
Alteration of monoamine receptor activity and glucose metabolism in paediatric patients with anticonvulsant-induced cognitive impairment

MATERIALS AND METHODS

Subjects

Intelligence quotient (IQ), including verbal IQ (VIQ), performance IQ (PIQ), and full-scale IQ (FSIQ) were assessed using the Chinese version of the Wechsler Intelligence Scale for Children (C-WISC) (1). IQ discrepancy refers to difference between VIQ and PIQ (VIQ-PIQ). Patients were considered to be in “Resistance” if they were failed to achieve sustained seizure free despite adequate anticonvulsants, or to be in “remission” if they had not had any seizures during the last year (2).

Data Analysis

Regions of interest (ROI) for the caudate nucleus, putamen (anterior and posterior), pallidum, thalamus and regional cortex were drawn in both hemispheres in the stereotactically normalized images (**Supplemental Fig. 1A**). The cerebellum was used as a reference region in ^{11}C -NMSP binding analysis as the low density of 5-HT_{2A} and D₂ receptors in this brain region allow for minimal levels of specific binding. The ^{11}C -NMSP PET images between 31 and 40 min, which demonstrated steady ratio of cortex to cerebellum, were selected for the image analysis (**Supplemental Fig. 1B**). In addition, the “ratio index” represents the slope of the striatum to cerebellum ratio over time and is a function of striatal Bmax (**Supplemental Fig. 1C**) (3).

RESULTS

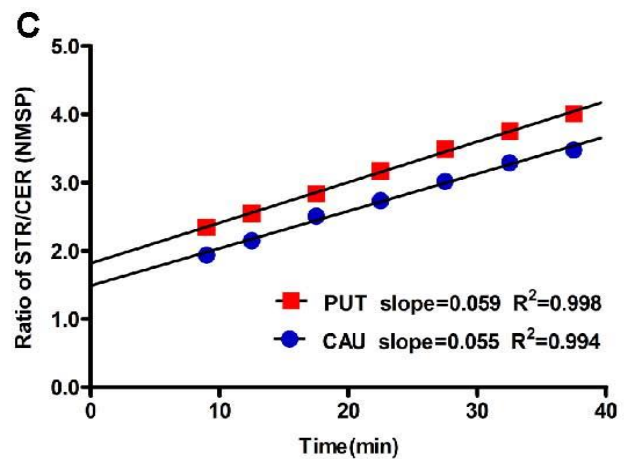
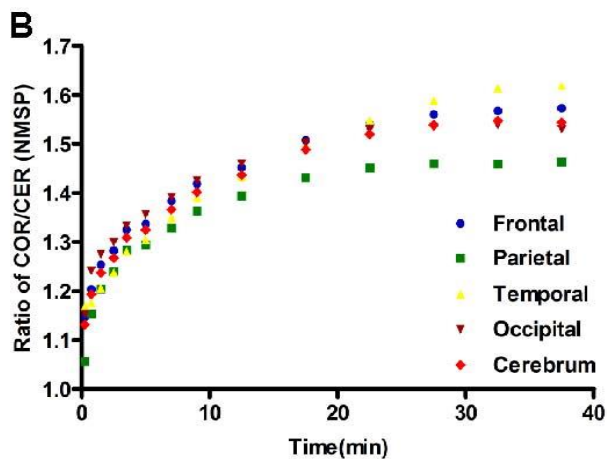
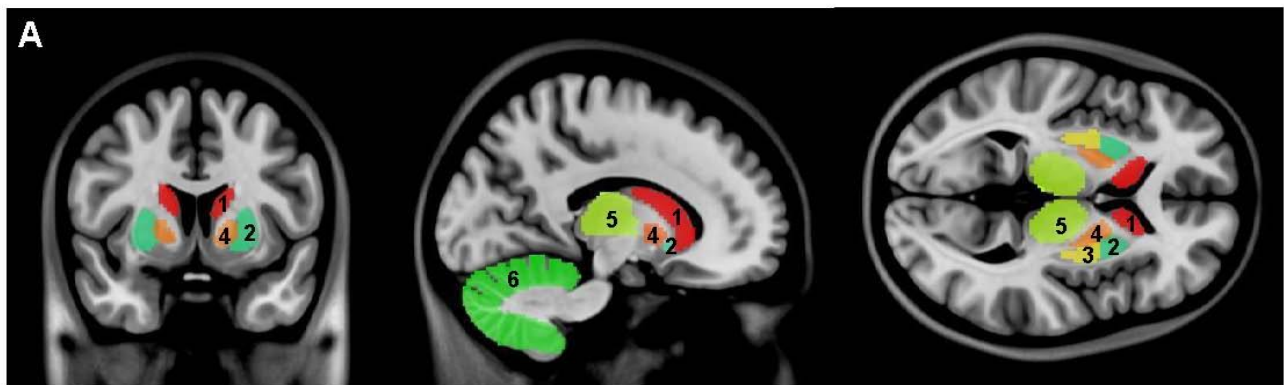
As shown in **Supplemental Figure 2**, significantly negative correlation was found between IQ discrepancy and PIQ ($r = -0.472$, $P = 0.017$) but not between IQ discrepancy and VIQ ($P = 0.627$). In addition, IQ discrepancy was significantly negatively correlated with ^{11}C -NMSP binding in right Broadman area 45 (BA45R) and Broadman area 46 (BA46R) ($r = -0.505$ and $r = -0.429$, respectively,

both $P < 0.05$). Among the 6 patients with significant IQ discrepancy ($|VIQ - PIQ| > 15$), 5 patients ($VIQ - PIQ < -15$) were confirmed to have epileptic foci in the left hemisphere, and 1 patient ($VIQ - PIQ > 15$) in the right hemisphere.

REFERENCES

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2. Dragoumi P, Tzetzzi O, Vargiami E, et al. Clinical course and seizure outcome of idiopathic childhood epilepsy: determinants of early and long-term prognosis. *BMC neurology*. 2013;13:206.
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Supplemental Figure 1 Region of interest (ROI) and dynamic change of ^{11}C -NMSP binding. **(A)** Outlining of ROIs in caudate (1), anterior putamen (2), posterior putamen (3), pallidum (4), thalamus (5) and cerebellum (6). **(B)** The ^{11}C -NMSP PET images between 31 and 40 min, which demonstrated steady ratio of cortex to cerebellum, were selected for the image analysis. **(C)** The slope of the striatum to cerebellum ratio over time is a function of B_{max} .



Supplemental Figure 2 Correlation between IQ discrepancy and ^{11}C -NMSP binding. **(A)** No significant correlation was found between IQ discrepancy and verbal IQ ($P = 0.627$). **(B)** IQ discrepancy was significantly negatively correlated with performance IQ ($r = -0.472$, $P = 0.017$). **(C and D)** IQ discrepancy was significantly negatively correlated with ^{11}C -NMSP binding in the right Broadman area 45 (BA45R) and Broadman area 46 (BA46R) ($r = -0.505$ and $r = -0.429$, respectively, both $P < 0.05$).

