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Propofol Induced Unconsciousness Causes Impaired Cortical Top-Down Processing Indicated by Changes in EEG-fMRI Connectivity

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Introduction

Functional connectivity (FC) analyses of functional magnetic resonance imaging (fMRI) under propofol unconsciousness reported alterations in default networks of the resting brain [1]. These results are in accordance to recent electro-encephalographic (EEG) studies observing impaired top-down information processing during anesthesia [2]. To investigate neural mechanisms of propofol induced unconsciousness, fMRI FC and effective connectivity (EC) reflected by information flow in EEG were correlated in healthy subjects. Therefore fMRI blood oxygen dependent (BOLD) and high resolution EEG were simultaneously recorded during consciousness and un-consciousness.

Methods

Approved by the ethics committee, 15 volunteers were enrolled into the study. Volunteers were instructed to relax and close eyes while BOLD 3T-fMRI and 64-channel EEG baseline (BL) recordings were performed (figure 1). Subsequently propofol was infused until loss of consciousness (LOC) using a TCI pump and fMRI/EEG were measured. Independent components (ICs) of fMRI resting state networks (RSN) were identified using independent component analysis based on a standard processing pipeline in SPM5 [3]. Differences between BL and LOC were analyzed by two-sample t-tests (threshold $p < 0.05$ corrected). STEn quantifies the mutual information flow between two signals [4] and was computed over all EEG channel pair combinations (0.5-30 Hz total bandwidth, 10 s signals, 50 ms time delay) to reflect cortical EC. Effects of Propofol on STEn were computed in clustered electrode combinations according to 10-20 scheme by a Wilcoxon test (threshold $p < 0.05$). Correlation between FC (z-values) and EC from BL to LOC were indicated by a partial correlation analysis (threshold $p < 0.05$).

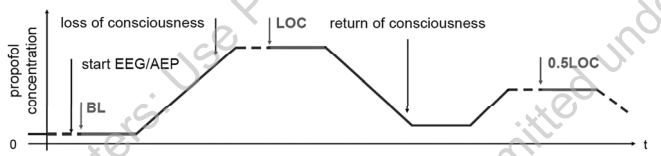

Figure 1: Diagram of the study period. BL: baseline recording, LOC: phase of unconsciousness with concentration obtained at loss of consciousness, 0.5LOC: phase of sedation.

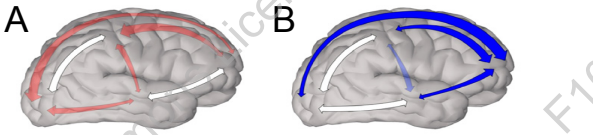

Figure 2: Illustration of dominant information exchange in EEG STEn during BL (A) and LOC (B) shows a decrease in the top–down information flow from frontal to posterior electrodes (red = anterior to posterior, blue = posterior to anterior, white = balanced).

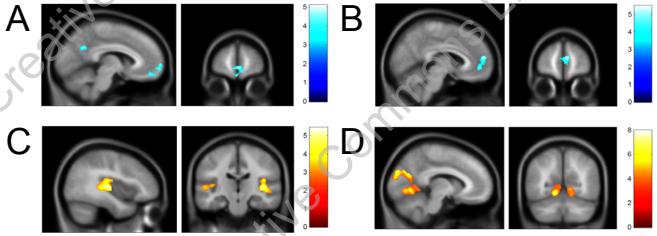

Figure 3: BOLD fMRI analysis of resting-state brain networks shows decreased FC from BL to LOC in the posterior (A) and anterior (B) default networks while the auditory (C) and visual (D) primary sensory networks show increased FC (decrease: dark to light blue, increase: red to yellow). Significant FC changes are displayed on the average T1 brain template of SPM 8 (full-factorial ANOVA: T-contrast of condition-specific effects at the same corrected cluster threshold $p < 0.05$).

Results

Table 1 shows changes in FC and EC between BL and LOC such as correlations between FC and EC. A decreased EC from frontal to posterior electrodes (figure 2) correlates with decreased FC in frontal (anterior default network) and increased FC in primary sensory networks (figure 3).

EC \ FC	anterior default ↓ (0.020)*	primary auditory ↑ (0.041)*	primary visual ↑ (0.029)*
frontal → parietal ↓ (0.005)*	+0.61 (0.004)*	-0.51 (0.087)	-0.45 (0.071)
frontal → temporal ↓ (0.009)*	+0.49 (0.122)	-0.61 (0.034)*	-0.73 (0.004)*
frontal → occipital ↓ (0.013)*	+0.57 (0.034)*	-0.53 (0.030)*	-0.39 (0.070)
temporal → occipital ↓ (0.009)*	+0.36 (0.248)	-0.62 (0.002)*	-0.58 (0.011)*

Table 1: Changes in FC / EC from BL to LOC (p-values, ↓: decrease, ↑: increase, *: $p < 0.05$ corrected) and correlation between FC and EC (p-values, +: positive, -: negative, *: $p < 0.05$).

Conclusions

EEG STEn reveals a propofol induced suppression of information feedback between frontal and posterior (parietal, temporal and occipital) brain regions which correlates to a decreased corticocortical FC within higher frontoparietal networks and increased FC in primary sensory areas. Increased connectivity within primary sensory cortices could result from a functional disconnection from higher cortical areas. Decrease of top-down feedback connection might be a general feature of unconsciousness and is compatible with theories attributing consciousness to the capacity of the brain to integrate distributed information [5,6].

References

[1] Anesthesiology 2010; 113: 1038-53 [2] PloS One 2011; 6 : e25155 [3] PNAS 2007; 104(47): 18760–5 [4] Phys Rev Lett 2008; 100: 158101 [5] Science 2008; 322: 876-80 [6] Science 2011; 332: 858-62