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HOW A DRUG CAN MAKE YOUR BRAIN FORGET THE WORDS? A LANGUAGE FUNCTIONAL MRI STUDY WITH TOPIRAMATE IN EPILEPSY AND HEADACHE.

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Abstract

We performed cognitive tests and language functional MRI (fMRI) study with healthy volunteers, patients with headache and others with epilepsy to demonstrate how TOPIRAMATE hampers words formation. We show poor cognitive performance and alterations on both brain activations and deactivations during the language paradigm fMRI.

Key words: *topiramate, functional MRI, language dysfunction.*

Introduction

Despite the excelent control of both seizures and headache, the drug TOPIRAMATE (TPM) can cause language (specially word finding difficulties) and memory impairment mostly unnoticed by subjects[1, 2]. So far, the mechanism for these side effects are not well understood. Here we applied cognitive tests and language fMRI to healthy controls, subjects with migraine/headache (HEAD) and others with temporal lobe epilepsy (TLE) to investigate dysfunction on brain activations and deactivations.

Results and Discussion

After Ethical approval, we performed a cross-sectional study, recruiting 24 healthy controls (18 women, mean age 42±13 years), 15 patients with migraine/headache taking TPM (HEAD-TPM,12 women, 39±12 years) and 12 patients with epilepsy using TPM (TLE-TPM,11 women, 39±13 years). Patients were recruited from both Epilepsy and Headache outpatient clinics at UNICAMP Hospital. All subjects underwent cognitive testing with language tests (1 minute for maximum word generation beginning with letter F, A, S and then 1 minute for animals); additionally, they performed a language fMRI study. in a 3T PHILIPS scanner with a blocked-design language paradigm (alternating task and rest every 20 seconds); subjects were instructed to covertly (silently, not loud) think about words beginning with different letters or think about the name of figures they were visually presented (letters, animals and fruits). MATLAB/SPM12(http://www.fil.ion.ucl.ac.uk/spm/software/spm12/) were used for imaging processing.

Groups were balanced for age (p=0.8) and gender (p=0.5). On multivariate analysis (with SPSS22) of language tests([$F_{(4,92)}$=6, p<0.0001, Pillai's Trace=0.4, partial η2=0.2]) we observed significant reduction of word production with letters *(FAS test)* for both HEAD-TPM and TLE-TPM (p<0.001) compared to controls (**Table 1**); no significant differences were observed for *categorical (animals)* word production (p>0.05) for these 2 groups, compared to controls.

On fMRI results (Figure1-2) we observed less activations and deactivations for both HEAD-TPM and EPI-TPM.

Table 1 – Language performance for 3 groups

	CONTROLS	HEAD/TPM	TLE/TPM
FAS	34±11	20±8	16±7
ANIMALS	19±7	15±5	17±6

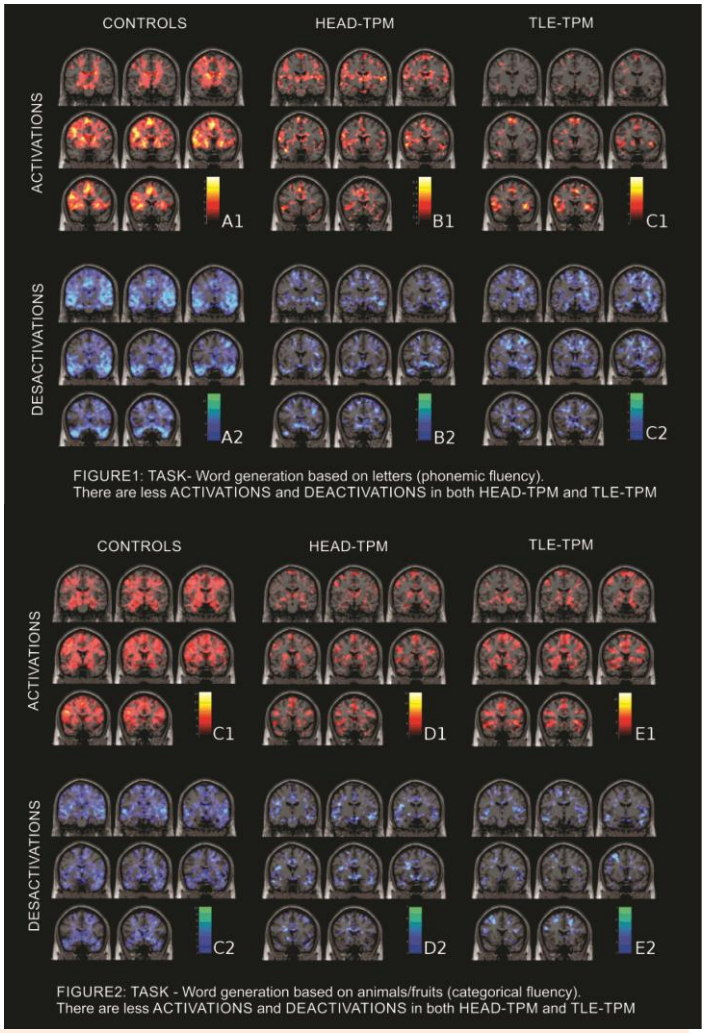

FIGURE1: TASK- Word generation based on letters (phonemic fluency). There are less ACTIVATIONS and DEACTIVATIONS in both HEAD-TPM and TLE-TPM

FIGURE2: TASK - Word generation based on animals/fruits (categorical fluency). There are less ACTIVATIONS and DEACTIVATIONS in both HEAD-TPM and TLE-TPM

Conclusions

TPM prevents normal brain activations and deactivations during language production, resulting in significantly impaired language performance. Careful attention is necessary to prescribe such drug to avoid excessive cognitive dysfunction, despite its efficacy.

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