Supporting Information

Magnin et al. 10.1073/pnas.0909710107

SI Methods

Intracerebral Recording Procedure. To explore the possibility of some decoupling between thalamic and cortical activities during sleep-wake cycles, we analyzed simultaneous thalamic and cortical recordings from 13 patients with refractory temporal lobe epilepsy. Based on the data from non invasive investigations including scalp video-EEG recording of seizures, none of the participating patients were suffering from a typical form of medial temporal lobe epilepsy eligible for a standardized anterior lobectomy. To delineate the extent of the cortical epileptogenic area and to plan a tailored surgical treatment, depth EEG recording electrodes were implanted according to the stereotactic technique of Talairach and Bancaud (1), a procedure that has proved useful to define the electro-clinical subgroups of refractory focal epilepsies (2). For each patient, the placement of the depth electrodes (diameter of 0.8 mm; 5–15 recording contacts, each 2 mm long, intercontact interval 1.5 mm) was determined by clinical criteria. The thalamus, and more specifically the medial pulvinar nucleus (PuM), was one of the targets of stereotactic implantation because, given its reciprocal connections with temporal cortical areas, it might be an important relay in the building of epileptic discharges (3). Intracortical exploration of temporal neocortical areas and of the PuM nucleus was possible using a single multicontact electrode, so that thalamic exploration did not increase the risk of the procedure by requiring an additional electrode track specifically devoted to the study of PuM activity. All patients were fully informed of the aim of this investigation and gave their written consent for the implantation and recording procedure, which was approved by the local ethics committee (Comité Consultatifs de Protection des Personnes se Prêtant à des Recherches Biomédicales Lyon – Centre Léon Bérard).

Data Acquisition and Analysis. Day and night recording under stereo-EEG video monitoring was conducted 5 days or more after electrode implantation. At that time, anticonvulsant drug intake had been reduced drastically for at least 1 week to record spontaneous epileptic seizures. Based on the criteria of Rechtschaffen and Kales (4), the states of vigilance were scored visually in 30-s periods by one of the authors (H.B.) who was blind to clinical data and positions of cortical recording sites. Sleep scoring was based on analysis of the cortical activity on 3–16 intracortical contacts per subject selected for absent or limited interictal epileptic activities and of electro-oculographic recordings. Bipolar EEG signals and electrooculograms were amplified, filtered (band pass: 0.33–128 Hz), and stored with a sampling frequency of 256 Hz (Micromed Systems).

To characterize cerebral activity, we used a nonlinear time series analysis and considered the dimension of activation (DA) (5), based on and derived from the dimensional complexity approach (6, 7). The non linear approach has been used for EEG analysis in several domains (8–15), mainly in sleep research (16–25) where it has been validated against conventional spectral measures (24, 25). To calculate the DA, we first applied a temporal lagging procedure termed "delay time embedding." The first 20 voltage values of the EEG signal $v(i)$, $v(i + t)$, $v(i+2t)$, ... were considered, time delay (t) being fixed at 15.6 ms, corresponding to the 20 coordinates of one vector (X_i) when embedded in a 20-dimensional phase space. This vector defined the state of the signal during the corresponding period. The operation was repeated taking the voltage value $v(i + t)$ as the origin of a second set of 20 successive voltage values, thus defining a second vector (X_{i+t}). This operation was performed until 1,000 vectors were embedded in the 20-dimensional phase space. Then, the correlation integral $C_n(r)$ was calculated based on the distances among all vectors. Repeating the process led to successive $C_n(r)$ values that allowed the building of a curve, (log $[C_n(r)]$/log(r), which represented the probability for the distance between two randomly selected vectors to be inferior to a predefined r value. The slope of this curve corresponded to the DA, which was estimated according to this procedure every 15.6 s. More details on mathematical aspects of DA calculation and its application on EEG signals are given in Guillemant et al. (5).

Original DA data obtained after this analysis were filtered (zero shift;−24 dB; low-pass filter with a 0.006-Hz cutoff frequency). Based on hypnograms, our study focused on variations in cerebral activity occurring at sleep onset in selected patients in whom the transition from wakefulness to sleep stage 4 was least interrupted by brief periods of reactivations. Significant changes in cerebral activities were defined as DA values differing by 2 SD from the DA values averaged during a period ranging from 10 to 50 min before sleep onset or after sleep stage 4 was reached (Fig. S1). The times at which a significant DA variation occurred in each cortical and thalamic recording site allowed the measurement of the time delay between cortical and thalamic deactivations. In addition, the dynamics of the transition from sleep onset to sleep stage 4 were evaluated by calculating the mean decrease in DA speed. A similar analysis for transitions from sleep stage 4 or stage 2 to awakening could not be performed because the duration of the preceding sleep stage or of the following waking period was too short.

Part of the data also was analyzed using a spectral method. Time–frequency analyses of the cerebral recordings were performed using the LetsWave software, and mean EEG power curves were calculated by averaging power values from 1 to 64 Hz (frequency resolution of 1 Hz) during successive nonoverlapping 30-s time windows (Fig. 2*A*). This strategy, instead of the usual spectral EEG bands analysis (26), was chosen to allow the comparison with DA data obtained from signals recorded in an identical 1–64 Hz frequency band. Significant changes in cerebral activities were defined as EEG power values differing by 2 SD from the EEG power values averaged during a period ranging from 10 to 50 min before sleep onset or after sleep stage 4 was reached. It should be emphasized that, unlike spectral analysis, the DA method allows an estimate of the complexity of a signal, which is independent of its amplitude. For this reason, DA and mean EEG power values at the wake–sleep transition show an opposite evolution (i.e., a decrease in DA versus a mean increase in EEG power). Nevertheless, the time delays between cortical and thalamic deactivations calculated by the spectral or DA approach are similar (Fig. 2*A*).

Anatomical Localization of Recording Sites. The thalamic and cortical electrode contact pairs used to perform the bipolar recordings were localized with the help of skull radiographs after electrode implantation and using the appropriate MR slices of patient's brains (MRIcro software) (27). The placement of the contacts within the PuM was assessed using Morel's atlas of the human thalamus (28). Thalamic contacts were located in the PuM in 11 patients; in two patients they were slightly anterior, lying in the central lateral, the mediodorsal, or the ventral posterior lateral nucleus (Fig. 3*C*). The position of the cortical contacts was localized with respect to the cortical anatomy in each patient and reported on the equivalent position on the anatomical model of normal brain proposed by the McConnell Brain Imaging Center of the Montréal Neurological Institute, McGill University, (http://www.bic.mni.mcgill.ca/brainweb/). All cortical lobes were explored with a larger sampling of the temporal cortex because of the suspected location of the epileptogenic area.

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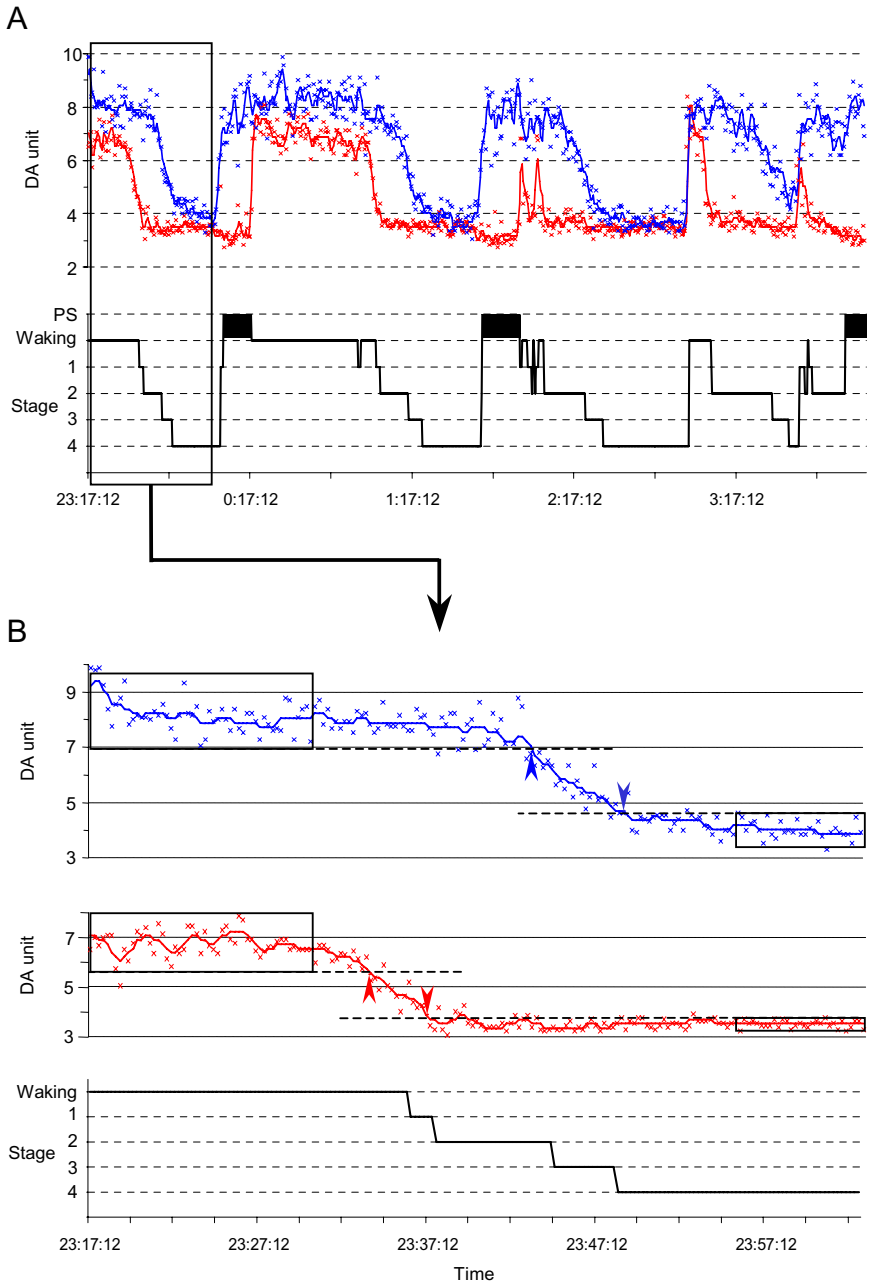

Fig. S1. Methodology for defining the time of significant changes in cerebral activities using DA analysis. (*A*) Example of the evolution of DA values obtained simultaneously at the thalamic (red trace) and cortical (blue trace) levels during sleep onset and the following night. For clarity, smoothed curves (low-pass filter with a cutoff frequency of 0.006 Hz) are plotted together with the original DA data represented by the symbol ×. The DA index of cortical activity exhibits cyclic changes that coincide with the different states of vigilance seen in the hypnogram underneath. Similar DA variations are observed at the thalamic level, except in paradoxical (rapid eye movement) sleep episodes, during which thalamic activity level could remain low (29). (*B*) Enlargement of the section in *A* focusing on DA evolution at sleep onset. To define the time at which a significant DA decrease occurred, DA values were averaged during the preceding wake period (black boxes). A DA value differing by 2 SD (dotted lines) from the DA mean was chosen as a significant DA decrease. A similar strategy was used to define the time when the DA value reached a stable level characterizing sleep stage 4.