

# ML of Striatum rs-fMRI Features Predicts TLE Diagnosis

**Yanchun Jiang**

Department of Neurology, the First Affiliated Hospital of Guangxi Medical University, Nanning

**Liluo Nie**

Department of neurology, Hengyang Central Hospital, Hengyang

**yanbo zhang**

Department of neurology, Nanxishan hospital of Guangxi Zhuang Autonomous Region, Guilin

**huihua Liu**

Department of neurology, Nanxishan hospital of Guangxi Zhuang Autonomous Region, Guilin

**jinou Zheng** (✉ [jinouzheng@163.com](mailto:jinouzheng@163.com))

Department of Neurology, the First Affiliated Hospital of Guangxi Medical University, Nanning

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## Research Article

**Keywords:** Resting State Functional Magnetic Resonance Imaging, ML, temporal lobe epilepsy, the striatum FC

**Posted Date:** June 30th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-638717/v1>

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# Abstract

**Objective:** To determine whether patients with temporal lobe epilepsy (TLE) exhibit aberrant resting-state functional magnetic resonance imaging (rs-fMRI)-functional connectivity and build an individualized TLE prediction model using ML (ML).

**Methods:** Sixty TLE patients and fifty-one controls underwent rs-fMRI scanning. The striatum was divided into 12 striatal seeds. rs-FC was compared between groups to enable TLE classification based on striatal FC using the SPM12, SVM and PRONTO softwares. Bilateral striatal FC values were extracted and significance values were obtained using leave-one-out (LOO) SVM analysis and permutation testing (2,000) for cross-validation.

**Results:** Patients with TLE exhibited a significantly decreased rs-FC between the left inferior ventral striatum and the right posterior central gyrus, left superior frontal gyrus; and between the left dorsal rostral putamen and right superior parietal lobule, right middle frontal gyrus. And between right dorsal caudate and left prefrontal lobe, and right middle temporal gyrus. rs-fMRI analysis revealed significantly increased FC between the left inferior ventral striatum seed and right anterior cingulate in TLE patients ( $p < 0.05$ ). Right dorsal caudate FC may distinguish individuals with TLE from controls with 79.08% Accuracy, including a 72.77% Sensitivity and 76.44% Specificity, resulting in an AUC of 0.71 ( $p < 0.01$ ). The areas informing classification included left prefrontal lobe, right middle temporal gyrus, and left superior parietal lobule.

**Conclusion:** Our findings demonstrate aberrant FC in certain brain regions, such as the right dorsal caudate, may play an important role as potential biomarkers of TLE and highlight the utility of ML-based models for clinical decision making.

## Introduction

Temporal lobe epilepsy (TLE) is the most common focal epilepsy, and it is likely to become refractory to therapy in adults. Neuroimaging studies have found structural abnormalities in several cerebral brain regions, including the hippocampus, the amygdala, the posterior superior temporal gyrus, and medial and inferior frontal gyri in TLE patients<sup>[1]</sup>. The literature reports that the TLE pathology involves the basal ganglia, namely the striatum and globus pallidus<sup>[2-3]</sup>. Previous neuroimaging studies have identified striatal atrophy and metabolic abnormalities in patients with TLE<sup>[4]</sup>. During seizures in these patients, regions of hyperperfusion in the striatum-caudate region may be involved in the spread of the epileptic activity and the initiation of inhibitory mechanisms. These findings suggest a neuronal network involvement in TLE seizures, and may explain the differences in clinical symptoms of right and left TLE seizures<sup>[5]</sup>. The centrality of the cortex, basal ganglia, and thalamus showed enhanced effects in the striatum, and these brain regions may represent potential critical regional network properties in TLE<sup>[6]</sup>. A recent study indicated that neuronal degeneration and damage caused by epileptic seizures mainly occur in striatum, and provide anatomical evidence to support their role in epilepsy<sup>[7]</sup>.

The striatum is one of the key components of the basal ganglia. Anatomy and interference studies have revealed functional heterogeneity in the striatum. In the current study, The subdivision of the striatum is associated with different cortical and subcortical structures forming channels that carry information related to marginal, associative, reward-guided and habitual behaviors, as well as cognition, amongst other functions<sup>[8-9]</sup>. The ventral rostral putamen and dorsal caudate receive projections from the dorsal prefrontal lobe, which is more closely related to executive functions<sup>[10]</sup>. Previous studies have found differences in the FC between different striatal divisions and multiple brain regions, such as the connection between the ventral striatum and the posterior cingulate gyrus, and between the dorsal putamen and occipitotemporal cortex. The striatum plays important role in the cortex-striatal ring. Recent studies show that the striatum is engaged in spread of epileptic seizures and the Gray matter(GM)of the striatum is negatively correlated with the age of onset at seizures<sup>[11]</sup>.

Resting-state Functional Magnetic Resonance Imaging (rs-fMRI) refers to a relaxed patient state with closed eyes, whereby the subject is instructed to avoid any structured thinking activity. rs-fMRI has gained widespread application in neuroimaging clinical research and may be used assess functional changes in the brain of patients with TLE<sup>[13]</sup>. Aberrant FC has been observed in the TLE and appears to span a wide range of neural networks. In the past few decades, many rs-fMRI studies investigating TLE have provided evidence for changes in functional connectivity (FC) in patients with TLE<sup>[14]</sup>. Current research shows that the FC between the seizure-associated network and ipsilateral temporal lobe structures decrease in TLE, while the FC between the seizure network and contralateral temporal lobe structures increases<sup>[15]</sup>. Disruption of the cerebellar-cerebral cerebellar functional network ipsilateral to the epileptic lesion side can cause two types of damage<sup>[16]</sup>. Compared with controls, TLE patients appear to have a disrupted FC between the right hippocampus and prefrontal cortex (PFC)<sup>[17]</sup>. However, no previous studies have investigated differences the effect of alterations in striatal FC to the pathology of TLE.

In recent years, machine learning (ML) have become a powerful and popular data analysis tool, and they are now increasingly applied to the study of functional magnetic resonance imaging data. Unlike traditional unit analysis methods, ML algorithms are a multi-modal analysis method which can fully explore the multi-element nature of functional magnetic resonance data and may thus be used for early diagnosis of brain diseases<sup>[18]</sup>. A previous study used the voxels of the brain area of the region of interest as features to train a an epilepsy classifier based on the Support vector Machine (SVM) Classification algorithm. SVM could classify individuals with epilepsy with 97.5% accuracy (sensitivity = 100%, specificity = 94.4%). The ten highest-ranked networks were found in the frontal, perisylvian, cingulo-insular, posterior-quadrant, thalamic, cerebello-thalamic, and temporo-thalamic regions<sup>[19]</sup>. Results by Del Gaizo et al, who applied SVM models in TLE, corroborate that abnormalities in the microstructure of the hippocampus may be used to identify various phenotypes of TLE in the future<sup>[20]</sup>. Another SVM study has furthermore demonstrated that the amplitude of low-frequency fluctuations (ALFF) and the whole brain rs-FC can predict TLE patients with an accuracy of up to 90%, and including the increased connectivity at 9-46v on the right back of TLE patients helps improve accuracy. Thus, ML models may help to diagnose TLE<sup>[21]</sup>.

So far, there are relatively few studies using ML to study the association between patients with TLE and individual differences, although this method has been successfully used in patients with depression, anxiety, and post-traumatic stress disorder<sup>[22]</sup>. In this study, we used rs-fMRI to evaluate the FC from the seeds of the striatum to the whole brain in TLE patients as well as age- and gender-matched healthy controls. Based on ML algorithms, we then developed a classifier based on the striatal FC to distinguish TLE patients from healthy controls. Studying functional abnormalities of affected brain areas may be beneficial to our understanding of the pathophysiological mechanism of the disease, and may also contribute the development of new biological markers.

## Material And Methods

### 2.1 Participants

We included 60 temporal lobe epilepsy patients (male/female: 34/26; average age:  $23.24 \pm 3.44$  years) and 51 healthy controls (male/female: 31/20; average age:  $24.09 \pm 3.08$  years) in this study. The mean duration of epilepsy in TLE patients was  $8.09 \pm 1.11$  years. All subject had normal or corrected-to-normal vision and were right-handed. All subjects were from recruited at the clinic of Department of Neurology of the First Affiliated Hospital of Guangxi Medical University between September 2019 and March 2021.

#### *TLE diagnosis.*

TLE diagnosis was made in compliance with the diagnostic criteria of the International League Against Epilepsy<sup>[23]</sup>. TLE patients in this study met two or more of the following criteria: (1) clinical symptoms suggesting that the epileptogenic focus is located in the temporal lobe, (2) imaging showing the presence of temporal lobe lesions, hippocampal sclerosis or atrophy, (3) seizure or seizure period EEG epileptic lesions are located in the temporal lobe, (4)no identifiable structural MRI abnormality in the subject's brain.

All participants scored  $> 24$  on the MMSE and participants with mental illness or generalized progressive neurological diseases were excluded. The study was approved by the Hospital Medical Ethics Committee. All subjects were informed of the details of the study and agreed to participate.

### 2.2. Scan acquisition

MRI scans were acquired using the Netherlands Philips company Achieva3.0T superconducting MRI scanner. Mission Stimulation was conducted using the SAMRTEC SA-9800 Stimulation System from Shenzhen Virtue Medical Electronics Technology Co., Ltd. The MRI protocol was as follows (1) Structure scanning: Spin echo sequence (T1 weighted), TR = 60 ms, TE = 16 ms, layer thickness = 5 mm, pitch = 1 mm, FOV =  $220 * 220$  mm; (2) Functional Image Scanning: Gradient Echo-Echo Plane Imaging Sequence, TR = 2000 ms, TE = 30 ms, Layer Thickness = 5 mm, Spacing = 1 mm, FOV =  $220 * 220$  mm, flip angle  $90^\circ$  scanning.

### 2.3. Data preprocessing

Imaging data of rs-fMRI were preprocessed using the statistical parametric mapping package SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/software/spm12/>) software<sup>[24]</sup> in MATLAB2016b. We conducted spatial preprocessing of the obtained data (including alignment, smoothing, and standardization), and then performed model estimation (convolving the stimulation time and interval with hemodynamic function, and conducting correlation analysis with the whole brain pixel signals). First, DICOM data were converted to NIFTI images. Second, slice timing was corrected; third, images were realigned, coregistered and resliced, excluding subject data where head movement exceeded 2 mm or head rotation exceeded 2°; fourth, we conducted spatial smoothing at 5-mm full-width using a half maximum Gaussian kernel and removed non-brain tissue using the brain extraction tool. Fifth, coregistration was conducted for alignment of the resting functional image with the structural image. Then, the images were normalized in order to fit the shape of functional images and structural images to a canonical average template. Lastly, spatial smoothing with a 6-mm full-width at half maximum Gaussian kernel was carried out<sup>[25]</sup>.

## 2.4 Functional connectivity analysis

We defined twelve subregions of the bilateral striatum as seed regions of interest (ROIs) based on a previous report<sup>[26]</sup>, with each subregion consisting of a radius of 2 mm: the inferior ventral striatum (MNI coordinates:  $x = \pm 9, y = 9, z = -8$ ), upper ventral striatum ( $x = \pm 10, y = 15, z = 0$ ), dorsal caudate nucleus ( $x = \pm 13, y = 15, z = -9$ ), dorsal putamen tail ( $x = \pm 28, y = 1, z = 3$ ), dorsal putamen head ( $x = \pm 25, y = 8, z = 6$ ), and ventral putamen head ( $x = \pm 20, y = 12, z = -3$ ). The average time series for each ROI area was extracted, and the Pearson correlation between the ROI and the rs-FC map for the subject were calculated. In order to improve the normality of the functional connection between other voxels of the brain, we used Fisher r-to-z transformation to render the single correlation matrix into a z-score matrix. The BrainNet Viewer (<https://helab.bnu.edu.cn/brainnet-viewer/>) was used to visualize the results.

## 2.5 ML-ProNTo toolkit for statistical analysis

SVM was applied using the Pattern Recognition for Neuroimaging Toolbox (PRoNTo) (<http://www.mlnl.cs.ucl.ac.uk/pronto>) in order to identify WM areas contributing most to TLE. The process was as follows: (1) Data was loaded and groups were divided into the TLE and control group. Age was added as a covariate in “modalities” in order to remove the influence of age on various indicators of brain function. (2) Next, the voxel-based feature set was prepared. (3) Then, a model was selected and calculated using “specify model and run model>: select classification modeling type modeling (classification)”. We opted for cross-validation using the leave one method. (4) The weights were computed and the PRT graph was generated using the AAL

template. (5) The results were displayed by importing the PRT graph generated in the previous step, obtaining the ROC curve graph, the total accuracy value and the confusion matrix graph, and the sensitivity and specificity were calculated. (6) The weights were presented using the function “displayweights”: the final PRT map was imported and weights per region were selected, arranged in the order of weight, and the top ten brain regions were selected. In the process of the result visualization, the temporary weight value of a single brain area was also calculated. Due to the limited sample size, we

used the leave-one-out-cross-validation (LOOCV) to evaluate the generalization rate of the support vector machine (SVM) classifier. The LOOCV results are expressed in sensitivity (SS) and specificity (SC), which were used to evaluate the performance of the classifier. SS represents the proportion of patients who are correctly classified, while SC represents the proportion of normal subjects who are correctly classified. We also used permutation testing and the ROC curve to evaluate the reliability of the classifier.

## 2.6 Statistical processing

Statistical analysis was performed on the data using SPSS 23.0 statistical software. The demographic data of the two study groups compared using independent sample t-tests, and gender comparison was carried out by  $\chi^2$ -test. The statistical module in the DPABI software was used for statistical analysis of the functional connectivity brain map. two-sample t-tests were used to analyze head movement parameters, age, gender, and education level as covariates, when the differences in the functional connectivity of striatal subregions between the two groups were compared. After 2000 permutation tests based on voxel levels and threshold-free cluster enhancement (TFCE) and multiple comparison correction, the brain area with  $P < 0.05$  (6 seed points on one side) after correction, that is,  $P < 0.01$ , was defined as the area with statistically significant differences. The FC values of brain areas with statistically significant differences between groups were further extracted.

## Results

### 3.1 Differences between controls and TLE patients in the rs-FC of subregions of the striatum

We found a significantly decreased rs-FC between the left inferior ventral striatum and the right posterior central gyrus, left superior frontal gyrus; and between the left dorsal rostral putamen and right superior parietal lobule, right middle frontal gyrus. And between right dorsal caudate and left prefrontal lobe, and right middle temporal gyrus. Conversely, rs-fMRI analysis revealed a significantly increased rs-FC between the left inferior ventral striatum seed and the right anterior cingulate in patients compared to controls ( $P < 0.05$ ).

There was no statistically significant difference in the FC of the bilateral superior ventral striatum seed, the right inferior ventral striatum seed, the right dorsal rostral putamen seed, the bilateral dorsal caudal putamen seed, the left dorsal caudate seed, and bilateral ventral rostral putamen seed between the TLE patients and healthy controls. Detailed information is shown in Figure 2 and Table 1. Figure 1 shows the template of the 6 striatal seed points in the left cerebral hemisphere.

### 3.2 ML discrimination of TLE patients and controls based on the right dorsal caudate FC

Eight brain areas regions were significantly different between TLE patients and controls and were selected as features, including the right middle temporal gyrus, the left superior parietal lobule, the right

precentral gyrus, the left prefrontal lobe, the left anterior cingulate, the right posterior cingulate, the left posterior cerebellum lobe, and the left inferior occipital gyrus.

The weight values corresponding to each of the abovementioned brain areas is shown in Table 2, and the weight diagram and ROC diagram are shown in Table 3 and Figure 3, respectively.

## Discussion

In the present study, compared with TLE patients, We found a significantly decreased rs-FC between partial subregions of the striatum and the right posterior central gyrus, left superior frontal gyrus, right superior parietal lobule, right middle frontal gyrus, left prefrontal lobe, and right middle temporal gyrus. Conversely, rs-fMRI analysis showed that TLE patients exhibited a significantly increased rs-FC between the left inferior ventral striatum seed and the right anterior cingulate gyrus. These results suggest that the striatal-cortical connection may be impaired in patients with TLE and confirm a decreased connectivity of the fronto-striatal connectivity which has been reported in previous studies in TLE<sup>[27]</sup>. The hyperconnectivity of the frontal striatum, parietal striatum, and temporal striatum projections may partly reflect the confusion of the circuits responsible for regulating cognitive control and motor functions.

The dorsal putamen is predominately projected to the sensorimotor cortex and is thought to play an important role in movement. Meanwhile, the dorsal rostral putamen plays an important role in the associative and motor aspects of decision-making and the ventral putamen–dorsolateral prefrontal circuitry is involved in executive function. Symptoms of epilepsy, including as cognitive impairment, decreased concentration, and dyskinesia, may be caused by an interruption of these projections which are related to defects in reward processing and emotional regulation. Our results did not reveal a difference in the FC of the bilateral superior ventral striatum seed, the right inferior ventral striatum seed, the right dorsal rostral putamen seed, the bilateral dorsal caudal putamen seed, the left dorsal caudate seed, and the bilateral ventral rostral putamen seed. There have been no previous reports on differences in the FC of the dorsal caudate putamen, which suggests that the primary motor network may not be directly involved in pathophysiology in TLE. Conversely, the increased left inferior ventral striatum seed and the right anterior cingulate FC may represent a compensation mechanism to prevent or delay cognitive impairment in TLE. Overall, the differences in the striatal-cortex circuitry between TLE patients and controls may expand our understanding of the interaction between epileptic activity, functional striatal-cortical structures, and neurocognitive processes in TLE.

Impairment of the temporal lobe occurs in several neurological disorders, such as TLE, memory impairment, hearing and balance disorders, and speech disorders. The functions of the middle temporal gyrus are complex and diverse. It is predominantly involved in general intersensory conflict, but may also be strongly associated with cognitive processing, acquisition of non-abstract semantic features, and synthesis of different semantic representations or connections<sup>[28]</sup>. In this study, we found that TLE patients exhibited a decreased rs-FC between the right dorsal caudate seed and middle temporal gyrus which implies that cognitive processing and language function may be impaired as a result of damage to

the striatal-middle temporal gyrus FC. A previous rs-fMRI study showed that patients with TLE exhibit abnormal local activity in the middle temporal gyrus<sup>[29]</sup> and previous studies using rs-fMRI have shown that the middle temporal gyrus is a language processing network. Local activity abnormalities in this region may therefore lead to cognitive processing abnormalities, including the the language system of patients with TLE. In addition, rs-fMRI studies have shown that middle temporal gyrus activity abnormalities may also cause cognitive processing abnormalities, such as observed in the language system in TLE patients<sup>[30]</sup>.

The posterior central gyrus plays an important role for the main sensorimotor cortex. In the present study, we found that the FC of the right dorsal putamen seed and the bilateral posterior central gyrus was lower in TLE patients than in controls which suggested that these patients may have an impaired putamen-posterior central gyrus connection. rs-fMRI studies have shown that patients with TLE exhibit a reduced spontaneous activity in the posterior central gyrus<sup>[31]</sup> alongside hypometabolism<sup>[32]</sup>, and reduced blood perfusion<sup>[33]</sup>. Moreover, studies have proposed that abnormal activity of the posterior central gyrus may affect the sensory processing of the sensorimotor network, leading to sensory disturbances in patients with TLE<sup>[34]</sup>. In this study, we show that the FC of the local functional connections in patients with TLE is increased in certain regions, such as the midbrain and cerebellum. These findings indicate that seizures with impaired consciousness in TLE are related to functional connection abnormalities between the subcutaneous arousal system, the cortical network, and the interruption of the information processing. Pathway abnormalities involved in TLE may provide insights into the mechanisms of loss of consciousness associated with seizures. The striatum is a key node in the cortical pathway composed of the cortex, basal ganglia and thalamus<sup>[35]</sup>. We found that the FC of striatum-middle temporal gyrus and the posterior central gyrus to the prefrontal lobe is involved visual spatial images, contextual memory retrieval, self- processing, and transfer of consciousness and attention in patients with TLE. Earlier studies have shown that this default network area includes the medial frontal lobe/anterior cingulate gyrus, inferior temporal lobe, posterior cingulate gyrus/precuneus and posterior parietal lobe; later studies found that the medial temporal lobe area is also related to this network. Consistent with previous evidence, patients with TLE may have default network damage<sup>[36]</sup>.

The current study uses ML to determine whether the bilateral striatum-FC distinguishes patients with TLE from controls. The results show that the striatum FC, in the area of the right caudate and the prefrontal lobe, insula, superior temporal gyrus, amongst others, plays the most important role for discrimination of patients from controls. We attempted an extensive search for suitable training features covering all possible measures using resting fMRI images. Our results suggested that functional brain alterations in TLE patients may indeed be detectable using ML. ML models can utilize resting fMRI information to separate TLE patients from age- and gender-matched healthy controls with 79.08% accuracy. Notably, features separating TLE patients and healthy controls were located throughout the entire brain, not just within the temporal lobe, which is consistent with previous findings<sup>[37]</sup>. Several articles have described the development of reliable ML models to make accurate decisions from complex clinical data sets. For example, there are previous reports on using ML for classification models to distinguish between patients

with TLE and HCs which aimed to determine which resting state measurements and frequency range combinations produce the best classification model. Finding better ML models will not only help TLE diagnosis, but also these abnormal networks connection may be reflect epileptogenesis in TLE [38–39].

Our results suggest that the heterogeneous response of the spatial distribution in the striatum (right dorsal caudate) FC is relevant for the differentiation TLE patients from controls, and further supports the hypothesis that the pathogenesis of TLE involves individual differences. In the striatal (right dorsal caudate) FC, the identification rate accuracy between the TLE group and controls was 79.08% with a diagnostic efficacy (AUC) of 0.71 and a specificity of 76.44%. We performed permutation tests and ROC curves on this classification, and our results showed that the performance of the classifier was appropriate. The model used the FC of the right dorsal caudate as a biological marker for patients with TLE. These results further demonstrate that temporal lobe epilepsy is a disease related to abnormalities in the whole brain. Although our classification accuracy is moderate, they have potential significance for future clinical applications. With our current study, we found evidence that whole-brain right dorsal caudate FC distinguished individuals with TLE from controls.

## Conclusion

This study uses ML methods and rs-fMRI to study changes in the FC of the striatum in TLE. We found that, based on whole brain FC, ML methods can distinguish temporal lobe epilepsy patients from controls with a classification recognition rate of 79.08%. Abnormal striatal functional network function may be related to a variety of cognitive dysfunctions in patients, and this FC dysfunction may be used as a potential biological marker for clinical diagnosis and treatment of TLE. For the first time, this study is characterized striatum rs-fMRI data using ML methods to distinguish patients with TLE from healthy controls, and obtained an appropriate accuracy rate. Our results suggest that the FC of the striatum can be used for the individualized diagnosis of TLE.

## Declarations

### **Ethics approval and consent to participate**

This research was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Informed consent

Informed consent was obtained from all individual participants included in the study.

### **Consent for publication**

Written informed consent for publication was obtained from all participants.

### **Availability of data and material**

All data generated or used during the study appear in the submitted article.

## Competing interests

The authors declare they have no competing interests.

## Funding

This work was supported by a grant from the Natural Science Foundation of China (No. 81560223) and Natural Science Foundation of Guangxi Province (2018GXNSFAA050149).and ZJO professor designed the study.

## Authors' contributions

Yanchun Jiang conceived and Jinou Zheng designed the study. Liluo Nie,Yanbo Zhang,HuihuaLiu performed the research. Yanchun Jiang and HuihuaLiu contributed to data analysis. Yanchun Jiang and HuihuaLiu supervised the data analysis. Yanchun Jiang wrote the original article. All authors reviewed,edited the manuscript gave final approval of publication.

## Acknowledgements

The authors are grateful to all study participants. The authors also are grateful for access to the MATLAB and SPSS software.The authors would like to express their gratitude to mjeditor (<https://www.mjeditor.com/index/pay/index.html>) for the expert linguistic services provided.

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## Tables

Table 1 Statistical analysis results for the striatal regions of interest

Brain region	cluster size voxels	MIN coordinates			t	p value
		x	y	z		
<b>Left inferior ventral striatum</b>						
Right posterior central gyrus	349	31	49	1	-2.53	p<0.001
Left superior frontal gyrus	261	-23	44	1	-1.79	p<0.001
<b>Left dorsal rostral putamen</b>						
Right superior parietal lobule	394	17	-30	56	-3.12	p<0.001
Right middle frontal gyrus	186	44	40	3	-3.48	p<0.001
<b>Right dorsal caudate</b>						
Left prefrontal lobe	425	-21	60	4	-2.71	p<0.001
Right middle temporal gyrus	331	43	42	0	-3.24	p<0.001
Right anterior cingulate	247	27	15	-6	2.65	p<0.001

Note: FC: functional connectivity; Min: Montreal Neurological Institute;

Table 2 SVM Classification performance.

	Accuracy (%)	Sensitivity (%)	Specificity (%)	AUC	Permutation	P-value
Left inferior ventral striatum	49.06	37.69	42.33	0.47	2000	0.001
Left dorsal rostral putamen	51.67	40.24	43.56	0.34	2000	0.001
Right dorsal caudate	79.08	72.77	76.44	0.71	2000	0.001

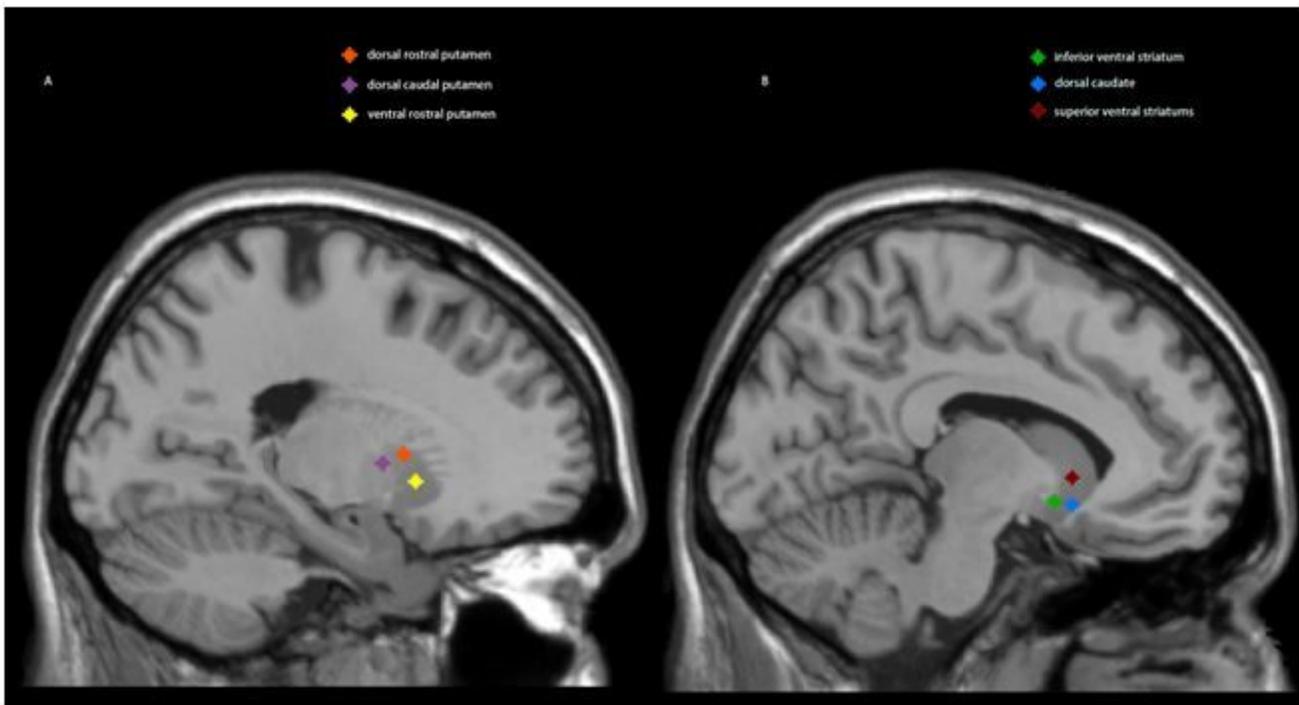
AUC, area under the ROC curve.

Table 3 Model weights per regions of interest

regions of interest	ROI Weight(%)	ROI Size(voxels)	MIN Coordinates		
			x	y	z
Right middle temporal gyrus	1.67	466	29	44	-8
Left superior parietal lobule	1.50	274	-29	-56	49
Right precentral gyrus	1.12	54	-32	-28	56
Left prefrontal lobe	1.35	328	-23	51	-12
Left anterior cingulate	1.45	152	-13	45	4
Right posterior cingulate	1.17	269	15	-38	26
Left posterior cingulate	1.36	195	-25	-38	-36
Left inferior occipital_Gyrus	1.40	107	-38	-74	-13

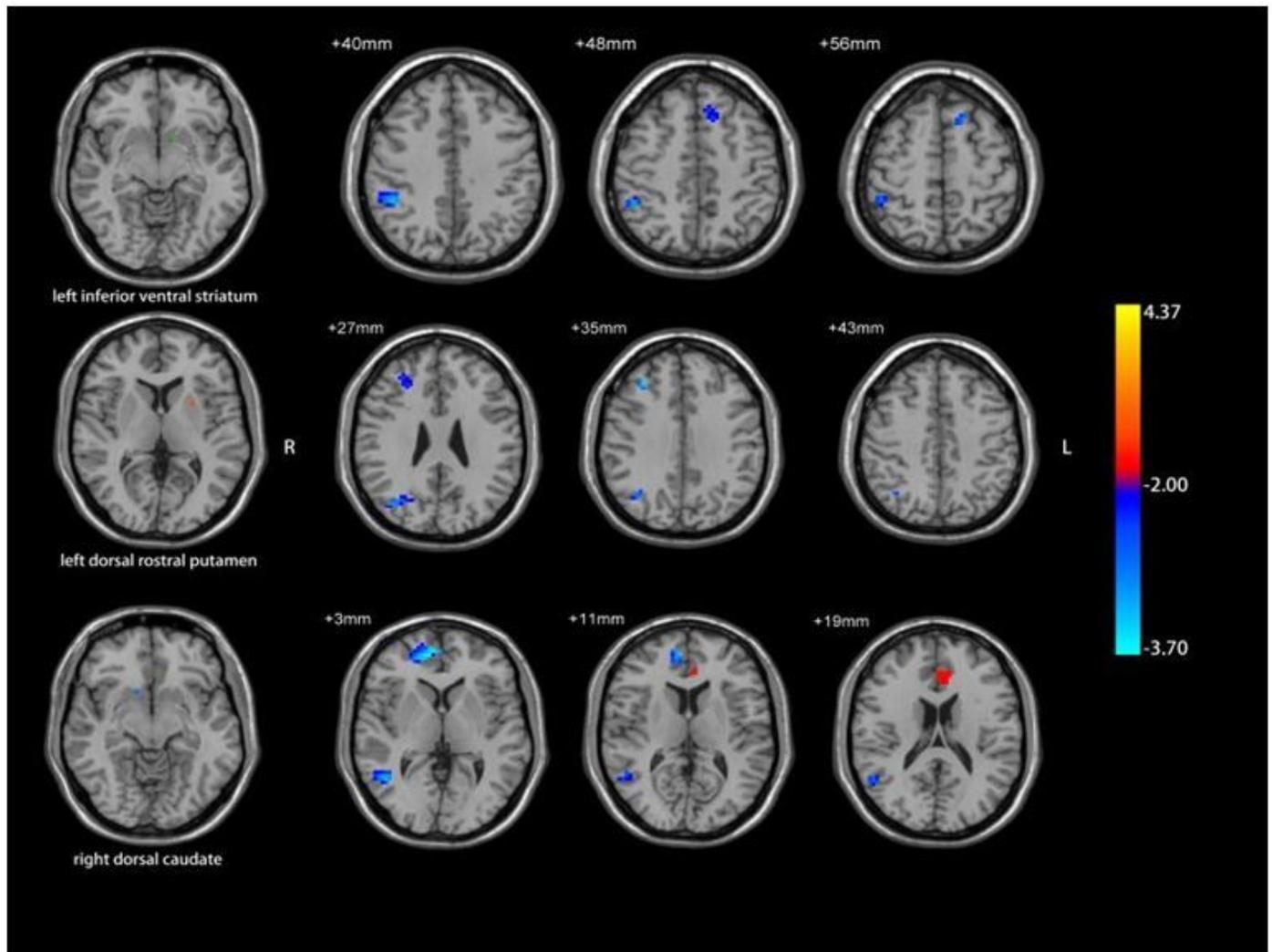
Note Reported regions represent the top 10% of regions based on weights. The weight was determined by the contribution of that region divided by the total contribution of all regions and is displayed as a percentage. Expected ranking reflects how stable the ranking of each region was across folds. MNI, Montreal Neurological Institute.

## Figures



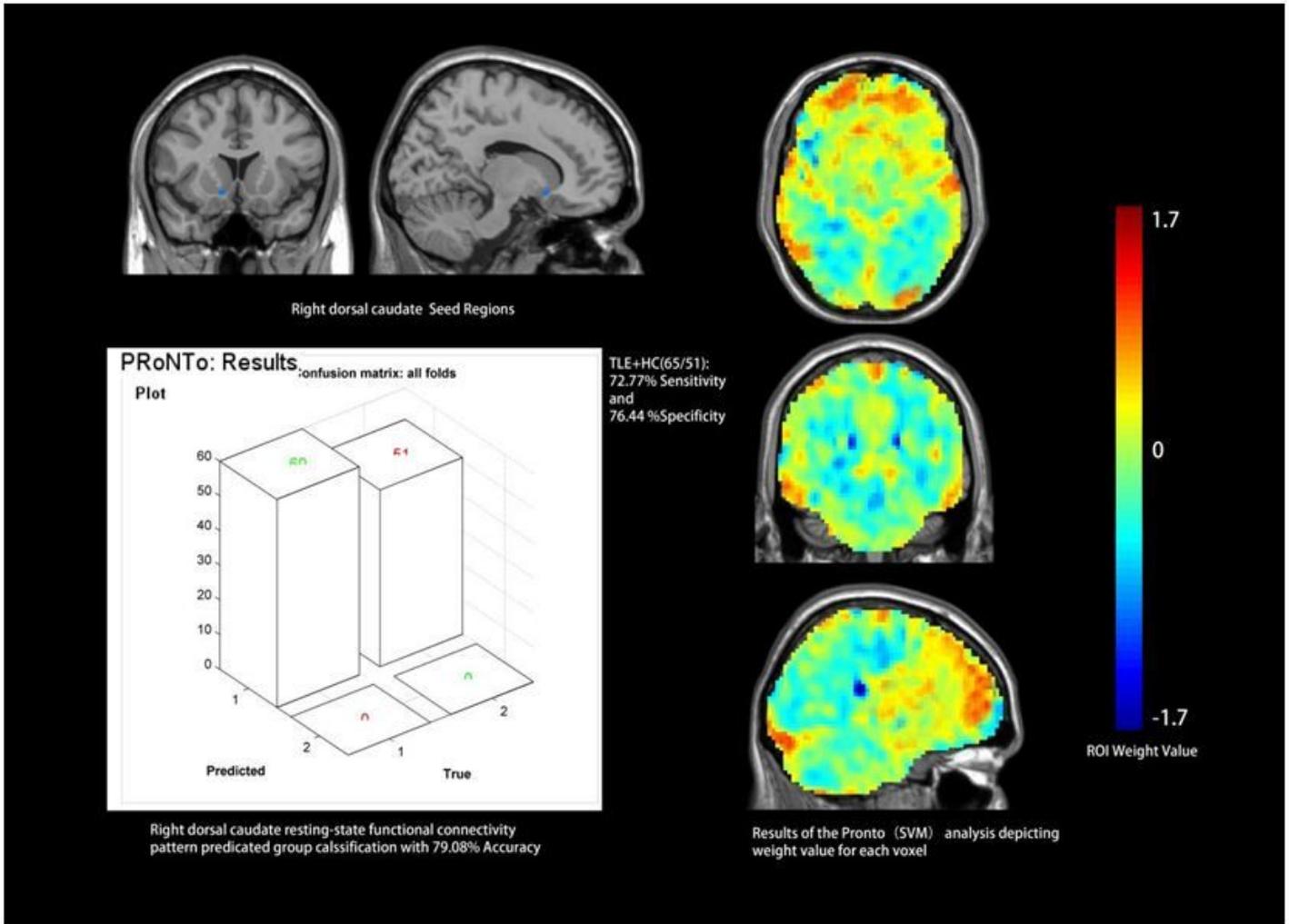
## Figure 1

The template of the 6 striatal seed points in the left cerebral hemisphere. X coordinate values provided by the Montreal Institute of Neurology.



## Figure 2

Brain regions with different functional connectivity between patients with TLE (n=60) and controls (n=51) L left, R right; (1) The left inferior ventral striatum seed-based FC maps in the TLE patients compared with healthy control subjects. (2) The left dorsal rostral putamen seed-based FC maps in the patients with TLE compared with healthy controls. (3) The right dorsal caudate seed-based FC maps in the patients with TLE compared with healthy controls. The values shown in the figure express the relative distance between the axial image and the coordinates of the Montreal Institute of Neurology (x=0, y=0, z=0).



**Figure 3**

The weight map derived from the ML tool PRoNTo, evaluating the difference between TLE patients and healthy controls.