**Valproate acid influence in the cortical surface of epilepsy’s patients brain structures**

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**Introduction:** Macro and micro-structural abnormalities are common findings in epilepsy. However, the pathogenesis and associated factors of these changes are not fully understood. Recent studies found an association of valproate acid (VPA) with brain atrophy independent of the seizure type. VPA is a commonly used anti-epileptic drug (AED) for focal and generalized epilepsies. This study aims to analyze the involvement of VPA in brain atrophy observed in epilepsy patients.

**Materials and Methods:** Patients followed in our epilepsy service had their medical charts analyzed for VPA use during their treatment. MRI images were post-processed with the FreeSurfer program to determine the cortical thickness, volume and surface of brain structures. A control group (n=50) was included for comparison. Patients were divided according with VPA use in two groups: a) never used VPA, but used other AEDs (VPA-, n=21) and b) were currently taking VPA when the MRI was taken (VPA+, n=13). Patients with major structural abnormalities were excluded from the analyses. The Student t-test was used for statistical analysis.

**Results:** We found that patients currently taking VPA (VPA+) had increase brain surface in the temporal-parietal region when compared to patients that had never taken the drug (VPA-) and to healthy controls. The group taking AEDs, but that had never used VPA, showed decrease in brain surface when compared to the VPA+ group (Table).

Table: Areas of significant changes between patients’ groups and controls

|  |  |  |
| --- | --- | --- |
| Changes in VPA+ patients compared to VPA- patients**\*** | Changes in VPA+ patients compared to controls**\*** | Changes in VPA- patients compared to controls **\*** |
| LH Cuneus (surface) | LH Cuneus (surface) | = LH Cuneus (surface) |
| RH Parietal superior (surface) | RH Parietal superior (surface) | = RH Parietal superior (surface) |
| RH Entorrinal (surface volume volume) | = RH Entorrinal (surface and volume) | RH Entorrinal (surface and volume) |

\*T-Test with two samples, p<0,05. LH: left hemisphere; RH: right hemisphere.

**Discussion:** The results show increased brain surface areas in patients currently taking VPA when compared to healthy controls and patients that never used AED. Cortical surface areas are usually increased in regions with reduced cortical thickness because of the consequent increase in sulcation of the cortical mantle. The temporal-parietal regions affected may be related to the effects of VPA in cognition and behavior.

**Conclusion:** The present work showed a possible link between VPA use and areas of increased cortical surface. More studies are necessary to better understand the relation between this AED and the changes in brain structure.