SUPPLEMENTAL MATERIAL

eTable 1. Demographics of the study subjects by group.

	LGI1-AE	non-LGI1-AE	AD	NC	p-value*
N (f/m)	13 (5/8)	15 (10/5)	11 (6/5)	10 (5/5)	0.530
Mean age (range) (y)	65 (48–78)	60 (18–77)	66 (49–84)	60 (42–93)	0.575

* Fischer's exact test for sex distribution, Kruskal-Wallis test for age comparison between groups

AD = Alzheimer's disease; f = female; LGI1-AE = LGI1 autoimmune encephalitis; m = male; NC = negative controls; non-LGI1-AE = non-LGI1 autoimmune encephalitides

eTable 2. Putaminal and mediotemporal metabolic activity measured with [^{18}F]FDG-PET in patients with LGI1 and non-LGI1 autoimmune encephalitis and Alzheimer's disease, and in negative controls.

[^{18}F]FDG-PET-index	LGI1-AE Median (IQR)	non-LGI1-AE Median (IQR)	AD Median (IQR)	NC Median (IQR)	p-value*
P-SUVRg	1.39 (0.16)	1.20 (0.14)	1.22 (0.08)	1.12 (0.07)	<0.001
P/Th	1.38 (0.13)	1.18 (0.18)	1.25 (0.20)	1.16 (0.15)	0.002
P/Mi	1.53 (0.11)	1.24 (0.22)	1.29 (0.12)	1.30 (0.22)	<0.001
MTL-SUVRg	0.90 (0.14)	0.88 (0.21)	0.82 (0.09)	0.75 (0.03)	0.002
MTL/Th	0.89 (0.09)	0.90 (0.15)	0.83 (0.13)	0.79 (0.06)	0.006
MTL/Mi	0.96 (0.09)	0.94 (0.12)	0.84 (0.09)	0.86 (0.15)	<0.001

* Significant at the level of p<0.05

AD = Alzheimer's disease; IQR = interquartile range; LGI1-AE = LGI1 autoimmune encephalitis; Mi = Midbrain; MTL = mediotemporal lobe; NC = negative controls; non-LGI1-AE = non-LGI1 autoimmune encephalitis; P = Putamen; SUVRg = global brain normalized standardized uptake value ratio; Th = thalamus.

e-Table 3. Comparison of putaminal and mediotemporal metabolic activity, measured with [^{18}F]FDG-PET, in patients with LGI1 autoimmune encephalitis and subgroups of non-LGI1 autoimmune encephalitides.

[^{18}F]FDG-PET-index	LGI1-AE Median (IQR)	NMDAr-AE Median (IQR)	OTHER LE-LIKE Median (IQR)	SD-LE Median (IQR)	p-value*
P-SUVRg[#]	1.39 (0.16)	1.07 (0.23)	1.19 (0.09)	1.24 (0.22)	0.009
P/Th[#]	1.38 (0.13)	1.26 (0.25)	1.12 (0.14)	1.22 (0.21)	0.015
P/Mi[#]	1.53 (0.11)	1.23 (0.17)	1.19 (0.27)	1.35 (0.24)	0.002
MTL-SUVRg	0.90 (0.14)	0.80 (0.19)	0.91 (0.25)	0.90 (0.21)	0.504
MTL/Th	0.89 (0.09)	0.94 (0.20)	0.88 (0.22)	0.90 (0.25)	0.674
MTL/Mi	0.96 (0.09)	0.90 (0.14)	0.92 (0.15)	0.96 (0.19)	0.360

LGI1-AE = LGI1 autoimmune encephalitis; Mi = Midbrain; MTL = mediotemporal lobe; Other LE-like = patients with limbic encephalitis -like autoimmune encephalitis associated with GABA-B, CASPR2, Anti-Hu or GAD65-antibodies; P = Putamen; SD-LE = patients with limbic encephalitis -like autoimmune encephalitis associated with other autoimmune systemic disorders (i.e. Sjögren's syndrome, Hashimoto's encephalitis or antiphospholipid syndrome); SUVRg = global brain normalized standardized uptake value ratio; Th = thalamus.

* Overall Kruskal-Wallis test p-value, significant at the level of p<0.05

[#] Pairwise comparisons between groups with significant p-values (after Bonferroni correction)
for P-SUVRg: LGI1 vs. NMDA, p=0.006 (p=0.033) and LGI1 vs. OTHER LE-like, p=0.008 (p=0.050);
for P/Th: LGI1 vs. OTHER LE-like, p=0.002 (p=0.012);
for P/Mi: LGI1 vs. NMDA, p=0.006 (p=0.033) and LGI1 vs. OTHER LE-like, p= 0.001 (p=0.006)

eTable 4. Cut-off values of the putaminal [^{18}F]FDG-PET indices for differentiating patients with LGI1 autoimmune encephalitis (AE) from negative controls (NC), patients with non-LGI1-AE and Alzheimer's disease. The cut-off values with optimal sensitivity and specificity are defined by the highest Youden Index (J = Sensitivity + Specificity -1) using the co-ordinates from the receiver operating characteristic (ROC) curve analyses, and the respective positive likelihood and negative likelihood ratios are also presented.

	LGI1-AE vs. NC						LGI1-AE vs. non-LGI1-AE						LGI1-AE vs. AD					
	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-	Cut-off value	Se (%)	Sp (%)	J	LR+	LR-
P-SUVRg	1.21	92	100	0.92	∞	0.08	1.29	77	80	0.57	3.85	0.29	1.28	77	82	0.59	4.28	0.28
P/Th-ratio	1.32	77	100	0.77	∞	0.23	1.3	85	80	0.65	4.25	0.19	1.29	85	73	0.58	3.15	0.21
P/Mi-ratio	1.44	85	100	0.85	∞	0.15	1.45	85	93	0.78	12.14	0.16	1.46	85	100	0.85	∞	0.15

AD = Alzheimer's disease; J = Youden Index; LGI1-AE = LGI1 autoimmune encephalitis; LR+ = positive likelihood ratio; LR- negative likelihood ratio; NC = negative controls; non-LGI1-AE = non-LGI1 autoimmune encephalitis; P = putamen; Se = sensitivity; Sp = specificity; SUVRg = global brain normalized SUV-ratio; Th = thalamus

eTable 5. Regional brain metabolic abnormalities in patients with LGI1 autoimmune encephalitis (n=13) in frontal, parietal, occipital and lateral temporal lobe regions and non-putaminal subcortical regions of interest compared to negative controls (n=10) and measured as global normalized standardized uptake value ratios (SUVRg) of [^{18}F]FDG.

ROI	LGI1-AE *Median (IQR)*	NC *Median (IQR)*	*% difference of medians*	*p-value**
Olfactory gyrus	1.02 (0.14)	0.90 (0.06)	+11.4 %	0.003
Opercular part of inferior frontal gyrus	1.10 (0.09)	1.15 (0.05)	-4.7 %	0.008
Triangular part of inferior frontal gyrus	1.08 (0.06)	1.15 (0.04)	-6.6 %	<0.001
Orbital part of inferior frontal gyrus	1.02 (0.06)	1.07 (0.06)	-5.0 %	0.021
Medial orbital part of superior frontal gyrus	1.02 (0.08)	1.09 (0.06)	-6.3 %	0.003
Gyrus rectus	1.03 (0.07)	1.10 (0.05)	-7.2 %	0.010
Angular gyrus	1.11 (0.10)	1.19 (0.09)	-6.9 %	0.021
Inferior parietal lobe	1.11 (0.09)	1.18 (0.07)	-6.8 %	0.030
Fusiform gyrus	1.05 (0.05)	0.98 (0.05)	+5.9 %	<0.001
Occipital inferior gyrus	1.20 (0.11)	1.11 (0.10)	+7.2 %	0.026
Caudate	0.85 (0.22)	0.76 (0.09)	+12.5 %	0.006
Pallidum	1.10 (0.11)	1.02 (0.11)	+7.4 %	0.015
Pons	0.74 (0.08)	0.69 (0.09)	+7.3 %	0.030

* Significant at the level of p<0.05

LGI1-AE = LGI1 autoimmune encephalitis; NC = negative control; IQR = interquartile range; ROI = region of interest

eTable 6. Short-term changes in mediotemporal and putaminal metabolism, measured with [^{18}F]FDG-PET, in eight patients with LGI1 autoimmune encephalitis after immunosuppressive treatment.

[^{18}F]FDG-PET -index	Baseline Median (IQR)	Follow-up Median (IQR)	% difference of medians	p-value
MTL-SUVRg	0.88 (0.14)	0.78 (0.14)	-11.3 %	0.050[#]
MTL/Th-ratio	0.89 (0.10)	0.78 (0.16)	-12.0 %	0.050[#]
MTL/Mi-ratio	0.96 (0.07)	0.91 (0.08)	-5.1 %	0.069
P-SUVRg	1.40 (0.19)	1.24 (0.19)	-11.2 %	0.012*
P/Th-ratio	1.39 (0.11)	1.25 (0.15)	-9.9 %	0.036*
P/Mi-ratio	1.53 (0.11)	1.42 (0.16)	-7.0 %	0.123

*   significant at the level of p<0.05
[#]   significant at the level of p=0.05
[§]   Spearman's rho

IQR = interquartile range; Mi = Midbrain; mRS = modified Rankin Scale; MTL = mediotemporal lobe; P = Putamen; Th = thalamus; SUVRg = global normalized standardized uptake value ratio

eTable 7. Short-term changes in mediotemporal and putaminal metabolism, measured as global normalized standardized uptake value ratio (SUVRg) of [18F]FDG, in patients with LGI1 autoimmune encephalitis after immunosuppressive treatment and stratified by clinical disability at the time of short-term follow-up PET.

[18F]FDG-PET -index	LGI1-AE subgroup	Baseline *Median (IQR)*	Follow-up *Median (IQR)*	*% difference of medians*	*Effect Size*	*p-value*
MTL-SUVRg	mRS ≤ 2	0.90 (0.10)	0.72 (0.09)	-19.8 %	-0.90	0.043
	mRS > 2	0.80 (na)	0.85 (na)	+6.0 %	0.00	1.000
P-SUVRg	mRS ≤ 2	1.41 (0.23)	1.23 (0.20)	-12.5 %	-0.90	0.043
	mRS > 2	1.39 (na)	1.26 (na)	-9.9 %	-0.93	0.109

IQR = interquartile range; mRS = modified Rankin Scale; MTL = mediotemporal lobe; P = Putamen; SUVRg = global normalized standardized uptake value ratio; LGI1-AE = LGI1 autoimmune encephalitis

eTable 8. Brain metabolism in the cingulate subregions at the initial [^{18}F]FDG-PET in patients with LGI1 autoimmune encephalitis (n=13), stratified by long-term clinical outcome at the latest clinical follow-up and measured with modified Rankin Scale.

ROI	Good outcome (mRS≤2) median (range)	Poor outcome (mRS>2) median (range)	% difference of medians	p-value
Cingulate Ant# (SUVRg)	0.99 (0.21)	0.87 (0.01)	-12.5 %	0.026*
Cingulate Mid (SUVRg)	1.13 (0.19)	1.05 (0.02)	-6.9 %	0.026*
Cingulate Post (SUVRg)	1.14 (0.41)	1.00 (0.15)	-12.1 %	0.231

* Significant at the level of p<0.05

Anterior cingulate hypometabolism at baseline remained significantly associated with worse long-term outcome in a multiple regression model when including time from symptom onset to the initial PET imaging, age and baseline mRS as covariates (standardized coefficient -0.753, t-value -2.441, p=0.041; overall regression p=0.009).

mRS = modified Rankin Scale; ROI = region of interest. SUVRg = global normalized standardized uptake value ratio

e-Table 9. Mediotemporal and putaminal brain metabolism at the initial [18F]FDG-PET in patients with LGI1 autoimmune encephalitis (n=13), stratified by long-term clinical outcome at the latest clinical follow-up and measured with modified Rankin Scale.

| [18F]FDG-PET -index	Good outcome (mRS≤2) median (range)	Poor outcome (mRS>2) median (range)	% difference of medians	p-value
MTL-SUVRg	0.88 (0.24)	0.94 (0.02)	+6.6 %	0.231
MTL/Th-ratio	0.89 (0.18)	0.92 (0.01)	+3.8 %	0.103
MTL/Mi-ratio	0.96 (0.16)	0.95 (0.01)	-0.6 %	1.000
P-SUVRg	1.33 (0.31)	1.48 (0.01)	+10.9 %	0.103
P/Th-ratio	1.36 (0.10)	1.45 (0.02)	+6.9 %	0.154
P/Mi-ratio	1.54 (0.13)	1.50 (0.05)	-2.5 %	0.513

Mi = Midbrain; mRS = modified Rankin Scale; MTL = mediotemporal lobe; P = Putamen; SUVRg = global normalized standardized uptake value ratio; Th = thalamus

eFigure 1. Longitudinal changes in disability after immunosuppressive treatment in patients with LGI1 autoimmune encephalitis. The level of disability is measured with modified Rankin Scale (mRS) at baseline (n=13), at short-term follow-up (n=8) and at long-term follow-up (n=13).
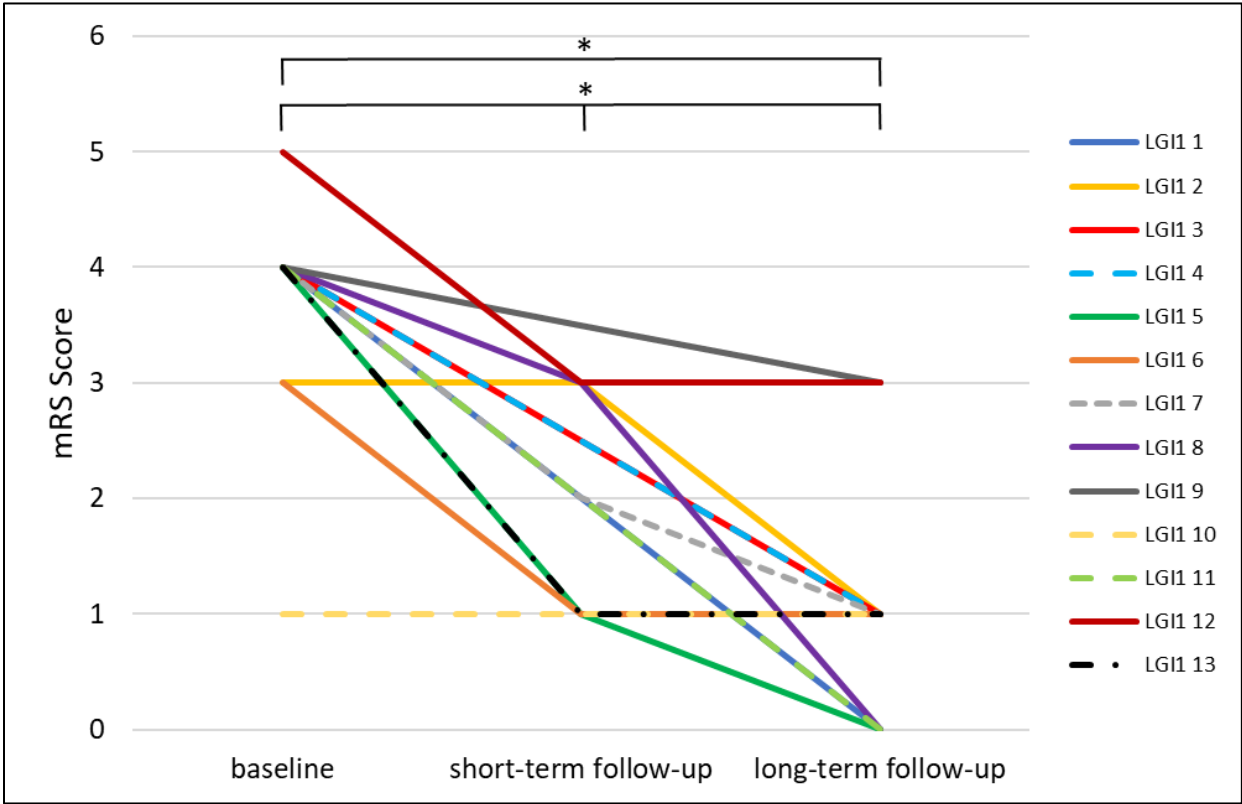
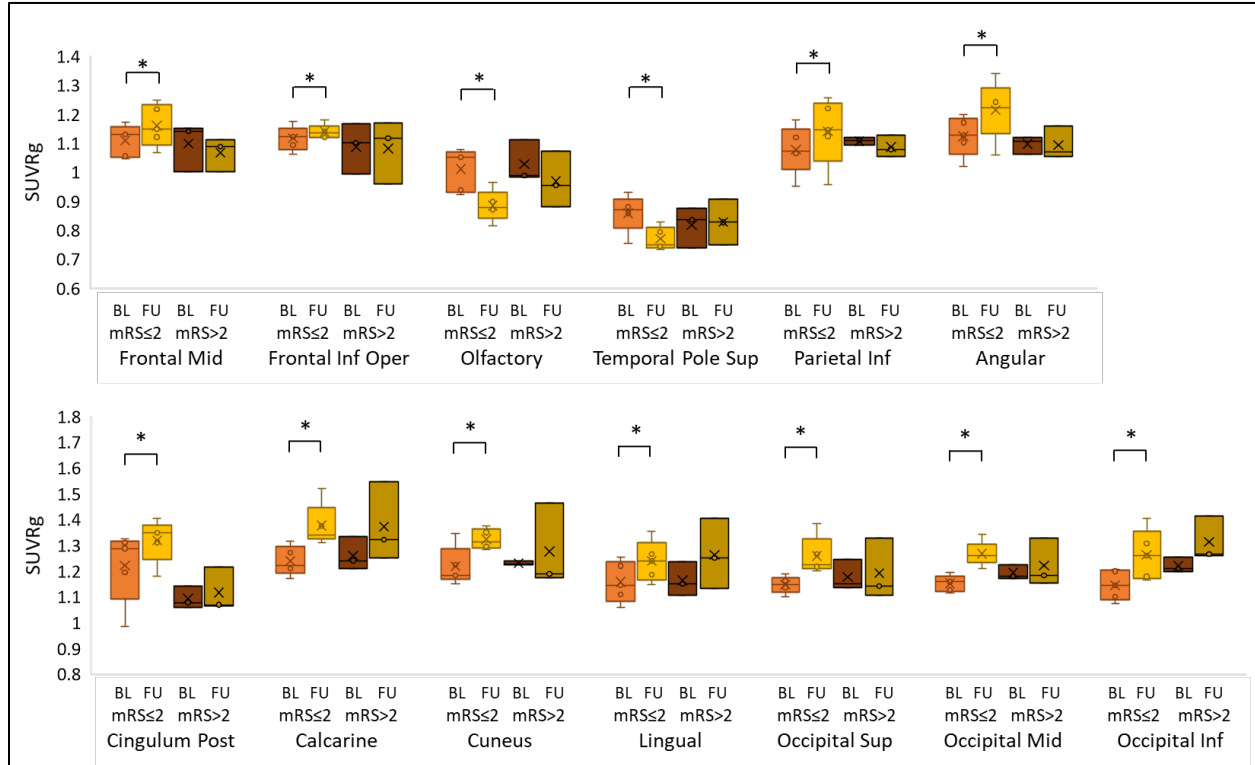* significant at the level of p<0.05

eFigure 2. Short-term changes in mediotemporal and putaminal metabolic activity associate with clinical short-term outcomes in LGI1-AE. The level of disability is stratified by the patients' short-term clinical outcome as good (mRS≤2, n=5) or poor (mRS>2, n=3) at the time of the short-term follow-up PET.
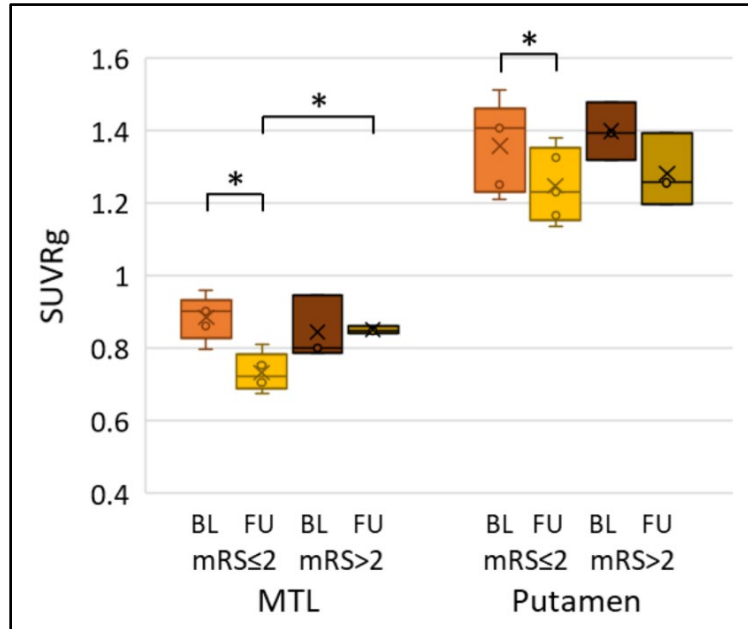
BL = baseline; FU = follow-up, mRS = modified Rankin Scale; MTL= mediotemporal lobe; SUVRg = global normalized standardized uptake value ratio

* significant at the level of p<0.05

eFigure 3. Associations between short-term changes in cortical metabolic activity and clinical short-term outcome in LGI1-AE. The level of disability is stratified by the patients' short-term clinical outcome as good (mRS≤2, n=5) or poor (mRS>2, n=3) at the time of the short-term follow-up PET.

Frontal Inf Oper = opercular part of inferior frontal gyrus; Inf = Inferior; Mid = middle; mRS = modified Rankin Scale; Post = posterior; Sup = Superior; SUVRg = global brain normalized standardized uptake value ratio

* p<0.05 (significant at the level of p<0.05)