# LORETA and sleep

Strijkstra, Arjen; Boerema, A.S.; Zavada, Andrei; Beersma, Dominicus

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# LORETA AND SLEEP: OVER-NIGHT DIFFERENCES IN NREM SLEEP SLOW WAVE CURRENT DENSITY

Arjen M. Strijkstra, Ate S. Boerema, Andrei G. Zavada,
Domien G.M. Beersma
Chronobiology, University of Groningen, The Netherlands.

## INTRODUCTION

Sleep homeostasis is achieved through two factors: sleep time and sleep intensity. Sleep intensity is reflected in the abundance and amplitude of cortical slow waves (1-4Hz), which can be expressed as slow wave power or slow wave activity (SWA). In the majority of sleep regulation research, central derivations (C3/C4) have been used, as proclaimed standard by Rechtschaffen and Kales (1968)[1]. This method has been widely accepted to standardize sleep recording, but underestimates the complexity of sleep processes. For example, measuring EEG on more electrodes at different locations shows that sleep regulation is organised differently in frontal and occipital regions[2].

Scalp EEG is an expression of electrical brain activity in the upper layers of the cortex under the skull. Using mathematical methods based on physical properties of electrical currents in the cortex, one can attempt to localize cortical sources of electrical activity. Low resolution electromagnetic tomography (LORETA) is such a method, estimating current density of electrical activity sources in the cortex, imageable in 2394 voxels[3]. LORETA allows for (low resolution) localization of (multiple and diffuse) current density sources, based on 16 or more simultaneous scalp EEG recordings. We used LORETA to explore localization of slow wave quantitative dynamics during sleep.

## METHODS

From an earlier experiment, 9 baseline sleep recordings were used. Healthy young subjects (18-27 years) were asked to participate in an experiment using visual stimulation. They did not smoke nor use drugs, and abstained from consumption of alcohol and coffee throughout the experiment. They did not rate as extreme morning or evening types. Subjects signed an informed consent form. The experiment was approved by the Medical Ethics Committee of the Academic hospital of the University of Groningen. A more elaborate description of the experiment has been given earlier[4].

Subjects were asked to come to the lab for a habituation sleep night and a baseline sleep night before the actual experiment took place on the third day. For the present analysis, only data from baseline sleep nights were used. Before both habituation and baseline sleep nights, subjects were at home doing their normal routine, until they came to the lab at 20:00 for application of the electrode cap. Subjects were subsequently asked to perform computerized tests series of ~35 min duration at 22:00 and 23:00. The test series contained questionnaires and event related potential trials, and did not include extensive visual stimulation. Subjects

prepared to go to sleep at 23:40 and were put in bed and connected to the EEG amplifiers around 23:55. At 00:00 hours, lights were turned off until 08:00 hours the next morning.

EEGs were recorded using a cap system with Ag/AgCl electrodes (Electro-Cap International, Inc., U.S.A.), on 26 positions on the scalp (F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, P9, P10, PO7, PO8, O1, Oz, O2, PO9, PO10, O9, O10). The left earlobe was used as reference, and the inion was used as ground. Data were amplified (500μV/V), sampled at 100 Hz and band-pass filtered between 0.16Hz–30Hz. Besides EEGs, also EOG of the left eye was obtained, and EMG was measured on neck muscles. EEGs were staged on a 30 sec basis using the criteria of Rechtschaffen and Kales (1968). Non-REM sleep EEG traces were screened for artifacts using the EEG analysis program BrainVision (Brain Products, Germany) and 256 point clean data traces were exported for further analysis by LORETA. Statistical analysis was done with non-parametric permutation tests provided by LORETA software.

## RESULTS AND DISCUSSION

Subjects slept for 7.84 (SEM 0.07) hours during the ~8 hours sleep window, of which 1.88 (SEM 0.08) hours was spent in REM sleep, 5.42 (SEM 0.12) hours in NREM sleep, and 0.54 (SEM 0.09) hours in wake or movement time. Sleep latency was 0.23 (SEM 0.05) hours. All sleep recordings showed a gradual decline in slow wave power after the first NREM episode on central derivations (not shown).

For imaging of SWA dynamics, individual LORETA images were calculated for the 1-2Hz range of the NREM sleep EEG spectrum and averaged for each 30 sec. Subsequently, NREM sleep LORETA images were averaged over the first half and the second half of sleep time. The two resulting LORETA images were contrasted statistically to investigate the distribution of the reduction of SWA current density in cortical 1-2Hz EEG current density sources.

Figure 1A shows the cortical current density source distribution found during NREM sleep in the first half of sleep. The distribution is diffuse, although some dominant sources in parietal and in particular occipital cortices occur, the latter possibly related to the dominance of occipital electrodes used. Figure 1B shows SWA current density sources during the second half of sleep, where a qualitatively similar pattern can be observed, albeit somewhat reduced in strength. Figure 1C shows the distribution of significant differences in 1-2Hz NREM sleep EEG source current density (LORETA non-parametric permutation tests, $p<0.05$). Differences were found for several structures in the anterior half of the brain, mostly frontal lobe and limbic lobe structures, including the (anterior) cingulate gyrus. In view of the known frontal predominance of SWA occurrence and considering the SWA decrease during the first half of the sleep period, the result is according to expectation.

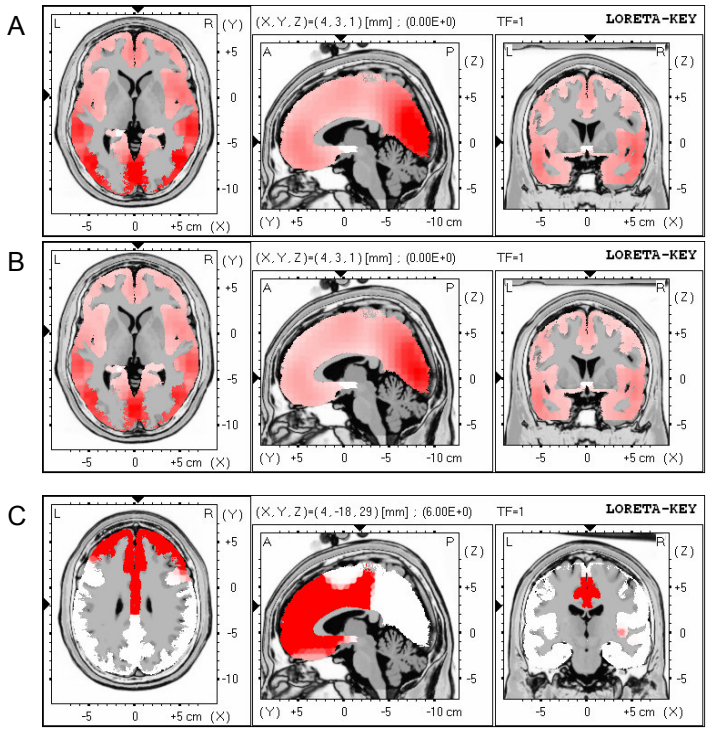


**Figure 1.** Average (N=9) LORETA current density source distribution of 1-2Hz component of the NREM sleep EEG during the first 50% of a normal night's sleep time (A), and during the second 50% of sleep time (B). Sources are diffusely distributed, and some parietal and occipital hotspots can be observed in both (A) and (B), albeit that the sources appear generally higher in (A). Panel (C) shows the distribution of significant differences between (A) and (B)(LORETA statistical non-parametric mapping; $p<0.05$), showing a pronounced frontal distribution.

The results suggest that (1) LORETA may be used for investigating sleep regulation in deeper cortical EEG source locations in a quantitative way, (2) the SWA reduction observed during the night may be caused primarily by a reduction in frontal SWA generators, and, (3) since occipital SWA current density appears to decrease less overnight as compared to frontal SWA generators, sleep regulation may be differently organized in these areas. Investigating these possible regulatory differences requires modelling of sleep debt dynamics of these different brain areas[5].

## REFERENCES

[1] Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques and scoring system for sleep stages in human subjects. US Government Printing Office, Washington DC.

[2] Cajochen C, Foy R, Dijk DJ (1999) Frontal Predominance of a Relative Increase in Sleep Delta and Theta EEG Activity after Sleep Loss in Humans. SRO 2:65-69.

[3] Pascual-Marqui RD, Michel CM, Lehmann D (1994) Low resolution electromagnetic tomography: a new method fopr localizing electrical activity in the brain. J. Psychophysiol. 18:49-65.

[4] Boerema AS, Van Bunnik BAD, Strijkstra AM, Wijers AA, Beersma DGM, Daan S (2003) Unilateral visual stimulation results in increased subjective sleepiness. . In Sleep-wake

Research in the Netherlands Vol.14, Van Bemmel AL, Beersma DGM, Hofman WF, Ruigt GSF, Vos PJE (Eds.), NSWO, Leiden, The Netherlands, pp 15-17.

[5] Zavada AG, Strijkstra AM, Boerema AS, Beersma DGM (in prep) Mapping the homeostatic sleep process in young healthy subjects.