to be a necessary condition for P3a elicitation in the auditory modality (Alho et al., 1998). Winter et al. (1995) explained the variation in the P210 amplitude on the basis of the different refractoriness pattern of the neural elements involved in the processing of the standard and deviant tone. However, this does not necessarily explain the enhancement of this positive wave during sleep as compared with wakefulness. Hull and Harsh (2001) also found an early central positive wave (220 ms) to auditory tones during the transition from wakefulness to stage 2 of NREM sleep. In their study, two stimuli (1000 versus 1500 Hz) defined as target or non-target in wakefulness were presented with different probabilities in 3 different conditions (target appeared infrequently, target appeared so many times as non-target, and target appeared frequently). The P220 during sleep showed the largest amplitude to the target and non-target tones when they occurred infrequently. The topography, latency, and the effect of probability on the P220 amplitude strongly suggest that this waveform might be equivalent to waking-P3a. However, the target P220 amplitude was significantly smaller overall than the non-target P220 in contrast to the findings of a larger P3a amplitude following attended versus ignored stimuli (Woods et al., 1992). Like in the Winter et al. (1995) study, the effects of stimulus probability on P220 amplitude reported by Hull and Harsh (2001) could be due to a release of the refractoriness for those neurons involved in the processing of stimuli presented more infrequently. Although the results reviewed above point out some common characteristics between the early positive waveforms recorded during stage 2 of NREM sleep and the waking-P3a, not all the parameters are modulated in the same way, and in the most cases it is not preceded by N1 or MMN, suggesting that both ERP components are involved in different functions in each brain state.

Results obtained during REM are relatively similar to those found during NREM sleep. Sallinen et al. (1996) recorded a larger P210 during tonic than phasic REM periods, and with larger amplitude in REM than in wakefulness. However, this waveform was preceded by any trigger component, such as the N1 or the MMN, so that this P210 may not be considered as the equivalent to the P3a component. In another study reviewed above (Atienza et al., 2001; Section 2.2), deviant tones occurring at the beginning of tone trains always elicited two positive waves: an early one, with a dominant frontal scalp distribution, and a late one, with a centro-parietal topography (Fig. 1). Both waves showed variations in their amplitudes during REM sleep with the prolongation of the intertrain interval, suggesting that the temporal stimulus probability determined the amplitude of these ERP components. However, these two potentials were not equally modulated by the position of the deviant tone within the train. The later P3 was larger to deviant tones in position 1, whereas the earlier P3 showed larger amplitudes for the deviant tones presented in later positions within the train. This result rules out that this positive waveform be the P2 component as its generators are thought to be more active for a stimulus in position 1, after a silent interval, than for a stimulus in a later position within the train. Therefore, several factors, such as scalp topography, latency, the enhanced amplitude for the later positions within the train, and the previous elicitation of MMN, suggest that the early positive wave recorded during REM sleep in the Atienza et al. (2001) study to the deviant tones may be the equivalent to the waking early phase of the P3a (Escera et al., 1998). The elicitation of a P3a-like response during REM sleep has also recently been supported by the study of Cote and Campbell (1999b). These authors found a frontal positive waveform at about 250 ms to deviant stimuli that highly deviated in intensity (90 dB) from the standard stimulation (70 dB). This positive response was accompanied by a large centro-parietal positive wave, similar to the P3b recorded in wakefulness. Taken together, all these results indicate that highly intrusive stimuli are able to generate an involuntary orienting response to such a type of stimuli also during human REM sleep.

The frontal P3a generation, together with the N1 and MMN elicitation during sleep, particularly to widely deviant stimuli, is a strong support for the hypothesis that changes in the acoustic environment can be pre-consciously detected by the sleeping brain, making the awakening to such changes possible.

5. The N300 and N550: two sleep-specific ERP components

5.1. Determinants of the N300 and N550

The N300 and N550 are two negative ERP components typically recorded during stages 1 and 2 of NREM sleep. Although these two ERPs are frequently accomplished by two other positive waveforms, P400 and P900, respectively, the N300 and N550 are the most studied. These two negative waveforms have different scalp distributions, suggesting different brain generators. The N300 reaches its maximum amplitude at central areas whereas the N550 shows a more frontal distribution (e.g. Harsh et al., 1994; Niiyama et al., 1995; Cote et al., 1999; Perrin et al., 1999, 2000; Gora et al., 2001). Furthermore, the amplitude of these two waves is selectively modulated by different stimulus factors. Thus, the N550 is mainly affected by the contextual and physical features of the stimulus, such as its novelty (Sallinen et al., 1994), salience (Bastien and Campbell, 1992), or stimulation rate (Colrain et al., 1999). The N300 amplitude, although is affected by intensity, novelty, and in some instances by the stimulus probability (e.g. Nielsen-Bohlman et al., 1991; Bastien and Campbell, 1992), it seems to be more sensitive to the intrinsic meaning of the stimulus. For instance, Perrin et al. (1999) found that the N300 (as well as the P400) showed a larger amplitude after their subject's own names when compared with the appearance of other equiprobable names, even when the N550 (and the P900) was not elicited (Perrin et al., 2000). In addition, a considerable number of studies have reported that the N300 can be evoked in the absence of the N550 not only during sleep onset (Ogilvie et al., 1991; Webster and Colrain, 1998; Colrain et al., 2000; Nittono et al., 2001) but also in the stage 2 of sleep (Nielsen-Bohlman et al., 1991; Bastien and Campbell, 1992; Harsh et al., 1994; Niiyama et al., 1994, 1995; Sallinen et al., 1994, 1997; Perrin et al., 2000; Gora et al., 2001). These findings clearly indicate that the N300 and the N550 are two independent neural events that probably subserve different functions.

Despite the evidence supporting the N300 and N550 as independent ERP components, several studies have suggested that the K-complex – one of the major graphoelements of the human sleep EEG – contributes to the generation of these two components (e.g. Ujszászi and Halász, 1986; Sallinen et al., 1994, 1997; Niiyama et al., 1995). Bastien and Campbell (1992; see also Sallinen et al., 1997) found the amplitude of the N300 to be larger when it was followed by the occurrence of the N550. This led the authors to hypothesize that the N300 might act as a trigger for the N550 component. Against this hypothesis, however, recent evidence indicates that the N300 amplitude is independent of the N550 elicitation (Gora et al., 2001). In this study, the N300 elicitation was exclusively associated with the vertex sharp waves whereas the N550 was associated with the K-complexes. Gora et al. (2001) classified their EEG trials into 4 different subgroups: presence of K-complexes, presence of vertex sharp waves, presence of the two types of events, and absence of the two types of events. The N300 was elicited only when trials with vertex sharp waves were included in the average, whereas the N550 was seen only when the K-complex trials were averaged. The reason for which Bastien and Campbell (1992) found a different result can be explained by the different way in which they classified phasic events in their averaging procedures. These authors sorted out the trials depending on the presence or absence of K-complexes, whereas Gora et al. (2001) took also into account the presence or absence of vertex waves. It is likely that the proportion of trials containing a vertex wave in the study of Bastien and Campbell (1992) was larger when K-complexes were present compared to when they were absent, leading to an enhanced N300 in the presence of K-complexes. Taken together, these results suggest that the N300 and N550 reflect different processes and only the N550 seems to be part of the K-complex.

5.2. Functional role of the N300 and N550 in information processing during sleep

Ujszászi and Halász (1988) proposed that the N300 (as well as the P400) – considered by the authors as the earliest phase of the K-complex – could be mainly involved in the information processing of external stimuli. Some evidence reviewed above supports this hypothesis, in particular the results recently obtained by Perrin et al. (1999, 2000). These authors not only found that the stimulus significance affected the amplitude of the N300 and P400, but also that their scalp topography was similar to the waking N2–P3 complex elicited by the subject's own name, suggesting some functional equivalence between these ERP components. However, the functional role of the N550 (as well as the P900) – considered the late phase of the evoked K-complex (Ujszászi and Halász, 1988) – is much more difficult to elucidate. Some evidence obtained in patients with thalamic lesions with or without hemineglect suggests that the N550–P900 complex may be conceived as a response similar to the wakefulness orienting response. Indeed, K-complexes were not recorded over the damaged hemisphere of patients with spatial hemineglect, whereas they were elicited bilaterally by stimuli administered contralateral and ipsilateral to the lesion in patients with no signs of hemineglect (Weisz et al., 1995). Given that hemineglect is considered to be caused by a loss of the orienting response (Heilman et al., 1978), the absence of K-complexes in the hemisphere ipsilateral to the lesion might be a proof supporting their role as a sign of arousal.

The set of ERPs that are considered to be influenced by evoked K-complexes has been demonstrated to facilitate the cognitive processing during stage 2 of sleep. This is supported by the ERP results obtained in the Niiyama et al. (1995) study. In their study, subjects were presented, during two consecutive nights, with frequent tones of 1000 Hz and rare tones of 2000 Hz, the latter stimulus being target or non-target under different experimental conditions in previous wakefulness. K-complexes occurred more frequently after rare tones, and were accompanied, often, by a negative response (300–800 ms) of maximum amplitude over fronto-central regions (Fig. 4). This long-lasting ERP waveform showed a larger amplitude to rare stimuli to which the subjects were instructed to respond in wakefulness (target), as well as in those cases in which a K-complex was simultaneously elicited. This result suggests an improvement in the cognitive processing of external stimuli associated with the occurrence of K-complexes. Similar conclusions can be drawn by the results reported by Sallinen et al. (1994). These authors demonstrated that K-complexes are a necessary condition for the elicitation of MMN. Further studies examining the elicitation of MMN during stage 2 of sleep have reported negative results (see Section 3.2), probably because in none of those studies, trials with and without K-complexes were averaged separately. These findings indicate that MMN, an electrophysiological index of automatic-change detection, may occur only during specific brain microstates of stage 2, probably those associated with an increment in the arousal level, as indicated by ERP components associated with evoked K-complexes.

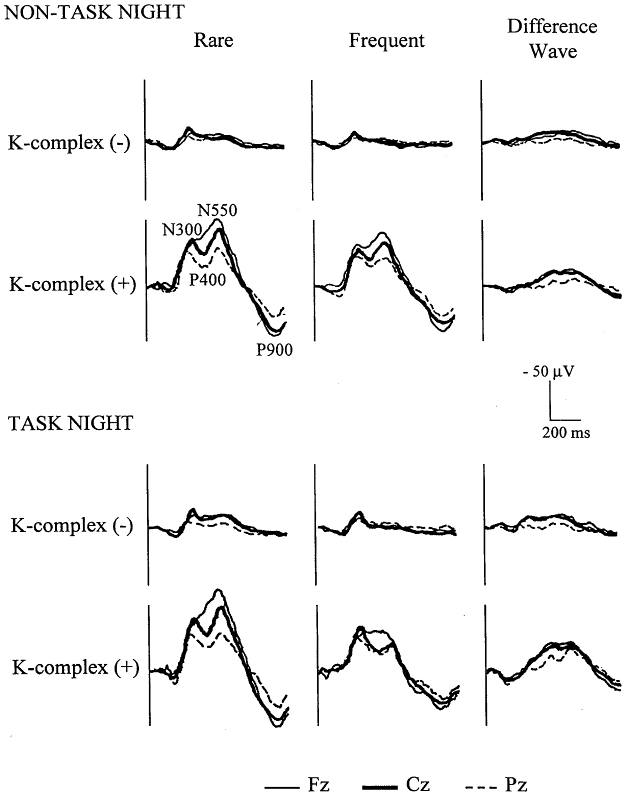

Fig. 4. Grand averages ($n = 7$) of ERPs to rare (left column) and frequent stimuli (middle column) and of the difference waves (right column) obtained at Cz by subtracting ERPs to frequent tones from ERPs to rare tones, in the non-task (when subjects were not asked to consciously detect the deviant stimuli in the waking prior to sleep) and task night (when subjects were required to respond to the deviant stimuli in the waking prior to sleep). In both nights, ERPs were obtained after averaging EEG segments with (+) and without (−) K-complexes. Note that the long-lasting negative responses appearing in the difference waves from EEG segments with K-complexes (+) showed a larger amplitude in the task night than in the non-task night (Adapted from Niiyama et al. (1995). Copyright 1995 Elsevier Science Ireland Ltd. Reprinted with permission.)

Summarizing, the N300 and N550 are two sleep-specific ERP components which have been proposed to be associated with the evoked vertex waves and K-complexes, respectively. The N300, with maximum amplitude at central areas, is mainly modulated by the significance of the stimulus; the N550, in turn, has a predominant fronto-central topographic distribution, and is more sensitive to changes in the salience and novelty of the stimulus. These waveforms may be independently elicited one of each other, supporting the notion that the two waveforms subserve different functions, the N300 being more related with sensory processing whereas the N550 may be mainly involved in the arousal rising during sleep, which, in turn, could facilitate the stimulus processing.

6. Conclusions

The studies reviewed here indicate that even the early phases of auditory processing are selectively affected across the different stages of sleep, and even within the sleep stages themselves, as suggested by an improved sensory processing when this is accompanied by K-complexes during sleep stage 2.

The formation of auditory feature traces and the subsequent neural representation of a discrete incoming auditory stimulus, thought to be reflected in the N1 and the MMN ERP components, respectively, seem to be severely affected during sleep. This is indicated by the decreased amplitudes of N1 and MMN, particularly remarkable during NREM sleep. This amplitude reduction during sleep may result from inhibited responses in cortical neurons, which may, in turn, be accounted for by changes occurring at thalamic level in the auditory pathway. We have pointed out another physiological condition, which might explain the amplitude differences in N1 and MMN between sleep and wakefulness: the deactivation of frontal regions contributing to these ERP components during sleep. Extensive evidence corroborates the involvement of frontal regions in N1 and MMN generation, presumably associated with involuntary switching of attention towards unattended stimuli. However, these regions, specifically a vast area of the dorsolateral pre-frontal cortex seems to be deactivated during both NREM and REM sleep, as revealed by neuroimaging studies. In terms of information processing, it is likely that the activity of the supratemporal neural populations contributing to the N1 and MMN has to exceed a higher threshold during sleep as compared with wakefulness to activate the generator mechanisms responsible for triggering conscious stimulus perception. This hypothesis is supported by the fact that a P3a-like activity, which indexes the engagement of attention, has only been elicited during sleep when particularly salient stimuli occurred in the auditory stimulation.

In conclusion, the acoustic environment can be analyzed during sleep using neural mechanisms similar to those used in wakefulness (e.g. generator mechanisms of N1, MMN, P3a) as well as sleep-specific mechanisms (e.g. generator mechanisms of N300, N550). The outcome of this analysis is the capacity to form a neural representation in sensory memory that permits the automatic detection of changes occurring in the surrounding context. Such change detection can lead occasionally to an increase in the arousal level, as revealed by the elicitation of the N550 (associated with the presence of K-complexes) during stage 2, which may facilitate awakening. The neural mechanisms determining the occasional increase in the arousal level remain unknown. The results gathered in the present review support the conclusion that the early stages of information processing characteristic of waking-processing are severely affected during sleep, but that the auditory system continues preserving 'essential services' in order to maintain contact with the surrounding environment.

Acknowledgements

The authors would like to thank anonymous reviewers for their helpful comments. This review was written while the two first authors (M.A. and J.L.C.) were visiting researchers in the Department of Psychiatry at Harvard Medical School, supported by fellowships of the NATO Scientific Program and the Spanish Ministry of Education, respectively. This study was also supported by grants to C.E. from the Spanish Ministry of Science and Technology (PM99-00167) and the Generalitat de Catalunya (1999SGR-00264).

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