

## Gap-junction is a new target for epileptic therapy in human gelastic seizures with hypothalamic hamartoma

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Human hypothalamic hamartoma (HH) is a rare developmental malformation usually characterized by gelastic seizures. Almost all HH patients are refractory to antiepileptic drugs (AEDs). Since the epileptogenic mechanisms of gelastic seizures are unknown, there is no available AEDs that can effectively control seizure activity. Previously, we have reported that the neurons within HH tissue are distributed in clusters of variable size, and that most (~90%) of HH neurons are small, GABAergic neurons with pacemaker-like firing. We believe that these neuronal clusters represent the functional unit for seizure initiation within HH tissue, and that hypersynchrony of these small, intrinsically-firing GABAergic neurons is a mechanistic component of ictogenesis. In the present study, we tested a new hypothesis that neuronal gap-junctions are highly expressed in HH tissue and play an important role in generating seizures. Immunostaining and Western-blot experiments show that neuronal type of gap-junction protein connexin 36 (Cx36) is highly expressed in human HH tissues freshly resected from gelastic seizure patients. Electrophysiological recordings from HH slices demonstrate that there are spontaneous epileptiform discharges in HH slice in normal artificial cerebrospinal fluid (ACFS) at  $33 \pm 1$  °C. Bath-application of gap-junction blocker (carbenoxolone) significantly eliminates these spontaneous discharges in a concentration-dependent manner. Our results suggest that the gap-junction is likely an important target for epileptogenesis within HH lesion, and pharmacological block of gap-junction is a novel therapeutic strategy for patients with refractory gelastic seizures and perhaps other forms of intractable epilepsy.

### Biography

Jie Wu has completed his M.D. at the age of 26 years from Xuzhou Medical College (China), his Ph.D at the age of 33 years from Sun-Yat-Sen University of Medical Science (China) and postdoctoral studies from both Tohoku University Medical College (Japan) and New Mexico University School of Medicine (USA). Now, He is a professor of neurology, the director of Epilepsy Research and the head of Electrophysiological Laboratory in Barrow Neurological Institute. He has published more than 107 peer-reviewed papers in reputed journals and serving as an editorial board member of several reputed journals.

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