



HAL
open science

The squirrel monkey model in clinical neuroscience

Julie Royo, Stephanie J Forkel, Pierre Pouget, Michel Thiebaut de Schotten

► **To cite this version:**

Julie Royo, Stephanie J Forkel, Pierre Pouget, Michel Thiebaut de Schotten. The squirrel monkey model in clinical neuroscience. *Neuroscience and Biobehavioral Reviews*, 2021, 10.1016/j.neubiorev.2021.06.006 . hal-03260008

HAL Id: hal-03260008

<https://hal.sorbonne-universite.fr/hal-03260008v1>

Submitted on 14 Jun 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Journal Pre-proof

The squirrel monkey model in clinical neuroscience

Julie Royo, Stephanie J. Forkel, Pierre Pouget, Michel Thiebaut de Schotten



PII: S0149-7634(21)00243-8

DOI: <https://doi.org/10.1016/j.neubiorev.2021.06.006>

Reference: NBR 4210

To appear in: *Neuroscience and Biobehavioral Reviews*

Received Date: 29 January 2021

Revised Date: 27 April 2021

Accepted Date: 1 June 2021

Please cite this article as: { doi: <https://doi.org/>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier.

The squirrel monkey model in clinical neuroscience

Julie Royo ^{1,2}, Stephanie J. Forkel ^{1,3,4}, Pierre Pouget ^{1,2*}, Michel Thiebaut de Schotten ^{1,3*}

¹ Brain Connectivity and Behaviour Laboratory, Sorbonne Universities, Paris, France

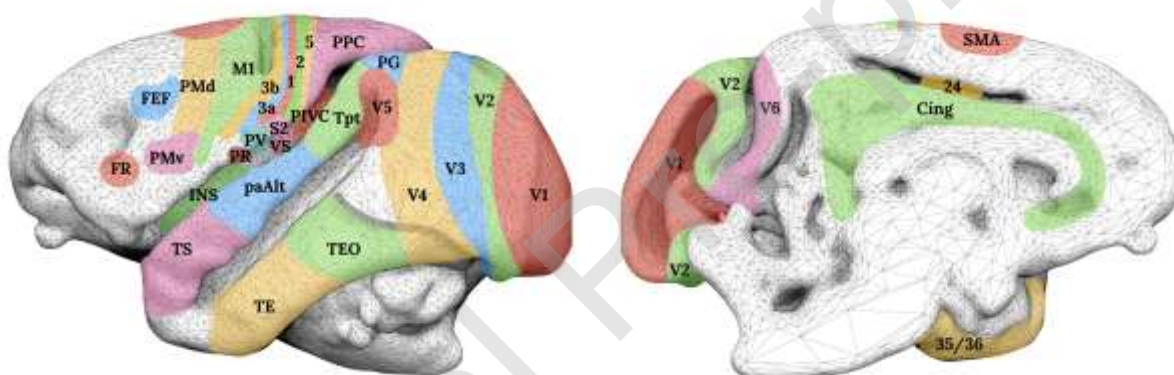
² Sorbonne University, Inserm U1127, CNRS UMR7225, UM75, ICM, Movement Investigation and Therapeutics Team, Paris, France.

³ Groupe d'Imagerie Neurofonctionnelle, Institut des Maladies Neurodégénératives-UMR 5293, CNRS, CEA University of Bordeaux, Bordeaux, France

⁴ Department of Neuroimaging, Institute of Psychiatry, Psychology and Neurosciences, King's College London, UK

*Contributed equally.

Graphical abstract



HIGHLIGHTS

- Squirrel monkey can be investigated in meaningful samples.
- Squirrel monkey cognition is far superior to marmoset monkeys.
- Squirrel monkey develops age-related cerebral impairments similar to humans.
- Squirrel monkey will fuel new translational discoveries for humans

Abstract

Clinical neuroscience research relying on animal models brought valuable translational insights into the function and pathologies of the human brain. The anatomical, physiological,

and behavioural similarities between humans and mammals have prompted researchers to study cerebral mechanisms at different levels to develop and test new treatments. The vast majority of biomedical research uses rodent models, which are easily manipulable and have a broadly resembling organisation to the human nervous system but cannot satisfactorily mimic some disorders. For these disorders, macaque monkeys have been used as they have a more comparable central nervous system. Still, this research has been hampered by limitations, including high costs and reduced samples. This review argues that a squirrel monkey model might bridge the gap by complementing translational research from rodents, macaque, and humans. With the advent of promising new methods such as ultrasound imaging, tool miniaturisation, and a shift towards open science, the squirrel monkey represents a window of opportunity that will potentially fuel new translational discoveries in the diagnosis and treatment of brain pathologies.

Keywords: Primates, Clinical Neuroscience, Translational, Animal Model, Neuroimaging.

Introduction

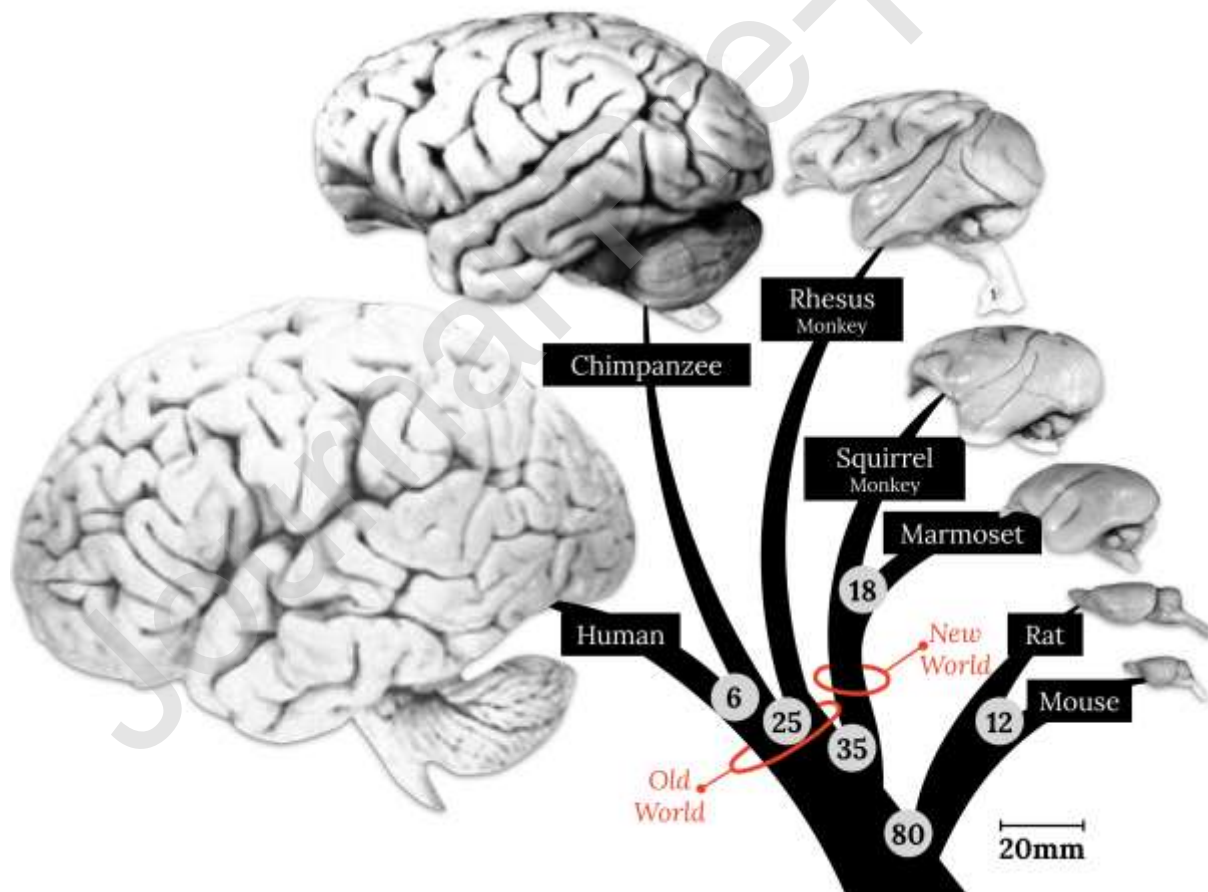


Figure 1: Evolutionary tree of the main species studied as a surrogate for the human brain. Numbers indicate the phylogenetic distance in millions of years between each species. (true to scale, modified from <http://neuroscielibrary.org>)

Non-human primates are the closest relatives to humans and share common cerebral characteristics in the organisation and functioning of the brain and cognition (Bernardi and Salzman, 2019; Friedrich et al., 2020; Hendrickx and Binkerd, 1990). The evolution of primates is characterised by an increase in the surface of the cerebral cortex and expansion and subdivision of the neocortex (Friedrich et al., 2020; Lewis and Van Essen, 2000). Likewise, there is an increase in functional fields related to the acquisition of higher cognitive functions, such as executive control, episodic memory, and communication (Kaas, 2012). The brain of non-human primates has a larger prefrontal cortex than rodents, and the patterns of neural activities in interconnected circuits are comparable to humans (Perretta, 2009). This phylogenetic, functional, and anatomical proximity to humans makes non-human primates a good model for testing the efficacy and the safety of treatments before entering clinical trials in humans (see the evolutionary tree in Figure 1). Among non-human primate models, Old World monkeys (e.g. baboons, macaques, vervet monkeys) and New World monkeys (e.g. capuchin monkeys, titi monkeys, marmosets) are frequently used in cognitive and clinical neuroscience studies.

In contrast, Great Apes (gorillas, orangutans, chimpanzees and bonobos) are rarely used for understandable ethical reasons and handling cost. Prosimians (grey mouse lemurs, galagos) are also seldom used because they are phylogenetically distant from humans (Phillips et al., 2014). Despite the valuable clinical application, research in non-human primates represents less than 1% of all animal models studied (Phillips et al., 2014). Several reasons may explain this discrepancy. The controversial use of non-human primates and their proximity to humans has led to strict ethical guidelines on their keeping and breeding conditions. Additionally, the high costs, constraints (e.g. lower number of animals and longer lifespan), and the high degree of expertise required for non-human primate (NHP) researchers are also drastically limiting the broader use of the model. Therefore, there is an urgent need for the neuroscientific community to adopt a model that will combine the small animals' advantages (e.g. low cost, fast-breeding) with non-human primates advantages (e.g. anatomical and behavioural similarities to humans).

The development and standardisation of procedures, methods (e.g. micro-surgery, ultrasound imaging), and tool miniaturisation (e.g. micro-electrodes, micro-manipulator) are offering novel

possibilities to study smaller non-human primate species such as marmosets or squirrel monkeys (i.e. *Saimiri sciureus*). The squirrel monkey is a non-human primate endemic of Central America and equatorial South America. They belong to the suborder Haplorhini and to the Cebidae family, which includes small, omnivorous primates. Their large tribes (between 20 and 75 animals) are distributed from primary forests to degraded forest remains (Defler, 2004). Compared to the marmoset, the squirrel monkey has a bigger brain with more pronounced gyration (such as the arcuate sulcus see Figure 1). Compared to macaques, squirrel monkeys have a shorter lifespan (~21 years in captivity compared to ~35 years for macaques)(Brady, 2000), a smaller body size (318 mm for males and 316 mm for females), mass (554 g - 1150 g for males and 651 g - 1250 g for females) (Bernarcky et al., 2002; Rowe, 1996) and are easily bred and raised in captivity. Their smaller size makes it possible to host larger colonies than macaques at lower maintenance costs. Their small brain size is another advantage for new methods such as ultrasound imaging and high field MRI imaging that will allow full brain coverage in high-resolution acquisition of anatomy and function (Blaize et al., 2020; Dizeux et al., 2019). Cognitively, they are considered superior to marmoset monkeys (see (Williams and Glasgow, 2000) for an extensive review of squirrel monkey behavioural research).

For instance, squirrel monkeys released in the wild appeared to dominate the marmoset population (e.g. marmoset spent less time foraging and more time in vigilance (alertness) than squirrel monkeys during interactions). The apparent competitive advantage of the squirrel monkey led to the recommendation of management measures to control their expansion (Camarotti et al., 2015). In laboratory conditions, a delayed-response task demonstrated a larger working memory span in squirrel monkeys conditions than marmosets (Tsujiimoto and Sawaguchi, 2002). These differences may be attributed to a higher ratio between the neocortex and the rest of the brain in squirrel monkeys ($15541 / 22572 \text{ mm}^3 = 69\%$) than in marmoset ($4371 / 7241 \text{ mm}^3 = 60\%$)(Sawaguchi, 1992). Additionally, the squirrel monkey develops age-related cerebral impairments similar to neurodegenerative disorders in ageing humans (Elfenbein et al., 2007; Emborg, 2007), rendering it a very apt model for neurological clinical translational studies. Despite its physiological and neurodegenerative similarities with humans that will make this species an ideal model for clinical neurosciences, the use of the squirrel monkey in research has been steadily decreasing over the past 20 years (see Figure 2). Therefore, the present review gathers the central neuroscientific literature in squirrel monkeys to summarise the exceptional contribution of this species to our current understanding of clinical neuroscience and promote its potential for future study.

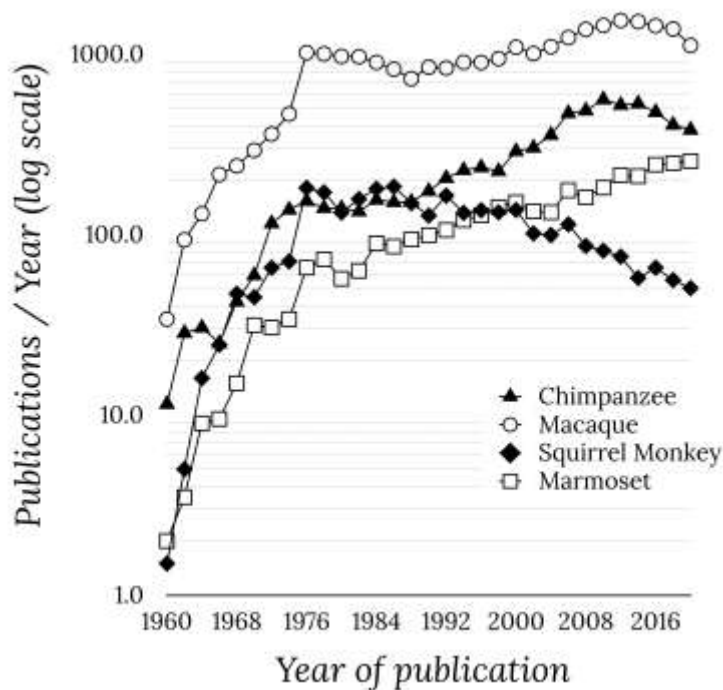


Figure 2: Number of PubMed peer-reviewed publications per primate species (date: 26.11.2020)

Cerebral anatomy

The brain of the squirrel monkey weighs approximately 22g (Hofman, 2014) which resembles a ratio with the body mass close to other primates (Fleagle and Seiffert, 2016; Friedrich et al., 2020; Roth and Dicke, 2012; van Dongen, 1998). The neuroanatomy of the squirrel monkey can be derived from several atlases (Akert, 1963; Gao et al., 2014; MacLean, 1962; Schilling et al., 2017, 2019a; Sun et al., 2015). MacLean and Akert atlases present brain structures delineated based on cyto- and myelo-architecture (Nissl and myelin stained sections); however, the lack of a digital version of these atlases limits the possibility to register and compare across individual monkeys (Akert, 1963; MacLean, 1962). In contrast, the atlases by Gao *et al.* (Gao et al., 2014) and Schilling *et al.* (VALiDATe29) (Schilling et al., 2017) used *in vivo* and *ex vivo* MRI acquisitions but in turn lack histological information. A recent atlas integrates histology with MRI data (CHIASM) (Schilling et al., 2019a) by including Nissl and myelin stains and anatomical and diffusion MRI contrasts from the same animal. We provide a comprehensive overview of the surface and the subcortical anatomy of the squirrel monkey in line with these references.

Surface

Similar to mammals and other primates, including humans, the brain of the squirrel monkey is covered by meninges which are composed of the dura mater, the arachnoid membrane, and the pia mater (Barcellos et al., 2011).

In primates, the amount of neocortical folding and sulci is proportional to the cerebral volume (Heuer et al., 2019). Accordingly, the squirrel monkey brain is not strictly lissencephalic, and it presents more sulci than the marmoset (as shown in Figure 1). Post mortem dissections and neuroimaging investigations in squirrel monkeys indicate the existence of a lateral fissure (Barcellos et al., 2011) that separates the temporo-occipital from the fronto-parietal cortices. A central sulcus separates the frontal from the parietal cortices and the primary motor cortex (M1) from the primary somatosensory cortex (area 3b). A superior precentral dimple (SPCd) separates the primary motor cortex from the premotor cortex (PMd and PMv). As in other non-human primates, the squirrel monkey's frontal eye field (FEF) is located in the front of the premotor cortex and limited anteriorly by the arcuate sulcus (As). Area 5 and the posterior parietal cortex (PPC) can only be dissociated from the somatosensory areas based on electrophysiological observations (Benjamin and Welker, 1957; Kaas et al., 2016) as the cytoarchitecture of the parietal cortex has not yet, to our knowledge, been parcellated in squirrel monkeys. Similar to macaques, the temporal lobe of the squirrel monkey can be divided into several regions, including the temporalis superior cortex (TS), lateral parakoniocortex (paAlt), temporo-parietal region (Tpt), temporo-occipital region (TEO), and temporal region (TE)(Weller et al., 2006). Areas 35 and 36 of the perirhinal cortex are located between the inferior temporal sulcus and the rhinal sulcus. Medially, the squirrel monkey's brain displays a wealth of familiar features similar to the human brain, such as a calcarine fissure typically indicating the location of primary visual areas. From there, the parieto-occipital medial sulcus separates the occipital lobe from the parietal and limbic lobes, respectively. A cingulate gyrus circles from the medial frontal to the medial temporal lobe around the corpus callosum. The medial frontal lobe is split into a dorsal and ventral portion by the rostral sulcus. An occipitotemporal sulcus separates the lateral portion of the temporal from the medial portion of the temporal lobe, where cytoarchitectural areas 35 and 36 will correspond to the perirhinal cortex in humans (see Figure 3).

Despite a small number of gyri and circumvolutions, the six-layered cortex ratio (i.e. the weight of the cerebral cortex relative to the total weight of the brain) of the squirrel monkey is 68.4%. This value is higher than in rodents (mouse: 43.0%; rat: 44.6%), grey mouse lemurs (50.5%), and owl monkeys (67.5%); but lower than in marmosets (71.5%), capuchins (75.0%), baboons

(79.5%), macaques (79.9%), and Great Apes (i.e. Humans: 81.7%)(Herculano-Houzel et al., 2015). Hence, the cortex of squirrel monkeys is close to the brain of macaques and very similar to humans except for some gyri and sulci that are also absent in the other monkeys.

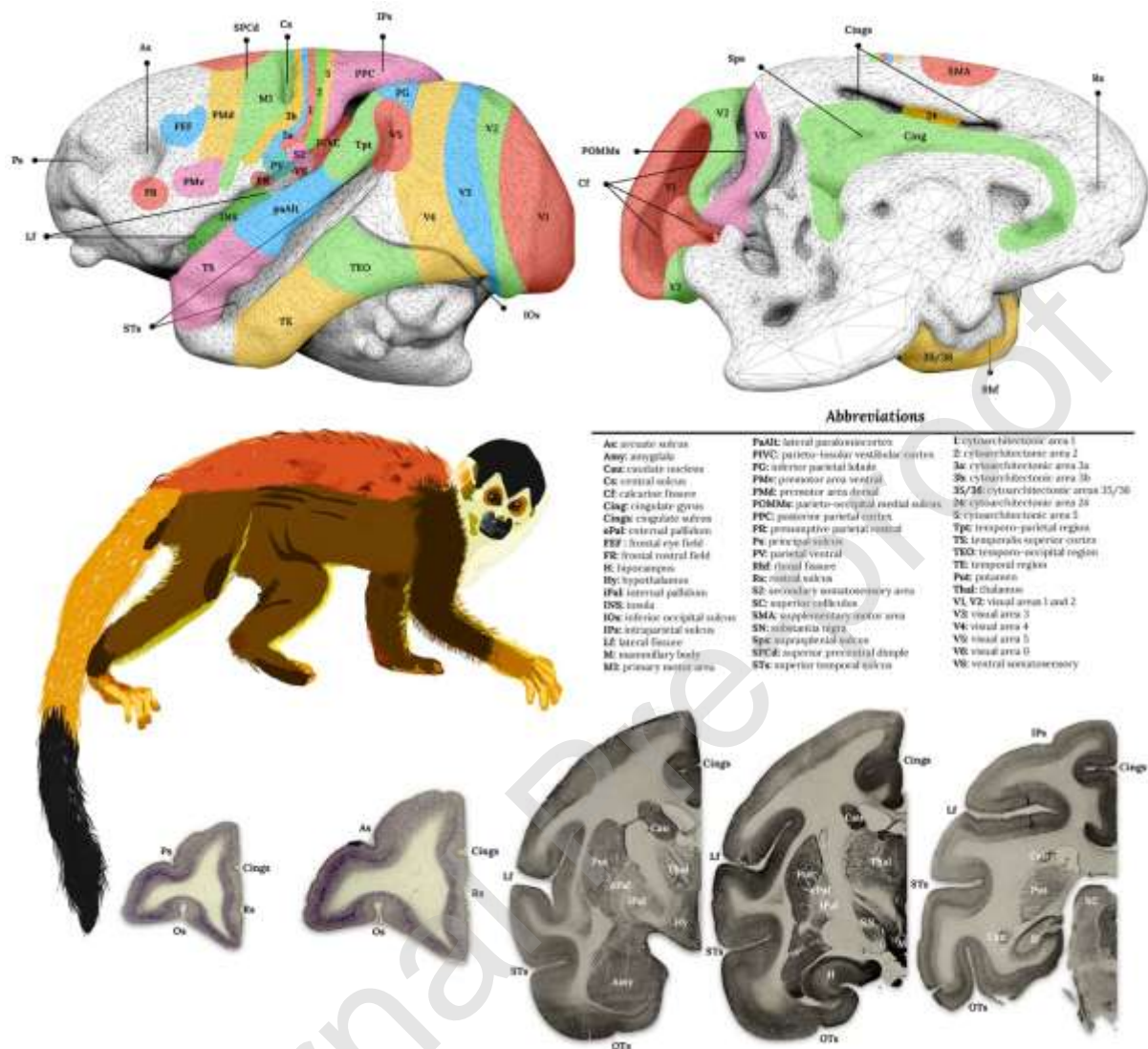


Figure 3: Gross anatomy of the squirrel monkey brain. The top panel displays a digital 3D reconstruction of the left hemisphere of a squirrel monkey derived from magnetic resonance imaging. The bottom panel shows post mortem coronal sections (modified from <http://neuroscielibrary.org> and Gergen and MacLean atlas (Gergen and MacLean, 1962) demonstrating the existence of sulci in the squirrel monkey brain and the close similarity of the subcortical anatomy with humans.

Subcortical

The brain of the squirrel monkey also has most of the subcortical areas identified in the human brain (see Figure 3). For instance, the diencephalon includes the pineal gland, thalamus, hypothalamus, hypophysis, and colliculi are visible and proportional to the brain size of the squirrel monkey. The lateral geniculate nucleus (part of the thalamus) of the squirrel monkeys, like Old World monkeys (e.g. rhesus monkey), is composed of six layers, including two ventral magnocellular layers and four dorsal parvocellular layers (Rosenblum and Coe, 1987) receiving input alternatively from the contralateral and ipsilateral eyes.

The telencephalon of squirrel monkeys contains the cerebral hemispheres, including the cerebral cortex and some subcortical structures. The subcortical structures of the telencephalon include the amygdala, the hippocampus, the basal ganglia, the septal nuclei, the basal nuclei of Meynert, and the nucleus accumbens (Emmers and Akert, 1963; Vanier et al., 2019).

In the brainstem of the squirrel monkey, the main structures such as the tectum, tegmentum, cerebral peduncles, and the superior and inferior colliculi are also well visible to the naked eye and with imaging methods.

Hence, the brain of squirrel monkeys harbours a wealth of structures comparable to humans and Great Apes (Dyce et al., 2010). In contrast, the rodent brain differs from humans with a smooth (rather than convoluted) cortex and a dorsally located hippocampus (instead of a ventral and medial position). The sensory system partially overlaps with the motor system in rodents and has a larger olfactory sensory cortex (i.e. considerably larger olfactory bulb) that includes a dedicated whisker sensory system (contrary to the importance of touch and taste in primates), the visual cortex is located lateral, and its brain circuitry is less complex (Snyder et al., 2018). The comparability of these structures in squirrel monkeys and humans is crucial as they allow more translational clinical investigations of functional systems that are not available or not developed in rodents.

Brain circuits and functional systems

Functional systems are defined here as brain regions working together via large circuits of neurons and connections to achieve main functions such as, for example, motor actions or the processing of sensory information. In squirrel monkeys, the connections of functional systems have been demonstrated using several techniques such as postmortem axonal

tracing (e.g. (Huerta et al., 1987, 1986)) or in vivo diffusion-weighted imaging (Gao et al., 2018, 2016, 2013; Schilling et al., 2019c, 2019b).

Visual system

Primate visual functions require primary visual inputs (i.e. retinogeniculate or retinotectal), good coordination between the two brain hemispheres for stereoscopy, and higher-level visual processing along the ventral and dorsal visual stream to quickly detect food and potential predators. In other words, in primates, visual functions are possible only through the integrative effort of different structures in a complex network.

Squirrel monkeys, like other primates, have an optical chiasma, although the proportion of non-crossing fibres remains, to our knowledge, unknown. Their ocular fibres terminate in the lateral geniculate nucleus (LGN) (Rosenblum and Coe, 1987) and their LGN of the thalamus projects between layers IV α /IV β and layer IIIB of the striate cortex (V1) (Lachica et al., 1993). However, in contrast with other monkeys, columns of ocular dominance in layer IV are less well segregated but still visible in squirrel monkeys (Horton and Hocking, 1996; Rosenblum and Coe, 1987), which opens up the question of the functioning/existence of eye dominance in squirrel monkeys (Livingstone, 1996). This difference suggests potential binocular interactions and differences between squirrel monkeys and Old-World monkeys that remain to be scrutinised in future research.

Visual interhemispheric coordination in squirrel monkeys is also very similar to macaques and humans (Gazzaniga, 2000; Rosenblum and Coe, 1987), with posterior callosal connections projecting preferentially to V1 and V2 (Gould et al., 1987). Visual information is also further processed along the dorsal (where) and the ventral (what) streams in the squirrel monkey, similar to macaques (Ungerleider and Mishkin, 1982; Weller, 1988). Accordingly, the ventral stream complex of squirrel monkeys is composed of a chain of local interconnected regions linking hierarchically successive functional modules along the occipital-temporal lobe (V1, V2, V3, and V5) (Tigges et al., 1981). These modules are systematically interconnected with the posterior thalamus—the pulvinar (Kaas and Lyon, 2007). The dorsal stream of the squirrel monkey runs in parallel to the ventral stream in the squirrel monkey. Area V2 is sending significant connections to area 19 (V4-6), albeit more moderately than macaques and humans (Cusick and Kaas, 1988).

Further along, the most anterior portion of area 19 (front of the parieto-occipital sulcus corresponding to V6) is connected with the frontal eye field (FEF) in squirrel monkeys, located near the arcuate sulcus and responsible for saccadic eye movements (Huerta et al., 1987).

The subcortical connections of the FEF in squirrel monkeys are comparable to macaque monkeys suggesting homology and conservation or convergent evolution (Huerta et al., 1986; Percheron et al., 2015). Overall, the structural organisation of the visual system in squirrel monkeys, albeit mapped incompletely, appears to be a much more accurate model of human visual functions than rodents where FEF has not been identified yet (Laubach et al., 2018).

Somatosensory system

The somatosensory system is contingent on primary sensory inputs, fast interpretation of threatening stimulation (i.e. pain), body representation, and sensory-motor integration.

The primary somatosensory cortex of the squirrel monkey, like its primate counterpart, is somatotopic and has the same somatic sensory fields described in other primates (Cusick and Kaas, 1988). For example, in the primary somatosensory cortex, Brodmann's areas (1, 2, and 3) and the subdivisions of 3 into 3a and 3b have also been demonstrated in squirrel monkeys (Sanides, 1968). In the squirrel monkey, area 1 of the somatosensory cortex is involved in tactile discrimination. It receives strong connections from other cytoarchitectonic regions of the somatosensory cortex (i.e. 2, 3a and 3b), the parietal lobe (5), the primary motor cortex (M1), the dorsal and ventral premotor cortex (PMd and PMv), the supplementary motor area (SMA), and the second somatosensory regions (i.e. S2, parietal ventral (PV), and two divisions of ventral somatosensory (VS) areas) (Ashaber et al., 2014; Cerkevich and Kaas, 2019; Friedman et al., 2020; Pálfi et al., 2018; Wang et al., 2013). This circuit has been mapped with axonal tracing. The cortical projections in squirrel monkeys are similar to the pattern of connections in macaques (Nelson et al., 1980; Pons and Kaas, 1986; Sur et al., 1982) and, putatively, humans.

Like in other primates, a sensory and an affective functional network processes pain in squirrel monkeys. The sensory network links primary (area 3b) and secondary somatosensory (areas S2, PV and 2 divisions of VS) cortices together with the posterior parietal cortex in squirrel monkeys. The affective network of the squirrel monkey involves connections between the whole cingulate cortex with the insula. These two networks interact at the system level via strong interconnections between S2 and the insula (Wu et al., 2017).

Additionally, squirrel monkey somatosensory cortex (3aV) connections to the rest of the brain (motor, M1 and premotor, PMd/PMv, posterior parietal, PPC, limbic, thalamus, 24 insula together with the primary and secondary somatosensory cortex) are putatively responsible for the representation of the body comparably to humans (Pacella et al., 2019; Pacella and Moro, 2020; Stevens et al., 1993).

Sophisticated techniques, such as electrical intracortical microstimulation with optical imaging, allow the mapping of inter-areal and intra-areal connections in vivo primates (Friedman et al., 2020; Liao et al., 2013). This approach revealed that the somatosensory and motor cortices are tightly connected in squirrel monkeys. For example, area 2 projects to areas 1, 3a, 3b, and M1. Similarly, area 3a is connected to areas 1, 2, 3b, and area 3b is connected to M1 and area 1. As in other primates, this dense sensorimotor integration was proposed to be mediated by short u-shaped connections recently discovered in humans (Catani et al., 2012). Functionally this dense network supports control and fine motor skills through connections between the different representations of each digit in area 3b with areas 1, 2, 3a, M1, parietal ventral/somatosensory cortex (PV/S2) and ventroposterior lateral nucleus of the thalamus (Liao et al., 2013, 2016).

The structural organisation of the somatosensory system in the squirrel monkey is more comparable to humans and Old World monkeys than rodents. A modest parietal lobe size and a limited range of behaviours restrict detailed sensorimotor and body representation investigations in NHP (Kaas et al., 2018).

Motor system

The motor system receives inputs from the prefrontal cortex to facilitate the planning of action sequences. The motor system is also connected to the parietal lobe to coordinate actions within a reference system (e.g. reaching a target or defending your peripersonal space). Fine-tuning of motor initiation (e.g. monitoring and planning) is orchestrated by cortico-subcortical interactions (i.e. striato-thalamic and ponto-cerebellar) within each hemisphere. The interaction between both hemispheres is required for bimanual coordination.

In the squirrel monkey, activity related to the elaboration of a motor plan would converge in the frontal rostral field (FR) before reaching the PMd, PMv and M1 (Dancause et al., 2008) and further processing along the fronto-parietal network. Like in other primates, the fronto-parietal network of the squirrel monkey can be divided into three systems that help to coordinate the action in a reference system for reaching (PMd, M1 to dorsal PPC), grasping (PMv, M1 to ventral PPC), and defending the peripersonal space (PMv, M1 to mid PPC)(Gharbawie et al., 2011; Kaas et al., 2016; Stepniewska et al., 2014). These fronto-parietal connections can therefore be considered as sensory-effector modules dedicated to actions. This network has been described in other primates as well, including owl monkeys (Stepniewska et al., 2006, 1993), galagos (Fang et al., 2005; Fogassi et al., 1994; Stepniewska et al., 2009, 2005) and macaques (Godschalk et al., 1995; Luppino et al., 1999;

Matelli et al., 1998; Tanné-Gariépy et al., 2002) suggesting their conservation during evolution (Gharbawie et al., 2011; Kaas et al., 2016).

The motor network extends to subcortical structures. The squirrel monkey motor and premotor cortices project to the putamen (Lapper et al., 1992) and then to the internal pallidum and the motor thalamus (Lavoie et al., 1989). The information is directed back to the supplementary motor area (SMA) via the ventrolateral nucleus divisions of the motor thalamus and to a lesser extent via the rostral motor thalamus in squirrel monkeys (Gharbawie et al., 2010).

Finally, with the help of axonal tracers, Dancause *et al.* (Dancause et al., 2007) identified several interhemispheric connections of PMv in squirrel monkeys, which participate in the coordination of bimanual movements. These included interhemispheric connections of PMv and SMA and the posterior parietal cortex (PPC) and inferior parietal cortex (PG).

In sum, the motor system in squirrel monkeys seems highly comparable to other non-human primates. It might, therefore, serve as a valuable model for the investigation of human motor disorders. The SMA region is located at the dorsomedial margin of the frontal lobe (Jürgens, 1984; Welker et al., 1957) but is not connected with the insula, area 3a, and PPC as has been described in other primates (Guldin et al., 1992).

Limbic system

In primates, including humans, the limbic system integrates visceral sensations, memory, and spatial orientation and introspective self-directed thinking (Catani et al., 2013). The visceral sensation can be triggered by olfactory senses and is highly developed in squirrel monkeys (Laska et al., 2000) with easily identifiable structures such as the piriform cortex, olfactory bulbs, trigone and tractus (MacLean, 1962). Viscero-receptive thalamic neurons of the squirrel monkey are also present in the ventral posterior lateral portion of the thalamus. Like humans, these thalamic neurons are responsive to bladder, colon, and oesophagus stimulation in squirrel monkeys (Brüggemann et al., 1994). The squirrel monkey visceral sensations are further enriched with affective representation through their interaction with S2 and the insula (Wu et al., 2017).

In primates, memory and spatial orientation are typically attributed to the hippocampus (Sosa et al., 2018). The hippocampus and entorhinal area of squirrel monkeys receive projections from the prefrontal and the orbitofrontal cortex (Leichnetz and Astruc, 1976a, 1975). Additionally, tracers injected in the hippocampal formation of squirrel monkeys identified projections to the medial septal area, the basal forebrain, anterior and laterodorsal thalamic

nuclei, reuniens and periventricular nuclei of the thalamus, lateral hypothalamus, and the dorsal and superior raphe nuclei (DeVito, 1980).

The default mode network is the primary network activated during mind wandering and self-thinking (Kucyi et al., 2016). Whilst mind wandering and self-thinking are challenging to quantify in animals, the existence of some critical structures and connections suggests that squirrel monkeys might have a default mode network comparable to apes. The anterior cingulate cortex of the squirrel monkey has connections to other cortical areas (e.g. frontal cortex, insula), subcortical structures (e.g. claustrum, thalamus), and brainstem nuclei (e.g. Raphe nuclei, nucleus coeruleus)(Jürgens, 1982). Most of these areas appear to be involved in the default mode network in humans (Alves et al., 2019). This network is anatomically mimicked in squirrel monkeys and may present a unique opportunity to investigate its clinical role and manipulate its function pharmacologically.

Vestibular system

Several studies suggest a close similarity between the vestibular system in macaques and squirrel monkeys (Cavada and Goldman-Rakic, 1989; Guldin et al., 1992; Neal et al., 1987). The vestibular system of the squirrel monkey takes roots in the parieto-insular vestibular cortex (PIVC), which is homologous to the PIVC in macaques (Pandya and Sanides, 1973). Further reciprocal connections between PIVC, 2, 3a, PPC and FEF are essential for the processing of vestibular information in squirrel monkeys (Guldin et al., 1992). The squirrel monkey somatosensory-proprioceptive system, together with the visual movement system (V5, see the previous sections on *Somatosensory and visual systems*), also participates in the vestibular network via a relay in the temporo-parietal region (Tpt). Hence, squirrel monkeys might be an excellent model to investigate therapeutics for symptoms like vertigo.

Auditory-vocal system

Studying primates rather than rodents offers a unique opportunity to tap into primitive vocal communication as a precursor for language evolution (Balezeau et al., 2020).

Like other primates, squirrel monkeys can cackle, growl, chirp, trill, or quack (Winter et al., 1966) and relevant brain structures have already been identified for cackling and growling (Jürgens and Ploog, 1970). Cackling and growling share the same network of regions involving the midbrain, the thalamus, and the subcallosal gyrus. However, cackling uniquely involves connections between the midbrain and the hypothalamus via the dorsal longitudinal fasciculus of squirrel monkeys (Winter et al., 1966). Crackling also requires thalamic projections to the

amygdala and the ventral temporal lobe via the inferior thalamic peduncle and the anterior cingulate cortex via the anterior thalamic radiations. In the squirrel monkey, growling, on the other hand, involves thalamic projections to the nucleus accumbens, which is interconnected with the hippocampus and the subcallosal gyrus via the fornix.

The auditory system of the squirrel monkey has been limited to the study of the lateral parakoniocortex (paAlt) in the superior temporal gyrus, which has a tonotopic organisation (Cheung et al., 2001). The parakoniocortex of squirrel monkeys can analyse complex auditory signals (Wollberg and Newman, 1972) and is finely tuned to intraspecies vocalisation (Funkenstein et al., 1970).

Prefrontal system

The investigation of the prefrontal system beyond motor tasks remains, to our knowledge, unexplored in squirrel monkeys. However, preliminary evidence derived from the unilateral partial ablations in the medial granular frontal cortex of the squirrel monkey revealed fibre degeneration along connections to the rest of the brain, including the limbic (via the cingulum), the contralesional hemisphere (via the corpus callosum), subcortical structures (via the internal capsule), the temporal lobe (via the uncinate fascicle) (Leichnetz and Astruc, 1976b), and the parietal lobe (via the superior longitudinal fasciculus) (Kaas et al., 2016). This wealth of connections with the rest of the brain is compatible with the putative 'conductor' role of the prefrontal cortex in cortical and subcortical limbic mechanisms. Hence, specific symptoms observed in humans with brain injury, such as behavioural disinhibition or strategies for their compensation, could be explored in squirrel monkeys.

Behaviour and cognition

The functional systems described above are involved in a wealth of behavioural and cognitive functions. Most of these functions can be tested given that the tasks performed in rodents and other primates can be adapted to the behavioural specificity of squirrel monkeys. For instance, in behavioural research studies, it is possible to investigate the reaching and grasping of objects in squirrel monkeys. In translational neurological studies, the squirrel monkey model can facilitate the study of neurologic lesions on the motor system and cognitive performances or drug effects on learning and memory skills (Williams and Glasgow, 2000).

We review here the typical tasks that have already been successfully adopted

Vision

Vision is one of the primary senses of primates, and the impact of its manipulation on behaviour in squirrel monkeys has been studied through variation of colour wavelength, duration, frequency, form, discrimination and co-orientation.

When it comes to colour perception, male squirrel monkeys are dichromatic, which can lead to colour vision deficiency similar to humans (De Valois et al., 1974; Jacobs, 1983; Jacobs and Blakeslee, 1984; Jacobs and Neitz, 1985; Miles, 1958). Dichromatism makes male monkeys less sensitive to long-wave-length light (640nm - red-orange hue). Females can either have dichromatic or a pseudo-trichromatic vision as they only have 2 classes of cones (Jacobs, 1977). The pseudo-trichromatic vision can be explained by an allelic variant of the gene for long wavelengths on each X chromosome. For instance, the combination of M/LWS alleles, 535 and 562, compared to the 550/562 and 535/550 associations, allows the animals to discriminate better greens and reds (De Araujo et al., 2006). Squirrel monkeys also seem to display a preference (i.e. selective attention) for the colour of the visual stimulation rather than its form (Ploog, 2011). Nevertheless, the presentation of attractive forms (i.e. prey) improves their performance, whereas repulsive forms (i.e. predators) induce fear reactions and an increase of gaze frequency (Humphrey, 1972; Murray and King, 1973). Significantly for these visual paradigms, repetitive visual stimulation induces habituation. For instance, the presentation of the picture of prey such as a moth or a spider to the squirrel monkey causes habituation after 120-130sec during the first session and up to 20-50sec after the tenth session (Marriot, 1976). Squirrel monkeys show visual co-orientation (i.e. the monkey will fixate an object when a human is fixating it), although less frequently than in macaques (Anderson et al., 2005; Anderson and Mitchell, 1999; Ferrari et al., 2000). These results demonstrate that the exploration of the visual behaviour in squirrel monkeys is appropriate to investigate the mechanisms subserving pathological behaviour and therapeutic strategies of the extended visual system (e.g. hemianopia, agnosias, visual neglect).

Olfaction

Squirrel monkeys exhibit a higher olfactory sensitivity which is very similar to human and other NHPs but less sensitive than other species such as rats or dogs (Laska et al., 2000). Anatomically, fMRI studies in sedated squirrel monkeys revealed robust odorant-induced activations in several brain areas similar to the human olfactory system (Waymel et al., 2020). These squirrel monkey brain areas include the orbitofrontal cortex, the cerebellum and the piriform cortex (Boyett-Anderson et al., 2003). These results suggest that sedated squirrel monkeys and conscious humans share similar neural substrates in olfactory processing. As

squirrel monkeys have an excellent sense of smell, its investigation may help to understand the critical role of olfaction in primate behaviour across several domains from social cognition (e.g. oxytocin), neurological symptoms (e.g. anosmia in Covid), and as an early disease biomarker (e.g. neurodegeneration). This opens up exciting new avenues previously not available to neurosciences reliant on rodent studies with limited translational power.

Audition

The audible frequency range of squirrel monkeys (0.125 kHz to 46 kHz) is higher pitched than the human range (0.02 kHz to 15 kHz). The maximum sensitivity is 8 kHz, and auditory stimulation, typically white noise, distracts squirrel monkeys and reduces their performance (Hornbuckle, 1972).

Auditory localisation can be assessed using a modified Wisconsin General Test Apparatus (i.e. two speakers separated by a central partition with boxes concealing a food reward). This study design has revealed auditory spatial maps in squirrel monkeys (Capps and Ades, 1968). The complexity of their vocal repertoire also demonstrates well-developed auditory abilities (Schott, 1975). Squirrel monkeys can use familiar vocal conspecific cues to reach a hidden distant goal area (Fragaszy, 1980). Auditory discrimination (i.e. sequences of low and high pitch sounds) studies even indicated that squirrel monkeys could detect variations of an ABnA grammar beyond the habituation patterns (Ravignani et al., 2013). However, these findings have been criticised (Ghirlanda, 2017), highlighting the lack of statistical robustness of the results (i.e. omission of data points, dichotomisation of the response variable). Additionally, according to Ghirlanda et al. (2017), it remains unclear whether the detection of variation relied on perceptual similarity rather than grammar. Further research will be required to settle this debate.

Hence, albeit criticised (Ghirlanda, 2017), audition in squirrel monkeys seems to show primitive elements of vocalisation and simple grammar that could be harvested to assess the mechanisms and the rehabilitation of auditory-verbal disorders. Additionally, while the existence of auditory-spatial maps in squirrel monkeys has been confirmed, they are still poorly understood and offer a strategic target for future studies of visual neglect rehabilitation.

Eye movements

During spontaneous eye movements, execution of saccades, and smooth pursuit tasks, the oculomotor behaviour of squirrel monkeys and macaques is similar (Heiney and Blazquez, 2011). Squirrel monkeys, however, exhibit a smaller oculomotor range, weaker performance

for horizontal saccades above 10 degrees and smaller gains for smooth horizontal pursuit. The smaller range of saccades and pursuit gains in squirrel monkeys may indicate that eye movements play a lesser role for gaze control than in macaques and are compensated for by more frequent head movements (Gdowski et al., 2000; McCrea and Gdowski, 2003; Roy and Cullen, 2001). Even if slightly more distractible than macaques during experimental sessions, gaze orienting can be investigated in squirrel monkeys and opens up some exciting possibilities for studying attention and related disorders.

Whether squirrel monkeys can perform anti-saccades still awaits confirmation. The ability of squirrel monkeys to correctly execute inhibitory control (see inhibitory control section) suggests that they might perform anti-saccades after training.

Reaching and grasping

Manual dexterity and fine motor coordination during manual prehension and manipulation tasks are testable in squirrel monkeys. However, in the absence of visual input, the prehension in squirrel monkey is not as sharp as macaques and humans (Zander et al., 2013), limiting the exploration of neuropsychological syndromes such as, for instance, ideational apraxia. On the other hand, squirrel monkeys are better than most of the other non-human primates for the prehension of a rapidly moving object (Fragaszy, 1983; Welles, 1976), a process that is typically impaired in optic ataxias.

Like macaques (Chatagny et al., 2013), squirrel monkeys also have a slight hand preference that may vary according to the task. While no preference can be observed for fruit grasping, squirrel monkeys preferentially use their left hand to catch their prey (Pouydebat et al., 2014). Further investigation of lateralised behaviour might suggest a potential brain functional lateralisation.

Inhibitory control

A typical experimental setup to study inhibitory motor control requires a squirrel monkey to choose a smaller amount of food over a larger amount of food. The latter would be a natural choice that has to be inhibited. Squirrel monkeys can achieve this inhibition and maintain it for up to eight months (Anderson et al., 2004). However, when increasing the cognitive load during an inhibition task, squirrel monkeys perform less well than other primates. For example, for a fine motor inhibition task, squirrel monkeys usually perform an inappropriate movement (e.g. pulling candy off a wire) rather than the target movement (e.g. move candy along the

wire to come off) (Davis and Leary, 1968). As such, squirrel monkeys are appropriate to investigate inhibitory control but using experimental designs with a low task load.

Social dimensions

In primates, recognition of individuals is a critical ability to form and maintain social groups. Like Old World monkeys, squirrel monkeys can detect subtle differences in facial features, which allows them to distinguish individuals within their species (Nakata and Osada, 2012). Social contact with their peers also facilitates task-directed behaviour and increases their acquisition of an instrumental response (Benjamin and Welker, 1957). Importantly, for the squirrel monkey living in social groups, the isolation during cognitive tests is a significant stress factor leading to distractibility and restless behaviour (Rosenblum and Coe, 1987). A comparison could be drawn here that could be interesting to explore in finding strategies to compensate or prevent the psychological danger of social distancing in humans (Sikali, 2020).

Memory

Working memory skills are comparable between macaques and squirrel monkeys, although squirrel monkeys are more distractible during delayed response tasks (Goldberg et al., 1980; Rosenblum and Coe, 1987).

Squirrel monkeys can accurately remember lists containing up to 20 items (Overman et al., 1983) and build long-term spatial memories (Burdyn et al., 1984; Ludvig et al., 2003). Their information retention period is also comparable to humans (Overman et al., 1983). Squirrel monkeys succeed at reversal learning tasks, although their performance is more modest than macaques (Rosenblum and Coe, 1987). Squirrel monkeys can remember newly learned rules even after a 5-year interval (Adachi et al., 2011). Therefore, albeit slower learners than macaques, squirrel monkeys' long-term memory abilities appear to be comparable to human memory. In combination with their ability to succeed in reverse learning tasks, they are a valuable model for investigating the anatomy and disorders of memory.

Healthy ageing and neurological pathologies

Ageing is defined as the progressive alteration of the organism's functions, accompanied by an increased risk of developing pathologies. With a life span of 35-40 and 25-30 years (Fischer and Austad, 2011; Tigges et al., 1988; Walker et al., 1990), macaques and squirrel monkeys are the most extensively studied primate models in ageing research. Some neuropathological changes characteristic of ageing or Alzheimer's disease in humans are also present in these senescent monkeys, and age-related deficits in memory tasks exist in squirrel monkeys similar to humans (Fischer and Austad, 2011).

Ageing

Similar to cognitive decline in humans, cognitive functions are affected in ageing squirrel monkeys (Fischer and Austad, 2011). For example, aged squirrel monkeys make more errors than younger animals during variations of a two-choice, spatial delayed-response task. However, the reduced accuracy in older squirrel monkeys was not due to a memory deficit per se, as the difference between the two groups was independent of the delay interval (King and Michels, 1989). Indeed, older squirrel monkeys perform comparably to younger animals in learning and memory tasks (Lyons et al., 2004). However, for motor inhibition tasks, there is a detectable effect of age as these are more challenging for older squirrel monkeys. This decline correlates with the overall white matter volume (Tigges et al., 1988). Cortisol treatment can also accentuate this decline in elderly squirrel monkeys (Lyons et al., 2000). This is of particular interest as, with ageing, humans develop endogenous hypercortisolism associated with cognitive impairment. Hence future research in older squirrel monkeys can shed light on the cascade of events that happens during ageing and help discover new targets for treatment.

Alzheimer's disease

An estimated 1 out of 15 people over the age of 65 years is affected by Alzheimer's disease (Qiu et al., 2009). The high presence of β -amyloid peptides (leading to senile plaques) and tau proteins (leading to neurofibrillary tangles) in the limbic system is a defining characteristic of Alzheimer's disease in humans (Ballard et al., 2011; Braak and Braak, 1997). However, establishing a suitable animal model for this disorder is challenging as no other mammals seem to compare exactly with humans with regards to this pathology. For instance, whilst squirrel monkeys β -amyloid peptide is identical to humans (Levy et al., 1995), its deposit ($A\beta$) preferentially affects capillaries, rather than neurons, in the form of cerebral β -amyloid angiopathy (CAA) around the age of 13-14 years (Oikawa et al., 2010; Walker, 1997, 1993; Walker et al., 1990). Aged squirrel monkeys present with relatively few senile plaques, predominantly distributed in the third and fifth layers of the cerebral cortex and are smaller

than those present in macaques and humans (Walker et al., 1990). Their presence in the squirrel monkey has been observed in the hippocampus in severe cases, similarly to humans (Ogomori et al., 1989).

In sum, squirrel monkeys naturally develop a deposit of β -amyloid peptide ($A\beta$) which is one advantage over rodent models. However, in squirrel monkeys, the deposits cause cerebral β -amyloid angiopathy (CAA) and not Alzheimer's disease. Future genetics research might shed light on neurodegenerative processes leading to the squirrel monkey as a model for Alzheimer disease. For instance, squirrel monkeys and humans present with 99.5% similarities for amyloid beta-protein precursors (β PP) (Levy et al., 1995). This substitution of nucleotides in the β PP gene (involved in neural plasticity or the regulation of synapse formation) could be one cause of human Alzheimer's disease.

Parkinson

The incidence of Parkinson's disease is estimated at around 1% of the population over 70 years. In non-human primates, the MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is a toxin that destroys neurons in the substantia nigra leading to the neurochemical, pathological, and behavioural characteristics of Parkinson's disease (Emborg, 2007; Porras et al., 2012). In MPTP squirrel monkeys, profound Parkinsonism and severe nerve cell destruction in the substantia nigra are evident within a day after toxin injection (Irwin et al., 1990). After one week, the number of dopaminergic neurons in the substantia nigra of squirrel monkeys decreased by 10%, and after one month, the neuronal loss is as high as 40% (Purisai et al., 2005). Squirrel monkeys injected with MPTP develop motor abnormalities similar to those observed in humans with Parkinson's disease, such as bradykinesia, rigidity, and postural abnormalities but recover quickly and spontaneously, preventing chronic motor symptoms in this species (Petzinger et al., 2006). Like humans, squirrel monkeys respond positively to L-DOPA treatment which is the primary drug for treating Parkinson's disease (Boyce et al., 1990). Apart from the neuronal loss in the substantia nigra, alpha-synuclein proteins tend to aggregate in neuronal tissues and form Lewy Bodies when combined with other proteins. Squirrel monkeys' dopaminergic neurons that survived the toxicity of an MPTP injection show alpha-synuclein proteins, albeit with a slightly different genetic signature than humans (Vermilyea and Emborg, 2015). These alpha-synuclein proteins, particularly in aged squirrel monkeys, aggregate into Lewy Bodies in the substantia nigra, the amygdala-parahippocampal region, the locus coeruleus, the basal nucleus of Meynert, the Raphe nuclei, and the dorsal motor nucleus of the vagus nerve (Forno et al., 1995, 1993, 1986). The difference between the inclusions in squirrel monkeys and human cortical Lewy Bodies is the orientation of the

filaments in the inclusion bodies. Contrary to the random orientation in human Lewy Bodies, squirrel monkeys present with curving bundles arranged in a ball or cap adjacent to the nucleus (Forno et al., 1995).

In sum, the MPTP model of squirrel monkeys shows many similarities with human Parkinsonism. However, it is essential to remember that the genetic code of some Parkinson Disease's actors varies (i.e. alpha-synuclein proteins), which may explain the spontaneous recovery of symptoms in squirrel monkeys and lead to differences in the efficiency of future treatments.

Stroke

It is estimated that one out of six people will suffer a stroke during their lifetime. Stroke is the second leading cause of death in the western world. Stroke has a detrimental toll on public health as patients find themselves amputated for life from a part of their mind. The current COVID-19 crisis has recently aggravated this number (Hernández-Fernández et al., 2020). However, as it stands, clinicians cannot yet predict the clinical outcome after a stroke. There is an urgent need for a suitable animal model for stroke that captures some of the complexity of clinical–physiological processes and the influence of psychodynamic mechanisms on human behaviour and cognition after stroke. A suitable animal would permit elaborating informative models for stroke recovery that can be translated to humans. While the occurrence of a stroke by an occlusion (i.e. ischemic infarct) can be mimicked in many animals, studying the mechanisms of recovery is limited to only a few. Squirrel monkeys have already been considered better suited than rodents, cats, or dogs to model brain circulation and vasculature (Waltz and Sundt, 1967) and have been used preferentially for thrombolytic therapy research (Sundt et al., 1969; Sundt and Waltz, 1967). Experimental stroke studies in squirrel monkeys initiated an occlusion in the middle cerebral artery, which, if permanent, causes a large infarct in the brain (Waltz and Sundt, 1967). In the two hours following an occlusion in squirrel monkeys, cerebral blood flow does not necessarily cease entirely. Still, it decreases but decreases to a critical level of 80 to 50% compared to the normal flow (Sundt and Waltz, 1971). Restoration of blood flow in the artery of the squirrel monkey within three hours after occlusion potentially allows for the survival of salvageable brain tissues (Sundt and Michenfelder, 1972). These results demonstrated that, if taken care of in time, the ischemic effects are potentially reversible and improved the lives of countless stroke survivors (Fassbender et al., 2013). Squirrel monkey models have also been used to investigate motor behaviour recovery. Findings indicate that the degree of motor deficit and the time required for recovery depends on the size of the injury. For instance, small acute lesions involving 35%

of M1 hand area lead to altered motor skills in squirrel monkeys with a behaviour similar to sensory agnosia (Barbay et al., 2006; Nudo et al., 2003). Particularly in the case of large lesions, squirrel monkeys use the impaired hand only when they cannot use the intact hand even two years after infarct comparably to patients with motor neglect (Laplaine and Degos, 1983).

Hence the model of stroke in squirrel monkeys allows dissociating the different trajectories of behavioural recovery according to lesion size and location and might be informative for rehabilitation.

Spongiform encephalopathies or prion diseases

Each year, spongiform encephalopathies (i.e. prion diseases) are estimated to affect 1-2 persons per million, equivalent to 8000 to 15000 people worldwide (Chen and Dong, 2016). Spongiform encephalopathies can also impact other mammals such as primates. For instance, the inoculation of bovine spongiform encephalopathy in squirrel monkeys leads to a similar clinical presentation as Creutzfeldt-Jakob in humans (Piccardo et al., 2012). The disease develops between 29 and 46 months after the inoculation in squirrel monkeys, with evolution over 2 and 5 months. The disease is characterised by prominent deposits of tau and prion proteins in several brain areas, including the cerebellum, with occasional and abnormal tau-immunoreactive neurites and neurons. These deposits are associated with progressive behavioural, cognitive, motor, and cerebellar alterations such as ataxia, tremors, loss of balance, jerky and uncoordinated movements, bradykinesia as well as a generalised weakness (Piccardo et al., 2012). However, neurofibrillary tangle formation remains, to our knowledge, to be explored in squirrel monkeys (Heuer et al., 2012; Oikawa et al., 2010).

In conclusion, squirrel monkeys can exhibit behavioural similarities with Creutzfeldt-Jakob disease in humans and therefore offers a potential line of investigation into its biological, behavioural, and cognitive features.

Conclusion

This review summarised the available literature on the squirrel monkey brain regarding its anatomy, functional systems, behaviour, normal ageing, and pathologies.

The squirrel monkey diverged from the human lineage 10 million years before the macaque monkey. Instead of a step back in evolution, the squirrel monkey offers a step forward in neuroscience by providing an opportunity to model better the evolution of the primate brain (Friedrich et al., 2020). Besides answering questions on the origins of the modern human,

understanding the phylogeny of the primate brain will allow for targeted studies matching human brain mechanisms to their phylogenetic counterpart. Further, it may also help discover neuroprotective agents allowing for resilience to disease in animals.

Squirrel monkeys also offer a point of comparison to the anatomical, physiological, and behavioural knowledge that has been derived from rodents, macaques, and humans. With a cortex representing $\frac{2}{3}$ of its brain, the squirrel monkey has a higher ratio than rodents but lower than most other primates. However, compared to macaques, its smaller brain is ideal for new methods such as ultrasound imaging and high field MRI imaging that will soon allow full high-resolution acquisition of the anatomy and the functioning of the brain (Blaize et al., 2020; Dizeux et al., 2019; Norman et al., 2021). As the squirrel monkey is smaller in body size but more social than the macaque, it is possible to host larger colonies at lower maintenance costs. Likewise, and in contrast to rodents, the long-life expectancy of squirrel monkeys offers an opportunity for studying brain ageing, neurodegenerative diseases, and recovery mechanisms after stroke. Their highly developed five senses allow estimating the impact of brain damage and disease on their behaviour with unprecedented accuracy.

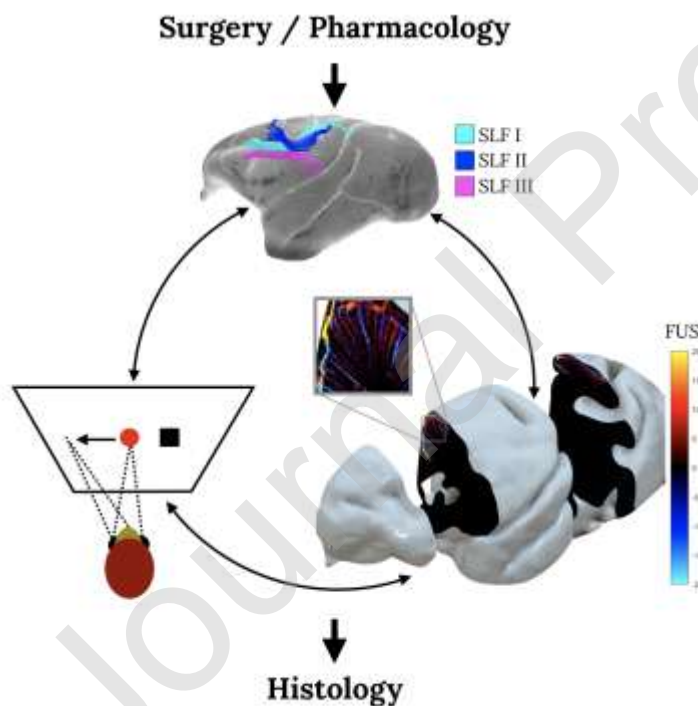


Figure 4: Perspective on the clinical neuroscience research in squirrel monkey that will allow assessing with unprecedented precision the effect of surgical and pharmacological lesions on in vivo brain anatomy, function and cognition as well as its relationship with post-mortem histological findings. Top panel: *In vivo* virtual dissection of the fronto-parietal network SLF (superior longitudinal fasciculus I, II and III) using diffusion tractography. Typical anti-saccade

paradigm (left) and corresponding functional ultrasound imaging (FUS) in the frontal and the parietal lobes.

With the advent of new methods such as micro-surgery, tool miniaturisation and open science, the squirrel monkey will allow for an advanced in vivo investigation between the standard surgery/pharmacology and histology (see Figure 4). Structural, behavioural, and functional exploration of the living squirrel monkey brain will give unique access to the mechanisms supporting cognitive impairment and its spontaneous or pharmacologically boosted recovery in meaningful samples. In doing so, the squirrel monkey has the potential to become a cornerstone to clinical neuroscience. Its use in research will allow to translate and extend the work carried out in rodents to primate. Also, it will allow for the replication of the work published in macaques in larger samples before its translation to humans and will help to bridge the gap between magnetic resonance neuroimaging and histological findings. Hence, the squirrel monkey represents a window of opportunity that will potentially fuel new translational discoveries for humans and should be encouraged for future research.

Acknowledgements

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No. 818521) and the Marie Skłodowska Curie Programme (grant agreement 101028551). We sincerely thank Chantal François for helpful and resourceful discussion.

Bibliography

- Adachi, I., Anderson, J.R., Fujita, K., 2011. Reverse-reward Learning in Squirrel Monkeys (*Saimiri sciureus*): Retesting After 5 Years, and Assessment on Qualitative Transfer. *J. Comp. Psychol.* 125, 84–90. <https://doi.org/10.1037/a0021041>
- Akert, R., 1963. *Stereotaxic Atlas of the Brain of the Squirrel Monkey*. University of Wisconsin Press.
- Alves, P.N., Foulon, C., Karolis, V., Bzdok, D., Margulies, D.S., Volle, E., Thiebaut de Schotten, M., 2019. An improved neuroanatomical model of the default-mode network reconciles previous neuroimaging and neuropathological findings. *Commun. Biol.* 2, 1–14. <https://doi.org/10.1038/s42003-019-0611-3>

- Anderson, J.R., Awazu, S., Fujita, K., 2004. Squirrel Monkeys (*Saimiri sciureus*) Choose Smaller Food Arrays: Long-Term Retention, Choice With Nonpreferred Food, and Transposition. *J. Comp. Psychol.* 118, 58–64. <https://doi.org/10.1037/0735-7036.118.1.58>
- Anderson, J.R., Kuroshima, H., Hattori, Y., Fujita, K., 2005. Attention to combined attention in new world monkeys (*Cebus apella*, *Saimiri sciureus*). *J. Comp. Psychol.* 119, 461–464. <https://doi.org/10.1037/0735-7036.119.4.461>
- Anderson, J.R., Mitchell, R.W., 1999. Macaques but not lemurs co-orient visually with humans. *Folia Primatol.* 70, 17–22. <https://doi.org/10.1159/000021670>
- Ashaber, M., Pálfi, E., Friedman, R.M., Palmer, C., Jákli, B., Chen, L.M., Kántor, O., Roe, A.W., Négyessy, L., 2014. Connectivity of Somatosensory Cortical Area 1 Forms an Anatomical Substrate for the Emergence of Multifinger Receptive Fields and Complex Feature Selectivity in the Squirrel Monkey (*Saimiri sciureus*). *J Comp Neurol* 522, 1769–1785. <https://doi.org/10.1002/cne.23499>
- Balezeau, F., Wilson, B., Gallardo, G., Dick, F., Hopkins, W., Anwander, A., Friederici, A., Griffiths, T.D., Petkov, C.I., 2020. Primate auditory prototype in the evolution of the arcuate fasciculus. *Nat. Neurosci.* 23, 611–614.
- Ballard, C., Gauthier, S., Corbett, A., Brayne, C., Aarsland, D., Jones, E., 2011. Alzheimer's disease. *Lancet* 377, 1019–1031. <https://doi.org/10.1016/S0140>
- Barbay, S., Plautz, E.J., Friel, K.M., Frost, S.B., Dancause, N., Stowe, M., Nudo, R.J., 2006. Behavioral and neurophysiological effects of delayed training following a small ischemic infarct in primary motor cortex of squirrel monkeys 169, 106–116. <https://doi.org/10.1007/s00221-005-0129-4>. Behavioral
- Barcellos, J.F.M., Branco, É., Fioretto, E.T., Imbeloni, A.A., Muniz, J.A.P.C., Lima, A.R., 2011. Macroscopic aspects of *Saimiri sciureus dura mater*. *Pesqui. Vet. Bras.* 31, 7–10. <https://doi.org/10.1590/S0100-736X2011001300002>
- Benjamin, R.M., Welker, W.I., 1957. Somatic receiving areas of cerebral cortex of squirrel monkey (*Saimiri sciureus*). *J. Neurophysiol.* 20, 286–299.
- Bernarcky, B.J., Gibson, S. V., Keeling, M.E., Abee, C.R., 2002. Nonhuman Primates, in: *Medicine, A.C. of L.A. (Ed.), Laboratory Animal Medicine*. Elsevier Inc., pp. 675–791. <https://doi.org/10.1016/b978-1-4832-0051-4.50010-2>

- Bernardi, S., Salzman, C.D., 2019. The contribution of nonhuman primate research to the understanding of emotion and cognition and its clinical relevance. *Proc. Natl. Acad. Sci. U. S. A.* 116, 26305–26312. <https://doi.org/10.1073/pnas.1902293116>
- Blaize, K., Arcizet, F., Gesnik, M., Ahnine, H., Ferrari, U., Deffieux, T., Pouget, P., Chavane, F., Fink, M., Sahel, J.-A., Tanter, M., Picaud, S., 2020. Functional ultrasound imaging of deep visual cortex in awake nonhuman primates. *Pro. Natl. Acad. Sci. USA* 117, 14453–14463. <https://doi.org/10.1073/pnas.1916787117/-/DCSupplemental>
- Boyce, S., Rupniak, N.M.J., Steventon, M.J., Iversen, S.D., 1990. Characterisation of dyskinesias induced by l-dopa in MPTP-treated squirrel monkeys. *Psychopharmacology (Berl)*. 102, 21–27. <https://doi.org/10.1007/BF02245739>
- Boyett-Anderson, J.M., Lyons, D.M., Reiss, A.L., Schatzberg, A.F., Menon, V., 2003. Functional brain imaging of olfactory processing in monkeys. *Neuroimage* 20, 257–264. [https://doi.org/10.1016/S1053-8119\(03\)00288-X](https://doi.org/10.1016/S1053-8119(03)00288-X)
- Braak, H., Braak, E., 1997. Frequency of Stages of Alzheimer-Related Lesions in Different Age Categories. *Neurobiol. Aging* 18, 351–357.
- Brady, A.G., 2000. Research techniques for the squirrel monkey (*Saimiri* sp.). *ILAR J.* 41, 10–18. <https://doi.org/10.1093/ilar.41.1.10>
- Brüggemann, J., Shi, T., Apkarian, A.V., 1994. Squirrel monkey lateral thalamus. II. Viscerosomatic convergent representation of urinary bladder, colon, and esophagus. *J. Neurosci.* 14, 6796–6814.
- Burdyn, L.E., Noble, L.M., Shreves, L.E., Thomas, R.K., 1984. Long-term memory for concepts by squirrel monkeys. *Physiol. Psychol.* 12, 97–102. <https://doi.org/10.3758/BF03332174>
- Camarotti, F.L.M., Silva, V.L. da, Oliveira, M.A.B. de, 2015. The effects of introducing the Amazonian squirrel monkey on the behavior of the northeast marmoset. *Acta Amaz.* 45, 29–34. <https://doi.org/10.1590/1809-4392201400305>
- Capps, M.J., Ades, H.W., 1968. Auditory frequency discrimination after transection of the olivocochlear bundle in squirrel monkeys. *Exp. Neurol.* 21, 147–158. [https://doi.org/10.1016/0014-4886\(68\)90133-7](https://doi.org/10.1016/0014-4886(68)90133-7)
- Catani, M., Dell'Acqua, F., Thiebaut de Schotten, M., 2013. A revised limbic system model for

- memory, emotion and behaviour. *Neurosci. Biobehav. Rev.* 37, 1724–1737. <https://doi.org/10.1016/j.neubiorev.2013.07.001>
- Catani, M., Dell'Acqua, F., Vergani, F., Malik, F., Hodge, H., Roy, P., Valabregue, R., Thiebaut de Schotten, M., 2012. Short frontal lobe connections of the human brain. *Cortex* 48, 273–291. <https://doi.org/10.1016/j.cortex.2011.12.001>
- Cavada, C., Goldman-Rakic, P.S., 1989. Posterior parietal cortex in rhesus monkey: I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. *J Comp Neurol* 287, 393–421. <https://doi.org/https://doi.org/10.1002/cne.902870402>
- Cerkevich, C.M., Kaas, J.H., 2019. Corticocortical projections to area 1 in squirrel monkeys (*Saimiri sciureus*) Christina. *Eur J Neurosci* 49, 1024–1040. <https://doi.org/10.1111/ejn.13884>
- Chatagny, P., Badoud, S., Kaeser, M., Gindrat, A.D., Savidan, J., Fregosi, M., Moret, V., Roulin, C., Schmidlin, E., Rouiller, E.M., 2013. Distinction between hand dominance and hand preference in primates: A behavioral investigation of manual dexterity in nonhuman primates (macaques) and human subjects. *Brain Behav.* 3, 575–595. <https://doi.org/10.1002/brb3.160>
- Chen, C., Dong, X.P., 2016. Epidemiological characteristics of human prion diseases. *Infect. Dis. Poverty.* <https://doi.org/10.1186/s40249-016-0143-8>
- Cheung, S.W., Bedenbaugh, P.H., Nagarajan, S.S., Schreiner, C.E., 2001. Functional organization of squirrel monkey primary auditory cortex: Responses to frequency-modulation sweeps. *J Neurophysiol* 85, 1732–1749. <https://doi.org/10.1152/jn.2001.85.4.1732>
- Cusick, C.G., Kaas, J.H., 1988. Cortical connections of area 18 and dorsolateral visual cortex in squirrel monkeys. *Vis Neurosci* 1, 211–237. <https://doi.org/https://doi.org/10.1017/s0952523800001486>
- Dancause, N., Barbay, S., Frost, S.B., Mahnken, J.D., Nudo, R.J., 2007. Interhemispheric Connections of the Ventral Premotor Cortex in a New World Primate. *J Comp Neurol* 505, 701–715. <https://doi.org/10.1002/cne.21531>
- Dancause, N., Duric, V., Barbay, S., Frost, S.B., Stylianou, A., Nudo, R.J., 2008. An additional motor-related field in the lateral frontal cortex of squirrel monkeys. *Cereb. Cortex* 18, 2719–2728. <https://doi.org/10.1093/cercor/bhn050>

- Davis, R.T., Leary, R.W., 1968. Learning of detour problems by lemurs and seven species of monkeys. *Percept. Mot. Ski.* 27, 1031–1034.
- De Araujo, M.F.P., Lima, E.M., Pessoa, V.F., 2006. Modeling Dichromatic and Trichromatic Sensitivity to the Color Properties of Fruits Eaten by Squirrel Monkeys (*Saimiri sciureus*). *Am. J. Pri* 68, 1129–1137. <https://doi.org/10.1002/ajp>
- De Valois, R.L., Morgan, H., Snodderly, D.M., 1974. Psychophysical studies of monkey vision. 3. Spatial luminance contrast sensitivity tests of macaque and human observers. *Vision Res.* 14, 75–81. [https://doi.org/10.1016/0042-6989\(74\)90118-7](https://doi.org/10.1016/0042-6989(74)90118-7)
- Defler, T., 2004. *Primates of Colombia*. Colombia: Conservation International.
- DeVito, J.L., 1980. Subcortical projections to the hippocampal formation in squirrel monkey (*Saimiri sciureus*). *Brain Res. Bull.* 5, 285–289. [https://doi.org/10.1016/0361-9230\(80\)90170-7](https://doi.org/10.1016/0361-9230(80)90170-7)
- Dizeux, A., Gesnik, M., Ahnine, H., Blaize, K., Arcizet, F., Picaud, S., Sahel, J.A., Deffieux, T., Pouget, P., Tanter, M., 2019. Functional ultrasound imaging of the brain reveals propagation of task-related brain activity in behaving primates. *Nat. Commun.* 10. <https://doi.org/10.1038/s41467-019-09349-w>
- Dyce, K.M., Sack, W.O., Wensing, C.J.G., 2010. *Tratado de anatomia veterinaria*, 4th editio. ed. Elsevier, Rio de Janeiro.
- Elfenbein, H.A., Rosen, R.F., Stephens, S.L., Switzer, R.C., Smith, Y., Pare, J., Mehta, P.D., Warzok, R., Walker, L.C., 2007. Cerebral β -amyloid angiopathy in aged squirrel monkeys. *Histol. Histopathol.* 22, 155–167. <https://doi.org/10.14670/HH-22.155>
- Emborg, M.E., 2007. Nonhuman Primate Models of Parkinson's Disease. *ILAR J* 48.
- Emmers, R., Akert, K., 1963. *A Stereotaxic Atlas of the Brain of the Squirrel Monkey : Saimiri Sciureus*. Madison : University of Wisconsin Press.
- Fang, P.C., Stepniewska, I., Kaas, J.H., 2005. Ipsilateral cortical connections of motor, premotor, frontal eye, and posterior parietal fields in a prosimian primate, *Otolemur garnetti*. *J Comp Neurol* 490, 305–333. <https://doi.org/https://doi.org/10.1002/cne.20665>
- Fassbender, K., Balucani, C., Walter, S., Levine, S.R., Haass, A., Grotta, J., 2013. Streamlining of prehospital stroke management the golden hour. *Lancet Neurol* 12, 585–596. [https://doi.org/10.1016/S1474-4422\(13\)70100-5](https://doi.org/10.1016/S1474-4422(13)70100-5)

- Ferrari, P.F., Kohler, E., Fogassi, L., Gallese, V., 2000. The ability to follow eye gaze and its emergence during development in macaque monkeys. *Proc. Natl. Acad. Sci. U. S. A.* 97, 13997–14002. <https://doi.org/10.1073/pnas.250241197>
- Fischer, K.E., Austad, S.N., 2011. The Development of Small Primate Models for Aging Research. *ILAR J.* 52, 78–88.
- Fleagle, J.G., Seiffert, E.R., 2016. *The Phylogeny of Primates, Second Edition*. Elsevier. <https://doi.org/10.1016/B978-0-12-804042-3.00061-0>
- Fogassi, L., Gallese, V., Gentilucci, M., Luppino, G., Matelli, M., Rizzolatti, G., 1994. The fronto-parietal cortex of the prosimian Galago: Patterns of cytochrome oxidase activity and motor maps. *Behav. Brain Res.* 60, 91–113. [https://doi.org/https://doi.org/10.1016/0166-4328\(94\)90067-1](https://doi.org/https://doi.org/10.1016/0166-4328(94)90067-1)
- Forno, L.S., Delanney, L.E., Irwin, I., Langston, J.W., 1995. Ultrastructure of eosinophilic inclusion bodies in the amygdala- parahippocampal region of aged squirrel monkeys treated with 1-methyl-4- phenyl-1,2,3,6-tetrahydropyridine, a dopaminergic neurotoxin. *Neurosci. Lett.* 184, 1–4.
- Forno, L.S., DeLanney, L.E., Irwin, I., Langston, W.J., 1993. Similarities and differences between MPTP-induced parkinsonism and Parkinson's disease. Neuropathologic considerations. *Adv Neurol* 60, 600–608.
- Forno, L.S., Langston, J.W., DeLanney, L.E., Irwin, I., Ricaurte, G.A., 1986. Locus ceruleus lesions and eosinophilic inclusions in MPTP- treated monkeys. *Ann. Neurol.* 20, 449–455. <https://doi.org/10.1002/ana.410200403>
- Fragaszy, D.M., 1983. Preliminary quantitative studies of prehension in squirrel monkeys (*Saimiri sciureus*). *Brain Behav. Evol* 23, 81–92.
- Fragaszy, D.M., 1980. Comparative Studies of Squirrel Monkeys (*Saimiri*) and Titi Monkeys (*Callicebus*) in Travel Tasks. *Z. Tierpsychol.* 54, 1–36. <https://doi.org/10.1111/j.1439-0310.1980.tb01061.x>
- Friedman, R.M., Morone, K.A., Gharbawie, O.A., Roe, A.W., 2020. Mapping mesoscale cortical connectivity in monkey sensorimotor cortex with optical imaging and microstimulation. *J Comp Neurol.* <https://doi.org/10.1002/cne.24918>

- Friedrich, P., Forkel, S.J., Amiez, C., Balsters, J.H., Coulon, O., Fan, L., Goulas, A., Hadj-Bouziane, F., Hecht, E.E., Heuer, K., Jiang, T., Latzman, R.D., Liu, X., Loh, K.K., Patil, K.R., Lopez-Persem, A., Procyk, E., Sallet, J., Toro, R., Vickery, S., Weis, S., Wilson, C., Xu, T., Zerbi, V., Eickhoff, S.E., Margulies, D., Mars, R.B., Thiebaut de Schotten, M., 2020. Imaging the primate brain evolution : the next frontier ? *Neuroimage*.
- Funkenstein, H.H., Winter, P., Nelson, P.G., 1970. Unit responses to acoustic stimuli in the cortex of awake squirrel monkeys, 4th ed. ed. *Fed Proc*.
- Gao, Y., Choe, A.S., Stepniewska, I., Li, X., Avison, M.J., Anderson, A.W., 2013. Validation of DTI Tractography-Based Measures of Primary Motor Area Connectivity in the Squirrel Monkey Brain. *PLoS One* 8. <https://doi.org/10.1371/journal.pone.0075065>
- Gao, Y., Khare, S.P., Panda, S., Choe, A.S., Stepniewska, I., Li, X., Ding, Z., Anderson, A., Landman, B.A., 2014. A brain MRI atlas of the common squirrel monkey, *Saimiri sciureus*. *Proc SPIE Int Soc Opt Eng* 9038. <https://doi.org/10.1117/12.2043589>.
- Gao, Y., Parvathaneni, P., Schilling, K.G., Wang, F., Stepniewska, I., Xu, Z., Choe, A.S., Ding, Z., Gore, J.C., Chen, L.M., Landman, B.A., Anderson, A.W., 2016. A 3D high resolution ex vivo white matter atlas of the common squirrel monkey (*Saimiri sciureus*) based on diffusion tensor imaging. *Proc SPIE Int Soc Opt Eng* 9784. <https://doi.org/10.1117/12.2217325>
- Gao, Y., Schilling, K.G., Stepniewska, I., Plassard, A.J., Choe, A.S., Li, X., Landman, B.A., Anderson, A.W., 2018. Tests of cortical parcellation based on white matter connectivity using Diffusion Tensor Imaging. *Neuroimage* 170, 321–331. <https://doi.org/10.1016/j.neuroimage.2017.02.048>
- Gazzaniga, M.S., 2000. Cerebral specialization and interhemispheric communication - Does the corpus callosum enable the human condition? *Brain* 123, 1293–1326.
- Gdowski, G., Boyle, R., McCrea, R.A., 2000. Sensory processing in the vestibular nuclei during active head movements. *Arch. Ital. Biol.* 138, 15–28.
- Gergen, J.A., MacLean, P.D., 1962. A stereotaxic atlas of the squirrel monkey's brain (*Saimiri sciureus*) /. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Bethesda, Md. : <https://doi.org/10.5962/bhl.title.114088>
- Gharbawie, O.A., Stepniewska, I., Burish, M.J., Kaas, J.H., 2010. Thalamocortical connections of functional zones in posterior parietal cortex and frontal cortex motor

- regions in new world monkeys. *Cereb. Cortex* 20, 2391–2410. <https://doi.org/10.1093/cercor/bhp308>
- Gharbawie, O.A., Stepniewska, I., Kaas, J.H., 2011. Cortical connections of functional zones in posterior parietal cortex and frontal cortex motor regions in new world monkeys. *Cereb. Cortex* 21, 1981–2002. <https://doi.org/10.1093/cercor/bhq260>
- Ghirlanda, S., 2017. Can squirrel monkeys learn an ABnA grammar? A re-evaluation of Ravnani et al. (2013). *PeerJ* 2017, 1–9. <https://doi.org/10.7717/peerj.3806>
- Godschalk, M., Mitz, A.R., van Duin, B., van der Burg, H., 1995. Somatotopy of monkey premotor cortex examined with microstimulation. *Neurosci. Res.* 23, 269–279. [https://doi.org/https://doi.org/10.1016/0168-0102\(95\)00950-7](https://doi.org/https://doi.org/10.1016/0168-0102(95)00950-7)
- Goldberg, R.B., Fuster, J.M., Alvarez-Peláez, R., 1980. Frontal cell activity during delayed response performance in squirrel monkey (*Saimiri sciureus*). *Physiol. Behav.* 25, 425–432. [https://doi.org/10.1016/0031-9384\(80\)90284-X](https://doi.org/10.1016/0031-9384(80)90284-X)
- Gould, H.J., Weber, J.T., Rieck, R.W., 1987. Interhemispheric connections in the visual cortex of the squirrel monkey (*Saimiri sciureus*). *J. Comp. Neurol.* 256, 14–28. <https://doi.org/10.1002/cne.902560103>
- Guldin, W.O., Akbarian, S., Grüsser, O. - J., 1992. Cortico- cortical connections and cytoarchitectonics of the primate vestibular cortex: A study in squirrel monkeys (*Saimiri sciureus*). *J. Comp. Neurol.* 326, 375–401. <https://doi.org/10.1002/cne.903260306>
- Heiney, S.A., Blazquez, P.M., 2011. Behavioral responses of trained squirrel and rhesus monkeys during oculomotor tasks. *Exp Brain Res* 212, 409–416. <https://doi.org/10.1007/s00221-011-2746-4>
- Hendrickx, A.G., Binkerd, P.E., 1990. Nonhuman primates and teratological research. *J. Med. Primatol.* 19, 81–108.
- Herculano-Houzel, S., Catania, K., Manger, P.R., Kaas, J.H., 2015. Mammalian Brains Are Made of These: A Dataset of the Numbers and Densities of Neuronal and Nonneuronal Cells in the Brain of Glires, Primates, Scandentia, Eulipotyphlans, Afrotherians and Artiodactyls, and Their Relationship with Body Mass. *Brain. Behav. Evol.* 86, 145–163. <https://doi.org/10.1159/000437413>
- Hernández-Fernández, F., Sandoval Valencia, H., Barbella-Aponte, R.A., Collado-Jiménez,

- R., Ayo-Martín, Ó., Barrena, C., Molina-Nuevo, J.D., García-García, J., Lozano-Setién, E., Alcahut-Rodriguez, C., Martínez-Martín, Á., Sánchez-López, A., Segura, T., 2020. Cerebrovascular disease in patients with COVID-19: neuroimaging, histological and clinical description. *Brain* 143, 3089–3103. <https://doi.org/10.1093/brain/awaa239>
- Heuer, E., Rosen, R.F., Cintron, A.F., Walker, L.C., 2012. Nonhuman Primate Models of Alzheimer-Like Cerebral Proteopathy. *Curr Pharm Des* 18, 1159–169.
- Heuer, K., Gulban, O.F., Bazin, P.L., Osoianu, A., Valabregue, R., Santin, M., Herbin, M., Toro, R., 2019. Evolution of neocortical folding: A phylogenetic comparative analysis of MRI from 34 primate species. *Cortex* 118, 275–291. <https://doi.org/10.1016/j.cortex.2019.04.011>
- Hofman, M.A., 2014. Evolution of the human brain: When bigger is better. *Front. Neuroanat.* 8, 1–12. <https://doi.org/10.3389/fnana.2014.00015>
- Hornbuckle, P.A., 1972. Delayed-response performance as a function of sensory stimulation in the squirrel and owl monkey. *J Comp Psychol* 79, 99–104.
- Horton, J.C., Hocking, D.R., 1996. Anatomical Demonstration of Ocular Dominance Columns in Striate Cortex of the Squirrel Monkey. *J. Neurosci.* 16, 5510–5522.
- Huerta, M.F., Krubitzer, L.A., Kaas, J.H., 1987. Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys II. cortical connections. *J. Comp. Neurol.* 265, 332–361. <https://doi.org/10.1002/cne.902650304>
- Huerta, M.F., Krubitzer, L.A., Kaas, J.H., 1986. Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys I. Subcortical Connections. *J. Comp. Neurol.* 253, 415–439.
- Humphrey, N.K., 1972. “Interest” and “pleasure”: two determinants of a monkey’s visual preferences. *Perception* 1, 395–416. <https://doi.org/10.1068/p010395>
- Irwin, I., DeLanney, L.E., Forno, L.S., Finnegan, K.T., Di Monte, D.A., Langston, J.W., 1990. The evolution of nigrostriatal neurochemical changes in the MPTP-treated squirrel monkey. *Brain Res.* 531, 242–252. [https://doi.org/10.1016/0006-8993\(90\)90780-F](https://doi.org/10.1016/0006-8993(90)90780-F)
- Jacobs, G.H., 1983. Within-species variations in visual capacity among squirrel monkeys (*Saimiri sciureus*) sensitivity differences. *Vision Res.* 23, 239–248.
- Jacobs, G.H., 1977. Visual Sensitivity: Significant Within-Species Variations in a Nonhuman

- Primate. *Science* (80-.). 197, 499–500.
- Jacobs, G.H., Blakeslee, B., 1984. Individual variations in color vision among squirrel monkeys (*Saimiri sciureus*) of different geographical origins. *J Comp Psychol* 98, 347–357.
- Jacobs, G.H., Neitz, J., 1985. Color vision in squirrel monkeys: Sex-related differences suggest the mode of inheritance. *Vision Res.* 25, 141–143. [https://doi.org/10.1016/0042-6989\(85\)90088-4](https://doi.org/10.1016/0042-6989(85)90088-4)
- Jürgens, U., 1984. The efferent and afferent connections of the supplementary motor area. *Brain Res* 300, 63–81. [https://doi.org/https://doi.org/10.1016/0006-8993\(84\)91341-6](https://doi.org/https://doi.org/10.1016/0006-8993(84)91341-6)
- Jürgens, U., 1982. Amygdalar vocalization pathways in the squirrel monkey. *Brain Res.* 241, 189–196. [https://doi.org/10.1016/0006-8993\(82\)91055-1](https://doi.org/10.1016/0006-8993(82)91055-1)
- Jürgens, U., Ploog, D., 1970. Cerebral representation of vocalization in the squirrel monkey. *Exp Brain Res* 10, 532–554.
- Kaas, J.H., 2012. The evolution of neocortex in primates. *Prog. Brain Res.* 195, 91–102. <https://doi.org/10.1016/B978-0-444-53860-4.00005-2>
- Kaas, J.H., Lyon, D.C., 2007. Pulvinar contributions to the dorsal and ventral streams of visual processing in primates. *Brain Res. Rev.* 55, 285–296. <https://doi.org/10.1016/j.brainresrev.2007.02.008>
- Kaas, J.H., Qi, H.X., Stepniewska, I., 2018. The evolution of parietal cortex in primates. *Handb. Clin. Neurol.* 151, 31–52. <https://doi.org/10.1016/B978-0-444-63622-5.00002-4>
- Kaas, J.H., Qi, H.X., Stepniewska, I., 2016. Evolution of Parietal-Frontal Networks in Primates. *Evol. Nerv. Syst. Second Ed.* 3–4, 287–297. <https://doi.org/10.1016/B978-0-12-804042-3.00084-1>
- King, J.E., Michels, R.R., 1989. Error analysis of delayed response in aged squirrel monkeys. *Anim. Learn. Behav.* 17, 157–162. <https://doi.org/10.3758/BF03207630>
- Kucyi, A., Esterman, M., Riley, C.S., Valera, E.M., 2016. Spontaneous default network activity reflects behavioral variability independent of mind-wandering. *Proc. Natl. Acad. Sci. U. S. A.* 113, 13899–13904. <https://doi.org/10.1073/pnas.1611743113>
- Lachica, E.A., Beck, P.D., Casagrande, V.A., 1993. Intrinsic connections of layer III of striate cortex in squirrel monkey and bush baby: Correlations with patterns of cytochrome

- oxidase. *J. Comp. Neurol.* 329, 163–187. <https://doi.org/10.1002/cne.903290203>
- Laplante, D., Degos, J.D., 1983. Motor neglect. *J. Neurol. Neurosurg. Psychiatry* 46, 152–158.
- Lapper, S.R., Smith, Y., Sadikot, A.F., Parent, A., Bolam, J.P., 1992. Cortical input to parvalbumin-immunoreactive neurones in the putamen of the squirrel monkey. *Brain Res.* 580, 215–224. [https://doi.org/10.1016/0006-8993\(92\)90947-8](https://doi.org/10.1016/0006-8993(92)90947-8)
- Laska, M., Seibt, A., Weber, A., 2000. “Microsmatic” Primates Revisited: Olfactory Sensitivity in the Squirrel Monkey. *Chem. Senses* 25, 47–53. <https://doi.org/10.1093/chemse/25.1.47>
- Laubach, M., Amarante, L.M., Swanson, K., White, S.R., 2018. What, if anything, is rodent prefrontal cortex? *eNeuro* 5. <https://doi.org/10.1523/ENEURO.0315-18.2018>
- Lavoie, B., Smith, Y., Parent, A., 1989. Dopaminergic innervation of the basal ganglia in the squirrel monkey as revealed by tyrosine hydroxylase immunohistochemistry. *J. Comp. Neurol.* 289, 36–52. <https://doi.org/10.1002/cne.902890104>
- Leichnetz, G., Astruc, J., 1976a. The squirrel monkey entorhinal cortex: Architecture and medial frontal afferents. *Brain Res. Bull.* 1, 351–358. [https://doi.org/10.1016/0361-9230\(76\)90027-7](https://doi.org/10.1016/0361-9230(76)90027-7)
- Leichnetz, G., Astruc, J., 1976b. The efferent projections of the medial prefrontal cortex in the squirrel monkey (*Saimiri sciureus*). *Brain Res.* 109, 455–472. [https://doi.org/10.1016/0006-8993\(76\)90027-5](https://doi.org/10.1016/0006-8993(76)90027-5)
- Leichnetz, G., Astruc, J., 1975. Preliminary evidence for a direct projection of the prefrontal cortex to the hippocampus in the squirrel monkey. *Brain. Behav. Evol.* 11, 355–364. <https://doi.org/10.1159/000123645>
- Levy, E., Amorim, A., Frangione, B., Walker, L.C., 1995. β -Amyloid precursor protein gene in squirrel monkeys with cerebral amyloid angiopathy. *Neurobiol. Aging* 16, 805–808. [https://doi.org/10.1016/0197-4580\(95\)00090-2](https://doi.org/10.1016/0197-4580(95)00090-2)
- Lewis, J.W., Van Essen, D.C., 2000. Mapping of architectonic subdivisions in the macaque monkey, with emphasis on parieto-occipital cortex. *J. Comp. Neurol.* 428, 79–111. [https://doi.org/10.1002/1096-9861\(20001204\)428:1<79::AID-CNE7>3.0.CO;2-Q](https://doi.org/10.1002/1096-9861(20001204)428:1<79::AID-CNE7>3.0.CO;2-Q)
- Liao, C.-C., Gharbawie, O.A., Qi, H.X., Kaas, 2013. Cortical Connections to Single Digit Representations in Area 3b of Somatosensory Cortex in Squirrel Monkeys and Prosimian

- Galagos. *J Comp Neurol* 521, 3768–3790. <https://doi.org/10.1002/cne.23377>
- Liao, C.C., Reed, J.L., Kaas, J.H., Qi, H.X., 2016. Intracortical connections are altered after long-standing deprivation of dorsal column inputs in the hand region of area 3b in squirrel monkeys. *J Comp Neurol* 524, 1494–1526. <https://doi.org/10.1002/cne.23921>
- Livingstone, M.S., 1996. Ocular dominance columns in New World monkeys. *J. Neurosci.* 16, 2086–2096. <https://doi.org/10.1523/jneurosci.16-06-02086.1996>
- Ludvig, N., Tang, H.M., Eichenbaum, H., Gohil, B.C., 2003. Spatial memory performance of freely-moving squirrel monkeys. *Behav. Brain Res.* 140, 175–183. [https://doi.org/10.1016/S0166-4328\(02\)00325-X](https://doi.org/10.1016/S0166-4328(02)00325-X)
- Luppino, G., Murata, A., Govoni, P., Matelli, M., 1999. Largely segregated parietofrontal connections linking rostral intraparietal cortex (areas AIP and VIP) and the ventral premotor cortex (areas F5 and F4). *Exp Brain Res* 128, 181–187. <https://doi.org/https://doi.org/10.1007/s002210050833>
- Lyons, D.M., Lopez, J.M., Yang, C., Schatzberg, A.F., 2000. Stress-level cortisol treatment impairs inhibitory control of behavior in monkeys. *J. Neurosci.* 20, 7816–7821. <https://doi.org/10.1523/jneurosci.20-20-07816.2000>
- Lyons, D.M., Yang, C., Eliez, S., Reiss, A.L., Schatzberg, A.F., 2004. Cognitive Correlates of White Matter Growth and Stress Hormones in Female Squirrel Monkey Adults. *J. Neurosci.* 24, 3655–3662. <https://doi.org/10.1523/JNEUROSCI.0324-04.2004>
- MacLean, J., 1962. *A Stereotaxic Atlas of the Squirrel Monkey's Brain (Saimiri sciureus)*. U.S. Department of Health, Education, and Welfare.
- Marriot, B.M., 1976. *Picture Perception in Squirrel Monkeys (Saimiri sciureus)*. University of Aberdeen.
- Matelli, M., Govoni, P., Galletti, C., Kutz, D.F., Luppino, G., 1998. Superior area 6 afferents from the superior parietal lobule in the macaque monkey. *J. Comp. Neurol.* 402, 327–352. [https://doi.org/10.1002/\(SICI\)1096-9861\(19981221\)402:3<327::AID-CNE4>3.0.CO;2-Z](https://doi.org/10.1002/(SICI)1096-9861(19981221)402:3<327::AID-CNE4>3.0.CO;2-Z)
- McCrea, R.A., Gdowski, G.T., 2003. Firing behaviour of squirrel monkey eye movement-related vestibular nucleus neurons during gaze saccades. *J. Physiol.* 546, 207–224. <https://doi.org/10.1113/jphysiol.2002.027797>

- Miles, R.C., 1958. Color vision in the squirrel monkey. *J Comp Physiol Psych* 51, 328–331.
- Murray, S.G., King, J.E., 1973. Snake avoidance in feral and laboratory reared squirrel monkeys. *Behaviour* 47, 281–289. <https://doi.org/10.1163/156853973X00120>
- Nakata, R., Osada, Y., 2012. The Thatcher illusion in squirrel monkeys (*Saimiri sciureus*). *Anim. Cogn.* 15, 517–523. <https://doi.org/10.1007/s10071-012-0479-9>
- Neal, J.W., Pearson, R.C.A., Powell, T.P.S., 1987. The cortico-cortical connections of area 7b, PF, in the parietal lobe of the monkey. *Brain Res.* 419, 341–346. [https://doi.org/https://doi.org/10.1016/0006-8993\(87\)90605-6](https://doi.org/https://doi.org/10.1016/0006-8993(87)90605-6)
- Nelson, R.J., Sur, M., Felleman, D.J., Kaas, J.H., 1980. Representations of the body surface in postcentral parietal cortex of *Macaca fascicularis*. *J. Comp. Neurol.* 192, 611–643. <https://doi.org/10.1002/cne.901920402>
- Norman, S.L., Maresca, D., Christopoulos, V.N., Griggs, W.S., Demene, C., Tanter, M., Shapiro, M.G., Andersen, R.A., 2021. Single-trial decoding of movement intentions using functional ultrasound neuroimaging. *Neuron* S0896-6273, 00151–3. <https://doi.org/10.1016/j.neuron.2021.03.003>
- Nudo, R.J., Larson, D., Plautz, E.J., Friel, K.M., Barbay, S., Frost, S.B., 2003. A squirrel monkey model of poststroke motor recovery. *ILAR J.* 44, 161–174. <https://doi.org/10.1093/ilar.44.2.161>
- Ogomori, K., Kitamoto, T., Tateishi, J., Sato, Y., Suetsugu, M., Abe, M., 1989. β -protein amyloid is widely distributed in the central nervous system of patients with Alzheimer's disease. *Am. J. Pathol.* 134, 243–251.
- Oikawa, N., Kimura, N., Yanagisawa, K., 2010. Alzheimer-type tau pathology in advanced aged nonhuman primate brains harboring substantial amyloid deposition. *Brain Res.* 1315, 137–149. <https://doi.org/10.1016/j.brainres.2009.12.005>
- Overman, W.H., McLain, C., Ormsby, G.E., Brooks, V., 1983. Visual recognition memory in squirrel monkeys. *Anim. Learn. Behav.* 11, 483–488. <https://doi.org/10.3758/BF03199805>
- Pacella, V., Foulon, C., Jenkinson, P.M., Scandola, M., Bertagnoli, S., Avesani, R., Fotopoulou, A., Moro, V., Thiebaut de Schotten, M., 2019. Anosognosia for hemiplegia as a tripartite disconnection syndrome. *Elife* 8, e46075.

<https://doi.org/10.7554/eLife.46075>

- Pacella, V., Moro, V., 2020. Anatomy and disorders of motor awareness, in: Elsevier (Ed.), *Encyclopedia of Behavioural Neuroscience 2nd Edition*.
- Pálfi, E., Zalányi, L., Ashaber, M., Palmer, C., Kántor, O., Roe, A.W., Friedman, R.M., Négyessy, L., 2018. Connectivity of neuronal populations within and between areas of primate somatosensory cortex. *Brain Struct. Funct.* 223, 2949–2971. <https://doi.org/10.1007/s00429-018-1671-8>
- Pandya, D.N., Sanides, F., 1973. Architectonic parcellation of the temporal operculum in rhesus monkey and its projection pattern. *Z Anat Entwicklungsgesch* 139, 127–161. <https://doi.org/https://doi.org/10.1007/bf00523634>
- Perretta, G., 2009. Non-human primate models in neuroscience research. *Scand. J. Lab. Anim. Sci.* 36, 77–85. <https://doi.org/10.23675/sjlas.v36i1.171>
- Petzinger, G.M., Fisher, B., Hogg, E., Abernathy, A., Arevalo, P., Nixon, K., Jakowec, M., 2006. Behavioral Motor Recovery in the 1-Methyl-4-Phenyl-1,2,3,6- Tetrahydropyridine-Lesioned Squirrel Monkey (*Saimiri sciureus*): Changes in Striatal Dopamine and Expression of Tyrosine Hydroxylase and Dopamine Transporter Proteins. *J. Neurosci. Res.* 83, 332–347.
- Phillips, K.A., Bales, K.L., Capitanio, J.P., Conley, A., Paul, W., Hart, B.A., Hopkins, W.D., Hu, S., Miller, L.A., Michael, A., Nathanielsz, P.W., Rogers, J., Shively, C.A., Lou, M., 2014. Why Primate Models Matter. *Am J Primatol* 76, 801–827. <https://doi.org/10.1002/ajp.22281>
- Piccardo, P., Cervenak, J., Yakovleva, O., Gregori, L., Pomeroy, K., Cook, A., Muhammad, F.S., Seuberlich, T., Cervenakova, L., Asher, D.M., 2012. Squirrel Monkeys (*Saimiri sciureus*) Infected with the Agent of Bovine Spongiform Encephalopathy Develop Tau Pathology. *J. Comp. Pathol.* 147, 84–93. <https://doi.org/10.1016/j.jcpa.2011.09.004>
- Ploog, B.O., 2011. Selective attention to visual compound stimuli in squirrel monkeys (*Saimiri sciureus*). *Behav. Processes* 87, 115–124. <https://doi.org/10.1016/j.beproc.2010.12.015>
- Pons, T.P., Kaas, J.H., 1986. Corticocortical connections of area 2 of somatosensory cortex in macaque monkeys: A correlative anatomical and electrophysiological study. *J. Comp. Neurol.* 248, 313–335. <https://doi.org/10.1002/cne.902480303>

- Porras, G., Li, Q., Bezard, E., 2012. Modeling Parkinson's disease in primates: The MPTP model. *Cold Spring Harb. Perspect. Med.* 2, 1–10. <https://doi.org/10.1101/cshperspect.a009308>
- Pouydebat, E., Borel, A., Chotard, H., Fragaszy, D., 2014. Hand preference in fast-moving versus slow-moving actions in capuchin, *Sapajus* spp., and squirrel monkeys, *Saimiri sciureus*. *Anim. Behav.* 97, 113–123. <https://doi.org/10.1016/j.anbehav.2014.09.008>
- Purisai, M.G., McCormack, A.L., Langston, W.J., Johnston, L.C., Di Monte, D.A., 2005. α -Synuclein expression in the substantia nigra of MPTP-lesioned non-human primates. *Neurobiol. Dis.* 20, 898–906. <https://doi.org/10.1016/j.nbd.2005.05.028>
- Qiu, C., Kivipelto, M., Von Strauss, E., 2009. Epidemiology of Alzheimer's disease: occurrence, determinants, and strategies toward intervention. *Dialogues Clin Neurosci* 11, 111–128.
- Ravnigani, A., Sonnweber, R.S., Stobbe, N., Fitch, W.T., 2013. Action at a distance: Dependency sensitivity in a New World primate. *Biol. Lett.* 9, 2013–2016. <https://doi.org/10.1098/rsbl.2013.0852>
- Rosenblum, L.A., Coe, C.L., 1987. Handbook of Squirrel Monkey Research, *The Journal of Zoo Animal Medicine*. <https://doi.org/10.2307/20094819>
- Roth, G., Dicke, U., 2012. Evolution of the brain and intelligence in primates, 1st ed, *Progress in Brain Research*. Elsevier B.V. <https://doi.org/10.1016/B978-0-444-53860-4.00020-9>
- Rowe, N., 1996. *The pictorial guide to the living primates*.
- Roy, J.E., Cullen, K.E., 2001. Passive Activation of Neck Proprioceptive Inputs Does Not Influence the Discharge Patterns of Vestibular Nuclei Neurons. *Ann. N. Y. Acad. Sci.* 942, 486–489. <https://doi.org/10.1111/j.1749-6632.2001.tb03776.x>
- Sanides, F., 1968. The architecture of the cortical taste nerve areas in squirrel monkey (*saimiri sciureus*) and their relationships to insular, sensorimotor and prefrontal regions. *Brain Res.* 8, 97–124.
- Sawaguchi, T., 1992. The Size of the Neocortex in Relation to Ecology and Social Structure in Monkeys and Apes. *Folia Primatol.* 58, 131–145. <https://doi.org/10.1159/000156620>
- Schilling, K., Gao, Y., Christian, M., Janve, V., Stepniewska, I., Landman, B.A., Anderson, A.W., 2019a. A Web-Based Atlas Combining MRI and Histology of the Squirrel Monkey

- Brain. *Neuroinformatics* 17, 131–145. <https://doi.org/10.1007/s12021-018-9391-z>
- Schilling, K., Gao, Y., Stepniewska, I., Janve, V., Landman, B.A., Anderson, A.W., 2019b. Histologically derived fiber response functions for diffusion MRI vary across white matter fibers—An ex vivo validation study in the squirrel monkey brain. *NMR Biomed.* 32, 1–17. <https://doi.org/10.1002/nbm.4090>
- Schilling, K., Gao, Y., Stepniewska, I., Wu, T.-L., Wang, F., Landman, B.A., Gore, J.C., Chen, L.M., Anderson, A.W., 2017. The VALiDATe29 MRI Based Multi-Channel Atlas of the Squirrel Monkey Brain. *Neuroinformatics* 15, 321–331. <https://doi.org/10.1007/s12021-017-9334-0>
- Schilling, K., Yeh, F.C., Nath, V., Hansen, C., Williams, O., Resnick, S., Anderson, A.W., Landman, B.A., 2019c. A fiber coherence index for quality control of B-table orientation in diffusion MRI scans. *Magn. Reson. Imaging* 58, 82–89. <https://doi.org/10.1016/j.mri.2019.01.018>
- Schott, D., 1975. Quantitative analysis of the vocal repertoire of squirrel monkeys (*Saimiri sciureus*). *Z Tierpsychol* 38, 225–250. <https://doi.org/10.1111/j.1439-0310.1975.tb02002.x>
- Sikali, K., 2020. The dangers of social distancing: How COVID-19 can reshape our social experience. *J. Community Psychol.* 48, 2435–2438. <https://doi.org/10.1002/jcop.22430>
- Snyder, J.M., Hagan, C.E., Bolon, B., Keene, C.D., 2018. *Nervous System, Comparative Anatomy and Histology*. Elsevier Inc. <https://doi.org/10.1016/B978-0-12-802900-8.00020-8>
- Sosa, M., Gillepsie, A.K., Franck, L.M., 2018. Neural Activity Patterns Underlying Spatial Coding in the Hippocampus. *Curr Top Behav Neurosci.* 37, 43–100. https://doi.org/10.1007/7854_2016_462
- Stepniewska, I., Fang, P.C., Kaas, J.H., 2005. Microstimulation reveals specialized subregions for different complex movements in posterior parietal cortex of prosimian galagos. *Proc. Natl. Acad. Sci. U. S. A.* 102, 4878–4883. <https://doi.org/10.1073/pnas.0501048102>
- Stepniewska, I., Fang, P.C.Y., Kaas, J.H., 2009. Organization of the Posterior Parietal Cortex in Galagos: I. Functional Zones Identified by Microstimulation. *J Comp Neurol* 517, 765–782. <https://doi.org/10.1002/cne.22181>

- Stepniewska, I., Gharbawie, O.A., Burish, M.J., Kaas, J.H., 2014. Effects of muscimol inactivations of functional domains in motor, premotor, and posterior parietal cortex on complex movements evoked by electrical stimulation. *J. Neurophysiol.* 111, 1100–1119. <https://doi.org/10.1152/jn.00491.2013>
- Stepniewska, I., Preuss, T.M., Kaas, J.H., 2006. Ipsilateral cortical connections of dorsal and ventral premotor areas in New World owl monkeys. *J. Comp. Neurol.* 495, 691–708. <https://doi.org/https://doi.org/10.1002/cne.20906>
- Stepniewska, I., Preuss, T.M., Kaas, J.H., 1993. Architectonics, somatotopic organization, and ipsilateral cortical connections of the primary motor area (M1) of owl monkeys. *J Comp Neurol* 330, 238–271. <https://doi.org/10.1002/cne.903300207>
- Stevens, R.T., London, S.M., Vania Apkarian, A., 1993. Spinothalamocortical projections to the secondary somatosensory cortex (SII) in squirrel monkey. *Brain Res.* 631, 241–246. [https://doi.org/10.1016/0006-8993\(93\)91541-Y](https://doi.org/10.1016/0006-8993(93)91541-Y)
- Sun, P., Parvathaneni, P., Schilling, K.G., Gao, Y., Janve, V., Anderson, A., Landman, B.A., 2015. Integrating histology and MRI in the first digital brain of common squirrel monkey, *Saimiri sciureus*. *Proc SPIE Int Soc Opt Eng* 9417. <https://doi.org/10.1117/12.2081443>
- Sundt, T.J., Waltz, A.G., 1971. Cerebral ischemia and reactive hyperemia: Studies of cortical blood flow and microcirculation before, during, and after temporary occlusion of middle cerebral artery of squirrel monkey. *Circ. Res.* 28, 426–433.
- Sundt, T.M., Grant, D., Garcia, J.H., 1969. Restoration of Middle Cerebral Artery Flow in Experimental Infarction. *J. Neurosurg* 31, 311–321. <https://doi.org/https://doi.org/10.3171/jns.1969.31.3.0311>
- Sundt, T.M., Michenfelder, J.D., 1972. Focal Transient Cerebral Ischemia in the Squirrel Monkey. *Circ. Res.* 30, 703–712. <https://doi.org/10.1161/01.res.30.6.703>
- Sundt, T.M., Waltz, A.G., 1967. Hemodilution and anticoagulation. Effects on the microvasculature and microcirculation of the cerebral cortex after arterial occlusion. *Neurology* 17, 230–238. <https://doi.org/10.1212/wnl.17.3.230>
- Sur, M., Nelson, R.J., Kaas, J.H., 1982. Representations of the body surface in cortical areas 3b and 1 of squirrel monkeys: Comparisons with other primates. *J. Comp. Neurol.* 211, 177–192. <https://doi.org/10.1002/cne.902110207>

- Tanné-Gariépy, J., Rouiller, E.M., Boussaoud, D., 2002. Parietal inputs to dorsal versus ventral premotor areas in the macaque monkey: evidence for largely segregated visuomotor pathways. *Exp Brain Res* 145, 91–103. <https://doi.org/https://doi.org/10.1007/s00221-002-1078-9>
- Tigges, J., Gordon, T.P., McClure, H.M., Hall, E.C., Peters, A., 1988. Survival rate and life span of rhesus monkeys at the Yerkes regional primate research center. *Am. J. Primatol.* 15, 263–273. <https://doi.org/10.1002/ajp.1350150308>
- Tigges, J., Tigges, M., Anschel, S., Cross, N.A., Letbetter, W.D., McBride, R.L., 1981. Areal and laminar distribution of neurons interconnecting the central visual cortical areas 17, 18, 19, and MT in squirrel monkey *Saimiri*. *J. Comp. Neurol.* 202, 539–560. <https://doi.org/10.1002/cne.902020407>
- Tsujimoto, S., Sawaguchi, T., 2002. Working memory of action: A comparative study of ability to selecting response based on previous action in New World monkeys (*Saimiri sciureus* and *Callithrix jacchus*). *Behav. Processes* 58, 149–155. [https://doi.org/10.1016/S0376-6357\(02\)00041-4](https://doi.org/10.1016/S0376-6357(02)00041-4)
- Ungerleider, L.G., Mishkin, M., 1982. Two cortical visual systems, in: Ingle, D.J., Goodale, M.A., Mansfield, R.J.W. (Eds.), *Analysis of Visual Behavior*. Cambridge : MIT Press, pp. 549–586.
- van Dongen, P.A.M., 1998. Brain Size in Vertebrates, in: *The Central Nervous System of Vertebrates*. Springer, Berlin, Heidelberg. https://doi.org/https://doi.org/10.1007/978-3-642-18262-4_23
- Vanier, D.R., Sherwood, C.C., Smaers, J.B., 2019. Distinct Patterns of Hippocampal and Neocortical Evolution in Primates. *Brain. Behav. Evol.* 93, 171–181. <https://doi.org/10.1159/000500625>
- Vermilyea, S.C., Emborg, M.E., 2015. α -Synuclein and nonhuman primate models of Parkinson's disease. *J. Neurosci. Methods* 255, 38–51. <https://doi.org/10.1016/j.jneumeth.2015.07.025>
- Walker, L.C., 1997. Animal models of cerebral β -amyloid angiopathy. *Brain Res. Rev.* 25, 70–84. [https://doi.org/10.1016/S0165-0173\(97\)00017-9](https://doi.org/10.1016/S0165-0173(97)00017-9)
- Walker, L.C., 1993. Comparative neuropathology of aged nonhuman primates. *Neurobiol. Aging* 14, 667. [https://doi.org/10.1016/0197-4580\(93\)90064-I](https://doi.org/10.1016/0197-4580(93)90064-I)

- Walker, L.C., Masters, C., Beyreuther, K., Price, D.L., 1990. Amyloid in the brains of aged squirrel monkeys. *Acta Neuropathol.* 80, 381–387. <https://doi.org/10.1007/BF00307691>
- Waltz, A.G., Sundt, T.J., 1967. The microvasculature and microcirculation of the cerebral cortex after arterial occlusion. *Brain* 90, 681–694.
- Wang, Z., Chen, L.M., Negyessy, L., Friedman, R.M., Mishra, A., Gore, J.C., Roe, A.W., 2013. The relationship of anatomical and functional connectivity to resting state connectivity in primate somatosensory cortex. *Neuron* 78, 1116–1126. <https://doi.org/10.1016/j.neuron.2013.04.023>
- Waymel, A., Friedrich, P., Bastian, P.A., Forkel, S.J., Thiebaut de Schotten, M., 2020. Anchoring the human olfactory system within a functional gradient. *Neuroimage* 216, 116863. <https://doi.org/10.1016/j.neuroimage.2020.116863>
- Welker, W.I., Benjamin, R.M., Miles, R.C., Woolsey, C.N., 1957. Motor effects of stimulation of cerebral cortex of squirrel monkey (*Saimiri sciureus*). *J Neurophysiol* 20, 347–364. <https://doi.org/https://doi.org/10.1152/jn.1957.20.4.347>
- Weller, R.E., 1988. Two cortical visual systems in Old World and New World primates. *Prog. Brain Res.* 75, 293–306. [https://doi.org/10.1016/S0079-6123\(08\)60487-2](https://doi.org/10.1016/S0079-6123(08)60487-2)
- Weller, R.E., LeDoux, M.S., Toll, L.M., Gould, M.K., Hicks, R.A., Cox, J.E., 2006. Subdivisions of inferior temporal cortex in squirrel monkeys make dissociable contributions to visual learning and memory. *Behav. Neurosci.* 120, 423–446. <https://doi.org/10.1037/0735-7044.120.2.423>
- Welles, J.F., 1976. A comparative study of manual prehension in anthropoids. *Sauget. Mitt.* 24, 26–38.
- Williams, L., Glasgow, M., 2000. Squirrel monkey behavior in research. *ILAR J.* 41, 26–36. <https://doi.org/10.1093/ilar.41.1.26>
- Winter, P., Ploog, D., Latta, J., 1966. Vocal repertoire of the squirrel monkey (*Saimiri sciureus*), its analysis and significance. *Exp. Brain Res.* 1, 359–384. <https://doi.org/10.1007/BF00237707>
- Wollberg, Z., Newman, J.D., 1972. Auditory Cortex of Squirrel Monkey: Response Patterns of Single Cells to Species-Specific Vocalizations. *Science* (80-.). 175, 212–214. <https://doi.org/10.1126/science.175.4018.212>

Wu, R., Wang, F., Yang, P.F., Chen, L.M., 2017. High-resolution functional MRI identified distinct global intrinsic functional networks of nociceptive posterior insula and S2 regions in squirrel monkey brain. *Neuroimage* 155, 147–158. <https://doi.org/10.1016/j.neuroimage.2017.04.067>

Zander, S.L., Weiss, D.J., Judge, P.G., 2013. The interface between morphology and action planning: A comparison of two species of New World monkeys. *Anim. Behav.* 86, 1251–1258. <https://doi.org/10.1016/j.anbehav.2013.09.028>

Journal Pre-proof