Epilepsy Research (2011) **97**, 225—228

journal homepage: www.elsevier.com/locate/epilepsyres

SHORT COMMUNICATION

Differences in cerebral blood flow between missed and generalized seizures with electroconvulsive therapy: A positron emission tomographic study

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Received 28 February 2011; received in revised form 5 August 2011; accepted 14 August 2011
Available online 13 September 2011

KEYWORDS
Electroconvulsive therapy;
Positron emission tomography;
Cerebral blood flow;
Generalized seizure;
Centrencephalic system

Summary While examining the acute effects of electroconvulsive therapy (ECT) on regional cerebral blood flow (rCBF), we could compare the changes in rCBF between missed (not generalized) and generalized seizures using $H_2{}^{15}O$ positron emission tomography in patients with depression under anesthesia. In contrast to missed seizures, rCBF was increased extensively, particularly in the centrencephalic structures in generalized seizures. These results further support the centrencephalic theory of seizure generalization.

Introduction

Electroconvulsive therapy (ECT), widely used to treat major psychiatric disorders, induces generalized tonic—clonic seizures safely in the human brain (McNally and Blumenfeld, 2004). Recent neuroimaging studies have demonstrated that ''generalized'' seizures appear to selectively involve certain focal cortical and subcortical networks most intensely, while other brain regions are relatively spared (Blumenfeld et al., 2003; Enev et al., 2007). We have examined the acute effects of ECT on cerebral blood flow (CBF) in patients with depression using serial positron emission tomography (PET) and found that CBF increases during ECT and decreases soon after ECT-induced seizures (Takano et al., 2007). During this study, we could, by chance, compare the changes in CBF between generalized and missed (not generalized) seizures. We believe that elucidating the differences in the

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doi:10.1016/j.eplepsyres.2011.08.007

neuroanatomy involved in generalized seizures and missed seizures might help us understand the neural mechanisms of the propagation of generalized tonic—clonic seizures as well as the underlying therapeutic mechanisms of ECT.

Methods

Subjects

As described previously (Takano et al., 2007), six inpatients (four men and two women; mean age, 55.0 years; standard deviation (SD), 16.1 years) with major depressive disorder without other major medical illnesses participated in this study. All patients provided written informed consent. This study was approved by the Intramural Research Board of the National Centre of Neurology and Psychiatry.

Experimental procedure

This experiment was performed in association with our previous study (Takano et al., 2007). PET studies were performed on each patient during the first ECT session. Electroencephalograms (EEGs) were recorded using disc electrodes placed at F3, F4, P3, P4, Fz, Cz, and Pz; A1 and A2 electrodes were used as reference electrodes. Propofol and vecuronium bromide were used as anesthetics. Patients were kept under controlled ventilation with a respirator. ECT was administered through the bilateral temporal regions using a Thymatron DGx (Somatics Inc., Lake Bluff, IL). The stimulation dose was titrated and the dose was increased in cases of unsuccessful, missed seizures (no spike-and-wave complex observed on EEG, i.e., no seizure generalization). To perform scanning during ECT, patients were injected with $H_2{}^{15}O$ just prior to receiving electrical stimulation in all scans.

PET procedure

PET images were acquired using a Siemens ECAT EXACT HR 961 scanner in the three-dimensional mode, as in our previous study (Takano et al., 2007). The resolution of the scanner was 3.8 mm × 3.8 mm × 4.7 mm after filtered back projection with a Hanning filter (cut-off frequency, 0.5 cycle/pixel). Prior to the acquisition of emission data, a 10-min transmission scan was obtained using a retractable rotating $^{68}Ga/^{68}Ge$ source with three rods for attenuation correction. To obtain each scan, a bolus of 259 MBq $H_2{}^{15}O$ was automatically flushed intravenously for 15 s. The scanning was started manually 1 s after the initial increase in head count, and it was continued for 90 s. We inspected the EEGs to verify complete generalized seizures. When an ECT-induced seizure was missed, we stimulated the brain again with a higher dose of electricity and injected $H_2{}^{15}O$ after approximately 10 min.

Data analysis

The PET images were analyzed using Statistical Parametric Mapping 2 (SPM2) software (Wellcome Department of Cognitive Neurology, London, UK). The stereotaxically normalized scans contained 68 planes, and a final image with a resolution of 17 mm × 17 mm × 20 mm was produced by smoothing with a 10-mm Gaussian kernel.

Global CBF (gCBF) was calculated as the sum of the gray matter CBF after spatial normalization. Relative changes in rCBF were compared using multi-subjects with different conditions with proportional scaling in SPM2. The significance level was set at $p < 0.001$ (uncorrected), and the minimum cluster size (k) was set at 100 voxels. One-way analysis of variance (ANOVA), followed by Bonferroni's multiple comparison test was used to compare the gCBF among 3 groups.

Relative changes in regional CBF (rCBF) were compared using multiple subjects with different conditions with proportional scaling in SPM2. The significance level was set at $p < 0.005$ (uncorrected), and the minimum cluster size (k) was set at 100 voxels.

Results

We obtained three scans for each patient and a total of 18 pre-ECT scans while the patients were under anesthesia. We also obtained six scans during successful ECT-induced generalized seizures for all six patients. In addition, five scans for missed ECT in three patients were unexpectedly obtained (two scans in two patients and one scan in one patient) because we used a titration method to determine the dose of electrical stimulation (electrical doses administered for generalized seizures; mean, 122 mC; SD, 51.4; for missed seizures; mean, 116 mC; SD, 22.5). Thus, each patient had one successful ECT scan and 0—2 unsuccessful ECT scans.

In the case of successful ECT-induced seizures, the EEGs indicated that the mean duration of seizure activity was 67.5 s (SD, 26.1 s; range, 50—120 s). In contrast, in missed seizures, no evident spike-and-wave activities were observed.

Global CBF (gCBF) was increased during generalized seizures as compared to that at pre-ECT under anesthesia. In missed seizures, gCBF was at intermediate levels between these two conditions. One-way ANOVA revealed a significant difference in gCBF values among pre-ECT under anesthesia (mean, 20.5 mL 100 g^{-1} min^{-1}; SD, 4.8 mL 100 g^{-1} min^{-1}), missed ECT (mean, 28.1 mL 100 g^{-1} min^{-1}; SD, 7.5 mL 100 g^{-1} min^{-1}), and successful ECT (mean, 37.5 mL 100 g^{-1} min^{-1}; SD, 8.9 mL 100 g^{-1} min^{-1}) scans ($df = 29$, $F = 17.4$, $p < 0.0001$; Fig. 1). Post hoc analysis with Bonferroni's correction demonstrated a significant increase between pre-ECT and successful ECT ($p < 0.0001$), while trend level increased

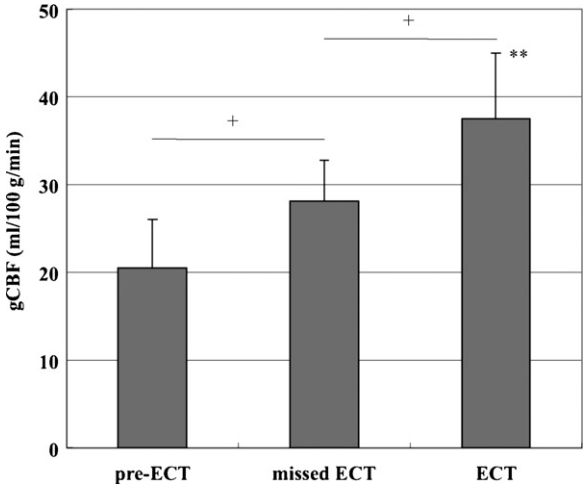

Figure 1 Global cerebral blood flow (gCBF) under anesthesia (pre-ECT), at missed and successful electroconvulsive therapy (missed ECT and ECT). $^{**}p < 0.001$ as compared to pre-ECT; $^{+}p < 0.1$ between missed ECT and pre-ECT, and pre-ECT and ECT, respectively.