

# Using eigenvector centrality to measure the effect of Propofol-induced sedation on functional connectivity

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**Introduction.** Propofol (Disoprivan®) is an anesthetic agent widely used in clinical practice. At low doses propofol affects episodic memory (Veselis et al. 2004) but the exact mechanism causing this effect is still unclear. Here we investigated whether propofol has a region-specific effect on functional connectivity in fMRI data. Test subjects were scanned under the influence of propofol or placebo while performing tasks involving episodic and semantic memory as well as evaluative judgments. Functional connectivity was assessed using an algorithm new to fMRI data analysis called 'eigenvector centrality'. This algorithm attributes a centrality value to each voxel in the brain. A voxel receives a larger value if it is highly correlated with many other nodes that are themselves central within the network. Google's PageRank algorithm is a variant of eigenvector centrality.

**Data and Methods.** The study was approved by the local ethics committee. All subjects gave informed consent. MRI data were acquired of 26 right-handed male volunteers on a 3T MRI scanner (Siemens Trio) using TR=2 sec, TE=40ms, 3x3 mm<sup>2</sup> in-plane resolution, 3 mm slice thickness, 1mm gap between slices. Each scanning session lasted for 70 minutes. One subject fell asleep so that his data had to be excluded. The session started with a T1-weighted scan, after which EPI scanning began while propofol or a placebo was administered (no task was presented during this period). After 10 minutes all subjects who received propofol were mildly sedated but remained responsive throughout the experiment. Over the following 30 minutes, dosages were maintained while subjects performed evaluative judgement (Zysset et al, 2002) as well as episodic and semantic memory tasks including face recognition. 8 of the 26 subjects received a placebo, 9 subjects received 0.6 µg/ml propofol, and 9 subjects received 0.12 µg/ml propofol.

All data sets were initially registered to an AC/PC coordinate system where the data were resampled to an isotropic voxel grid with a resolution of 3x3x3 mm<sup>3</sup>. We manually defined a mask containing about 42,000 voxels covering the entire cerebrum. We then computed a correlation matrix containing pairwise correlations between fMRI time series of the 30 minutes during which subjects performed the experimental tasks. Note that experimental design information such as stimulus onset times was not used for this analysis. The components of the normalized eigenvector belonging to the largest eigenvalue of the similarity matrix indicate node centrality, provided all entries in the matrix are positive. Note that negative entries in the matrix may lead to multiple eigenvalues, so that uniqueness is only guaranteed by adding +1 to all correlation values (by the Perron-Frobenius theorem). For each subject, we obtained an eigenvector centrality map (ECM). Voxels having a large ECM value are highly correlated with many other voxels that are themselves well connected. Immediately following the scanning, subjects were tested for their memory performance. Three performance levels were identified based on those tests. Level 0 was the placebo group, level 1 was a group of subjects who had received propofol and performed relatively well, the level 2 group had also received propofol but performed poorly.

**Results.** Figure 1 shows the results of a regression analysis thresholded at  $p < 0.05$  (corrected) using memory performance as a covariate. Areas shown in red had higher ECM values with decreased memory performance, blue denotes the reverse. We found a network of regions associated with evaluative judgement (anterior frontomedian cortex, Zysset 2002), and memory processes (middle frontal gyrus, hippocampus) showing a relative increase of ECM values. On the other hand, we found a strong bilateral decrease in the posterior cerebellum.

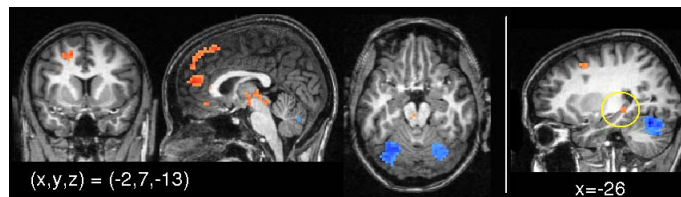


Figure 1: Effect of propofol on ECM values.

**Discussion.** In applying eigenvector centrality to fMRI data of propofol-sedated subjects, we found a set of brain regions that were differentially affected by the drug. Some areas – in particular those associated with task performance - showed a relative increase of ECM under propofol. This might indicate an increased effort against the effect of sedation in performing the experimental task which made demands on both judgment and working memory. The bilateral ECM decrease in the posterior cerebellum may be explained in light of recent findings on memory-related roles of the cerebellum (e.g. Fliessbach et al. 2007). Our results suggest that the well known impairment of episodic memory after propofol infusion is related to an impaired function of cerebellar regions known to be involved in memory encoding.

## References.

1. Veselis et al (2004). *Anesthesiology*, 101(4):831-41.
2. Zysset et al. (2002). *NeuroImage* 15, 983–991.
3. Fliessbach et al. (2007). *NeuroImage* 35, 1330–1337.