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EEG MEASURES INDICATING ANAESTHESIA INDUCED CHANGES OF CORTICAL INFORMATION PROCESSING

Jordan D[1], Ilg R[2], Schneider G[1,3], Stockmanns G[4], Kochs EF[1]

[1]Department of Anaesthesiology, Klinikum rechts der Isar, Technische Universität München, Germany
[2]Department of Neurology, Klinikum rechts der Isar, Technische Universität München, Germany
[3]Department of Anaesthesiology, Witten/Herdecke University, HELIOS Clinic Wuppertal, Germany
[4]Hochschule Niederrhein, FB Elektrotechnik und Informatik, Krefeld, Germany

d.jordan@lrz.tum.de

Abstract: *Consciousness is related to the brains ability to process information. This is inline with EEG studies observing decreased signal "complexity" under anaesthesia induced unconsciousness. In the present investigation, 64-channel electroencephalogram (EEG) of 15 volunteers was analyzed during consciousness, propofol induced sedation and unconsciousness. Univariate EEG parameters (spectral power, Higuchi fractal dimension, permutation entropy) and cortico-cortical information exchange in EEG based on symbolic transfer entropy (STE) were analysed to indicate effects of anaesthetics on the systemic information processing of the brain. The STE revealed affected interaction between frontal and parietal brain regions during unconsciousness.*

Keywords: *Electroencephalogram, consciousness, anaesthesia, propofol, entropy*

Introduction

Information processing in the human brain is an active field of research and is investigated with respect to specific paradigms [1]. It has been suggested that unconsciousness results from an impaired ability of the brain to integrate information. Functional magnetic resonance imaging (fMRI) studies on the effects of anaesthesia induced sedation and unconsciousness on the functional connectivity (FC) of the resting brain reported a disintegration of higher cortical networks [2]. Further, electroencephalographic (EEG) studies indicated an uncoupling of electrical coherence or suppression of long-range synchronization during unconsciousness when compared to wakefulness [3]. Beyond classical spectral power analyses of the EEG, new techniques were introduced to quantify the content of processed information. Approaches include state space methods such as fractal dimensions and information theoretic methods based on entropy analysis [4]. More recently, asymmetric multivariate analysis has facilitated the detection of directional interdependences from time series. Within the framework of ordinal signal analysis, symbolic transfer entropy (STE) was introduced to distinguish driving and responding subsystems in complex non-linear dynamics and to detect asymmetry in their mutual interaction [5]. STE combines advantages of a stringent concept to infer the direction of interactions with robustness and performance of non-linear symbolic analysis. In contrast to the univariate EEG permutation entropy (PE) [6], which has been suggested as reliable non parametric measure of anaesthetic depth [7], STE may more specifically indicate effects of anaesthetics on the systemic information processing level of the brain. In the present investigation, the ability of STE to quantify cortical processing in EEG during consciousness, propofol sedation and unconsciousness was evaluated.

Methods

Approved by the local ethics committee, 15 male volunteers (age 21-32 years) were enrolled into the study. After a resting period, volunteers were instructed to relax and close their eyes while 64-channel EEG recordings were performed under three conditions: After 15 minutes baseline (BL condition) recordings, propofol was infused until loss of consciousness (LOC) using a target controlled infusion (TCI) pump (Open TCI, Braun Medical, Melsungen, Germany). TCI concentrations were maintained stable for 15 minutes (LOC condition). After that, a phase of sedation was maintained during another 15 minutes at 50% of the initial LOC concentration (0.5LOC condition). Standard monitoring parameters (electrocardiogram (ECG), blood pressure, respiratory frequency, pulse oxymetry) were continuously measured with a Datex anaesthesia monitor (Datex-Ohmeda Division Instrumentation Corp., Helsinki, Finland) and recorded together with TCI concentrations. EEG recordings were performed using a 64-channel electrode cap with equidistant electrodes (Easycap, Herrsching, Germany) and two 32-channel EEG amplifiers (Brain Products, Gilching, Germany). Basic artefact rejection (EEG with amplitudes exceeding 250μV), average reference and independent component analysis for blind source separation of non cortical signal components were performed.

In the present study power spectral density in θ- (4-8Hz), α- (8-12Hz) and β-band (12-30Hz), Higuchi's fractal dimension (HD) [4], PE (dimension $m = 5$) [6] and STE [5] were analysed on all EEG channels at the end of the three conditions BL, 0.5LOC and LOC (signals of 10s length, zero phase digital filtered with 0.5-30Hz bandwidth, 200Hz sampling frequency). STE indicates information flow from system Y (time series y of length N) to system X (time series x of length N) through

$$\mathrm{STE}_{Y\rightarrow X} = \sum p(\hat{x}_i, \hat{x}_{i-\delta}, \hat{y}_{i-\delta}) \log_2\left(\frac{p(\hat{x}_i | \hat{x}_{i-\delta}, \hat{y}_{i-\delta})}{p(\hat{x}_i | x_{i-\delta})}\right). \quad (1)$$

Therefore, amplitude orders $\hat{x}_i, \hat{y}_i$ of sequences $x_i = \{x(i), x(i+l), \ldots, x(i+(m-1)l\}$ and y_i along x, y ($i \in \{1, \ldots, N-(m-1)l\}$) are analyzed with respect to embedding parameters m (dimension) and l (time lag). $p(A|B)$ is the conditional probability that A occurs under condition B, $p(A,B)$ is the joint probability of A and B. The directionality index denoted by STE quantifies the preferred direction of flow between systems X and Y, i.e.

$$\mathrm{STE} = \mathrm{STE}_{X \to Y} - \mathrm{STE}_{Y \to X} \,. \qquad (2)$$

STE is expected to attain positive values for unidirectional coupling with X as the driver and negative values for Y driving X. Assuming $\mathrm{STE}_{X \to Y}, \mathrm{STE}_{Y \to X} > 0$, a value STE = 0 indicates balanced bidirectional coupling. STE was computed in all EEG channel pair combinations using a dimension m = 5 and a transfer delay δ = 35-50 ms mainly reflecting cortico-cortical information transfer in the EEG β-band [1].

Discrimination of Pθ, Pα, Pβ, HD, PE and STE between BL, 0.5LOC (consciousness) and LOC (unconsciousness) was evaluated using the area under the receiver characteristic curve (AUC) and 95% percentile bootstrap confidence intervals (CI) at a corrected threshold of $p < 0.05$ Therefore, parameters were averaged in frontal, parietal, temporal and occipital EEG electrodes.

Results

Fig. 1 shows value distribution of Pθ, Pα, Pβ, HD, PE and STE at (A) BL, (B) 0.5LOC and (C) LOC. Only results of frontal (Pθ, Pα, Pβ, HD, PE) and frontal-parietal (STE) EEG leading to highest AUC is reported. Power spectral density Pθ, Pα, Pβ did not indicate loss of consciousness ($p > 0.05$). In contrast, HD, PE and STE provided significant separation of consciousness and unconsciousness as summarized in Tab. 1.

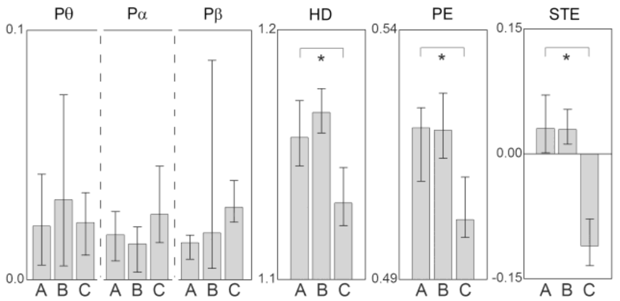

Figure 1: Median and 50% interquartile range of frontal EEG parameters Pθ, Pα, Pβ, HD, PE and frontal-parietal STE during (A) BL, (B) 0.5LOC and (C) LOC. *: Significant separation of consciousness (BL, 0.5LOC) and LOC.

In particular, during unconsciousness HD indicated a decrease of "dimensionality" in EEG, and PE indicated a decrease of "information content". Based on frontal-parietal EEG, STE showed a reliable separation of consciousness and unconsciousness, indicating a shift from predominantly fronto-parietal feedback (consciousness: STE > 0) to parieto-frontal feed forward "information processing" during LOC (STE < 0). This was induced by a decreased feedback ($\mathrm{STE}_{X \to Y}$) during LOC ($p < 0.05$).

Table 1: AUC including 95% CI at corrected threshold $p < 0.05$ of HD, PE and STE for separation of consciousness (BL, 0.5LOC) and LOC.

EEG parameter		AUC (CI)
HD	(frontal EEG)	↓ 0.89 (0.68-1.00)
PE	(frontal EEG)	↓ 0.90 (0.69-1.00)
STE	(frontal-parietal EEG)	↓ 0.99 (0.92-1.00)

Discussion

While EEG spectral analyses only showed weak effects of propofol, nonlinear analyses may provide additional information related to the dynamics of the brain. The observed decrease of HD and PE in frontal electrodes of the EEG could indicate a decline of higher-level cortical information processing during unconsciousness [1]. To further address whether consciousness is related to the brains ability to process information between cortical areas, EEG STE was found to be an adequate measure. STE indicated that long-range frontoparietal communication pathways (corresponding to default and attention control networks in fMRI) may be particularly affected. In contrast to unconsciousness, during propofol sedation the information exchange seemed to be largely preserved. This supports the hypothesis that the transition from consciousness to unconsciousness emerges from an on-off phenomenon [1] and is consistent with the reported persistence of the default mode network during sedation [2]. As a mechanism based measure that reliably differentiates consciousness from unconsciousness in frontal-parietal EEG, STE represents a promising approach for future techniques in EEG monitoring the "depth of anaesthesia".

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