

Supplemental information

**Dynamics of AMPA receptors regulate
epileptogenesis in patients with epilepsy**

Tsuyoshi Eiro, Tomoyuki Miyazaki, Mai Hatano, Waki Nakajima, Tetsu Arisawa, Yuuki Takada, Kimito Kimura, Akane Sano, Kotaro Nakano, Takahiro Mihara, Yutaro Takayama, Naoki Ikegaya, Masaki Iwasaki, Akitoyo Hishimoto, Yoshihiro Noda, Takahiro Miyazaki, Hiroyuki Uchida, Hideaki Tani, Nobuhiro Nagai, Teruki Koizumi, Shinichiro Nakajima, Masaru Mimura, Nozomu Matsuda, Kazuaki Kanai, Kazuhiro Takahashi, Hiroshi Ito, Yoji Hirano, Yuichi Kimura, Riki Matsumoto, Akio Ikeda, and Takuya Takahashi

Patient	Gender/age,y	Onset age,y	Duration,y	Seizure type	Estimated epileptogenic focus
1	M/33	11	22	FIAS/FAS	Left temporal lobe
2	M/48	25	23	FIAS/FAS	Right temporal lobe
3	M/26	26	1	FIAS	Left temporal lobe
4	M/38	11	27	FIAS	Right temporal lobe
5	M/38	29	9	FIAS/FAS	Frontal lobe

Table S1. Patient characteristics of focal onset seizures without generalized seizure, Related to Figure 1 and 2.

FIAS: Focal impaired awareness seizure, FAS: Focal aware seizure.

Patient	Gender /age,y	Onset age,y	Duration,y	Seizure type	Estimated epileptogenic focus
6	M/25	0	25	FIAS/FAS+FBTCS	Right hypothalamus
7	M/21	13	8	FIAS+FBTCS	Left temporal lobe
8	M/50	10	40	FIAS+FBTCS	Bilateral temporal lobe
9	M/25	9	16	FAS +FBTCS	Right frontal lobe
10	M/55	53	2	FIAS+FBTCS	Right frontal lobe
11	M/35	6	29	FAS +FBTCS	Left occipital lobe
12	M/39	18	20	FIAS+FBTCS	Right frontal lobe
13	M/45	31	14	FIAS+FBTCS	Unknown
14	M/30	28	2	FIAS+FBTCS	Right temporal lobe
15	M/31	14	17	FIAS+FBTCS	Left temporal lobe
16	M/21	15	6	FAS +FBTCS	Left frontal lobe
17	M/46	4	42	FIAS+FBTCS	Unknown
18	M/30	20	10	FIAS+FBTCS	Right frontal lobe
19	M/31	11	14	FIAS+FBTCS	Left frontal lobe
20	M/50	42	8	FIAS+FBTCS	Left temporal lobe
21	M/26	20	6	FIAS+FBTCS	Left temporal lobe
22	M/47	10	37	FIAS/FAS+FBTCS	Left temporal lobe

Table S2. Patient characteristics of focal to bilateral tonic clonic seizures, Related Figure 1 and 3

FIAS: Focal impaired awareness seizure, FAS: Focal aware seizure, FBTCS: Focal to bilateral tonic clonic seizure.

Patient	Gender /age,y	Onset age,y	Duration,y	Seizure type
23	M/28	12	16	GOTC
24	M/23	14	9	GOTC
25	M/20	12	8	GOTC
26	M/29	15	14	GOTC
27	M/49	13	36	GOTC
28	M/37	24	2	GOTC
29	M/26	24	2	GOTC
30	M/29	24	5	GOTC

Table S3. Patient characteristics of generalized onset seizures, Related to Figure 4

GOTC: Generalized onset tonic clonic.

Figure S1

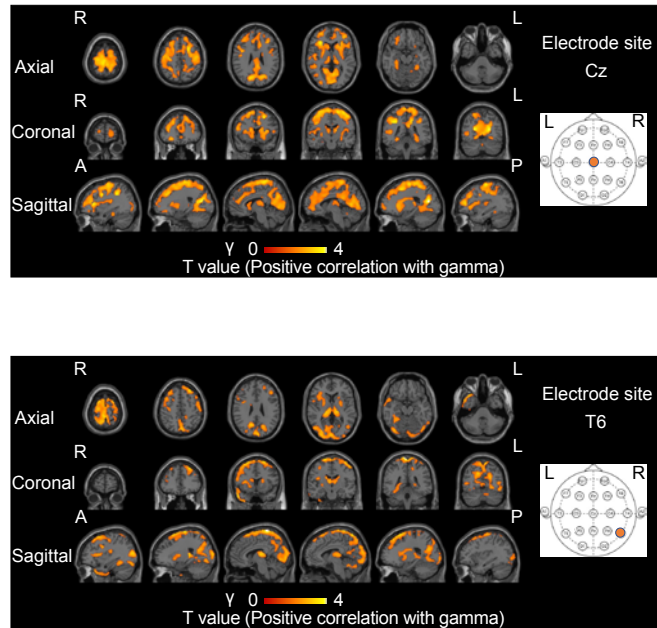


Figure S1. Positive correlation between the amount of cell surface AMPAR and the amplitude of gamma activity in focal epilepsy detected by multiple electrode sites, Related to Figure 1

SPM analysis of [¹¹C]K-2 in patients with the focal onset seizures identifies the brain regions showing a significant positive correlation between $SUVR_{30-50 \text{ min}}$ with white matter as a reference and the amplitude of gamma activity in Cz, T6 electrode site ($p < 0.05$, $T > 1.72$, one-tailed, FDRc). Scale bar indicates T value of this correlation. R: right side, L: left side, A: anterior side, P: posterior side.

FigureS2

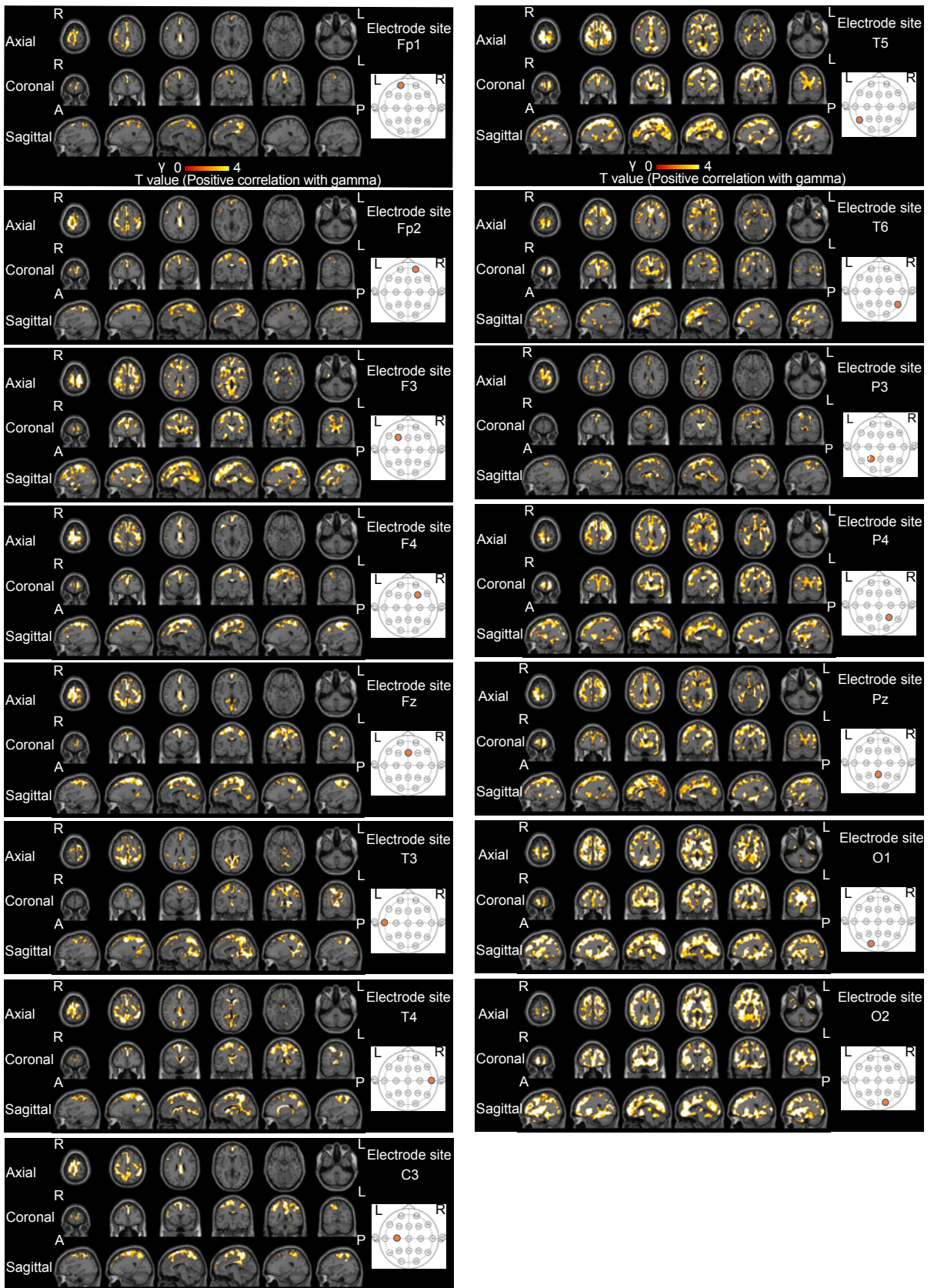


Figure S2. Positive AMPAR-gamma activity couplings are observed in patients with the focal onset seizures without generalized seizure detected by multiple electrode sites, Related to Figure2

SPM analysis of [¹¹C]K-2 in patients with the focal onset seizures without generalized seizure identifies the brain regions showing a significant positive correlation between $SUVR_{30-50 \text{ min}}$ with white matter as a reference and the amplitude of gamma activity in Fp1, Fp2, F3, F4, Fz, T3, T4, C3, T5, T6, P3, P4, Pz, O1, O2 electrode site ($p < 0.05$, $T > 2.35$, one-tailed, FDRc). Scale bar indicates T value of this correlation.

R: right side, L: left side, A: anterior side, P: posterior side.

Figure S3

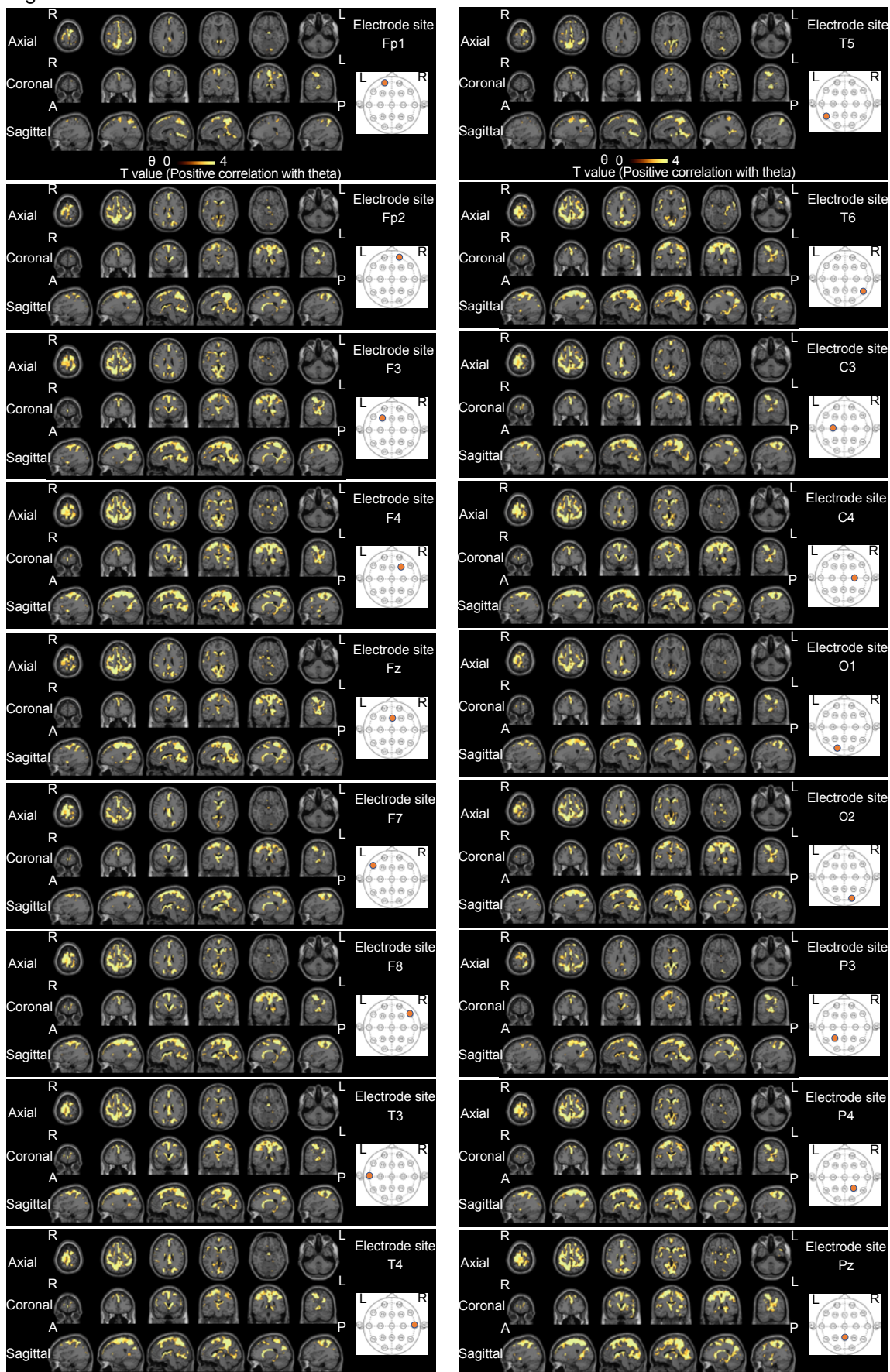


Figure S3. Positive AMPAR-theta activity couplings are observed in patients with the focal onset seizures without generalized seizure detected by multiple electrode sites, Related to Figure2

SPM analysis of [¹¹C]K-2 in patients with the focal onset seizures without generalized seizure identifies the brain regions showing a significant positive correlation between $SUVR_{30-50 \text{ min}}$ with white matter as a reference and the amplitude of theta activity in Fp1, Fp2, F3, F4, Fz, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, Pz, O1, O2 electrode site ($p < 0.05$, $T > 2.35$, one-tailed, FDRc). Scale bar indicates T value of this correlation. R: right side, L: left side, A: anterior side, P: posterior side.

Figure S4

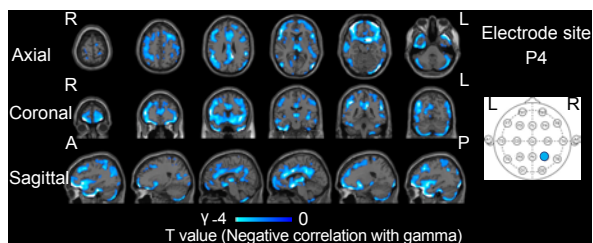
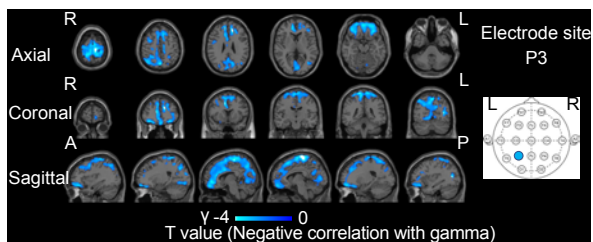
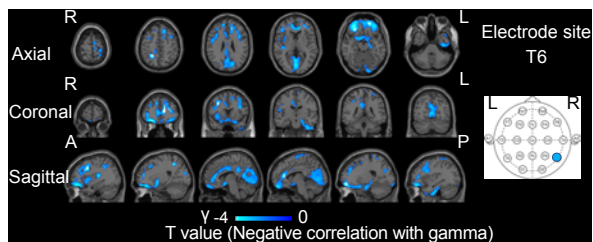
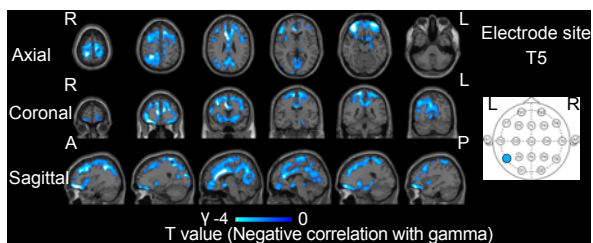
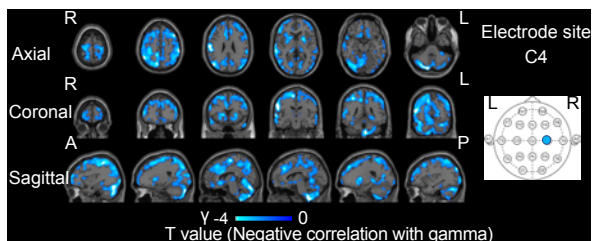
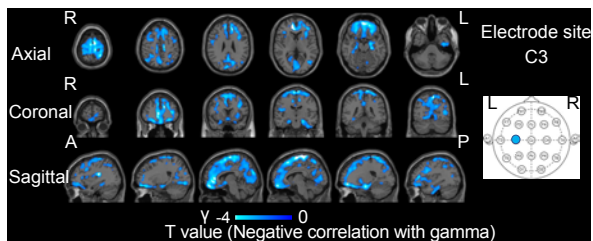


Figure S4. Generalized onset seizure downregulates AMPAR levels detected by multiple electrode sites, Related to Figure 4

SPM analysis of [¹¹C]K-2 in patients with the generalized onset seizures identifies the brain regions showing a significant negative correlation between SUVR_{30-50 min} with white matter as a reference and the amplitude of gamma activity in C3, C4, T5, T6, P3, P4 electrode sites ($p < 0.05$, $T > 1.94$, one-tailed, FDRc). Scale bar indicates T value of this correlation. R: right side, L: left side, A: anterior side, P: posterior side.