

Topiramate disrupts Graph Theory properties of brain connectivity in epilepsy and migraine patients.

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Abstract

Patients taking topiramate having a common effect of cognitive disfunction. This study investigates patients brain connectivity comparing to paired controls, using a graph theory approach. Results suggests losses of local connections and relevant hubs.

Key words:

Topiramate, graph theory, epilepsy.

Introduction

Despite the efficacy for epilepsy and migraine, cognitive dysfunction (mainly language) is a relatively common side effect of topiramate (TOP), for subjects with and without epilepsy. Here we applied Graph theory (GT) to evaluate the impact of TOP on functional connectivity (on both global and local properties), comparing parameters between controls and subjects taking TOP (patients with epilepsy and others with migraine).

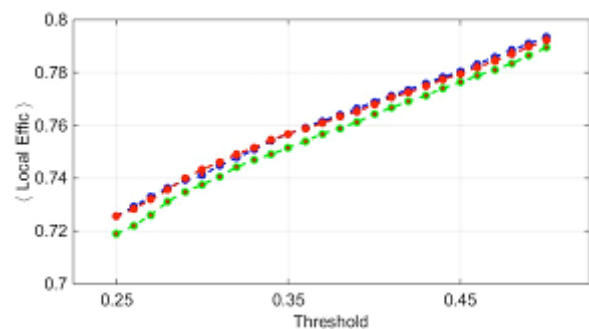
Results and Discussion

Resting-state fMRI (RS) was acquired from 38 healthy controls [without topiramate], 19 TLE patients (TLE-TOP) and 19 migraine patients (MIG-TOP), both groups taking TOP. All subjects underwent neuropsychological evaluation, with verbal fluency (FAS tests) and category fluency tests (naming animals). Each RS-fMRI was preprocessed with an in-house routine for SPM12/MATLAB, using a method to detect, characterize and remove motion volumes; Then parcellated into 90 regions of interest (based on AAL); by computing Pearson correlation values between all pairs, we finally constructed 90x90 matrices. Patients and controls were paired by number of remanoid volumes, age and gender.

Global and local parameters of GT (clustering coefficient, path length, local and global efficiency, transitivity, betweenness centrality, modularity and small world index) were calculated for a range of sparsity values. We also found hubs distribution in the whole networks for each group. Finally, the significance between-group comparison procedure were examined at each sparsity on SPSS22, with Tukey's HSD test. Cognitive tests were examined with MANOVA.

Both groups of patients presented lower performance for verbal fluency and category, compared to controls ($p < 0.05$). MIG-TOP performed similarly to TLE-TOP. Considering GT parameters (for a sparsity range between 0.25 – 0.5), statistical analysis revealed that MIG-TOP presented reduction of local efficiency (Image 1) and transitivity (Image 2) related to controls; in addition there were no differences between MIG-TOP and TLE-TOP groups ($p > 0.05$). Considering the relevance of each hub distribution for networks, we found nineteen significant AAL regions for controls, fifteen significant regions for TLE-TOP and fourteen regions of interest for MIG-TOP. This parameter showed decreased

number of regions with network importance comparing



controls to MIG-TOP and TLE-TOP groups.

Image 1. Local efficiency Parameter (Green – MIG-TOP; Red – TLE-TOP; Blue – CT).

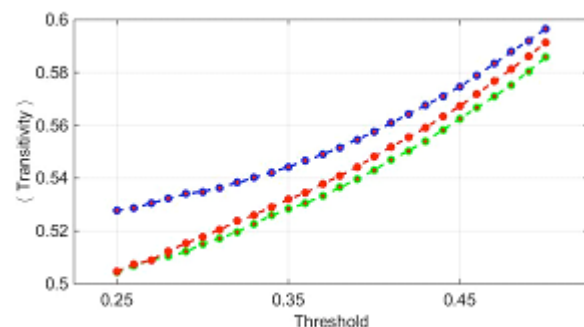


Image 2. Transitivity Parameter (Green – MIG-TOP; Red – TLE-TOP; Blue – CT).

Conclusions

These results suggest that MIG-TOP behave similarly to TLE-TOP regarding cognition and brain connectivity. The lowest performance of local GT parameters for MIG-TOP suggest a negative impact of TOP on brain connectivity which may be associated with cognitive dysfunction commonly observed in subjects taking this drug.

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