



Auditory Thalamus Neurons During Sleep: Changes in Frequency Selectivity, Threshold, and Receptive Field Size

Jean-Marc Edeline, Elizabeth Hennevin, Yves Manunta

► To cite this version:

Jean-Marc Edeline, Elizabeth Hennevin, Yves Manunta. Auditory Thalamus Neurons During Sleep: Changes in Frequency Selectivity, Threshold, and Receptive Field Size. *Journal of Neurophysiology*, 2000, 84 (2), pp.934-52. <10.1152/jn.2000.84.2.934>. <hal-02397206>

HAL Id: hal-02397206

<https://hal.science/hal-02397206v1>

Submitted on 11 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

Auditory Thalamus Neurons During Sleep: Changes in Frequency Selectivity, Threshold, and Receptive Field Size

Jean-Marc Edeline, Elizabeth Hennevin, Yves Manunta

► To cite this version:

Jean-Marc Edeline, Elizabeth Hennevin, Yves Manunta. Auditory Thalamus Neurons During Sleep: Changes in Frequency Selectivity, Threshold, and Receptive Field Size. *Journal of Neurophysiology*, American Physiological Society, 2000. hal-02397206

HAL Id: hal-02397206

<https://hal.archives-ouvertes.fr/hal-02397206>

Submitted on 11 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Auditory Thalamus Neurons During Sleep: Changes in Frequency Selectivity, Threshold, and Receptive Field Size

JEAN-MARC EDELINE, YVES MANUNTA, AND ELIZABETH HENNEVIN

Laboratoire de Neurobiologie de l'Apprentissage, de la Mémoire et de la Communication, UMR 8620, Centre National de la Recherche Scientifique et Université Paris-Sud, 91405 Orsay Cedex, France

Received 22 February 2000; accepted in final form 5 May 2000

Edeline, Jean-Marc, Yves Manunta, and Elizabeth Hennevin.

Auditory thalamus neurons during sleep: changes in frequency selectivity, threshold, and receptive field size. *J Neurophysiol* 84: 934–952, 2000. The present study describes how the frequency receptive fields (RF) of auditory thalamus neurons are modified when the state of vigilance of an unanesthetized animal naturally fluctuates among wakefulness (W), slow-wave sleep (SWS), and paradoxical sleep (PS). Systematic quantification of several RF parameters—including strength of the evoked responses, response latency, acoustic threshold, shape of rate-level function, frequency selectivity, and RF size—was performed while undrugged, restrained guinea pigs presented spontaneous alternances of W, SWS, and PS. Data are from 102 cells recorded during W and SWS and from 53 cells recorded during W, SWS, and PS. During SWS, thalamic cells behaved as an homogeneous population: as compared with W, most of them (97/102 cells) exhibited decreased evoked spike rates. The frequency selectivity was enhanced and the RF size was reduced. In contrast during PS, two populations of cells were identified: one (32/53 cells) showed the same pattern of changes as during SWS, whereas the other (21/53 cells) expressed values of evoked spike rates and RF properties that did not significantly differ from those in W. These two populations were equally distributed in the different anatomical divisions of the auditory thalamus. Last, during both SWS and PS, the responses latency was longer and the acoustic threshold was higher than in W but the proportion of monotonic versus nonmonotonic rate-level functions was unchanged. During both SWS and PS, no relationship was found between the changes in burst percentage and the changes of the RF properties. These results point out the dual aspect of sensory processing during sleep. On the one hand, they show that the auditory messages sent by thalamic cells to cortical neurons are reduced both in terms of firing rate at a given frequency and in terms of frequency range. On the other hand, the fact that the frequency selectivity and the rate-level function are preserved suggests that the messages sent to cortical cells are not deprived of informative content, and that the analysis of complex acoustic sounds should remain possible. This can explain why, although attenuated, reactivity to biologically relevant stimuli is possible during sleep.

INTRODUCTION

One of the most striking differences between the waking and sleeping states obviously concerns the relationship of the organism to its environment, reactivity to external sensory stimuli being progressively reduced as sleep deepens. Nonetheless, the sleeping organism remains able to react to salient and

behaviorally relevant environmental stimuli; this sets sleep apart from other states such as coma and anesthesia. Despite the number of studies performed from the early 1960s to assess the sleep-related changes in sensory processing, how and where ascending sensory information is modulated during the different sleep stages remain open questions. Answering them constitutes important challenges intersecting the fields of sensory physiology and sleep research.

Understanding how sensory systems process information, whether during sleep or during any other states, requires comprehensive analysis of the operations performed by sensory neurons in their receptive fields (RF). Whatever the sensory modality, a minimal prerequisite to unravel sensory coding is to determine the size of the peri-threshold RF and the supra-threshold selectivity for a given dimension of the sensory stimuli. Other important measures include neuronal threshold, response latency, and the dynamic range of neuronal responses to increasing intensity of the stimulus. These measurements, which have long been used in sensory physiology experiments performed in anesthetized animals, have not yet been done in naturally sleeping animals. Indeed, if we except some observations in the visual cortex (Livingstone and Hubel 1981), all the studies that have been carried out so far have only described how neuronal responsiveness to a single sensory stimulus changed across behavioral states.

This is typically the case for the four single-unit studies that have been performed in the central auditory system: all of them only reported sleep-related changes in evoked responses to a selected acoustic stimulus. They showed that at the first relay (cochlear nucleus), an increase in evoked responses was the dominant change occurring when the animal shifted from waking (W) to slow-wave sleep (SWS), as well as from SWS to paradoxical sleep (PS) (Pena et al. 1992). At the two subsequent relays (lateral superior olive and inferior colliculus), almost equivalent proportions of increased and of decreased responses were observed in SWS relative to W, and in PS relative to SWS (Morales-Cobas et al. 1995; Pedemonte et al. 1994). At all these subthalamic levels only 15–35% of the cells showed unchanged evoked responses, but surprisingly, at the cortical level, most of the cells (63%) exhibited unchanged responses in SWS and PS (Pena et al. 1999). No study was performed at the thalamic level.

Address for reprint requests: J.-M. Edeline, NAMC, UMR 8620, Université Paris-Sud, Bât 446, 91405 Orsay Cedex, France (E-mail: Jean-Marc.Edeline@ibaic.u-psud.fr).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

The present experiment represents the first attempt to determine how the sensory coding performed by auditory thalamus neurons is modified across the wake-sleep states. Systematic quantification of frequency RF parameters was conducted while undrugged, restrained guinea pigs presented spontaneous alternances of W, SWS, and PS. A preliminary report concerning parts of these data was presented in an abstract form (Hennevin et al. 1995).

METHODS

Animal preparation

Single-unit activity was recorded from chronically implanted micro-electrodes rather than from moveable electrodes for two reasons. First, this technique maximizes the probability of long-duration recordings required in the present study. Second, as it involves less manipulations above the animal's head than the other one, it is less stressful, which increases the probability that the animal falls asleep and presents nonfragmented sleep episodes.

Thirty-three adult male Hartley guinea pigs (380–450 g) underwent surgery under anesthesia [atropine sulfate 0.08 mg/kg, diazepam (Valium) 8 mg/kg, pentobarbital sodium (Nembutal) 20 mg/kg] (see Evans 1979). Three silver-ball electrodes were inserted between bone and dura: one was used as reference during the recording sessions; the other two, placed over the frontal and parietal cortex, served to monitor the cortical electroencephalogram (EEG). A bipolar electrode was lowered in the right hippocampus (3 mm under pia) for the recording of hippocampal electroencephalographic (HEG) activity. Two silver wires were inserted into the dorsal neck muscles to record the electromyogram (EMG). An array of five tungsten electrodes ($\sim 1.0\text{ M}\Omega$ at 1 kHz, spaced 200–300 μm in the rostrocaudal axis) was lowered in the auditory thalamus, either unilaterally or bilaterally, under electrophysiological control. A pedestal in dental acrylic cement including two cylindrical threaded tubes was built to allow atraumatic fixation of the animal's head during the subsequent recording sessions. An antiseptic ointment (neomycine sulfate, Cidermex, Rhone-Poulenc Rorer) was liberally applied in the wound around the pedestal, and an antibiotic (josamycine propionate, Josacine, 8 mg/kg, Rhone-Poulenc Rorer) was administered during the 5 days following surgery. All surgical procedures were performed in conformity with national (JO 887-848) and European (86/609/EEC) legislations on animal experimentation, which are similar to those described in the *Guidelines for the Use of Animals in Neuroscience Research of the Society of Neuroscience*. In addition, regular inspections of our laboratory by accredited veterinarians designed by Paris-Sud University attested that cares were taken to maximize the animals' health and comfort throughout the different phases of the experiment.

Three days after surgery, each animal was adapted for several days to restrained conditions in an acoustically isolated chamber (IAC, model AC2). It was placed in a hammock with the head fixed for increasing periods of time (2–6 h/day). It was also accustomed to hear sequences of pure tone bursts. At the end of this period of adaptation, alternations of W, SWS, and PS were obtained. We stress the fact that none of the animals was drugged or sleep deprived before the recording sessions.

Recording procedures

The signal coming from the electrode was amplified (band-pass 600–10,000 Hz, gain 5,000) and sent in parallel to an audio monitor and to a voltage window discriminator (Frederic Haer, model 74-60-1). As no waveform sorting system was used, only one single-unit waveform was isolated from the signal coming from a given electrode. The waveform of the unit and the corresponding pulses generated by the discriminator were constantly displayed on the screen of a digital

oscilloscope. During each recording session, meticulous care was taken to ensure that the same unit was recorded throughout the session, and data collection was immediately stopped when the waveform was unstable. The TTL pulses generated by the window discriminator were sent to the acquisition board (PCLab, PCL 720) of a 33 MHz 486 PC computer. Using a subroutine written in assembly language, the time of occurrence of the TTL pulses corresponding to each action potential was known with a resolution of 50 μs . The single-unit waveforms were digitized (GW Instruments, Superscope software, 50-kHz sampling rate) during 63/102 recording sessions.

Stimulus generation

The sound generating system was exactly the same as in previous studies (Edeline et al. 1999; Manunta and Edeline 1997, 1999). Pure tone frequencies were generated by a remotely controlled wave analyzer (Hewlett-Packard, model HP 8903B) and attenuated by a passive programmable attenuator (Wavetek, P557, maximal attenuation 127 dB); both were controlled by a computer via an IEEE bus. Contralateral tones were delivered through an earphone (Sony MDR-W05) mounted in a small stainless steel container filled with foam. The opening of the container was fitted into the ear canal to deliver the stimuli close to the tympanic membrane. The determination of the power output of the sound delivery system was made with respect to a reference tone (1 kHz at 94 dB re 20 μPa) generated by a sound level calibrator (Bruel and Kjaer, model 4230). A condenser microphone/preamplifier (B and K, models 4133 and 2639T) was placed inside the opening of the calibrator. The output was sent to the wave analyzer, and the value obtained, together with the microphone calibration curve supplied by B and K (free field curve), allowed the conversion of additional values into absolute sound pressure level (SPL) values. The microphone/preamplifier was then placed in front of the opening of the sound transmission tube at approximately the same location as the tympanic membrane with respect to the end of the sound tube during the experiments. For each frequency passing through the earphone and the microphone/preamplifier, the power output for that frequency was determined by the wave analyzer. The values were converted into SPL values. A calibration curve was produced by converting the deviations from the intensity of the reference tone into absolute values for each frequency. Six ascending sequences of 11 isointensity tones were used: 0.1–1.1 kHz (stepping frequency, 100 Hz); 0.3–2.3 kHz (step, 200 Hz); 1–11 kHz (step, 1 kHz); 5–15 kHz (step, 1 kHz); 10–20 kHz (step, 1 kHz); 15–35 kHz (step, 2 kHz). The sound-delivery system can deliver tones of 90 dB up to 20 kHz and of 70 dB up to 35 kHz. Harmonic distortion products were 60 dB down from the fundamental. Although the intensities used were calibrated with respect to the SPL scale, the intensities expressed here are best viewed as relative values, given that a sealed sound system cannot be used in awake animals.

Experimental protocol

After 3–6 days of adaptation, the signal coming from each electrode was regularly checked. Single-unit signals were obtained from 1 to 4 wk after surgery. It should be emphasized that not all of the implanted electrodes gave satisfactory signals: more than half gave multiunit signals from which it was never possible to isolate any single unit waveform. The electrodes implanted in 14 (of 33) animals never gave appropriate signals. In the remaining 19 animals, 94 electrodes gave correct single-unit (SU) signals during at least one session. SU activity was recorded only once for 68 electrodes; it was recorded twice for 18 electrodes, three times for 6 electrodes, and four times for two electrodes. Recordings from the same electrode were spaced by at least 3 days.¹

¹ It is unlikely that the same cell was recorded twice for the following reasons. First, in the dorsal and medial divisions of the auditory thalamus, the

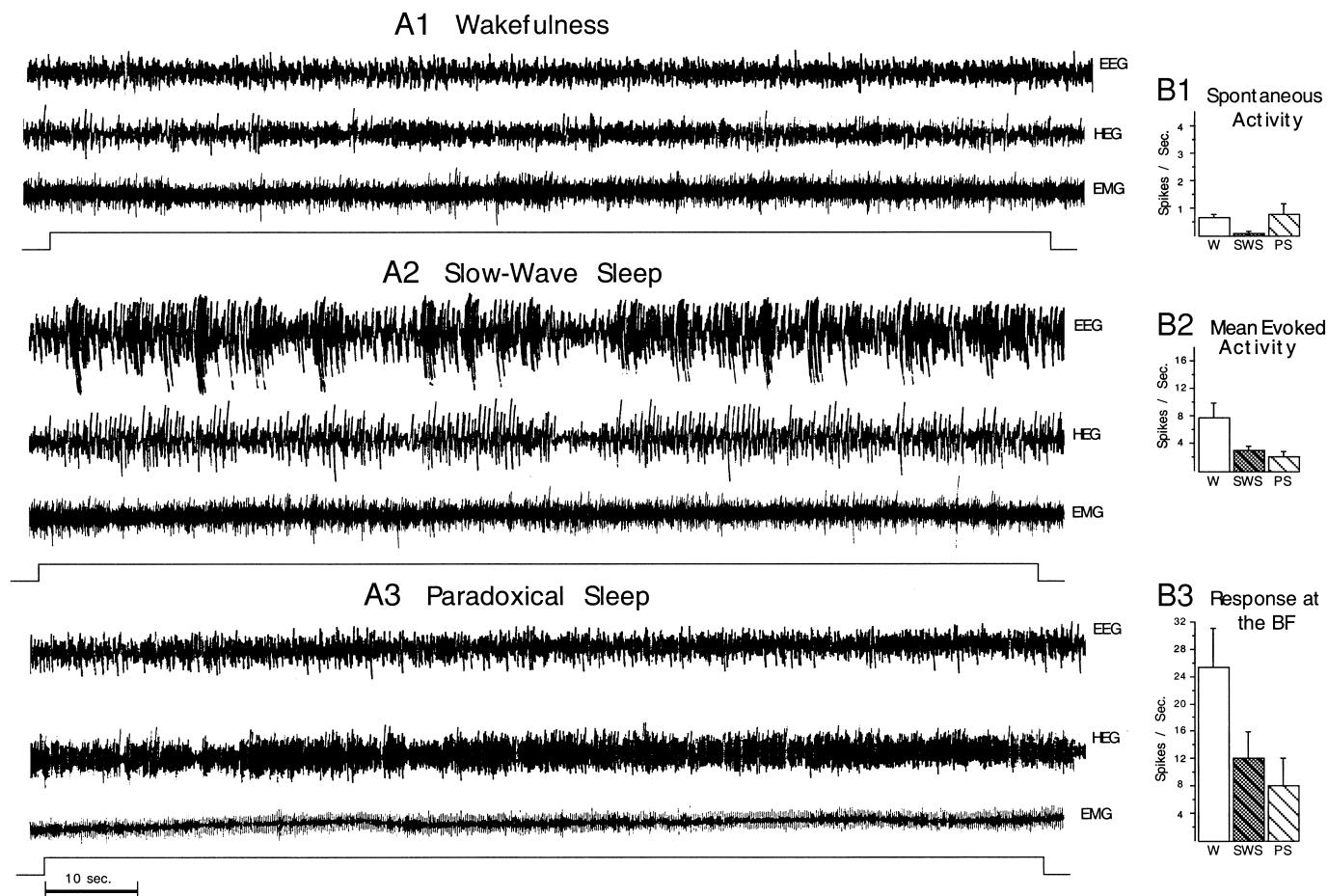


FIG. 1. Examples of polygraphic recordings obtained in the different states of vigilance. The cortical electroencephalogram (EEG), the hippocampal electroencephalogram (HEG), and the electromyogram (EMG) are displayed during the 110 s (represented by the TTL pulse below the EMG recording) required to test the frequency response function at a given intensity. Compared to wakefulness (W; A1), the EEG and the HEG exhibited a typical pattern of high-voltage slow rhythm during slow-wave sleep (SWS; A2). During paradoxical sleep (PS; A3), a typical theta rhythm was observed on the HEG, while the EMG became almost flat, revealing cardiographic activity. For the cell (GP23bv2) recorded during these periods, the spontaneous activity was decreased in SWS and unchanged in PS (B1), the mean evoked response was decreased in both SWS and PS (B2) and so was the response at the best frequency (BF; B3).

At each recording session, once a clear single-unit waveform was observed, repeated ascending sequences of 11 pure tone frequencies (100-ms tone duration, 5-ms rise-fall time, 1-s intertone interval) were first delivered, until the sequence of tones the most appropriate to cover the neuron's receptive field was found. The selected sequence was then continuously presented. It was repeated 10 times at a given intensity; thus testing the frequency response function (FRF) at a given intensity lasted 110 s. The sequence was presented at different intensities, in a pseudo-random order, from 70–90 dB to the neuron's threshold (using 10-dB steps). The data corresponding to every test of the FRF were systematically stored on the hard drive of the computer. The EEG, HEG, and EMG were continuously monitored on a polygraph (Grass, model 7P511). The recording session was stopped each time a waveform different from that stored at the beginning of the session passed the threshold of the voltage window discriminator.

characteristic frequency of the cells recorded from the same electrode largely differed between successive recording sessions. Second, in the ventral division, of five cases of successive recordings with the same electrode, four had similar characteristic frequency (as expected from the tonotopic organization in this division), but the changes in vigilance state did not produce twice identical effects.

Data analysis

After each recording session, the polygraphic recordings were examined independently by the three investigators. Only the FRFs unambiguously recorded during continuous and stable periods of W, SWS, or PS were analyzed. As the vigilance state of the animals always fluctuated in an unpredictable manner, the probability that the 110 s corresponding to the determination of the FRF at a given intensity belonged entirely to a stable vigilance state was very low. The consequence was that only 10% of the FRFs obtained during a recording session were analyzed; the remaining 90%, obtained from mixed vigilance states, were not further considered. Figure 1 presents a representative example of recording obtained in each behavioral state.

The spontaneous activity was quantified during the 500 ms preceding each tone. Such quantification was found to be similar to that obtained when spontaneous activity was collected during longer periods (2 min) without tone presentation (Manunta and Edeline 1997, 1999). In agreement with the literature that has categorized the excitatory evoked responses in anesthetized animals (Bordi and Ledoux 1994; Calford 1983; Rodrigues-Dageff et al. 1989; Rouiller et al. 1989), we observed either "on" (phasic) responses or "sustained" (tonic) responses. On the basis of the observed pattern of response, a

time window (0–25, 0–50, or 0–100 ms) was selected to analyze the responses of a given neuron. Only excitatory responses were considered, inhibitory responses were not. We did not analyze either “off” responses and “labile” responses (i.e., responses which progressively habituated during repetition of the tone sequence even when the vigilance state was constant). Cells that could not be driven by any pure tone stimuli but that, in many cases, responded to click or complex stimuli were also discarded.

For each cell, the FRFs obtained at each intensity were plotted, and the following variables were analyzed. The mean evoked response (mean) was defined as the response averaged across the 11 frequencies used to determine the FRF at a given intensity. The best frequency (BF) was defined as the frequency eliciting the strongest evoked responses at that intensity. The signal-to-noise ratio (S/N) was computed at each intensity tested, by dividing the tone-evoked response by the spontaneous activity, using as signal the mean evoked response (mean/spon) and the response at the BF (BF/spon).

The frequency selectivity was quantified at each intensity using the following index: [(response at the BF – mean evoked response)/(response at the BF)] \times 100. A similar index is used in the visual system to quantify the orientation selectivity (Bienenstock et al. 1982; Frégnac et al. 1992). An index approaching 100 means that excitatory responses occurred only at the BF, whereas an index equal to 0 means that the cell gave similar responses at all the frequencies used to generate the FRF.

The latency of the tone-evoked responses was computed at each intensity used to test the FRF. At a given intensity, all the responses obtained for all the frequencies tested were considered, and the latency of the first spike after tone onset was computed (1-ms precision). For each cell and at each intensity, the variability of the latency was quantified by the standard deviation of the mean latency value.

The acoustic threshold was defined as the intensity eliciting at least 5/10 tone-evoked responses at the BF. The rate-level function was characterized when the evoked responses at the BF could be determined at least at five to seven different intensities. Monotonic and nonmonotonic rate-level functions were defined on the basis of the criteria used by Phillips and Kelly (1989), that is, if the sign of the gradient of the rate-response curve did not reverse over the range of intensities tested, the cell was classified as monotonic and if the gradient of the rate-response curve did change sign at suprathreshold tone levels, the cell was classified as nonmonotonic (changes in response strength $<10\%$ were not considered as gradient changes). In all cases, the cells classified as nonmonotonic exhibited excitatory responses that were attenuated by 60% compared with their maximal level, at least at the two to three highest intensities tested.

The RF size was quantified using two different indices. The first was the Q10dB (Kiang et al. 1965). With this index, the higher the value the sharper the RF size. The second was the square root transformation $\sqrt{f_2 - f_1}$, where f_2 and f_1 indicate the high and low limits of the FRF breadth at 20 dB above threshold. This measure is independent of the characteristic frequency (Calford et al. 1983; Whitfield 1968; Whitfield and Purser 1972). With this index, the lower the value the sharper the RF size.

To assess if changes in discharge mode occurred across states, a “burstiness index” (BI) was calculated for each cell in each vigilance state. As it has been done in other studies (Guido et al. 1992; Lu et al. 1992; Mukherjee and Kaplan 1995), we used an empirical gauge of the neurons burstiness by computing the percentage of intervals ≤ 4 ms in the interspike interval distribution. The BI was computed separately for periods of spontaneous activity (between tone presentations) and for periods of evoked activity (during tone presentations). For each cell, this analysis was performed both at the intensity producing the strongest evoked responses and at the intensity producing the smallest responses above threshold.

Three types of statistical comparisons were carried out. First, for each of the parameters measured, between-state comparisons were made using, in all cases, Student’s paired *t*-tests. Second, individual

comparisons were made for each cell to determine if the activity of the cell was significantly affected by behavioral state changes. At each tone intensity, the values of spontaneous and of evoked activity obtained for a cell during SWS or during PS were compared with those obtained for that cell during W, using paired *t*-test. The level of $P < 0.05$ was used to assign each cell to a given category: decreased, increased, or unchanged activity. Third, between-division comparisons were made using ANOVA to determine if the sleep-related changes were or not similar in the different anatomical divisions of the auditory thalamus.

Histology

At the end of the experiment, the animals received a lethal dose of Nembutal (200 mg/kg), and small electrolytic lesions were made by passing anodal current (10 μ A, 10 s) through the recorded electrodes. The animals were perfused intracardially with 0.9% saline (200 ml) followed by 2,000 ml of fixative (4% paraformaldehyde in 0.1 M phosphate buffer, pH 7.4). The brains were put in a 30% sucrose solution for 3–4 days. Then coronal serial sections of the brain were cut on a freezing microtome (50- μ m thickness). For 13 animals, all serial sections were counterstained with cresyl violet. For six animals, sections were collected in three parallel series. Sections from the first series were counterstained with cresyl violet. Sections from the second series were histochemically stained for reduced nicotinamide adenine dinucleotide phosphate diaphorase (NADPH-d) (Sandell et al. 1986; Sims et al. 1974). Sections from the third series were histochemically stained for acetylcholinesterase (AChE) (Koelle 1955). The combination of these stainings has been found to be useful for delineating the divisions of the auditory thalamus in the rabbit (Cabrero-Bleda et al. 1991), a species that is phylogenetically close to the guinea pig. The sections were examined under several microscopic magnifications, and the location of the recording sites was reconstructed using a camera lucida.

RESULTS

Of 130 neurons recorded in 19 animals, 102 gave tone-evoked responses sufficiently robust to provide reliable frequency response functions (FRF) in the waking state. All these 102 cells were tested during SWS, and 53 of them were tested during PS. The time period during which a cell was recorded ranged from 30 min to 4 h (mean 65 min). The spike amplitudes were from 200 to 800 μ V, with a noise level generally <100 μ V.

Figures 2–4 present the FRF of three cells recorded in three different animals. As can be seen, during SWS the three cells exhibited lower spontaneous and evoked activities than during W, and they responded to a smaller frequency range. Two of these cells were also recorded during PS. Both displayed higher spontaneous activity in PS than in W, but their evoked activity was differentially affected. For a cell (Fig. 3), the evoked responses were almost totally suppressed in PS. For the other cell (Fig. 4), the evoked responses partly recovered the level observed during W, and the cell responded for the same frequency range as in W.

As detailed in the following text, these profiles of changes are representative of those observed on the whole cells population, whatever the tone intensity used. Table 1 indicates the number of observations used to generate the group data.

Changes in spontaneous and evoked activities; consequences on the S/N ratio

Figure 5 presents the results obtained on the largest database available, i.e., over all the intensities tested. For most of the

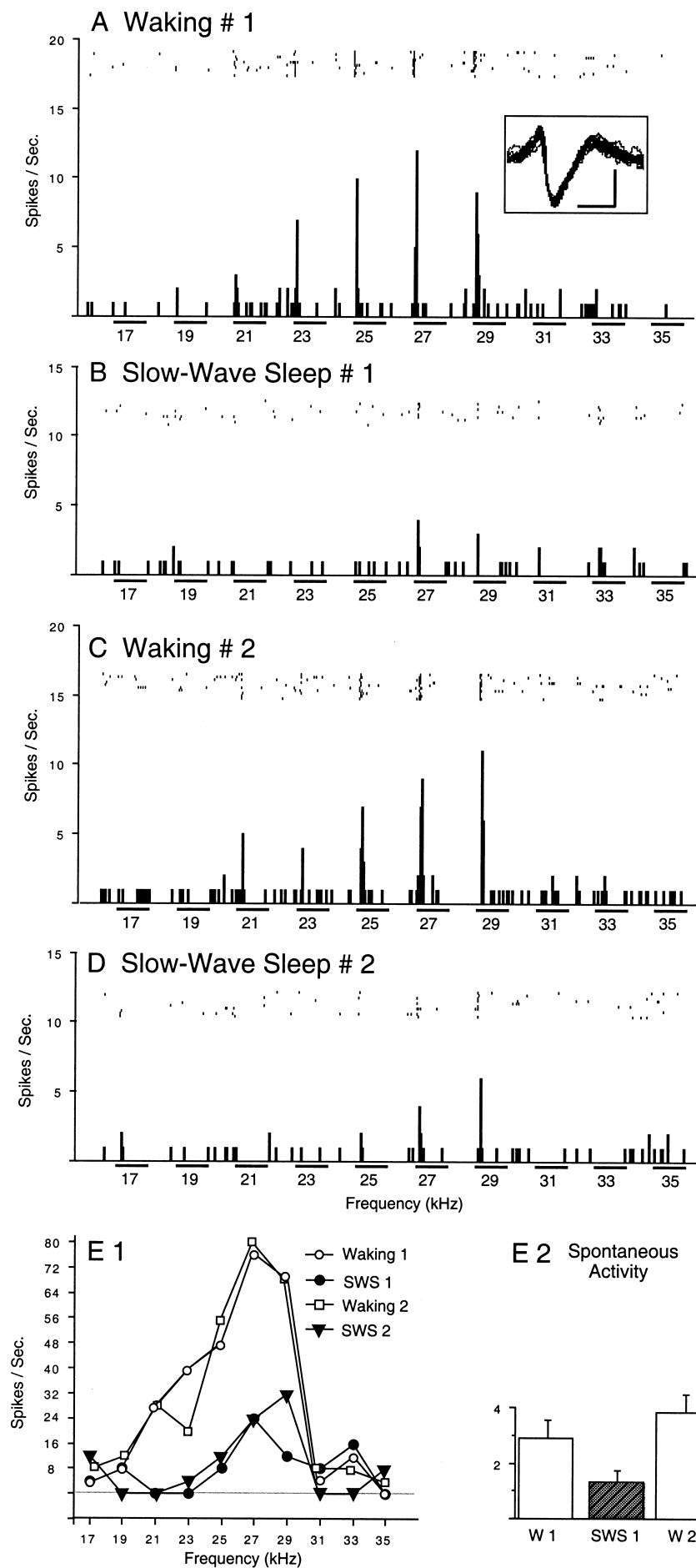


FIG. 2. Decrease in evoked and spontaneous activity during SWS for a neuron recorded in the ventral medial geniculate body (MGv). The histograms and rasters display the responses evoked at 20 dB in the receptive field (RF) of a cell (*GP17fv1*) located in MGv. At this intensity, the cell was tested twice during W and twice during SWS. During W, evoked responses were observed from 21 to 29 kHz (A and C). During SWS, responses, strongly reduced in magnitude, were only observed at 27 and 29 kHz (B and D). This cell was not tested during PS. The quantification of the evoked responses (E1) shows the stability of the responses within each state of vigilance, and the large decrease of the responses in SWS. The spontaneous activity was significantly decreased during the 2 tests performed in SWS (E2). In this figure, as in all the following individual figures, the histograms (5-ms bin) and rasters display the cell's activity during 10 repetitions of a sequence of 11 ascending frequencies. An evoked response was defined by the presence of tone-evoked action potentials elicited at least in 5/10 repetitions. The short bars below the x axis denote the 100 ms of tone duration, and only the 100 ms immediately preceding each tone is presented. The numbers below the short bars are the values of the frequencies in kHz. Inset: display of the waveform of the action potential (30 sweeps, 50-kHz sampling rate). Scale bars: 0.5 mV, 0.5 ms).

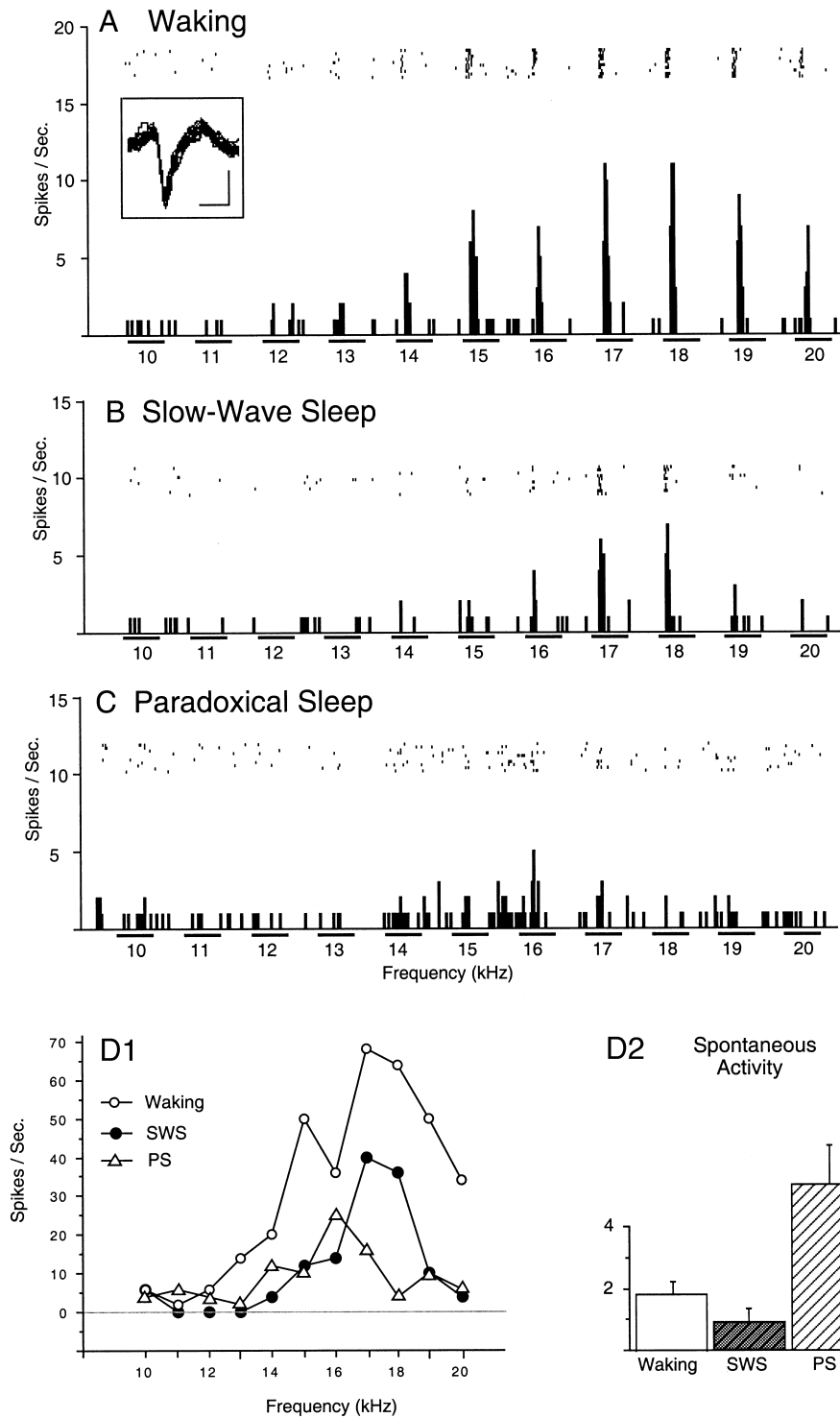


FIG. 3. Decrease in evoked activity during SWS and further decrease in PS for a neuron recorded in the medial division of the medial geniculate body (MGm). The histograms and rasters display the responses evoked at 30 dB in the RF of a cell (*GP13ov1*) located in MGm. At this intensity, the cell was tested during W, SWS, and PS. During W, evoked responses were observed from 13 to 20 kHz (A). During SWS, responses, reduced in magnitude, were observed from 16 to 18 kHz (B). During PS, weak evoked responses were observed at 16 and 17 kHz (C). The quantification of the evoked responses (D1) shows the decrease of the responses in SWS and their further attenuation in PS. Spontaneous activity was significantly decreased in SWS and significantly increased in PS (D2).

cells, spontaneous activity was decreased in SWS compared with W, whereas it was increased in PS (Fig. 5A). The mean evoked activity was decreased in SWS as well as in PS (Fig. 5B). This was also the case for the responses at the BF (data not shown). Between-state comparisons (paired *t*-test) attested that these changes were highly significant ($P < 0.0001$ in all cases). Comparison between SWS and PS indicated that the mean evoked response was higher in PS ($P = 0.02$), whereas the response evoked at the BF did not differ between the two states ($P = 0.76$).

The consequences of these changes on the S/N ratio are illustrated in Fig. 5C. The S/N ratio was unchanged in SWS compared with W ($P > 0.62$, using as signal either the mean evoked response or the response at the BF). In contrast, it was decreased in PS compared both to W and SWS (all $P < 0.0001$).

Similar changes were observed when the responses at selected intensities were considered. For example, at the intensity eliciting the strongest responses in W, the mean evoked re-

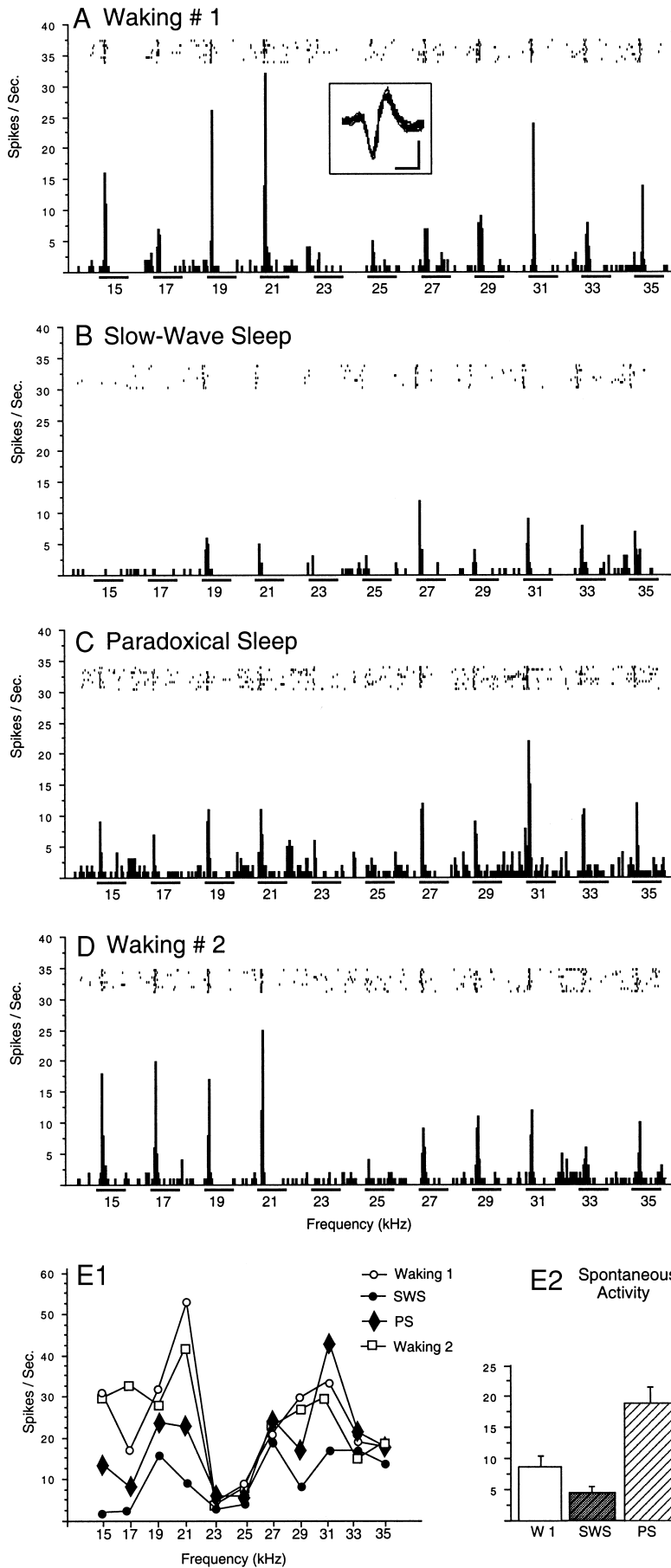


FIG. 4. Decrease in evoked activity during SWS and partial recovery during PS for a neuron recorded in the dorsal medial geniculate body (MGd). The histograms and rasters display the responses evoked at 70 dB in the RF of a cell (*GP17gv2*) located in MGd. At this intensity, the cell was tested during W, SWS, and PS. During W (A), evoked responses are shown from 15 to 35 kHz (at lower intensities, this cell responded to a limited frequency range; for example, at 40dB it was only responding between 21 and 29 kHz). During SWS, responses, reduced in magnitude, were observed from 19 to 35 kHz (B). During PS, evoked responses, slightly reduced in magnitude compared with W, were observed from 15 to 35 kHz (C). During a subsequent episode of W (D), the responses were similar to those obtained in the first waking episode. The quantification of the evoked responses (E1) shows their attenuation in SWS and their partial recovery in PS. Spontaneous activity was significantly decreased in SWS and significantly increased in PS (E2).

TABLE 1. Number of cells tested in each behavioral state and number of observations from which group data were obtained for the different parameters quantified

	W	SWS	PS
Total number of cells tested	102	102	53
Intensities tested			
Mean number (range)	3.65 (1–7)	3.53 (1–7)	2.20 (1–5)
Range of values (dB)	20–90	20–90	20–90
Total number of frequency response functions tested	373	361	117
Number of cells used to quantify the evoked responses			
At the highest intensity	102	102	31
At the lowest intensity	102	77	25
At the intensity producing the strongest response	102	102	44
Number of cells used to quantify the S/N ratio	102	102	53
Number of cells used to quantify the frequency selectivity	102	102	53
Response latency			
Number of frequency response functions allowing determination of the response latency	373	325	94
Number of cells from which the response latency was determined at the intensity producing the strongest response	102	95	35
Number of cells used to determine the acoustic threshold	102	82	42
Number of cells used to determine the rate-level function	94	74	20
Number of cells used to quantify the receptive field size	102	82	31

W, wakefulness; SWS and PS, slow-wave and paradoxical sleep, respectively.

sponse and the response at the BF were smaller during SWS than during W ($P < 0.0001$ in both cases). They were also reduced during PS ($P < 0.003$ for both comparisons; see Table 2). Comparable results were obtained at the highest and at the lowest intensity used to test the cells. Last, whatever the intensity and using as signal either the mean evoked response or the response at the BF, the S/N ratio did not differ between SWS and W (for high intensity, low intensity or intensity producing the strongest responses, lowest P value = 0.26). It was systematically lower in PS than in W and SWS (all $P < 0.01$).

The attenuation of evoked activity during sleep is also attested by the proportion of cells exhibiting significant ($P < 0.05$) changes in their evoked activity relative to W. During SWS, most of the cells (69/102, 68%) showed a significant decrease in activity. Similarly, during PS 32/53 cells (60%) showed a significant decrease in evoked response (see Table 3B and Fig. 6A), and this decrease was even more pronounced than that observed during SWS (see Fig. 6B). However, a substantial number of cells (21/53, 40%) behaved differently: their responses were stronger in PS than in SWS (Fig. 6D) and were comparable to those observed during W (Fig. 6C).

Changes in frequency selectivity

The frequency selectivity was determined for each cell and at each intensity, using an index that quantified the relative weight of the response at the BF compared with the responses evoked at the other frequencies (see METHODS). Figure 5D shows the results obtained over all the intensities tested. On average, the selectivity index was higher in SWS than in W [59.8 vs. 53.6; $t(360) = 8.61$, $P < 0.0001$] and than in PS [64.1 vs. 57.3; $t(108) = 4.64$, $P < 0.0001$]. It did not significantly differ between PS and W [57.3 in PS vs. 55.6 in W; $t(116) = 1.11$, $P = 0.26$]. Similar changes were observed when the data were analyzed at selected intensities. For example, at the intensity eliciting the strongest evoked responses, the selectivity index was increased from W to SWS [from 52.9 to 58.9;

$t(101) = 3.80$, $P < 0.0002$], whereas it was not significantly modified in PS [$t(43) < 1$; see Table 2]. However, a more detailed analysis revealed that the frequency selectivity in PS differentially evolved depending on whether the cells did or did not exhibit decreased evoked responses. It did not significantly differ from that in W for the 21 cells whose evoked responses were not depressed [$t(20) = 1.62$, $P = 0.12$], whereas it was increased for the 32 cells showing depressed evoked responses [$t(31) = 3.07$, $P < 0.005$].

Changes in responses latency

In the three states of vigilance, the latency of the evoked responses was determined at each intensity tested. In some cases, it could not be computed in SWS and/or in PS because the evoked responses were too depressed to allow latency quantification. Over all the intensities tested, the mean responses latency during W was 27.3 ms (range, 7–64 ms). This rather long latency was due to the fact that the latency increased as the response decreased in strength as a function of the intensity used, and that the data were from all the anatomical divisions of the auditory thalamus, including cells from the dorsal and medial divisions that have long latency responses (Calford 1983; Edeline et al. 1999). The mean responses latency was increased in SWS [$t(324) = 6.08$, $P < 0.0001$]. When the latency could also be determined during PS ($n = 94$), it appeared longer from W (26.7 ms) to SWS (28.2 ms; $P < 0.0001$) and to PS (31.1 ms; $P < 0.008$ for the comparison between PS and W; $t < 1$ for the comparison between PS and SWS). As presented on Fig. 7A, similar changes were observed at the intensity eliciting the strongest tone-evoked responses (see also Table 2). In addition, the variability of the responses latencies was increased during sleep. For the 94 FRFs from which the responses latencies could be determined in W, SWS, and PS, the variability increased from W to SWS (20.2 vs. 22.7 ms; $P < 0.01$) and it was further increased from SWS to PS (24.6 ms; $P < 0.0001$).

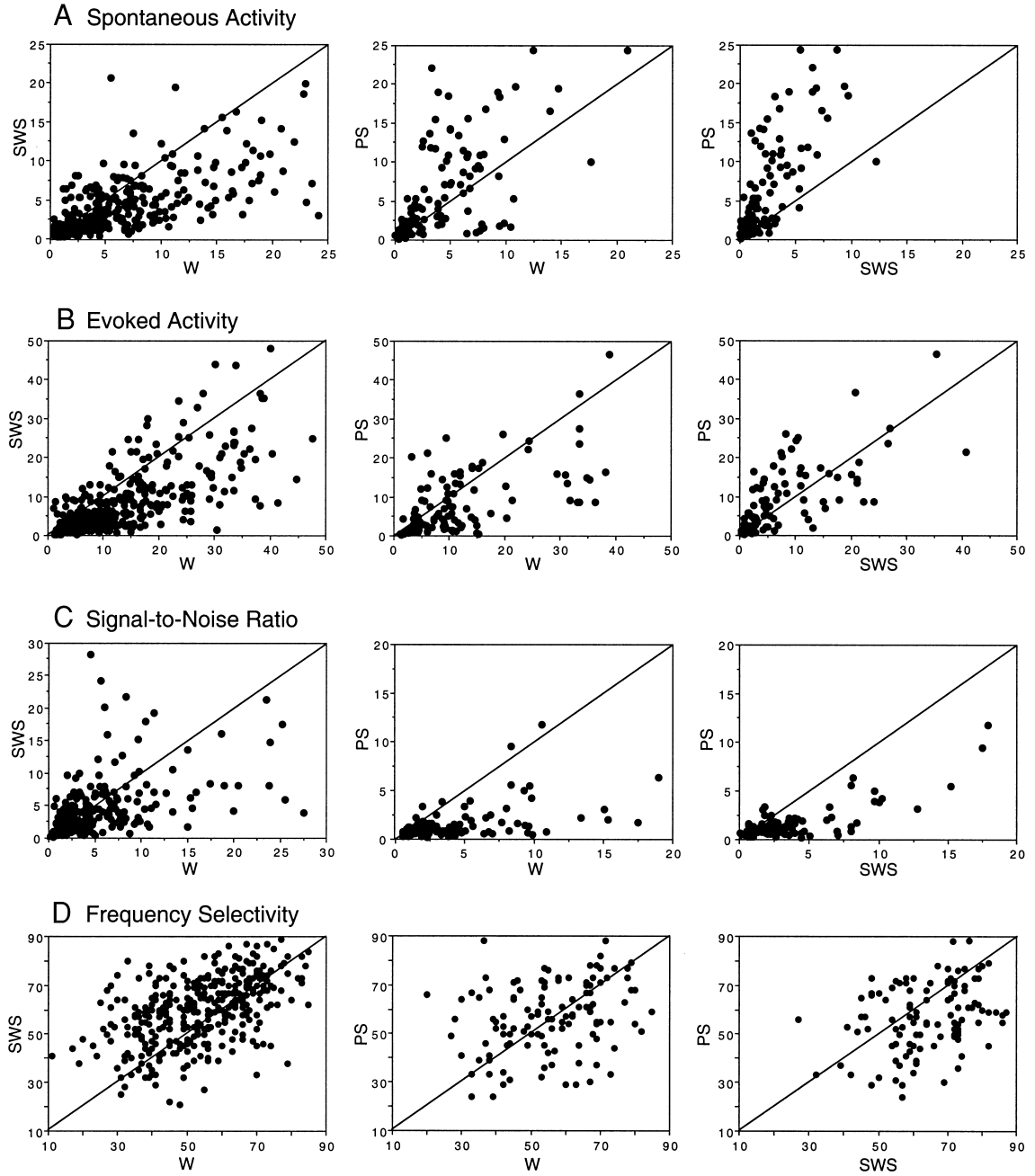


FIG. 5. Changes occurring across vigilance states for the 4 main parameters quantified over all the intensities tested. *Left*: scattergrams show the changes occurring in SWS compared with W. *Middle*: the changes occurring in PS compared with W. *Right*: the changes occurring in PS compared with SWS. For each cell, the data obtained at each intensity are represented individually. *A*: in most of the cases, spontaneous activity was decreased in SWS compared with W. It was increased in PS compared with both W and SWS. *B*: in most of the cases, the mean evoked activity was decreased in SWS compared with W. It was often (but not systematically) decreased in PS compared with W. It was mainly increased in PS compared with SWS. *C*: the signal-to-noise ratio was either increased or decreased in SWS compared with W. It was systematically decreased in PS compared with both W and SWS. *D*: in the majority of the cases, the frequency selectivity was increased in SWS compared with W. It was increased or decreased in PS compared with W. It was decreased in PS compared with SWS.

Changes in acoustic threshold and in rate-level function

The mean acoustic threshold obtained for the 102 cells tested during W was 40 dB. For some cells, the threshold could not be determined during SWS and/or PS because the evoked responses were too reduced or because an insufficient number of intensities was tested. The appropriate conditions were met for 82 cells in SWS and for 42 cells in PS. On average, the

threshold was higher in SWS than in W (51 vs. 41 dB; $P < 0.0001$); it was further increased in PS (64 dB; $P < 0.001$ for all paired comparisons). Indeed, as it can be seen from Fig. 7B, among the 42 cells tested in the three vigilance states, only one exhibited a lower threshold in SWS or PS than in W.

The rate-level function was determined for 94 cells during W; 49 exhibited monotonic functions and 45 nonmonotonic

TABLE 2. Changes in physiological parameters for 44 cells tested in each vigilance state at the intensity eliciting the strongest evoked responses in W

	W	SWS	PS
Spontaneous activity (spikes/s)	5.29	3.29*	6.80*
Mean evoked activity (spikes/s)	15.59	7.46***	8.82**
Response at best frequency (spikes/s)	33.97	19.23***	19.72**
Signal-to-noise ratio			
Mean/spon	5.35	4.51	2.05***
BF/spon	13.17	12.08	5.27***
Selectivity index	55.18	63.18***	57.79
Latency (ms)	24.69	29.80**	31.50***
Threshold (dB spl)	35.71	43.57**	49.63***
Receptive field size			
$\sqrt{f_2} - \sqrt{f_1}$	1.040	0.714***	0.859
Q10dB	1.935	3.117**	2.418
Burstiness index			
During spontaneous activity	11.51	22.21***	12.34
During tone presentation	36	49.28**	19.40***

Mean, mean evoked response; BF, response at the best frequency; spon, spontaneous activity. For other abbreviations, see Table 1.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$ (different from W; paired t -test).

functions. Among the 74 cells tested during SWS, 41 displayed monotonic functions and 33 nonmonotonic functions. It was possible to determine the rate-level function for only 20 cells

TABLE 3. Proportions of cells showing significant changes in spontaneous and/or evoked activity, as compared with W, for the 53 cells tested during SWS and PS

Spontaneous activity	Evoked activity, n (%)			
	Decrease	Increase	No change	Total
<i>During SWS</i>				
Decrease	26 (49)	0 (0)	4 (7)	30 (56)
Increase	1 (2)	0 (0)	2 (4)	3 (6)
No change	10 (19)	1 (2)	9 (17)	20 (38)
Total	37 (70)	1 (2)	15 (28)	53
<i>During PS</i>				
Decrease	10 (19)	0 (0)	1 (2)	11 (21)
Increase	11 (21)	4 (7)	11 (21)	26 (49)
No change	11 (21)	0 (0)	5 (9)	16 (30)
Total	32 (61)	4 (7)	17 (32)	53

The spontaneous activity and the mean evoked response obtained during SWS or PS were compared with the values obtained in W and the $P < 0.05$ level was used to assign a cell to a given category. Note that the dominant effect in SWS was a decrease of both spontaneous and evoked activity whereas in PS it was an increase of spontaneous activity and a decrease of evoked activity. n , number of cells. For other abbreviations, see Table 1.

during PS; 6 of them exhibited monotonic functions and 14 nonmonotonic functions. More interesting is the fact that in all but one cases, the shape of the rate-level function was not

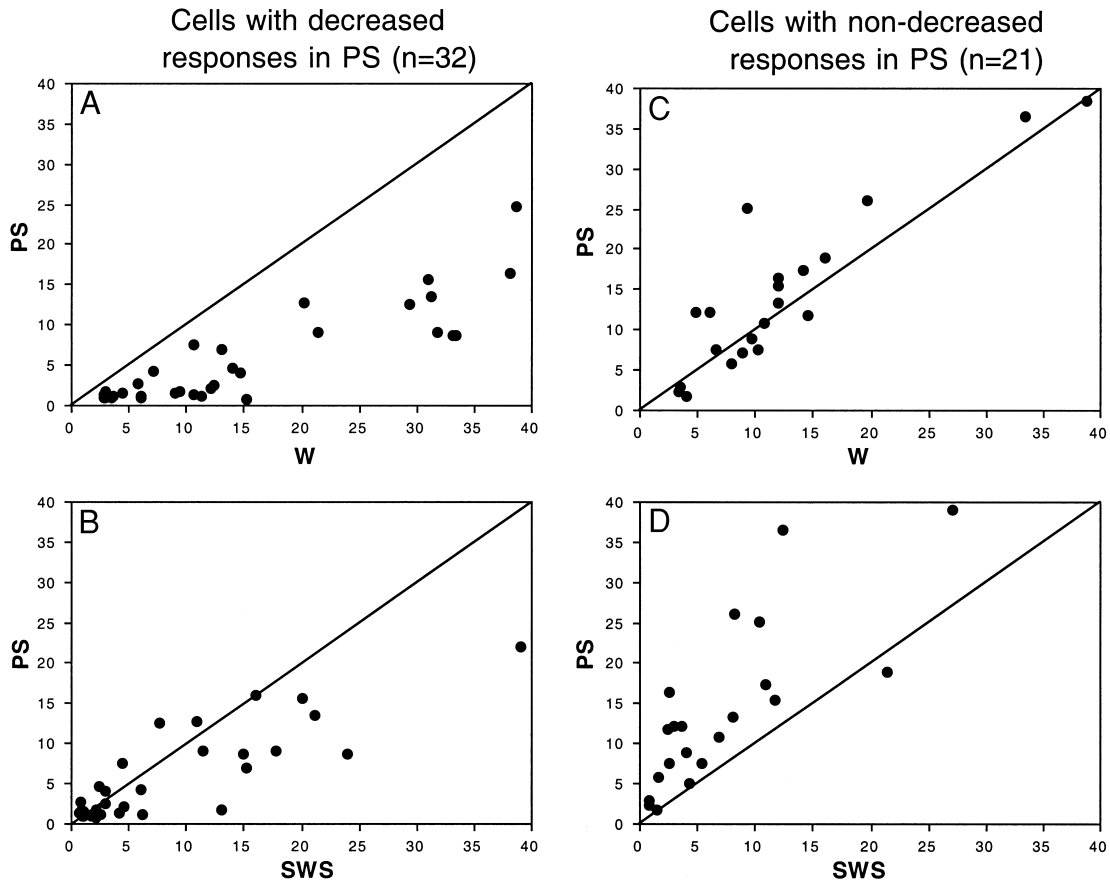


FIG. 6. Differential evolution of the responses evoked during PS. The scattergrams illustrate the fact that the evoked responses of the 53 cells tested during PS evolved in 2 different ways. For a first group of cells ($n = 32$) that individually exhibited significant attenuation of their responses in PS compared with W (A), the responses were generally more depressed in PS than in SWS (B). In contrast, for a 2nd group of cells ($n = 21$) whose responses were not statistically different in PS and W (C), the responses were stronger in PS than in SWS (D).

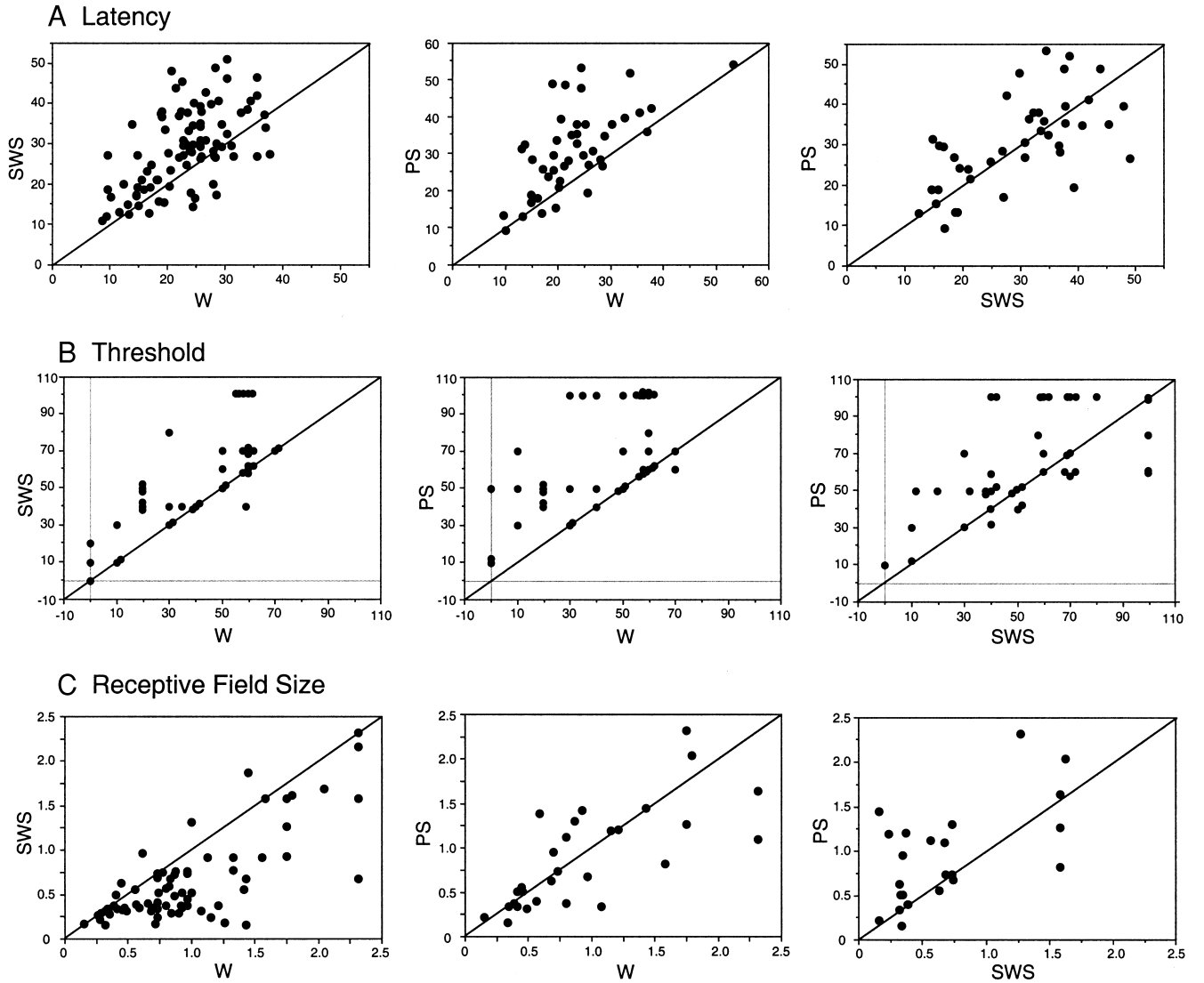


FIG. 7. Changes occurring across vigilance states for the latency, the acoustic threshold, and the RF size. *A*: the response latency was increased in SWS compared with W. It was also increased in PS compared with W. It was either increased or decreased in PS compared with SWS. Data are from the intensity allowing the strongest evoked response. *B*: the acoustic threshold was increased in SWS compared with W. It was increased in PS compared with both W and SWS. Note that an arbitrary value of 100 was assigned when the threshold could not be determined in SWS or PS due to weak evoked responses. *C*: the receptive field size was decreased in SWS compared with W. It was either increased or decreased in PS compared with W. It was increased in PS compared with SWS. Conventions as in Fig. 5.

affected by the state changes. This is illustrated in Fig. 8, *A* and *B*, which provides examples of a monotonic and of a nonmonotonic cell, respectively.

Changes in RF size

The size of the RFs was quantified by the square root transform ($\sqrt{f_2} - \sqrt{f_1}$) and the Q10dB. The use of these two indices was problematic here because it required to estimate the neuron's threshold in the three states of vigilance, to quantify in each state the neuron's FRF at, respectively, 20 and 10 dB above threshold, and to still observe unambiguous evoked responses at these intensities. These conditions were met for 82/102 neurons during SWS and for 31/53 neurons during PS.

Using the square root transform, a mean value of 0.897 was

obtained for the 102 cells tested during W. For the 82 cells whose bandwidths were quantified in SWS, the value of tuning was smaller in SWS than in W [0.64 vs. 0.92; $t(81) = 7.20$, $P < 0.0001$]. For the 31 cells whose bandwidths were quantified in PS, the value of tuning did not significantly differ from that in W [$t(30) < 1$]. Similar results were observed with the Q10dB: a higher value (indicating a smaller RF size) was obtained in SWS than in W [3.42 vs. 2.10; $t(81) = 5.93$, $P < 0.0001$], whereas there was no significant difference between PS and W [$t(30) = 1.70$, $P = 0.09$].

Thus on the basis of these two measures, the mean RF size was decreased during SWS compared with W. This reduction is illustrated by the scattergrams presented Fig. 7C and by the three examples of threshold tuning curves provided in Fig. 9. During PS, the RF size was, on average, not significantly modified relative to W. However, a more detailed analysis

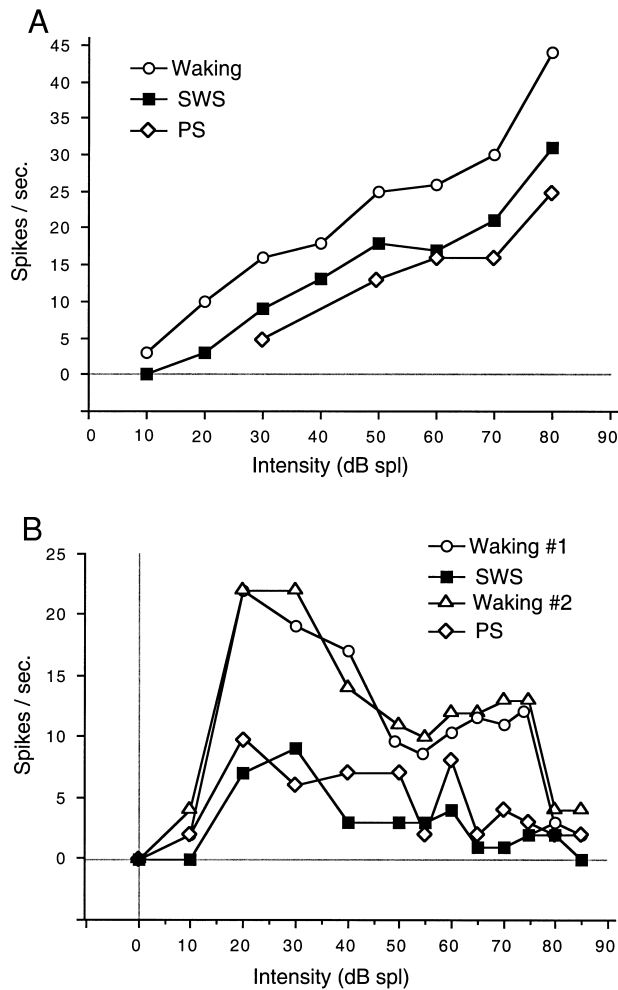


FIG. 8. Individual examples of rate-level functions obtained for 2 different cells in the 3 states of vigilance. *A*: the frequency tuning of this cell (*GP09hv1*) was tested between 10 and 80 dB. The responses obtained at the BF are presented for each intensity tested in W, SWS, and PS. This cell typically exhibited a monotonic rate-level function that was maintained in SWS and PS despite the attenuation of evoked responses. *B*: the frequency tuning of this cell (*Gp13pv1*) was first tested from 30 to 70 dB. As the recording was particularly stable, we also tested the rate-level function across vigilance states by presenting the BF at intensities ranging from 0 to 85 dB. During W, this cell typically exhibited a nonmonotonic rate-level function with a peak of response at 20–30 dB. During both SWS and PS, the evoked responses were largely decreased at all intensities, but the highest responses were still observed at 20–30 dB, while the lowest responses were obtained between 65 and 85 dB. Thus the nonmonotonic characteristic of the rate-level function was preserved whatever the state of vigilance.

revealed that this was true only for the cells whose evoked responses were not decreased in PS [$t(14) < 1$, for the square root transform]. For the cells whose evoked responses were decreased, the RF size was reduced [$t(15) = 2.36$, $P < 0.05$]. The examples presented in Fig. 9, *A* and *C*, illustrate these two opposite effects.

Changes in discharge mode: relationships with other parameters

During W, the mean value of the BI was higher during tone presentation than during spontaneous activity. This was true at the intensity producing the strongest evoked response (37.2 during tone period vs. 11.5 during spontaneous activity; $P <$

0.0001) as well as at the intensity producing the smallest evoked responses (30.2 vs. 12.3; $P < 0.0001$). During SWS, the BI value was higher than it was in W during both tone presentation and spontaneous activity. For example, at the intensity eliciting the strongest evoked responses, it was 50.8 during tone period (+36.5%; $P < 0.0001$) and 24.2 during spontaneous activity (+110%; $P < 0.0001$). Similar increases

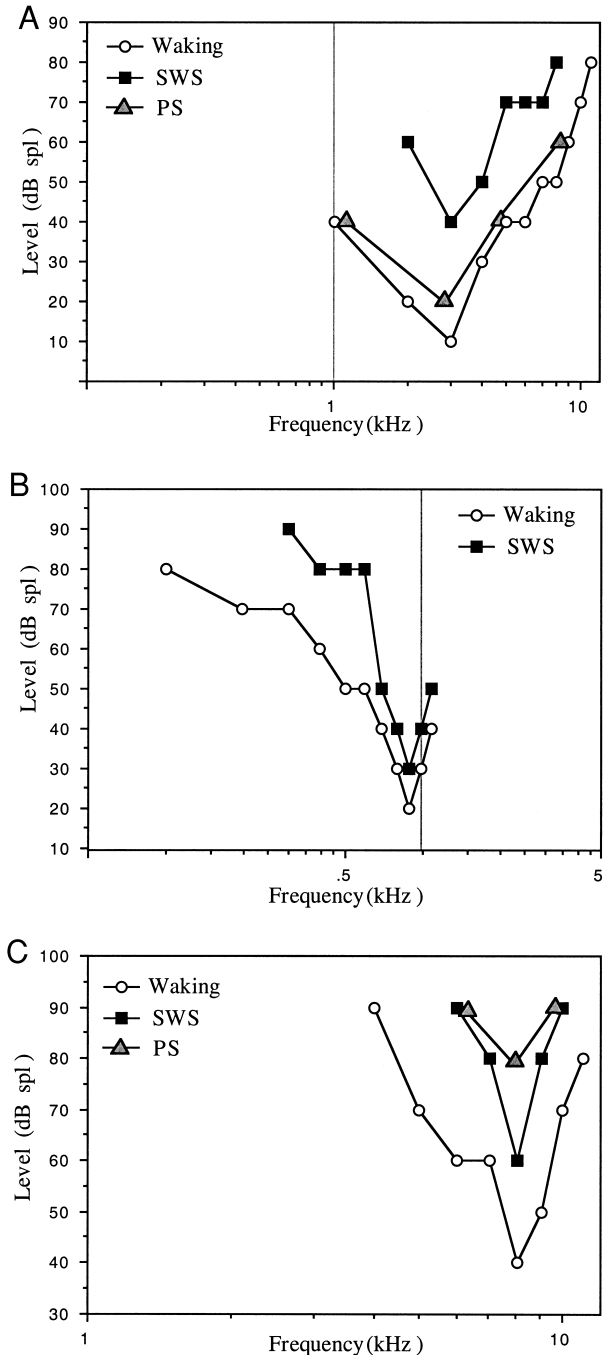


FIG. 9. Individual examples of threshold tuning curves (TC) in the different states of vigilance. *A–C*: the frequency TC for 3 different cells. For each cell, the frequency TC was constructed by plotting the value of the threshold measured at the different frequencies tested. Note that in the 3 cases, the RF size was smaller in SWS than in W. Two opposite cases are presented for PS: in the first one (*A*), the RF was close to that obtained in W, whereas in the second one (*C*), the RF was extremely reduced.

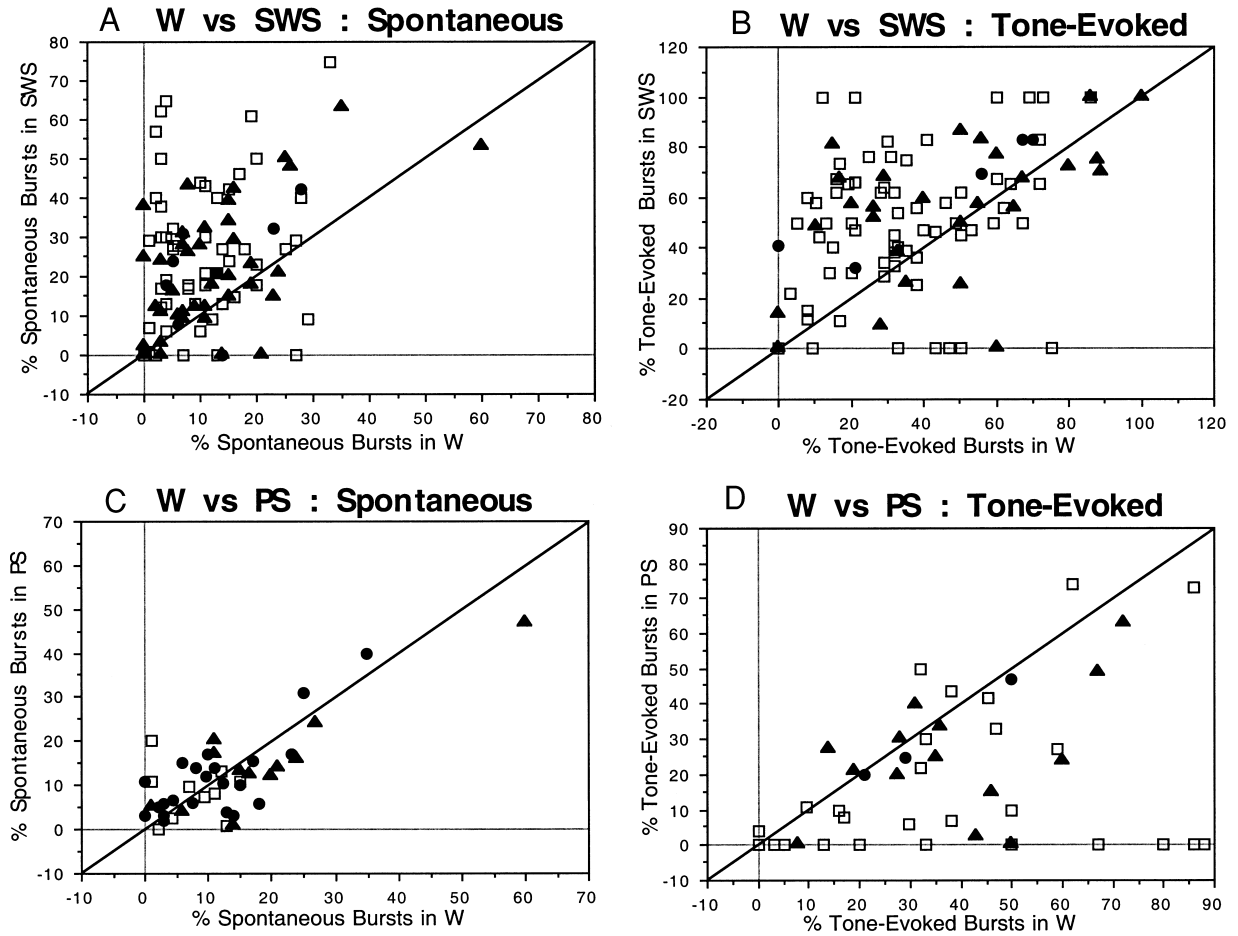


FIG. 10. Lack of relationships between changes in firing mode and changes in firing rate occurring from one state of vigilance to another. *A*: in most of the cases, the burstiness index (BI; see METHODS for definition) obtained during spontaneous activity was increased during SWS compared with W. This effect occurred for cells exhibiting increased (●), decreased (□), or unchanged (▲) spontaneous activity. *B*: in most of the cases, the BI obtained during evoked activity was increased in SWS compared with W. This effect occurred for cells exhibiting increased, decreased, or had unchanged evoked activity. *C*: in most of the cases, the BI obtained during spontaneous activity exhibited only minor changes during PS compared with W. Small increases or decreases occurred for cells exhibiting increased, decreased or unchanged spontaneous activity. *D*: in most of the cases, the BI obtained during evoked activity was decreased during PS compared with W. This effect occurred for cells exhibiting increased, decreased, or had unchanged evoked activity. Data are from the tone intensity producing the strongest evoked responses. Similar effects were obtained at the intensity producing the weakest evoked responses.

were observed at the intensity producing the smallest evoked responses. During PS (see Table 2), the BI value was similar to that obtained in W during spontaneous activity ($t < 1$), whereas it was lower during tone period ($P < 0.0001$). Such results indicate that the changes of the BI values do reflect state-dependent changes in discharge mode and not simply changes in spontaneous and evoked discharge rates. For example, although the evoked responses were reduced both in SWS and in PS, the BI value was increased in SWS whereas it was decreased in PS.

Systematic analyses were performed to determine whether the changes in firing mode influenced the other parameters quantified across states. First, it appeared again that the changes in discharge mode occurred independently of the changes in discharge rate. As shown in Fig. 10, the BI increased during SWS whatever the change in spontaneous (Fig. 10A) or in evoked (Fig. 10B) activity. Similarly during PS, the increase in spontaneous activity occurred with minor increases or decreases of the BI values (Fig. 10C), and the BI decreased

during tone period independently of the changes in evoked responses (Fig. 10D). Second, the changes in discharge mode from W to SWS did not account for the changes in the S/N ratio, the selectivity index, the response latency, the RF size (highest r value = 0.164, $P = 0.12$). For example, the changes in S/N ratio from W to SWS were not related to the changes in BI whether during tone period ($r = 0.108$; $P = 0.28$) or during spontaneous activity ($r = 0.122$; $P = 0.23$). This was confirmed when we focused on the cells that met a criterion of $\geq 20\%$ increase in BI (this criterion was met by 34/102 cells for spontaneous activity and by 37/102 cells for evoked activity). Indeed, like the whole cells population, these cells did not show significant changes in S/N ratio during SWS, whether the S/N ratio was computed with the mean or with the BF (lowest P value = 0.41). Note that these cells did show decreased S/N ratio during PS (all $P < 0.02$). Last, the monotonic cells exhibiting $\geq 20\%$ of change in BI from W to SWS ($n = 18$) did not change the slope of their rate-level function between the two states ($t < 1$).

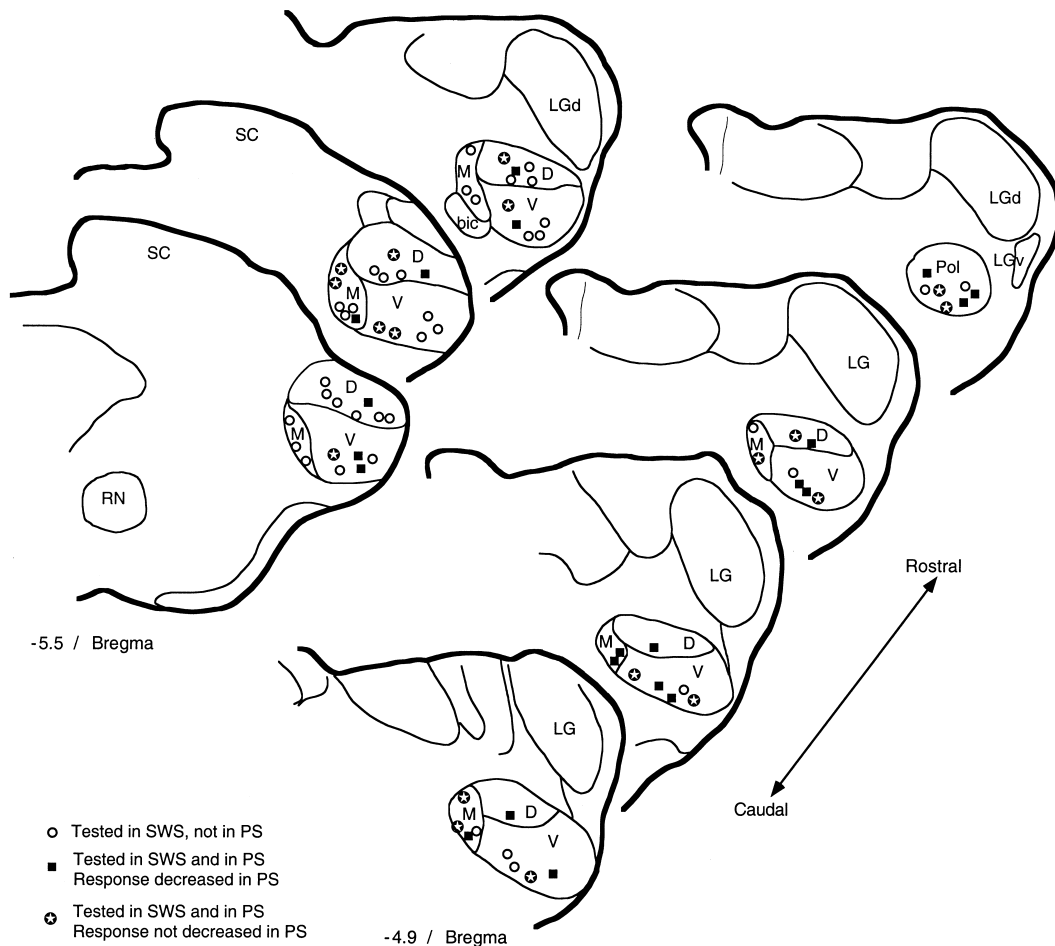


FIG. 11. Anatomical location of the recording sites. Coronal sections are from anterior -5.5 mm to anterior -4.1 mm, with bregma used as reference. The first 5 sections are $200\ \mu\text{m}$ apart, and the last 2 ones are $400\ \mu\text{m}$ apart. At all the locations, the cells were tested in W and SWS. Locations where the cells were also tested during PS were split into 2 groups according to the changes in evoked responses expressed by the cells during PS. Note that these 2 groups of cells are equally distributed in all the divisions of the auditory thalamus. bic, brachium of the inferior colliculus; D, dorsal division of the medial geniculate; LGd, dorsal lateral geniculate; LGv, ventral lateral geniculate; M, medial division of the medial geniculate; Pol, lateral part of the posterior nucleus; RN, red nucleus; SC, superior colliculus; V, ventral division of the medial geniculate.

Changes in the different anatomical divisions of the auditory thalamus

Figure 11 presents the locations of the recording sites in the different divisions of the auditory thalamus—the ventral (MGv), dorsal (MGd), and medial (MGm) parts of the medial geniculate body, and the lateral part of the posterior nucleus (Pol).

Whatever the subdivision, a majority of cells displayed a decrease in spontaneous and in evoked activity during SWS and an increase in spontaneous activity and a decrease in evoked activity during PS. None of the χ^2 tests performed revealed any significant differences between the different divisions (lowest P value = 0.12 for the spontaneous activity, and 0.19 for the evoked activity).

During W, the mean threshold values ranged from 33 ± 22 dB in MGv to 45 ± 13 dB in Pol, but there was no significant differences between subdivisions [$F(3,91) < 1$]. In contrast, the mean values of the responses latency and of the RF size differed among subdivisions [$F(3,91) = 2.71$, $P < 0.05$, and $F(3,91) = 6.20$, $P < 0.001$, respectively]: the latency was shorter in MGv (21 ± 6 ms) than in MGd ($26 \pm$

10 ms) and MGm (26 ± 7 ms; $P < 0.025$ in both cases), and the RF size was smaller in MGv (0.69 ± 0.34) and Pol (0.65 ± 0.29) than in MGd (1.14 ± 0.70) and MGm (1.07 ± 0.48 ; all $P < 0.025$).

An ANOVA analysis performed for each quantified parameter (spontaneous and evoked activity, S/N ratio, frequency-selectivity, latency, threshold, RF size, BI) failed to detect any significant interactions between the factors “anatomical subdivision” and “state of vigilance” (lowest P value = 0.11 for the RF size). Thus whatever the physiological parameter considered, the anatomical divisions of the auditory thalamus exhibited similar sleep-dependent changes.

DISCUSSION

Methodological considerations

It is first important to stress that the frequency RFs characterized here were obtained in totally undrugged and non-sleep-deprived animals and that only data collected during an unambiguous and uninterrupted state of vigilance ($\sim 10\%$ of the collected data) were included in the results.

Despite the weak proportion of PS in total sleep time in the guinea pig (Escudero and Vidal 1996; Pellet and Béraud 1967), 53 cells were tested at different tone intensities during PS. Some of them exhibited decreased evoked responses while others did not. This cannot be explained by the fact that some cells were rather tested in phasic PS and others in tonic PS (Berlucchi et al. 1967; Carli et al. 1967a,b; Mukhametov and Rizzolatti 1970). As the tone sequences were continuously presented and repeated 10 times within each PS episode, for every cell, tones indistinctly occurred during tonic and phasic PS periods.

The use of restrained animals allowed a constant distance between the speaker and the tympanic membrane during a recording session. Thus the alterations in responses observed during sleep were not the trivial consequence of changes of the acoustic signals reaching the tympanic membrane. Even if we cannot totally exclude the possibility that the activity of the middle-ear muscles (MEMs) modified sound transmission, this factor cannot account for our results for the following reasons. First, the MEMs are inactive during SWS (Baust et al. 1964; Dewson et al. 1965); still, most of the cells exhibited largely depressed evoked responses in SWS. Second, MEMs contractions are mostly pronounced during PS, particularly during phasic periods of PS (Baust et al. 1964; Berlucchi et al. 1967; Dewson et al. 1965; Irvine et al. 1970); thus maximal attenuation of evoked responses should have occurred in PS, which was not the case for 40% of the cells tested. Third, MEMs contractions mainly attenuate low-frequency sounds <2 kHz (Pickles 1988); still, the responses evoked during sleep were decreased whatever the neuron's best frequency.

The index we used to estimate the burstiness of the recorded cells is similar to that used in previous studies (Benoit and Chataignier 1973; McCarley et al. 1983). Unlike other authors (Guido et al. 1992; Lu et al. 1992; Mukherjee and Kaplan 1995), we did not require a silence period of 100 ms to be present before a burst occurrence because spontaneous 100-ms silence periods are unusual in undrugged animals and because presentation of acoustic stimuli can evoke burst response without a preceding silence period (Phillips and Sark 1991; Phillips et al. 1996). As a consequence, we could not distinguish bursts triggered by low-threshold spikes (which require a cell hyperpolarization >100 ms) from bursts triggered by high-threshold spikes (which require a cell depolarization). Nonetheless, using this index we observed during W a proportion of spontaneous bursts (11.5–12.3%) similar to that reported in previous studies (Guido and Weyand 1995), and as expected (McCarley et al. 1983), we detected a significant increase in burst proportion from W to SWS. Last, it is very unlikely that this index was affected by the cells firing rate: increased burst proportion was found during SWS while spontaneous and evoked activities were decreased; no change in spontaneous burst proportion was found during PS while spontaneous activity was increased.

Comparison with previous studies in unanesthetized animals

In accordance with previous studies (Bizzi 1966; Maffei et al. 1965; Marks et al. 1981; McCarley et al. 1983; Mukhametov and Rizzolatti 1970; Mukhametov et al. 1970; Sakakura 1968), for most of the cells, spontaneous activity was decreased during SWS and increased during PS. Also, as observed here, depressed evoked responses were repeatedly

found in SWS at the thalamic level (Coenen and Vendrik 1972; Livingstone and Hubel 1981; Maffei et al. 1965; Mariotti et al. 1989; Mukhametov and Rizzolatti 1970). The data obtained in PS showed more variability from one study to another: whereas some studies reported that the evoked responses were unchanged or increased in PS compared with W (Mariotti and Formenti 1990; Mukhametov and Rizzolatti 1970), others described very weak responses in PS (Gücer 1979). This variability could partly be explained by the present results which suggest the existence of two populations of thalamic relay cells: one exhibiting responses in PS equivalent to those in W (40% of the cells tested here), the other exhibiting strongly decreased responses in PS (60% of the cells tested here).

Sleep-related changes in S/N ratio at the thalamic level were examined in only two studies. Mukhametov and Rizzolatti (1970) found that the S/N values were decreased in SWS and not significantly altered in PS. Livingstone and Hubel (1981) mentioned that the S/N ratio increased on arousal from brief periods of drowsiness. The changes observed in the present experiment logically derived from the changes in spontaneous and in evoked activity. During SWS, as the spontaneous and the evoked activity were reduced to the same extent, the S/N ratio was unchanged. During PS, as the spontaneous activity was enhanced while the evoked activity was depressed or unchanged, the S/N ratio was always decreased.

An obvious question, which had never been addressed, was whether the alterations in evoked responses were dependent on tone intensity. Intuitively it might have been predicted that only loud sounds were able to elicit tone-evoked responses during sleep. However, the analyses performed here indicated that the responses were similarly reduced whatever the tone intensity. As classically described (Rodrigues-Dageaff et al. 1989; Rouiller et al. 1983), thalamic cells exhibited either monotonic or nonmonotonic functions. Despite the attenuation in evoked responses, the shape of the rate-level functions was preserved during SWS and PS. At the functional level, the consequence of decreased evoked responses independently of tone intensity and of preserved rate-level functions, could be the preservation, at least partial, of the intensity coding during sleep.

Very few studies looked at neuronal selectivity or RF size across natural behavioral states. In the somatosensory thalamus, two studies (Baker 1971; Hayward 1975) mentioned that the RFs seemed to remain constant in size and location over long periods of time despite changes in the animal's behavioral state. In the visual cortex, Livingstone and Hubel (1981) reported, on the basis of few examples, that the orientation selectivity was enhanced at the shift from SWS to W. The systematic quantification performed here indicated that, in SWS, the frequency selectivity was higher and the RF size smaller than they were in W. Comparable changes were observed in PS when the evoked responses were decreased. On the other hand, when the evoked responses in PS were not decreased, the frequency selectivity and the RF size did not differ from those in W. As our quantification of these two indices was based on independent measures, the fact that they were affected in a coherent way—the smaller the RF size the higher the frequency selectivity—validates the quantifications performed here.

Both in SWS and PS, the decrease in RF size and the increase in frequency selectivity were the direct consequence

of the attenuation in evoked responses. These changes are quite logical, given that when there is an attenuation of responses evoked within the neuron's RF, the responses at the RF borders tend to disappear. For example, it has long been known that lowering the sound intensity leads to smaller RF sizes (Aitkin 1973; Hind et al. 1963). Of course, an enhanced neurons' selectivity during sleep seems paradoxical, given that a higher selectivity is intuitively associated with the idea of more accurate processing. However, we should not forget that the increased selectivity observed here did not result from a selective facilitation of the response at the BF but from a reduction of RF size and from an attenuation of evoked responses, which may be viewed as an impoverishment of the message sent to cortical neurons.

Comparison with results from anesthetized animals

Several recent experiments have questioned the relationships between the firing mode and the physiological properties of lateral geniculate (LGN) cells during spontaneous (using extracellular recordings) or imposed (using intracellular recordings) changes from tonic to bursting mode in anesthetized cats. First, the spatial and temporal tunings of LGN cells were found similar during tonic and bursting mode of discharge (Guido et al. 1992; Lu et al. 1992).² Second, on the basis of results obtained using techniques of signal detection theory, it was proposed that the detection of a signal is better when cells are in bursting mode (Guido et al. 1995). Third, using sine-wave grating stimuli, it was shown that the low-threshold bursts response was evoked by an earlier phase of the stimulus than was the tonic response component (Guido et al. 1992). Last, lower latency variability was found during burst than during tonic firing (Guido and Sherman 1998). A totally different profile of changes was observed here during SWS, a state yet characterized by a high proportion of spontaneous and evoked bursts: compared with W, the cells frequency selectivity was increased, the S/N ratio was not improved, the acoustic threshold was higher, and the response latency was longer and more variable. In addition, we found no relationships between the changes in burst proportion and the changes in any of the other physiological parameters quantified.

Our results are also at variance with those of Wörgötter et al. (1998), who reported that under anesthesia the RF size of visual cortex neurons was larger during periods of synchronized EEG than during periods of desynchronized EEG (but see Armstrong-James and George 1988; Eggermont and Smith 1996).³ In contrast, as we already observed at the cortical level (Manunta and Edeline 1999), we found here that the RF size was smaller during EEG synchronized state (SWS) than during EEG activated states (W and PS).

Two obvious reasons can explain these discrepancies. First, state fluctuations occurring while the CNS is continuously under the control of an anesthetic agent are not equivalent to state changes occurring when the organism shifts from natural

W to natural SWS. Second, despite some apparent resemblances, natural SWS differs from an anesthetized state. The few studies that have directly compared neuronal activity in natural SWS and under anesthesia have pointed the differences existing between these two states (Cotillon and Edeline 1999; Destexhe et al. 1999; Kishikawa et al. 1995). For example, we recently found marked differences in neuronal responsiveness when the same thalamic and cortical recordings were tested first during SWS, then during anesthesia (Nembutal or urethan) (Cotillon and Edeline 1999). These differential effects likely result from a combination of factors, which could include differences in the balance of neuromodulators and in the dynamics of membrane potential fluctuations.

Potential mechanisms

Two nonexclusive possibilities can account for the alterations in evoked responses observed in the auditory thalamus across the vigilance states: they can reflect changes that already occur at subthalamic levels and/or they can be due to intrinsic events occurring within the thalamus. The first possibility was discarded in the visual system because sleep-related response alterations were observed for LGN neurons but not for optic tract fibers (Maffei et al. 1965; Mukhametov and Rizzolatti 1970). Similarly, in the somatosensory system, early evoked potential studies found unchanged responsiveness at subthalamic levels during SWS and tonic PS (Carli et al. 1967a,b; Favale et al. 1965). Recent studies also showed that during SWS, most of the trigeminal sensory neurons did not exhibit changes in evoked activity. During PS, those neurons displayed decreased responses to tooth pulp stimulation (Cairns et al. 1995, 1996) but increased responses to air puff stimuli (Cairns et al. 1996), which suggests that as early as the pons, sensory information can be differentially gated during PS.⁴ In the auditory system, changes in evoked responses were reported at all the subthalamic levels. The amplitude of the compound auditory nerve action potential and of the cochlear microphonic potential was increased in SWS and unchanged in PS as compared with W (Velluti et al. 1989). In the inferior colliculus, about the same percentages of cells exhibited increased (29%) and decreased (35%) responses in SWS relative to W, and about the same percentages of cells showed increased (32%) and decreased (35%) responses in PS relative to SWS (Morales-Cobas et al. 1995). Thus from the VIII nerve to the last prethalamic relay, the reported changes differed from those described here, which suggests that intrinsic mechanisms operate at the thalamic level to modify neuronal responsiveness.

The studies performed over the last three decades by Steriade and colleagues have demonstrated that the excitability of thalamic neurons is depressed during SWS as compared with brain-activated states of W and PS. Field potential recordings in various dorsal thalamic nuclei demonstrated that the postsynaptic component triggered in the thalamus by prethalamic stimulation was diminished during SWS, while the presynaptic component was unaffected (review in Steriade 1991; Steriade et al. 1997). The hyperpolarization of thalamic neurons during SWS (3–5 mV according to Fourment et al. 1985; Hirsch et al. 1983) can explain their decreased excitability and

² However, using lower rates of stimulus presentation, it was found that increased bursting activity was monotonically related to increased sharpening of the temporal tuning of LGN neurons (Mukherjee and Kaplan 1995).

³ Armstrong-James and George (1988) found that the RF size of somatosensory cortex neurons decreased as the degree of anesthesia deepened. Eggermont and Smith (1996) found that burst-firing produced a sharpening of the frequency tuning in the auditory cortex.

⁴ Neuronal responses evoked during PS were already modified at the level of the spinal cord: responses to tooth-pulp stimulation were attenuated (Soja et al. 1993), but responses to light touch were enhanced (Kishikawa et al. 1995).

be responsible of the attenuation of evoked responses, the elevation of acoustic thresholds and the longer responses latencies. For example, it has been shown that when auditory thalamus neurons are hyperpolarized by 5 mV, their responses are delayed by 10–17 ms (Hu 1995).

The reduced responsiveness observed during PS is more difficult to explain given that thalamic cells are tonically depolarized during PS (by ~10 mV relative to SWS) (Hirsh et al. 1983) and their excitability is enhanced (Fourment and Hirsch 1980; Glenn and Steriade 1982; Sakakura 1968). Thus other mechanisms have to be considered, including a decrease in synaptic transmission between the tectofugal afferences and the thalamic neurons. On the basis of field potentials evoked by orthodromic and antidromic stimulation, a presynaptic inhibition, with a postsynaptic facilitation, was suspected to occur at the thalamic level (Bizzi 1966; Dagnino et al. 1963; Iwama et al. 1966). However, it remains to explain why some cells showed largely depressed evoked responses, whereas others showed responses that tended to recover values comparable to those in W.

Thus while it seems possible to explain the decreased responsiveness in SWS by a unique mechanism, the hyperpolarization of thalamic cells, the changes occurring during PS are more complex. They might result from the interplay of several mechanisms: a depolarization of thalamic cells, a decrease in synaptic transmission at the thalamic level, and changes occurring at subthalamic levels.

Conclusions

From the present results, it appears that the message sent to cortical neurons is attenuated during sleep (the acoustic threshold is increased, the evoked responses are decreased) and that its spectral content is impoverished (the RF size is reduced). Even when the evoked responses are not depressed during PS, they occur on a background of intense spontaneous activity, which probably makes the sensory messages difficult to decode. The timing of the neuronal discharges is also altered during sleep: the responses latencies are longer than in W and, more important, their variability is increased. Thus any coding mechanism based on the exact timing of the neuronal discharges, or on the timing of neuronal interactions, should be affected. All these changes are, however, not sufficient to consider sleep as a brain-deafferented state. First, intensity coding seems to be preserved. Second, the RFs are smaller in size but are not disorganized, which suggests that topographic maps, fundamental to sensory processing (Kaas 1997), should be maintained. Third, the neurons' selectivity is kept the same or even enhanced. These preserved capabilities of sensory analyzers to process information could explain why the sleeping organism remains able to detect and react to behaviorally relevant acoustic stimuli.

We thank N. Weinberger and E. Rouiller for helpful and detailed comments on a previous version of this paper. We thank G. Dutrieux for outstanding help with the analysis software and V. Bajo and F. Nodal for help with the histological material.

This work was supported in part by grant CHRXCT930269 from the European Community "Human Capital and Mobility." Y. Manunta was supported by a doctoral fellowship from the French Ministère de la Recherche et

de l'Enseignement Supérieur. The bulk of the data were collected while E. Hennevin was on sabbatical leave from Paris X University.

REFERENCES

- ARTKIN LM. Medial geniculate body of the cat: response to tonal stimuli of neurons in medial division. *J Neurophysiol* 36: 275–283, 1973.
- ARMSTRONG-JAMES M AND GEORGE MJ. Influence of anesthesia on spontaneous activity and receptive field size of single unit in rat Sm1 neocortex. *Exp Neurol* 99: 369–387, 1988.
- BAKER MA. Spontaneous and evoked activity of neurones in the somatosensory thalamus of the waking cat. *J Physiol (Lond)* 271: 359–379, 1971.
- BAUST W, BERLUCCHI G, AND MORUZZI G. Changes in the auditory input in wakefulness and during the synchronized and desynchronized stages of sleep. *Arch Ital Biol* 102: 657–674, 1964.
- BENOIT O AND CHATAIGNIER C. Patterns of spontaneous unitary discharge in thalamic ventro-basal complex during wakefulness and sleep. *Exp Brain Res* 17: 348–363, 1973.
- BERLUCCHI G, MUNSON JB, AND RIZZOLATTI G. Changes in click-evoked responses in the auditory system and cerebellum of free-moving cats during sleep and waking. *Arch Ital Biol* 105: 118–135, 1967.
- BIENENSTOCK EL, COOPER LN, AND MUNRO PW. Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. *J Neurosci* 2: 32–48, 1982.
- BIZZI E. Discharge patterns of single geniculate neurons during the rapid eye movements of sleep. *J Neurophysiol* 29: 1087–1095, 1966.
- BORDI F AND LEDOUX J. Response properties of single units in areas of rat auditory thalamus that project to the amygdala. I. Acoustic discharge patterns and frequency receptive fields. *Exp Brain Res* 98: 261–274, 1994.
- CABALLERO-BLEDA M, FERNANDEZ B, AND PUELLES L. Acetylcholinesterase and NADPH-diaphorase chemoarchitectonic subdivisions in the rabbit medial geniculate body. *J Chem Neuroanat* 4: 271–280, 1991.
- CAIRNS BE, FRAGOSO MC, AND SOJA PJ. Activity of rostral trigeminal sensory neurons in the cat during wakefulness and sleep. *J Neurophysiol* 73: 2486–2498, 1995.
- CAIRNS BE, McERLANE SA, FRAGOSO MC, JIA WG, AND SOJA PJ. Spontaneous discharge and peripherally evoked orofacial responses of trigemino-thalamic tract neurons during wakefulness and sleep. *J Neurosci* 16: 8149–8159, 1996.
- CALFORD MB. The parcellation of the medial geniculate body of the cat defined by the auditory response properties of single units. *J Neurosci* 3: 2350–2365, 1983.
- CALFORD MB, WEBSTER WR, AND SEMPLE MM. Measurement of frequency selectivity of single neurons in the central auditory pathway. *Hear Res* 11: 395–401, 1983.
- CARLI G, DIETE-SPIFF K, AND POMPEIANO O. Transmission of sensory information through the lemniscal pathway during sleep. *Arch Ital Biol* 105: 31–51, 1967a.
- CARLI G, DIETE-SPIFF K, AND POMPEIANO O. Presynaptic and postsynaptic inhibition of transmission of somatic afferent volleys through the cuneate nucleus during sleep. *Arch Ital Biol* 105: 52–82, 1967b.
- COENEN ALM AND VENDRIK AJH. Determination of the transfer ratio of cat's geniculate neurons through quasi-intracellular recordings and the relation with the level of alertness. *Exp Brain Res* 14: 227–242, 1972.
- COTILLON N AND EDELINE J.-M. Tone-evoked oscillations in the thalamo-cortical auditory system are not present in undrugged animals. *Soc Neurosci Abstr* 25: 156.18, 1999.
- DAGNINO N, FAVALE E, LOEB C, MANFREDI M, AND SEITUN A. Presynaptic and postsynaptic changes in specific thalamic nuclei during deep sleep. *J Neurophysiol* 26: 668–684, 1963.
- DESTEXHE A, CONTRERAS D, AND STERIADE M. Cortically-induced coherence of a thalamic-generated oscillation. *Neuroscience* 92: 427–443, 1999.
- DEWSON JH, DEMENT WC, AND SIMMONS FB. Middle ear muscle activity in cats during sleep. *Exp Neurol* 12: 1–8, 1965.
- EDELINE J.-M, MANUNTA Y, NODAL FR, AND BAJO V. Do auditory responses recorded from awake animals reflect the anatomical parcellation of the auditory thalamus? *Hear Res* 131: 135–152, 1999.
- EGGERMONT JJ AND SMITH GM. Burst-firing sharpens frequency-tuning in primary auditory cortex. *Neuroreport* 7: 753–757, 1996.
- ESCUDERO M AND VIDAL PP. A quantitative study of electroencephalography, eye movements and neck electromyography characterizing the sleep-wake cycle of the guinea-pig. *Eur J Neurosci* 8: 572–580, 1996.
- EVANS EF. Neuroleptanesthesia for the guinea pig. *Arch Otolaryngol* 105: 185–186, 1979.

- FAVALE E, LOEB C, MANFREDI M, AND SACCO G. Somatic afferent transmission and cortical responsiveness during natural sleep and arousal in cat. *Electroencephalogr Clin Neurophysiol* 18: 354–368, 1965.
- FOURMENT A AND HIRSCH JC. Synaptic potentials in cat's lateral geniculate neurons during natural sleep with special reference to paradoxical sleep. *Neurosci Lett* 16: 149–154, 1980.
- FOURMENT A, HIRSCH JC, AND MARC ME. Oscillations of the spontaneous slow-wave sleep rhythm in lateral geniculate nucleus relay neurons of behaving cats. *Neuroscience* 14: 1061–1075, 1985.
- FRÉGNAC Y, SHULZ D, THORPE S, AND BIENENSTOCK E. Cellular analogs of visual cortical epigenesis. I. Plasticity of orientation selectivity. *J Neurosci* 12: 1280–1300, 1992.
- GLENN LL AND STERIADE M. Discharge rate and excitability of cortically-projecting neurons in the intralaminar thalamic nuclei during waking and sleep states. *J Neurosci* 2: 1387–1404, 1982.
- GÜÇER G. The effect of sleep upon the transmission of afferent activity in the somatic afferent system. *Exp Brain Res* 34: 287–298, 1979.
- GUIDO W AND SHERMAN SM. Response latencies of cells in the cat's lateral geniculate nucleus are less variable during burst than tonic firing. *Vis Neurosci* 15: 231–237, 1998.
- GUIDO W, LU S-M, AND SHERMAN SM. Relative contributions of burst and tonic responses to the receptive field properties of lateral geniculate neurons in the cat. *J Neurophysiol* 68: 2199–2211, 1992.
- GUIDO W, LU S-M, VAUGHAN JW, GODWIN DW, AND SHERMAN SM. Receiver operating characteristic (ROC) analysis of neurons in the cat's lateral geniculate nucleus during tonic and burst response mode. *Vis Neurosci* 12: 723–741, 1995.
- GUIDO W AND WEYAND T. Burst responses in thalamic relay cells of the awake behaving cat. *J Neurophysiol* 74: 1782–1786, 1995.
- HAYWARD JN. Response of ventrobasal thalamic cells to hair displacement on the face of the waking monkey. *J Physiol (Lond)* 250: 385–407, 1975.
- HENNEVIN E, MANUNTA Y, AND EDELINE J-M. How does the state of vigilance modify frequency receptive fields (FRF) in the guinea-pig auditory thalamus? *Soc Neurosci Abstr* 21: 379.2, 1995.
- HIND JE, GOLDBERG JM, GREENWOOD DD, AND ROSE JE. Some discharge characteristics of single neurons in the inferior colliculus of the cat. II. Timing of discharges and observations on binaural stimulation. *J Neurophysiol* 26: 321–341, 1963.
- HIRSCH JC, FOURMENT A, AND MARC ME. Sleep-related variations of membrane potential in the lateral geniculate body relay neurons of the cat. *Brain Res* 259: 308–312, 1983.
- HU B. Cellular basis of temporal synaptic signalling: an in vitro electrophysiological study in rat auditory thalamus. *J Physiol (Lond)* 483: 167–182, 1995.
- IRVINE DRF, WEBSTER WR, AND SACK KH. Effects of repetitive stimulation and state of arousal on cochlear potentials. *Exp Neurol* 29: 16–30, 1970.
- IWAMA K, KAWAMOTO T, SAKAKURA H, AND KASAMATSU T. Responsiveness of cat lateral geniculate at pre- and postsynaptic levels during natural sleep. *Physiol Behav* 1: 45–53, 1966.
- KAAS JH. Topographic maps are fundamental to sensory processing. *Brain Res Bull* 44: 107–112, 1997.
- KIANG NYS, WATANABE T, THOMAS EC, AND CLARK LF. *Discharge Patterns of Single Fibers in the Cat's Auditory Nerve*. Cambridge, MA: MIT Press, 1965.
- KISHIKAWA K, UCHIDA H, YAMAMORI Y, AND COLLINS JG. Low-threshold neuronal activity of spinal dorsal horn neurons increases during REM sleep in cats: comparison with effects of anesthesia. *J Neurophysiol* 74: 763–769, 1995.
- KOELLE GB. The histochemical identification of acetylcholinesterase in cholinergic, adrenergic and sensory neurons. *J Pharmacol* 114: 167–184, 1955.
- LIVINGSTONE MS AND HUBEL DH. Effects of sleep and arousal on the processing of visual information in the cat. *Nature* 291: 554–561, 1981.
- LU S-M, GUIDO W, AND SHERMAN SM. Effects of membrane voltage on receptive field properties of lateral geniculate neurons in the cat: contribution of the low-threshold Ca^{2+} conductance. *J Neurophysiol* 68: 2185–2198, 1992.
- MAFFEI L, MORUZZI G, AND RIZZOLATTI G. Influence of sleep and wakefulness on the response of lateral geniculate units to sinewave photic stimulation. *Arch Ital Biol* 103: 596–608, 1965.
- MANUNTA Y AND EDELINE J-M. Effects of noradrenaline on frequency tuning of rat auditory cortex neurons. *Eur J Neurosci* 9: 833–847, 1997.
- MANUNTA Y AND EDELINE J-M. Effects of norepinephrine on frequency tuning of auditory cortex neurons during wakefulness and slow-wave sleep. *Eur J Neurosci* 11: 2134–2150, 1999.
- MARIOTTI M AND FORMENTI A. Somatosensory transmission through the ventroposterolateral thalamic nucleus during sleep and wakefulness. In: *The Diencephalon and Sleep*, edited by Mancina M and Marini G. New York: Raven, 1990, p. 301–312.
- MARIOTTI M, FORMENTI A, AND MANCIA M. Responses of VPL thalamic neurones to peripheral stimulation in wakefulness and sleep. *Neurosci Lett* 102: 70–75, 1989.
- MARKS GA, FARBER J, AND ROFFWARG HP. Phasic influences during REM sleep upon dorsal lateral geniculate nucleus unit activity in the rat. *Brain Res* 222: 388–394, 1981.
- MCCARLEY RW, BENOIT O, AND BARRIONUEVO G. Lateral geniculate nucleus unitary discharge in sleep and waking: state- and rate-specific aspects. *J Neurophysiol* 50: 798–818, 1983.
- MORALES-COBAS G, FERREIRA MI, AND VELLUTI RA. Firing of inferior colliculus neurons in response to low-frequency sound stimulation during sleep and waking. *J Sleep Res* 4: 242–251, 1995.
- MUKHAMEDOV LM AND RIZZOLATTI G. The responses of lateral geniculate neurons to flashes of light during the sleep-waking cycle. *Arch Ital Biol* 108: 348–368, 1970.
- MUKHAMEDOV LM, RIZZOLATTI G, AND SEITUN A. An analysis of the spontaneous activity of lateral geniculate neurons and of optic tract fibers in free moving cats. *Arch Ital Biol* 108: 325–347, 1970.
- MUKHERJEE P AND KAPLAN E. Dynamics of neurons in the cat lateral geniculate nucleus: in vivo electrophysiology and computational modeling. *J Neurophysiol* 74: 1222–1243, 1995.
- PEDEMONTE M, PENA JL, MORALES-COBAS G, AND VELLUTI RA. Effects of sleep on the response of single cells in the lateral superior olive. *Arch Ital Biol* 132: 165–178, 1994.
- PELLET J AND BÉRAUD G. Organisation nyctémérale de la veille et du sommeil chez le cobaye (*Cavia porcellus*). *Physiol Behav* 2: 131–137, 1967.
- PENA JL, PEDEMONTE M, RIBEIRO MF, AND VELLUTI R. Single unit activity in the guinea-pig cochlear nucleus during sleep and wakefulness. *Arch Ital Biol* 130: 179–189, 1992.
- PENA JL, PÉREZ-PÉREIRA PL, BOUVIER M, AND VELLUTI RA. Sleep and wakefulness modulation of the neuronal firing in the auditory cortex of the guinea pig. *Brain Res* 816: 463–470, 1999.
- PERUZZI D, BARTLETT E, SMITH PH, AND OLIVER DL. A monosynaptic GABAergic input from the inferior colliculus to the medial geniculate body in rat. *J Neurosci* 17: 3766–3777, 1997.
- PHILLIPS DP AND KELLY JB. Coding of tone-pulse amplitude by single neurons in auditory cortex of albino rats (*Rattus norvegicus*). *Hear Res* 37: 269–280, 1989.
- PHILLIPS DP, KITZES LM, SEMPLE MN, AND HALL SE. Stimulus-induced spike bursts in two fields of cat auditory cortex. *Hear Res* 97: 165–173, 1996.
- PHILLIPS DP AND SARK SA. Separate mechanisms control spike numbers and inter-spike intervals in transient responses of cat auditory cortex neurons. *Hear Res* 53: 17–27, 1991.
- PICKLES JO. *An Introduction of the Physiology of Hearing* (2nd ed.). London: Academic, 1988.
- RODRIGUES-DAGAEFF C, SIMM G, DE RIBAUPIERRE Y, VILLA A, DE RIBAUPIERRE F, AND ROUILLER EM. Functional organization of the ventral division of the medial geniculate body of the cat: evidence for a rostro-caudal gradient of response properties and cortical projections. *Hear Res* 39: 103–126, 1989.
- ROUILLER E, DE RIBAUPIERRE Y, MOREL A, AND DE RIBAUPIERRE F. Intensity functions of single unit responses to tone in the medial geniculate body of cat. *Hear Res* 11: 235–247, 1983.
- ROUILLER EM., RODRIGUES-DAGAEFF C, SIMM G, DE RIBAUPIERRE Y, VILLA A, AND DE RIBAUPIERRE F. Functional organization of the medial division of the medial geniculate body of the cat: tonotopic organization, spatial distribution of response properties and cortical connections. *Hear Res* 39: 127–142, 1989.
- SAKAKURA H. Spontaneous and evoked unitary activities of cat lateral geniculate neurons in sleep and wakefulness. *Jpn J Physiol* 18: 23–42, 1968.
- SANDELL JH, GRAYBIEL AM, AND CHESSELET MF. A new enzyme marker for striatal compartmentalization: NADPH-diaphorase activity in the caudate nucleus and putamen. *J Comp Neurol* 243: 326–335, 1986.
- SIMS KL, KAUFFMAN FC, JONHSON EC, AND PICKEL VM. Cytochemical localization of brain nicotinamide adenine dinucleotide phosphate (oxidized)-dependent deshydrogenase. Qualitative and quantitative distribution. *J Histochem Cytochem* 22: 7–19, 1974.
- SOJA PJ, OKA JI, AND FRAGOSO MC. Synaptic transmission through cat lumbar ascending sensory pathways is suppressed during active sleep. *J Neurophysiol* 70: 1708–1712, 1993.

- STERIADE M. Alertness, quiet sleep, dreaming. *Cereb Cortex* 9: 279–357, 1991.
- STERIADE M, JONES EG, AND MCCORMICK DA. *Thalamus*. Amsterdam: Elsevier, 1997, vol. I.
- VELLUTI R, PEDEMONTE M, AND GARCÍA-AUSTT E. Correlative changes of auditory nerve and microphonic potentials throughout sleep. *Hear Res* 39: 203–208, 1989.
- WHITFIELD IC. The medial geniculate body of the cat. *J Sound Vib* 8: 108–117, 1968.
- WHITFIELD IC AND PURSER D. Microelectrode study of the medial geniculate body in unanaesthetized free-moving cats. *Brain Behav Evol* 6: 311–322, 1972.
- WINER JA, SAINTE MARIE RL, LARUE DT, AND OLIVER DL. GABAergic feedforward projections from the inferior colliculus to the medial geniculate body. *Proc Natl Acad Sci USA* 93: 8005–8010, 1996.
- WÖRGÖTTER F, SUDER K, ZHAO Y, KERSCHER N, EYSEL UT, AND FUNKE K. State-dependent receptive-field restructuring in the visual cortex. *Nature* 396: 165–168, 1998.