Tuberous sclerosis complex case series

2022

Retrospective longitudinal cohort study of 13 children with TSC, 3 to 6 serial ASL-MRI scans between 2 months and 7 years of age (53 scans in total), and an EEG examination performed within 2 months of the last MRI. Tuber cerebral blood flow (CBF) values were calculated in tuber segmentation masks, and tuber:cortical CBF ratios were used to study tuber perfusion. Logistic regression analysis was performed to identify which initial tuber characteristics (CBF value, volume, location) in the first MRI predicted tubers subsequently associated with EEG slow waves. Whole-brain and lobar CBF values were extracted for all patient scans and age-matched controls. CBF ratios were compared in patients and controls to study longitudinal changes in whole-brain CBF.

Results: Perfusion was reduced in tubers associated with EEG slow waves compared with other tubers. Low tuber CBF values around 6 months of age and large tuber volumes were predictive of tubers subsequently associated with EEG slow waves. Patients with severe developmental delay had more severe whole-brain hypoperfusion than those with no/mild delay, which became apparent after 2 years of age and were not associated with a higher tuber load.

Conclusions: Dynamic changes in tuber and brain perfusion occur over time. Perfusion is significantly reduced in tubers associated with EEG slow waves. Whole-brain perfusion is significantly reduced in patients with severe delay [1)].

2021

A study of Tong et al. investigated the dynamic and long-term efficacy of vagus nerve stimulation (VNS) in patients with drug-resistant epilepsy (DRE) induced by tuberous sclerosis complex (TSC). In addition, the impact of VNS on cognition and emotion after a one-year follow-up was evaluated.

A total of 17 patients diagnosed with DRE induced by TSC were retrospectively recruited between 2008 and 2019. Dynamic changes in seizure frequency were observed in the responders (≥50% reduction of seizure frequency at last follow-up) and non-responders. Clinical characteristics and seizure outcomes were comprehensively analyzed to determine factors associated with seizure outcomes. The Wechsler intelligence scale was applied in a subgroup of six pediatric patients, whereas the Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) were assessed in a subgroup of nine patients to determine the impact of VNS therapy on cognitive performance and emotional state.

The follow-up duration for the 17 patients who underwent VNS treatment ranged from 0.5 to 10 years (mean ± SD: 4.1 ± 3.2 years). Monthly seizures decreased significantly from three months to four years post-treatment ($p < 0.05$). At the last follow-up, 70.6% of the patients achieved at least a 50% reduction in seizure frequency, and three patients were completely seizure free. Comparatively, non-responder patients experienced deterioration of seizure frequency after the first year. Notably, after one-year follow-up the mean standard score of full-scale intelligence quotient increased from 67.33 to 69.5 ($p = 0.078$) while the mean, standard score of SDS decreased from 49.22 to 45.67 ($p = 0.003$) compared to preoperative neuropsychological evaluation results.

VNS is a safe and effective treatment for patients with DRE caused by TSC. Although early outcomes were encouraging, a follow-up of at least one-year was required to predict long-term outcomes in patients receiving VNS treatment. Moreover, VNS may improve depressive mood in patients with DRE caused by TSC. Further investigations are needed to validate the present results [2)].

Liu et al. reported a nationwide multicentre retrospective study and analyzed the long-term seizure and neuropsychological outcomes of epilepsy surgery in patients with tuberous sclerosis complex. There were 364 patients who underwent epilepsy surgery in the study. Patients' clinical data, postoperative seizure outcomes at 1-, 4-, and 10-year follow-ups, preoperative and postoperative intelligence quotients, and quality of life at 1-year follow-up were collected. The patients' ages at surgery were 10.35 ± 7.70 years (range: 0.5-47). The percentage of postoperative seizure freedom was 71% (258/364) at 1-year, 60% (118/196) at 4-year, and 51% (36/71) at 10-year follow-up. Influence factors of postoperative seizure freedom were the total removal of epileptogenic tubers and the presence of outstanding tuber on MRI at 1- and 4-year follow-ups. Furthermore, monthly seizure (versus daily seizure) was also a positive influence factor for postoperative seizure freedom at 1-year follow-up. The presence of an outstanding tuber on MRI was the only factor influencing seizure freedom at 10-year follow-up. Postoperative quality of life and intelligence quotient improvements were found in 43% (112/262) and 28% (67/242) of patients, respectively. Influence factors of postoperative quality of life and intelligence quotient improvement were postoperative seizure freedom and preoperative low intelligence quotient. The percentage of seizure freedom in the tuberectomy group was significantly lower compared to the tuberectomy plus and lobectomy groups at 1- and 4-year follow-ups. In conclusion, this study, the largest nationwide multi-centre study on resective epilepsy surgery, resulted in improved seizure outcomes and quality of life and intelligence quotient improvements in patients with tuberous sclerosis complex. Seizure freedom was often achieved in patients with an outstanding tuber on MRI, total removal of epileptogenic tubers, and tuberectomy plus. Quality of life and intelligence quotient improvements were frequently observed in patients with postoperative seizure freedom and preoperative low intelligence quotient [3)].

Brain MRIs of 110 TSC patients (mean age 11.5 years; age range 0.5-38 years; 52 female; 26 TSC1, 68 TSC2, 8 without mutation identified in TSC1 or TSC2, 8 not tested) were retrospectively evaluated. Signal and morphological abnormalities consistent with olfactory bulb hypo/aplasia or with olfactory bulb hamartomas were recorded. Cortical tuber number was visually assessed and a neurological severity score was obtained. Patients with and without rhinencephalon abnormalities were compared using appropriate parametric and non-parametric tests.

Eight of 110 (7.2%) TSC patients presented rhinencephalon MRI changes encompassing olfactory bulb bilateral aplasia (2/110), bilateral hypoplasia (2/110), unilateral hypoplasia (1/110), unilateral hamartoma (2/110), and bilateral hamartomas (1/110); olfactory bulb hypo/aplasia always displayed ipsilateral olfactory sulcus hypoplasia, while no TSC patient harboring rhinencephalon hamartomas had concomitant forebrain sulcation abnormalities. None of the patients showed overt olfactory deficits or hypogonadism, though young age and poor compliance hampered a proper evaluation in most cases. TSC patients with rhinencephalon changes had more cortical tubers (47 ± 29.1 vs 26.2 ± 19.6; $p = 0.006$) but did not differ for clinical severity ($p = 0.45$) compared to the other patients of the sample.

Olfactory bulb and/or forebrain changes are not rare among TSC subjects. Future studies investigating clinical consequences in older subjects (anosmia, gonadic development etc.) will define whether rhinencephalon changes are simply an imaging feature among the constellation of TSC-related brain changes or a feature to be searched for possible implications in the management of TSC subjects [4].

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