

## Fragmentation of fMRI resting state networks in deep non Rapid Eye Movement (REM) sleep as compared to wakefulness as revealed by a group probabilistic ICA analysis in healthy volunteers

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**Introduction:** In recent years, increasing interest has grown concerning spontaneous low-frequency BOLD fluctuations as observed in resting state fMRI. In particular, consistent spontaneously coherent connectivity patterns, or resting state networks have been found across healthy awake volunteers. However, the significance of these spontaneous BOLD fluctuations is not known. We here investigate spontaneous BOLD connectivity patterns in the same volunteers, studied in deep non REM sleep compared to wake. **Methods:** 25 non-sleep deprived human volunteers were studied in a single scanning session using simultaneous electroencephalography and functional MRI. In nine of these subjects, sufficiently long and stable periods of both stage 3-4 sleep and non artefacted wakefulness, as documented by a standard EEG-based sleep staging procedure. This selection resulted in 2 sessions of 178 scans long per subject, one in deep non REM sleep, one in the preceding awake period. These functional images were preprocessed using SPM5, including realignment, normalisation and smoothing. Subsequent analyses were carried out using Probabilistic ICA as implemented in MELODIC version 3.05, part of FSL. This method allows for an automatic estimation of the relevant number of independent components to be chosen, using probabilistic PCA as a preprocessing step. Two separate group analyses were performed, one on the awake period, and one on the sleep session, using a temporal concatenation approach. Results of the group analyses were thresholded for display at  $P > 0.66$ . Identification of 10 functionally relevant networks similar to those described by Damoiseaux et al. (1) was performed visually for the waking group. A spatial cross correlation analysis was then performed between these selected networks and the corresponding spatial maps obtained for the group sleep analysis, using unthresholded Z scores maps. Spatial correlations between sleep and wake networks were thresholded at coefficient 0.2. **Results:** For nine out of ten resting state networks, cross correlation analysis identified a fragmentation in at least two to four components in sleeping subjects as compared to wake. The only network which failed to show such segregation was a left-lateralized dorsal frontoparietal component, corresponding to network C in Damoiseaux et al. (1). Splitting of the networks seemed to follow a certain functional segregation among the areas involved. In particular, the dorsal and ventral streams of the visual system were segregated in sleep while they were clustered in the same visual component in awake state. The default network was fragmented in an anterior part, encompassing mainly medial prefrontal cortices, and a posterior part, involving mainly posterior cingulate/ precuneus and temporoparietal cortices. **Conclusion:** The main finding of this analysis is a fragmentation of resting state networks in deep non REM sleep compared to wakefulness, as studied in non sleep-deprived healthy volunteers. As the data obtained here come from the same volunteers acquired the same day, our findings do not support the hypothesis that spontaneous connectivity patterns as commonly found in awake resting state volunteers are merely and only due to anatomical connectivity. They suggest the contribution of a functional origin to the resting state networks, that can be modified depending of conscious state. Fragmentation of spontaneous connectivity patterns in sleep compared to wakefulness is likely to contribute to the decrease in consciousness during deep non REM sleep, and might profoundly modify responses to external stimuli.

1. Damoiseaux, J. S., Rombouts, S. A., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., & Beckmann, C. F. (2006) *Proc Natl Acad Sci U S A* **103**, 13848-13853.