

J-difference editing method to evaluate GABA may reveal the mechanism of ACTH therapy for infantile spasms as a useful predict biomarker.

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Introduction

Adrenocorticotrophic hormone (ACTH) therapy has been used for rapid and complete elimination of infantile spasms (West syndrome) which is one of intractable epilepsies. The purposes of this study were to evaluate the metabolic changes including GABA before and after ACTH administration for infantile spasms, and to find a useful biomarkers to predict efficacy of ACTH therapy.

Methods and Materials

Eight cases (mean 8.7m.) with infantile spasms were evaluated in this study. The same examination was conducted on eight cases (mean 9.1m.) who had non-specific headache without any neurological findings and excluded morphological abnormality as normal controls. Local ethics committee approval was granted and full patient's families consent obtained. All studies were performed with a 3T clinical scanner (Signa Excite HD 3.0T) with standard head coil. MEGA-PRESS and STEAM sequences were adapted in this study and the measurement region (VOI) was placed on the right parietal parenchyma. LCModel was used for quantified spectrum analysis of GABA and other metabolites using our original basis-sets obtained by the same conditions in this study. Pre, post and two or three months after measurement for ACTH administration were done for all patients. The area of brain parenchyma of MR images of both pre and post ACTH therapy on same level was measured to evaluate brain shrinkage.

Results and Discussion

The shrinkage of brain parenchyma of patients with infantile spasms was shown in fig.1. It was attributed to the administration of ACTH, but it was recovered soon after few months. Figure 2 showed the differences of metabolites concentration between normal and infantile spasms, and the high concentrations of GABA, Cr, Cho, and mIns were found in the patients. The changes of GABA, NAA and Glx after ACTH administration were shown in fig.3. GABA and NAA were reduced with significant differences after the therapy, and the reduction of GABA was maintained even in few months after ACTH administration although NAA had the tendency of recovery. These results suggested that ACTH administration produced the atrophy of brain parenchyma and suppressed metabolism in neurons, but the influence of ACTH for neurotransmitters such as GABA might be prolonged more than other metabolism and morphologic changes. This prolonged decrease of neurotransmitter agents may influence on the suppression of abnormal excitation in neurons.

Conclusions

Our result suggested that GABA measured by MEGA-PRESS would be a useful indicator to evaluate the efficacy of ACTH treatment for infantile spasms. The information of neurotransmitter agents will give us better insights for pathological backgrounds of functional abnormality in the brain.

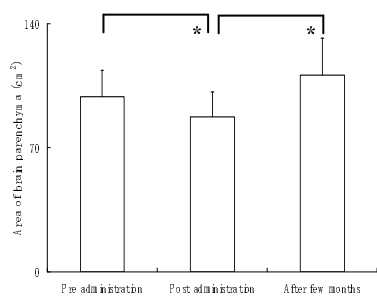


Fig.1 Changes of brain atrophy of

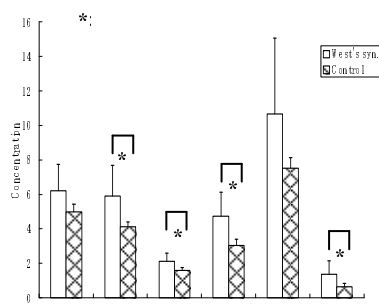


Fig.2 Metabolites concentration

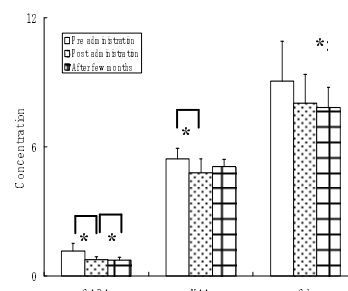


Fig.3 Changes of metabolism