Atlas of the Striatum and Globus Pallidus in the Tree Shrew: Comparison with Rat and Mouse

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Abstract The striatum and globus pallidus are principal nuclei of the basal ganglia. Nissl- and acetylcholinesterase-stained sections of the tree shrew brain showed the neuroanatomical features of the caudate nucleus (Cd), internal capsule (ic), putamen (Pu), accumbens, internal globus pallidus, and external globus pallidus. The ic separated the dorsal striatum into the Cd and Pu in the tree shrew, but not in rats and mice. In addition, computer-based 3D images allowed a better understanding of the position and orientation of these structures. These data provided a large-scale atlas of the striatum and globus pallidus in the coronal, sagittal, and horizontal planes, the first detailed distribution of parvalbumin-immunoreactive cells in the tree shrew, and the differences in morphological characteristics and density of parvalbumin-immunoreactive neurons between tree shrew and rat. Our findings support the tree shrew as a potential model for human striatal disorders.

Keywords Striatum · Globus pallidus · Basal ganglia · Reconstruction · Rodent · Parvalbumin

Introduction

The striatum and globus pallidus are principal nuclei of the basal ganglia, the striatum being the largest. In primates, the striatum is composed of the caudate nucleus (Cd), internal capsule (ic), putamen (Pu), and accumbens (Acb) [1, 2]. The globus pallidus contains the external globus pallidus (EGP) and the internal globus pallidus (IGP; known as the entopeduncular nucleus (EP) in rodents) [3]. The striatum receives afferents from most regions of the cerebral cortex, thalamus, hippocampus, and amygdala [4–8]. The striatum is the principal input nucleus of the basal ganglia and provides efferent projections to other basal ganglia nuclei (globus pallidus, subthalamic nucleus, and substantia nigra), the thalamus, and the bed nucleus of the stria terminalis [9–13]. The dorsal striatum (Pu, Cd, and ic) integrates these inputs for the control of motor and cognitive behaviors [14–16]. The ventral striatum (Acb) integrates various afferent projections and plays a specific role in reward-based decision-making and cocaine abuse [17–20].

Recently, the tree shrew, a close living relative of primates, has been used in studies of viral infections [21], stress-related disorders [22], pharmacological tests [23], and Parkinson's disease (PD) [24]. There are many antibodies (such as those for neuropeptide Y [25], NeuN [26], corticotropin-releasing factor [27], and tubulin [28]), pharmacological reagents (e.g., 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine [24], amyloid-beta peptide 1–40 [29], and morphine [30]), surgical methods (stereotaxic surgery [11], monocular deprivation [31], and intravenous drug self-

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administration [30]), disease models (of depression [22], breast cancer [32], fatty liver disease [33], acute stress [34, 35], glioblastoma [36], and hepatitis B virus infection [37]) and behavioral tests (open field test [38], conditioned place preference/aversion [30], sucrose preference [22], and visuo-spatial trials [39]) which have been used in biomedical research using tree shrews. The tree shrew has been successfully used to study the structure and function of the brain [40–42], PD [24], Alzheimer's disease [29], the visual system [43, 44], diffusion tensor imaging [45], and the limbic system [11, 46].

Previous studies have indicated that the morphological and anatomical characteristics of the striatum in the common tree shrew (*Tupaia glis belangeri*) resemble those in primates [47, 48]. The immunomarkers calcium-binding protein parvalbumin and acetylcholinesterase (AChE) have been used to define homologous nuclei among species [49–51]. The distribution of parvalbumin and AChE has been used to study the morphological characteristics of the caudate and putamen in tree shrews [25, 47]. A previous report indicated that the dorsal striatum in the tree shrew has many similarities to other mammals in the distribution of these markers [47]. The spiny output cells of the dorsal striatum receive afferents from the pulvinar nucleus in the tree shrew [6].

However, an anatomically comprehensive atlas of the striatum and globus pallidus in the tree shrew (*Tupaia belangeri chinensis*) has not been entirely explored. In the present study, we aimed to compare the anatomical features of the striatum and globus pallidus in the tree shrew with those in the rat and mouse. In addition, we provide detailed mapping and three-dimensional (3D) imaging of the striatum and globus pallidus in the tree shrew. Finally, we provide a comprehensive description of parvalbumin-immunoreactive (-ir) cells in these regions of the tree shrew and rat.

Materials and Methods

Animals

All adult male tree shrews (*Tupaia belangeri chinensis*), Sprague-Dawley rats, and C57/BL6J mice were housed in rooms under a 12-h dark/light cycle (lights off at 20:00). All animal procedures were performed in accordance with the Guide for the Care and Use of Laboratory Animals of the University of Science and Technology of China and were approved by the Animal Care and Use Committee at the University of Science and Technology of China.

Tissue Preparation

The tree shrews ($n = 4$, 10–19 months old), rats ($n = 4$, 6 months old), and mice ($n = 3$, 5 months old) were anesthetized with pentobarbital sodium (80 mg/kg, i.p.), then perfused with 0.9% saline and 4% paraformaldehyde (PFA). All brains were removed and segmented in the coronal plane according to brain atlases [52–55]. The forebrain was dehydrated in 30% sucrose and cut at 40 μm on a microtome (Leica CM1950, Wetzlar, Germany).

Nissl Staining

Three series of sections from tree shrews (24 sections at 320- μm intervals), rats (23 sections at 240- μm intervals), and mice (16 sections at 240- μm intervals) were rinsed in phosphate-buffered saline (PBS; 0.1 mol/L, pH 7.4), and then stained in 0.02% thionin acetate salt solution for 20 min [25]. The sections were dehydrated, coverslipped, and visualized under a light microscope (Olympus U-TV0.5XC-3, Tokyo, Japan).

Acetylcholinesterase Histochemistry

The sections were treated as previously described [25]. Briefly, another set of slides from tree shrews was incubated in 10 mL stock solution (50 mmol/L sodium acetate buffer, 4.0 mmol/L copper sulfate, 16 mmol/L glycine, pH 5.0, 11.6 mg acetylthiocholine iodide, and 0.3 mg ethopropazine hydrochloride) for 15 h. The slides were then rinsed and developed for 10 min in 1% sodium sulfide (pH 7.5). The sections were immersed for 8 h in 4% PFA, then dehydrated and coverslipped. The finished sections were visualized using the Olympus microscope (U-TV0.5XC-3).

Antibody Characterization and Immunohistochemistry

The specificity of the primary antibody, mouse monoclonal anti-parvalbumin (MAB1572, Millipore, Billerica, MA), was tested extensively in tree shrews [47] and rats [56]. Another two sets of adjacent sections were taken at the level of the striatum and globus pallidus of tree shrews (24 sections at 320- μm intervals) and rats (23 sections at 240- μm intervals). These sections were processed as previously described [57]. Briefly, floating sections were treated with 0.3% hydrogen peroxide and 0.5% Triton X-100 in PBS for 0.5 h. Then, following incubation with 5% normal horse serum (Solarbio, Beijing, China) in PBST (PBS containing 0.5% Triton X-100), the sections were incubated with mouse monoclonal anti-parvalbumin (MAB1572, Millipore; 1:2000) in 5% normal goat serum

Fig. 1 Coronal sections of the striatum and globus pallidus in the tree shrew, rat, and mouse. AChE-stained sections (A–C) and adjacent Nissl-stained sections (D–F) from rostral to caudal showing distinct subregions of the basal ganglia in the tree shrew. Coronal sections at similar levels show the organization of the basal ganglia in the rat (G–I) and mouse (J–L) in Nissl-stained sections. Dashed lines show the

borders of these structures. ac, anterior commissure; Acb, nucleus accumbens; cc, corpus callosum; Cd, caudate nucleus; CPu, caudate putamen (dorsal striatum); d, dorsal; EGP, external globus pallidus; ic, internal capsule; IGP, internal globus pallidus; l, lateral; LV, lateral ventricle; Pu, putamen. Scale bars, 1 mm.

Fig. 2 Schematic drawings showing the general morphology of the striatum and globus pallidus in the coronal plane from rostral to caudal in the tree shrew (A1-A58, referring to The Tree Shrew

(*Tupaia belangeri chinensis*) Brain in Stereotaxic Coordinates [52]). Colors represent distinct subregions of the basal ganglia. ICj, islands of Calleja. Scale bar, 1 cm.

for 24 h at 4°C. The sections were then incubated with biotinylated horse anti-mouse IgG (1:200; Vector Laboratories, Burlingame, CA) and avidin-biotin peroxidase complex (1:200; Vector Laboratories). The sections were stained with 0.05% 3,3'-diaminobenzidine (Sigma-Aldrich) as chromogen, dehydrated, and coverslipped.

Microphotographs were captured using an Imager.Z2 microscope with an automated acquisition system (TissueFAXS Plus, TissueGnostics GmbH, Vienna, Austria).

Some sections following parvalbumin immunoperoxidase labeling were stained with 0.02% thionin as described above. Then, sections were scanned using Imager.Z2 (Carl

Fig. 3 Rostral view of a 3D reconstruction of the striatum and globus pallidus based on serial histological sections of tree shrew brain (58 sections shown in Fig. 2).

Zeiss Microscopy GmbH, Jena, Germany) with an automated acquisition system (TissueFAXS Plus, TissueGnostics GmbH).

3D Reconstruction

Every third section (133.98 μm between sections) was photographed and drawn using Adobe software. The TIF-format images (12.68 μm per pixel) from camera lucida drawings were used to reconstruct 3D models. These images were aligned with The Tree Shrew Brain in Stereotaxic Coordinates [52]. Based on the manually-defined representative color of each structure, brain regions were calculated using Imaris 7.2.3. (Bitplane AG, Zurich, Switzerland) and the image properties were set. Then the reconstructed images and movie were generated and exported [58].

Digital Photomicrographs and Drawings

Neuroanatomical localization and designation of the striatum and globus pallidus were based on previously-published atlases for the tree shrew [52], rat [54], and mouse [53]. Light microscopic images were captured using a series scanning microscope (Olympus U-TV0.5XC-3) and an Imager.Z2 microscope (Carl Zeiss) with an automated acquisition system (TissueFAXS Plus, TissueGnostics GmbH). All digital microphotographs of sections were adjusted for cropping and brightness/contrast using Adobe Photoshop CS5 (Adobe Systems, San Jose, CA). All

drawings were depicted using Adobe Illustrator (Adobe Systems).

For quantitative analysis of the density of parvalbumin-ir cells, more than ten sections from each animal (4 tree shrews and 4 rats) were chosen for study. The density of positive cells was measured at 100 $\times$ total magnification. Automatic cell counting methods were used to analyze these sections based on previous studies [59]. In ImageJ, a random-offset grid (200 μm $\times$ 200 μm) was applied to each image. At least three grids were counted for each section. The density of parvalbumin-ir cells was determined from the number of positive cells per grid. The data for all grids in each animal were pooled.

Statistics

All data are presented as the mean $\pm$ SEM and no data were excluded. The unpaired *t*-test and Mann-Whitney U test were used to make statistical comparisons between the tree shrew and rat using SPSS 19 software (SPSS Inc., Chicago, IL). In all cases, a probability value of $P < 0.05$ was considered statistically significant. The histogram for the density of parvalbumin-ir cells was plotted using GraphPad Prism (GraphPad Software, San Diego, CA).

Results

In the coronal sections from tree shrews, the dorsal striatum was composed of the ic, Cd, and Pu (Fig. 1A–F). The ic was mainly white matter that separated the dorsal striatum into the Cd and Pu. In the rostral and middle parts of the dorsal striatum, the Cd and Pu were not completely segmented by the ic (Fig. 1A, B). The Cd was located along the lateral ventricle and the dorsal and medial borders of the ic. The Acb was a region of the ventral striatum (Fig. 1A, D), located in the rostral part of the striatum. The AChE-stained sections showed darkly-staining neurons and fibers in the Cd, Pu, and Acb but not in the ic (Fig. 1A–C). In addition to the striatum, the EGP and IGP were the principal structures of the basal ganglia (Fig. 1B, C, E, F). The EGP was medial to the Pu and adjacent to the IGP (Fig. 1C, F). These two structures were approximately round in coronal sections. The EGP contained a moderate density of AChE-stained neurons and fibers, whereas only numerous fibers were observed in the IGP (Fig. 1F).

In the rodents, coronal sections at similar levels were Nissl stained to show the organization of the basal ganglia of the rat (Fig. 1G–I) and mouse (Fig. 1J–L). The neuroanatomical characteristics of the striatum and globus pallidus were similar in rat and mouse. The striatum was inconspicuously subdivided by the ic (Fig. 1H, K), which

Fig. 4 Sagittal sections of the striatum and globus pallidus of the tree shrew, rat, and mouse. AChE-stained sections (A–C) and adjacent Nissl-stained sections (D–F) from lateral to medial show distinct subregions of the basal ganglia in the tree shrew. Sagittal sections at similar levels show the organization of the basal ganglia of the rat (G–I) and mouse (J–L) in Nissl-stained sections. Dashed lines show the

borders of these structures. ac, anterior commissure; Acb, accumbens nucleus; Cd, caudate nucleus; CPu, caudate putamen (dorsal striatum); d, dorsal; EGP, external globus pallidus; ic, internal capsule; ICj, islands of Calleja; LV, lateral ventricle; Pu, putamen; r, rostral. Scale bars, 1 mm.

Fig. 5 Schematic drawings showing the general morphology of the striatum and globus pallidus in the sagittal plane from lateral to medial in the tree shrew (A1–A31, referring to The Tree Shrew

(*Tupaia belangeri chinensis*) Brain in Stereotaxic Coordinates [52]). Colors represent distinct subregions of the basal ganglia. ICj, islands of Calleja. Scale bar, 2 cm.

was fused into most regions of the striatum. The shape of the EGP and EP was approximately elliptical and separated by the ic in the rat and mouse (Fig. 1I, L).

To display the striatum and globus pallidus of the tree shrew from rostral to caudal, a series of coronal sections was selected and referenced to the bregma (the reference zero point) (Fig. 2A1–A58). The ic, Cd, Pu, Acb, EGP, and IGP were clearly discernible in the coronal sections (Fig. 2). The outlines of the structures on the right side were derived from the left side of each section using mirror-image construction. In addition, deep brain structures were visualized by producing a translucent image of the 3D reconstruction using Imaris software (Fig. 3; Supplementary Material). The positional relationships among these brain regions were clearly represented in the 3D images.

In sagittal sections from the tree shrew, the dorsal striatum was separated into the Cd and Pu by the ic (Fig. 4A–F). The middle part of the Cd was larger than the outer and inner parts (Fig. 4D–F). In the rodents, sagittal sections at similar levels showed the anatomical

characteristics of the striatum and globus pallidus (Fig. 4G–L). The circular/oval-shaped ic was present in the outer part of the dorsal striatum in the rat and mouse (Fig. 4G, J). The strip-shaped ic was located in the inner part in the sagittal plane (Fig. 4E, H, K). The anterior commissure passed through the Acb in the sagittal sections (Fig. 4E, H, K). A series of sagittal sections was selected from lateral to medial in the tree shrew (Fig. 5). The outlines of the striatum and globus pallidus in the sagittal plane were depicted in the light of stained sections (Fig. 5).

In horizontal sections, the striatum and globus pallidus were delineated in the tree shrew and rat (Fig. 6). The dorsal striatum of the tree shrew was not adjacent to the Acb in horizontal sections through the ventral Acb (Fig. 6A, D). The dorsal striatum in the tree shrew formed a strip which was divided by the ic (Fig. 6B, C, E, F). However, the dorsal striatum and EGP in the rat formed an arch or bridge (Fig. 6G, H). The Acb was medial to the dorsal striatum and adjacent to the midline in the tree shrew and rat (Fig. 6E, H). The ic in the rat was seldom visible in the ventral part of the striatum in horizontal

Fig. 6 Horizontal sections of the striatum and globus pallidus in the tree shrew and rat. AChE-stained sections (A–C) and adjacent Nissl-stained sections (D–F) from ventral to dorsal show distinct subregions of the basal ganglia in the tree shrew. Horizontal sections at similar levels show the organization of the basal ganglia of the rat in Nissl-stained sections (G–I). Dashed lines show the borders of these

structures. ac, anterior commissure; Acb, accumbens nucleus; cc, corpus callosum; Cd, caudate nucleus; CPu, caudate putamen (dorsal striatum); D3V, dorsal 3rd ventricle; EGP, external globus pallidus; ic, internal capsule; ICj, islands of Calleja; IGP, internal globus pallidus; l, lateral; LV, lateral ventricle; Pu, putamen; R, rostral. Scale bars, 1 mm.

sections (Fig. 6G). The strip-shaped ic was found in the middle part of the striatum and oriented perpendicular to the pial surface (Fig. 6H). The circular- and oval-shaped ic was scattered in the dorsal part of the striatum (Fig. 6I). A series of horizontal sections was selected from ventral to dorsal in the tree shrew (Fig. 7). Based on AChE- and Nissl-stained sections, the morphology and location of the striatum and globus pallidus in the horizontal plane were determined in the tree shrew (Fig. 7).

Parvalbumin immunoreactivity was assessed in the striatum and globus pallidus of the tree shrew. Camera lucida drawings were made to present the distribution of

parvalbumin-ir cells throughout the striatum and globus pallidus from rostral to caudal (Fig. 8). The Acb contained a number of positive neurons and fibers (Fig. 9A). A moderate density of parvalbumin-ir cells and fibers was seen in the Cd and Pu (Fig. 9B, C). Immunoreactive neurons were absent from the ic (Fig. 9B). A high density of parvalbumin-ir neurons and fibers was found in the EGP and IGP of the tree shrew (Fig. 9D, E). However, a low density of parvalbumin-ir cells and fibers was scattered in the Acb and CPu of the rat (Fig. 9F, G). A high density of positive neurons and fibers was present in the rat EGP (Fig. 9H), while a moderate density was observed in the EP

Fig. 7 Schematic drawings showing the general morphology of the striatum and globus pallidus in the horizontal plane from ventral to dorsal in the tree shrew (A1–A28, referring to The Tree Shrew

(*Tupaia belangeri chinensis*) Brain in Stereotaxic Coordinates [52]). Colors represent distinct subregions of the basal ganglia. ICj, islands of Calleja. Scale bar, 2 cm.

(Fig. 9I). The EGP and IGP (EP) had the highest density of parvalbumin-ir cells in the striatum and globus pallidus of the tree shrew and rat (Fig. 10). The density of parvalbumin-ir cells in the Cd of the tree shrew was higher than that in the Pu (Fig. 10A). A higher density of parvalbumin-ir cells was located in the CPu, Acb, and IGP of the tree shrew than the rat (Fig. 10A, B).

Discussion

Our results present a detailed mapping of the striatum and globus pallidus in the Chinese tree shrew (*Tupaia belangeri chinensis*) in the coronal, sagittal, and horizontal planes. In addition, the morphological and anatomical features of the striatum and globus pallidus in all three planes in the tree

shrew are clearly compared with those in rodents. The neurochemical features of the dorsal striatum in the common tree shrew (*Tupaia glis belangeri*) have been examined in the coronal plane [47]. In this paper, Rice *et al.* [47] analyzed the neurochemical composition and distribution of the striosome and matrix compartments using immunohistochemistry, but positional information of the dorsal striatum sections was not provided. The neurochemical characteristics of the ventral striatum in the common tree shrew, rat, and monkey were examined in the coronal plane using immunohistochemistry and electron microscopic analysis in another paper by McCollum and Roberts [48]. Their results indicated that the ultrastructure in the tree shrew closely resembles the characteristics of the primate Acb [48]. Our present study has described the comparative anatomical organization of the

Fig. 8 Camera lucida drawings showing the distribution of parvalbumin-ir cells (dots) in the striatum and globus pallidus of the tree shrew from rostral to caudal (A–I). Representative coronal sections were selected, with reference to bregma. The density of dots represents the relative density of cells in the areas. Each dot

striatum and globus pallidus in the tree shrew, rat, and mouse. The dorsal striatum in the tree shrew contains the main anatomical feature of a well-developed ic that clearly separates the Cd and Pu, similar to previous reports in primates and humans [60, 61]. Actually, rats and mice present an under-developed ic in the striatum. The under-developed ic was scattered in most regions of the rostral and middle parts of the striatum in rat and mouse. The ic was absent in the dorsomedial part of the mid-striatum along the lateral ventricle in rat and mouse, resembling the well-developed Cd in the tree shrew. The morphological characteristics of the EGP and IGP in the tree shrew differed from those in rat and mouse. Although differences between the tree shrew and the rat have been reported in the organization within the Acb shell and the proportion of symmetrical and asymmetrical synapses formed by

represents approximately one parvalbumin-labeled neuron. ac, anterior commissure; Acb, accumbens nucleus; Cd, caudate nucleus; EGP, external globus pallidus; ic, internal capsule; IGP, internal globus pallidus; LV, lateral ventricle; Pu, putamen.

dopaminergic terminals [48], the morphological characteristics of the Acb were similar in these species in our study.

According to our data, the location of parvalbumin-ir neurons in the Acb, CPu, EGP, and IGP (EP) of the tree shrew is similar to that in rodents [62, 63]. However, the density of parvalbumin immunoreactivity in the globus pallidus and striatum differs between the tree shrew and rat. The density of parvalbumin neurons in the striatum of monkeys is higher than that in rats [64]. Similarly, a higher density of parvalbumin-ir neurons was present in the striatum of the tree shrew than in the rat. Previous work indicates that the density of parvalbumin-ir neurons in the striatum is related to behavioral performance in fear extinction and latent inhibition [65] and that the parvalbumin-expressing neurons in the basal ganglia play a role in regulating movement-related behaviors [66, 67]. Furthermore, the age of the animal affects the density of

Fig. 9 Photomicrographs of parvalbumin-ir staining in the nucleus accumbens (Acb; **A**), caudate nucleus (Cd; **B**), putamen (Pu; **C**), external globus pallidus (EGP; **D**), and internal globus pallidus (IGP;

E) in the tree shrew. Parvalbumin-ir neurons were also present in the Acb (**F**), caudate putamen (CPu; **G**), EGP (**H**), and entopeduncular nucleus (EP; **I**) of the rat. Scale bar, 100 μm.

parvalbumin-ir neurons [68], especially in the main olfactory bulb and septum [69, 70]. However, no significant age-related changes have been found in the number of parvalbumin-ir cells in the rodent striatum [70, 71]. A previous report has identified two classes of neurons in the rodent EP on the basis of their electrophysiological characteristics [72] and that it contains somatostatin-ir neurons and parvalbumin-ir neurons [73]. Wallace *et al.* [74] used large-scale single-cell transcriptional profiling and molecular analyses to reveal that the rodent EP contains at least three classes of projection neurons: glutamate/GABA co-releasing somatostatin neurons, glutamatergic parvalbumin neurons, and GABAergic parvalbumin neurons. These classes in the EP have functionally

and anatomically distinct outputs that differentially affect their targets, such as the epithalamus and thalamus [74].

It is possible that these differences in morphological and anatomical characteristics reflect species differences in their natural habitats. Wild tree shrews mainly live in an arboreal habitat [75], while rats and mice live mainly in burrow systems at ground level [76]. In addition, tree shrews in the laboratory prefer to jump, leap, and somersault in their cages [75]. Such a preference is not seen in rats and mice. The dorsal striatum receives numerous afferent projections from the motor cortex and somatosensory cortex [77, 78]. A recent report provides evidence that neuronal clusters in the dorsal striatum of mice encode locomotor information which is important for

Fig. 10 Quantitative analysis of the density of parvalbumin-ir cells in distinct subregions of the striatum and globus pallidus in the tree shrew (A) and rat (B) (* $P < 0.05$; ** $P < 0.01$ compared with rat; Mann–Whitney U test and unpaired t -test). Acb, accumbens nucleus;

Cd, caudate nucleus; CPu, caudate putamen; EGP, external globus pallidus; EP, entopeduncular nucleus; IGP, internal globus pallidus; Pu, putamen.

striatum-controlled behaviors [79]. The pulvinar in the tree shrew receives afferent inputs from the superior colliculus and projects to spiny output neurons in the Cd and Pu [6]. These subcortical circuits in diurnal tree shrews differ from those in rodents [80]. The rodents lack the apparent pulvinar nucleus observed in tree shrews [52–54].

Our data showed that the morphological and anatomical features of the striatum in the tree shrew are dissimilar to those in rodents. Rodent transgenic and neurotoxic models are widely used to study PD [81, 82], and although they have greatly improved our knowledge of its pathogenic and pathophysiological mechanisms [83], the rodent striatum differs significantly from that of primates, and this must be carefully taken into consideration when the findings in rodent models of PD are translated from laboratory species to human pathologies and clinical trials. The tree shrew has the potential for development as an animal model of PD because it is diurnal, small, easy to handle and feed, and has a short gestation period and duration of puberty [75]. Previous research indicates that tree shrews treated with the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine exhibit classic PD symptoms at a lower dose than in rodents [24].

There are several advantages of using the tree shrew as a model in which to study human diseases associated with the striatum. The tree shrew has a larger striatum than rodents [75], making it beneficial for magnetic resonance scanning and analysis. In addition, the tree shrew striatum displays clear-cut borders, providing a new animal model in which to study the subregional functions of the human striatum. The cytoarchitectonics of the striatum in tree shrews has similarities to that of primates [47]. These advantages may provide further insights into the human diseases associated with the striatum.

In summary, our results present a comprehensive comparison of the Cd, ic, Pu, Acb, EGP, and IGP (EP) in the tree shrew and rodents in the coronal, sagittal, and

horizontal planes. Moreover, our data provide detailed coronal, sagittal, and horizontal atlases of the striatum and globus pallidus in the Chinese tree shrew. The computer-based 3D images allow a better understanding of the position and orientation of the striatum and globus pallidus in relation to each other. In addition, the present findings provide the first detailed distribution of parvalbumin-ir cells in the tree shrew striatum and globus pallidus and demonstrate species differences in the density of positive neurons between tree shrew and rat. Our results support the tree shrew as a potential animal model for human striatal disorders which may help to further elucidate and understand pathogenic and pathophysiological mechanisms.

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Authors' Contributions RJN was involved in tissue processing, histochemical analysis, collection and interpretation of data, and writing the manuscript; ZHH and YMS were involved in tissue processing and data interpretation; YW was involved in 3D brain reconstruction; TL was responsible for revising the manuscript; and JNZ was responsible for experimental design and manuscript preparation.

Compliance with Ethical Standards

Conflict of interest All authors claim that there are no conflicts of interest.

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