Brain Connectivity in *Ateles geoffroyi*: Resting-State Functional Magnetic Resonance Imaging of Working Memory and Executive Control

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Keywords

Functional connectivity · Working memory · Executive control · Nonhuman primates · Brain evolution · New World monkeys

Abstract

The objective of this research was to describe the organization and connectivity of the working memory (WM) and executive control (EC) networks in *Ateles geoffroyi* in resting-state conditions. Recent studies have shown that resting-state activity may underlie rudimentary brain functioning, showing that several brain regions can be tonically active at rest, maximizing the efficiency of information transfer while preserving a low physical connection cost. Whole-brain resting-state images were acquired from three healthy adult *A-*

teles monkeys (2 females, 1 male; mean age 10.5 ± SD 2.5 years). Data were analyzed with independent component analysis, and results were grouped together using the GIFT software. The present study compared the EC and WM networks obtained with human data and with results found in the literature in other primate species. Nine resting-state networks were found, which were similar to resting networks found in healthy human adults in the prefrontal basal portion and frontopolar area. Additionally, components of the WM network were found to be extending into the hypothalamus and the olfactory areas. A key finding was the discovery of connections in the WM and EC networks to the hypothalamus, the motor cortex, and the entorhinal cortex, suggesting that information is integrated from larger brain areas. The correlated areas suggest that many elements of WM and EC may be conserved across primate species. Char-

acterization of these networks in resting-state conditions in nonhuman primate brains is a fundamental prerequisite for understanding of the neural bases underlying the evolution and function of this cognitive system. © 2019 S. Karger AG, Basel

Introduction

Working memory (WM) is the brain system that provides temporary storage and the ability to manipulate information over short time periods when perceptual input is temporarily absent [Baddeley, 1986; Just and Carpenter, 1992; Pasternak and Greenlee, 2005; Cowan, 2008; Rottschy et al., 2012]. Such information is necessary for complex cognitive functions such as language comprehension, learning, spatial orientation, and reasoning, which are essential to many human behaviors [Baddeley, 1986; Just and Carpenter, 1992; Pasternak and Greenlee, 2005; Cowan, 2008; Rottschy et al., 2012]. Unlike short-term memory, which only refers to information storage, WM includes the handling and transfer of inputs (e.g., visual or tactile sensory information) and outputs (e.g., manual actions or speech) [Baddeley, 2003; Engle and Kane, 2004; Rottschy et al., 2012]. Our understanding of the evolution of WM is limited [Carruthers, 2013]. Most comparative studies are based on cognitive experiments, with experimental paradigms that are often adapted from human studies [Ericsson and Kintsch, 1995; Inoue and Matsuzawa, 2007; Botvinick et al., 2009; Carruthers, 2013]. As such, there has been very little comparative research on WM abilities across species.

Neuroimaging studies that have attempted to explain the neural basis of WM in humans have found a correlation with the executive control (EC) function [Baddeley, 1986; Just and Carpenter, 1992; Carpenter et al., 2000]. EC serves to regulate the system that allocates and coordinates attentional resources for cognitive tasks [Baddeley, 1996]. It involves several brain regions, including the frontopolar area, the prefrontal cortex (PFC), and the anterior cingulate [Smith and Jonides, 1999; Bunge et al., 2000; Osaka et al., 2003; Harrison and Tong, 2009; Emrich et al., 2013; Lee et al., 2013; Sreenivasan et al., 2014]. Simpler processes such as the active organization, storage, and retrieval of information involve the mid-ventrolateral PFC (Brodmann area 46 y 9/46) [Curtis and D'Esposito, 2003]. In contrast, distinctive elements of WM [Baddeley, 2003; Curtis and D'Esposito, 2003], such as coding, scanning, and

active manipulation of information to perform additional tasks, primarily occur in the mid-dorsolateral PFC (Brodmann area 45 y 47/12) [Curtis and D'Esposito, 2003; Lee et al., 2013; Sreenivasan et al., 2014]. Additional studies, not limited to the analysis of regions of interest, have shown that the experimental tasks typically used to study WM actually activate a broader network that primarily involves the PFC, premotor regions, and certain regions of the parietal lobe, with significant variations being observed among other regions due to the type of task and stimulus used in each experimental paradigm [Niendam et al., 2012; Rottschy et al., 2012].

The memory and other cognitive skills of the spider monkey have been reported to be outstanding under experimental conditions, particularly in relation to its olfactory memory [Hernandez Salazar et al., 2003; Laska et al., 2003, 2006; Amici et al., 2008, 2010]. For example, Laska et al. [2003] conducted a comparative study originally proposed for assessing olfactory performance in an Old World primate, the macaque pig-tail. The spider monkeys were trained to answer a test that simulated olfactory foraging behavior based on discriminating between two odorants presented simultaneously in a paradigm of instrumental conditioning, rewarded with food. In the test, they were presented with a device with two containers fitted with strips of odorized paper indicating the presence or absence of a food reward inside one of the containers. On the basis of repeated tests, the spider monkeys learned to pay attention to the odor stimuli and to use them as indications to open the container and obtain a reward in the form of food. In this experiment, Laska et al. [2003] highlighted discriminatory ability, odor memory, and odor learning performance and concluded that the *Ateles* possess excellent retention of the reward value of the pairs of odors previously learned for up to 4 weeks. Amici et al. [2010] conducted a comparative study of cognitive abilities in four great apes and three monkey species (spider monkeys, capuchin monkeys, and long-tailed macaques). The delayed match-to-sample task, where three conditions were tested (no delay, a 30-s delay, and a 30-min delay) to evaluate memory, showed that spider monkeys performed better than the gorillas and other monkeys evaluated [Amici et al., 2010]. These studies support the existence of an information storage and handling system, as in other nonhuman primates, which operates under the same principles of using cognitive resources for handling information stored in short-term memory.

Resting-state functional magnetic resonance imaging (fMRI) involves the measurement of functional brain activity in the absence of task engagement. Low-frequency fluctuations (less than 0.1 Hz) in the blood oxygen level-dependent (BOLD) signals are detected [Fox and Greicius, 2010] and can be observed regardless of the type of anesthetic used [Horwitz, 2003; Vincent et al., 2007; Kanurpatti et al., 2008; Zhao et al., 2008; Hutchison et al., 2010; Wu et al., 2016]. Functional connectivity is defined as the temporal correlations between brain structures [Beckmann et al., 2005; Bonnefond et al., 2017]. Communication between brain regions plays a fundamental role in cognitive processes [Hampson et al., 2002; Proal et al., 2011].

Independent component analysis (ICA) is an ideal technique for identifying features that describe the activity in a dispersed network, by decomposing the time series of the BOLD fluctuations into components, or factors, in which the statistical independence of each with respect to the others is maximized [Hampson et al., 2002; Damoiseaux et al., 2006]. Data-driven approaches are useful when the regions involved in a particular network are unknown, since no hypothesis or model is assumed before analysis. ICA was used in the present research since functional connectivity networks are unknown in spider monkeys [Hampson et al., 2002; Beckmann et al., 2005; Damoiseaux et al., 2006]. Distinct networks with potential functional relevance have been identified in humans [Biswal et al., 1995; Raichle et al., 2001; Hampson et al., 2002; Greicius et al., 2003; Beckmann et al., 2005; Damoiseaux et al., 2006], and manifest in highly organized patterns of coherence across mammalian species [Rilling et al., 2007; Vincent et al., 2007; Pawela et al., 2008; Kojima et al., 2009; Cabral et al., 2011; Barks et al., 2015; Platas-Neri et al., 2015].

In this study, WM and EC networks in spider monkeys are described by comparing these connectivity networks with those obtained in other primates [Rilling et al., 2007; Vincent et al., 2007; Hutchinson and Everling, 2012] and humans [Biswal et al., 1995; Raichle et al., 2001; Hampson et al., 2002; Damoiseaux et al., 2006; Rottschy et al., 2012]. WM and EC networks are useful and interesting because they are related to higher-level cognitive abilities, which can reveal information about how the cognitive system operates and evolves [Rilling et al., 2007; Cabral et al., 2011]. Although WM and EC in humans have been intensively studied, little is known about their organization, connectivity, and evolution in the primate order. Studies using resting-state fMRI in nonhuman primates, although still incipient, represent a fundamental compo-

nent in the understanding of the neural bases of resting-state and complement cognitive experiments by helping to resolve matters of debate in the literature, such as the implications in the homologous brain connectivity regions [Rilling et al., 2007; Cabral et al., 2011; Carruthers, 2013].

Materials and Methods

Animal Study

Subjects. Whole-brain images were acquired from three healthy adult spider monkeys (2 females, 1 male; mean age $10.5 \pm \text{SD}$ 2.5 years). The animals were socially housed at the National Institute of Psychiatry, Ramón de la Fuente. The group and enclosure details can be seen in Platas-Neri et al. [2015].

Experimental Protocol. Animals were anesthetized for the acquisition of brain images, with a minimum dose of ketamine (10 mg/kg, Pisa[®]) and atropine (0.05 mg/kg, ABBOJECT[®]), and then maintained with Zoletil 50 tiletamine-zolazepam (0.2 mg/kg, Virbac[®]). The anesthetic allowed spontaneous respiration throughout the image acquisition protocol. A pediatric head immobilizer (Medihelp) was used to prevent motion-related artifacts. This equipment used plastic compartments filled with air to immobilize the animal's head, ensuring that head motion was <1.5 mm in all directions for the duration of the experiment. Once the image acquisition had been completed, the anesthetic was no longer administered and animals were placed in a recuperation cage for a period of 12 h. The animals were kept there until they responded to stimuli and all their vital signs were normal. After this period, animals were reintroduced into the group. During the experiment and recovery time, a veterinary team was present to measure the animals' physiological parameters and to monitor their well-being.

Image Acquisition. During a 50-min procedure (which included animal anesthesia and preparation in the scanner), anatomical images followed by resting-state sequences were acquired. Experiments were performed on a 3-T Achieva scanner (Philips Achieva, Best, Netherlands) using an eight-channel (SENSE knee) radiofrequency coil. A gradient-echo (GE) echo-planar imaging (EPI) sequence was used to obtain BOLD images of the resting state, with the following imaging parameters: 20 axial slices covering the whole of the brain, TR/TE = 2,200/30 ms, averages = 1, matrix 128×128 with a 1.90×1.90 mm in-plane resolution and slice thickness of 3 mm (no gap between slices). A total of 200 brain volumes were acquired during a scanning time of 7 min 20 s. An anatomical image was obtained using a T₁-3D-GE sequence; parameters employed were TR = 10.6 ms, TE = 5.18 ms, field of view 150×150 mm, matrix 256×256 with a 0.59×0.59 mm in-plane resolution, 1 mm slice thickness, and flip angle = 8° .

Data Processing. In order to identify resting-state networks in our subjects, MRI data were first preprocessed and then a grouped ICA was performed using the GIFT software (<http://icatb.sourceforge.net/>). A more detailed description of this analysis can be seen in previous reports [de Celis Alonso et al., 2014; Platas-Neri et al., 2015]. Batch preprocessing of images was carried out using the SPM12 software (<http://www.fil.ion.ucl.ac.uk/spm/>). First, functional and anatomical data were converted from DICOM to the ANALYZE format. Seven images from the resting-state batch were

eliminated to allow for stabilization of the T_1 signal. Images were then slice time-corrected (ascending interleaved), realigned to the first EPI volume analyzed for each subject, and then coregistered to their corresponding anatomical T_1 image. Due to the anesthetic, no relevant motion artifacts were found in our study: motion during scanning was always under the size of one voxel and never exceeded two degrees. As no standard template exists of the *Ateles* brain, the resting-state scans from all study subjects were then normalized to a mean image obtained from an average of the EPI data from the fMRI study of the first monkey (a male). As no template exists for these monkeys, it was impossible to mask cerebrospinal fluid and white matter in these data. It was also impossible to obtain nuisance measurements to be included in the analysis, so this was not done either. Analysis proceeded by smoothing the data with a kernel of $4 \times 4 \times 4 \text{ mm}^3$ (full width at half maximum). Finally, the data were de-trended (linear and quadratic trends) and filtered to keep frequencies between 0.001 and 0.1 Hz.

Grouped ICA. When the preprocessing was completed, resting-state networks were obtained by applying grouped ICA using the GIFT software toolbox. The standard grouped ICA analysis was completed, with parameter initialization, group reduction, ICA calculation, back reconstruction, component calibration, and group statistics. Forty independent components were suggested as of interest by the GIFT software, each of which was assessed under a $z > 3.33$ threshold ($p < 0.001$). The selection of the number of components is always arbitrary, but similar to those of previously published papers (e.g., grouped ICA of resting-state data) [Schöpf et al., 2010]. Noisy and artefactual components were eliminated, based on a visual comparison with human resting-state data obtained in healthy subjects (30 in total) [Biswal et al., 1995; Damoiseaux et al., 2006]. The remaining thirteen components were presented, with results projected onto the anatomical T_1 image of one subject. Our results were compared with those of human studies by highlighting the brain areas involved in both networks for both cases and after comparing the total number of activated voxels in each network.

Human Study

To compare *Ateles* findings with those of humans, data from three human volunteers were used to obtain their grouped resting-state networks. It is important to note that in order to perform a proper comparison, the same methodology as that used for the analysis of *Ateles* monkeys was employed here.

Subjects. All data were obtained from hospital records on healthy adult humans. Three adults (2 females, 1 male; mean age $25.6 \pm \text{SD } 6.5$ years) were considered. The age of the human subjects and the low number was chosen to mirror the monkey group.

Experimental Protocol and Image Acquisition. The human subjects were not anesthetized for this study. During the scanning, subjects were instructed to keep their eyes closed and relax, think of nothing in particular, and not fall asleep. In the procedure, anatomical followed by resting-state data were obtained. Experiments were performed on a 3-T Skyra scanner (Siemens, Erlangen, Germany) using an eight-channel head radiofrequency coil. A GE EPI sequence was used to obtain BOLD images of the resting state, with the following imaging parameters: 44 axial slices covering the whole of the brain, TR/TE = 1,500/30 ms, averages = 1, matrix 94×94 with a $2.66 \times 2.66 \text{ mm}$ in-plane resolution and slice thickness of 3.5 mm (with no gap between slices). A

total of 240 brain volumes were acquired during a scanning time of 6 min. An anatomical image was obtained using a T_1 -3D-GE sequence. Parameters employed were: TR = 10.6 ms, TE = 5.18 ms, field of view $250 \times 250 \text{ mm}$, matrix 320×320 with a $0.781 \times 0.781 \text{ mm}$ in-plane resolution, 3.5 mm slice thickness, and no flip angle.

Data Processing and Grouped ICA. Since the purpose of this part of the study was to mirror animal analysis, work on human data was performed in a way as similar as possible. This included not performing analytical steps commonly used for human data processing but not available for monkeys (e.g., no regression of nuisance variables and no use of brain atlases). The only difference between the analyses was that the smoothing kernel used in the human study was $5.3 \times 5.3 \times 5 \text{ mm}^3$. This was 50% more than the size of the voxels used in this study, and had the same proportion as the one followed for the *Ateles* monkeys study.

Number of Voxels in Resting-State Networks. In order to calculate the number of voxels which were part of a given resting-state network, each one was given a threshold value of $z > 3.33$ after opening them using the ImageJ software (ImageJ 1.51k, NIH, USA). Afterwards the number of voxels was counted using the measure and histogram options. Each resting-state network was calculated independently both on human and animal data. The number of voxels over the threshold was measured and then multiplied by $2 \times 2 \times 2 \text{ mm}^3$, which was the volume of a voxel in these sets of images. The mask of the whole brain produced during preprocessing steps was used in both cases (human and animal) to measure the total volume of the brain for each species. Percentages for each network were then calculated using this total brain volume as the 100% value.

Results

The group-level ICA yielded nine networks of interest, identified through spatial cross-correlation and with reference to the previous literature in healthy human brains [Damoiseaux et al., 2006]. The networks are named on the basis of their close correspondence with task-based networks: 2 executive function networks (WM and EC); striate network, visual network; 2 default-mode networks, 1 memory network (right), 1 motor network; and 1 auditory network [Damoiseaux et al., 2006] (Fig. 1). Various components were projected onto T_1 axial of the first subject (Fig. 1).

In order to mirror the animal networks obtained and to verify the consistency of the methodology followed in this study, the same analysis was performed on a human sample following the same methodology (Fig. 2). The group-level ICA yielded 11 networks of interest: 1 executive function network (in which WM and EC were merged); 1 language network; 1 visual network; 1 motor network; 1 dorsal salience network; 2 memory networks (left and right); 1 auditory network; 2 default-mode net-

Fig. 1. Resting-state networks in the spider monkey. Networks are presented overlaid on axial slices of a monkey's brain. The networks shown are executive control, working memory, visual, ventral salience, dorsal salience, right memory, audition, default parts 1 and 2, extrastriate, and motor (left and right). The pseudocolored scale indicates levels of statistical significance.

works; and 1 extrastriate network. Different components were projected onto T_1 axial of the first subject.

The main difference in the resting-state networks obtained was that the executive networks of the monkeys (EC and WM) were separated into two components and merged for the human group. Although memory networks are not addressed in this study, it is important to point out that another difference found was that *Ateles* only has one memory network, while the human group has two memory networks (Fig. 1, 2 and online suppl. Table S1; see www.karger.com/doi/10.1159/000499177 for all online suppl. material).

Resting-State Networks in Ateles (EC and WM)

Two networks were identified relating to EC and WM (online suppl. Table S2). The WM network included the medial prefrontal cortices and orbital prefrontal, spanning the cingulate cortex, septal areas, and olfactory

structures, as well as the olfactory bulb, both amygdalae, and the preoptic and hypothalamic areas (Fig. 3). A correlation was observed in a large number of structures at the base of the brain and the medial cortex. Figure 3a shows how correlation begins in the lower hypothalamus, rises to the primary olfactory areas, the olfactory band and bulb, and spreads to the mesial part of both temporal lobes at the level of the anterior hippocampus and the amygdala (Fig. 3b–e). At the top, the anterior preoptic, septum, and hypothalamic region is synchronized, occupying a discrete portion of the corpus callosum in regions II and III, and the anterior part of the internal frontal gyrus as well as the anterior middle cingulate (Fig. 3e, f). Finally, it rises as a small portion towards the anterior part of the cingulate gyrus (Fig. 3g). Significant regions were observed symmetrically across both hemispheres (i.e., bilaterally). The blue to yellow colors indicate z values, ranging from -10.0 to 10.0 (Fig. 3, 4).

Fig. 2. Resting-state networks in humans. Networks are presented overlaid on axial slices of a human's brain. Data was calculated with the same methodology as that in Figure 1. The networks shown are executive control and working memory (merged), visual, ventral salience, dorsal salience, right and left memory, audition, default parts 1 and 2, extrastriate, and motor (left and right). The pseudo-colored scale indicates levels of statistical significance.

The EC network in the *Ateles* emerged from the middle portion of the corpus callosum and septum, included the medial frontal cortex, and extended from the central cingulate area (Fig. 4a, b). In the section immediately above this, one can clearly see the correlation of the anterior cingulate, in front of the limit of the central sulcus

(Fig. 4a–c). This activation pattern is seen at the top of the brain, above the internal frontal gyrus in the anterior and superior part (Fig. 4d), covering a small area behind the central sulcus. In the paracentral areas in this site, it is also located at the level of the dorsal edge of the brain (Fig. 4e, f). Significant regions are observed symmetrically across

Fig. 3. Working memory brain activity in the spider monkey. The figure shows seven axial slices, with the spatial color-coded z map components overlaid on the echo-planar image obtained from the mean for the three subjects. A higher z score (yellow) represents a higher correlation between the time course of that voxel and the mean time course of this component. Mean components comprise the hypothalamus (**a**), the amygdalae (**b**), the medial and secondary olfactory areas (**c**), the olfactory structures (**d**), the olfactory tract and bulb (**e**), the septal areas (**f**), and the gyrus of the cingulum (**g**).

both hemispheres (i.e., bilaterally). There is also a connectivity pattern in the upper, bilateral prefrontal areas.

Resting-State Networks in Humans (WM-EC)

The following pattern was found, which is involved in the EC and WM networks [Beckmann et al., 2005; Damoiseaux et al., 2006]. The network emerges at the level of the dorsal border of the hemispheres in paracentral regions, predominating on the right side (Fig. 2, WM-EC, 1). There is also a correlation between the central and upper regions, at the level of convexity, with the right side predominating (Fig. 2, WM-EC, 2), and, discretely, in the middle parietal region of the convexity, it predominates on the right side and a portion of the precentral area (Fig. 2, WM-EC, 3). There is discrete connectivity in the medial parietal region (Fig. 2, WM-EC, 4, 5), and a bilateral cluster in the frontopolar, frontobasal, and anterior

cingulate areas, up to the knee of the corpus callosum without including it, going slightly above it (Fig. 2, WM-EC, 5–8). In both occipital poles, predominating on the right side, a discrete correlation is observed (Fig. 2, WM-EC, 8–10). Components are also observed in the cerebellum, particularly on the right side and at the junction with the anterior and lateral faces (Fig. 2, WM-EC, 11, 12). Similar components were found to those observed in healthy humans in the literature [Biswal et al., 1995; Raichle et al., 2001; Hampson et al., 2002; Greicius et al., 2003; Beckmann et al., 2005; Damoiseaux et al., 2006], consistent with what was found in *Ateles* (Fig. 3, 4), confirming the hypothesis of a possibly related WM system in spider monkeys.

As comparison between networks has been mainly qualitative up to now, an effort was made to obtain quantitative data. Online supplementary Table S1 presents the

Fig. 4. Executive control in the spider monkey. The figure shows seven axial slices, with the spatial color-coded z map components overlaid on the echo-planar image obtained from the mean for the three subjects. A higher z score (yellow) represents a higher correlation between the time course of that voxel and the mean time course of this component. Mean components comprise the corpus callosum (**a**), the medial cingulate cortex (**b**), the medial cingulate cortex and paracentral areas (**c**), the paracentral areas and frontal gyrus (**d**), and the paracentral areas (**e–g**).

number of activated voxels, which belong to each network for both groups. Calculations were performed on the averaged results, so no statistics are possible. Even if volume differences did not reach statistical significance when comparing all networks together with a Student t test ($p = 0.262$), it could be observed that 6 of the 9 networks were proportionately larger in humans, including the WM and EC networks.

Discussion

In this project, 9 resting-state functional connectivity networks were recognized in the spider monkey. These networks overlap considerably with resting-state brain activity in humans, macaques, and chimpanzees [Damoiseaux et al., 2006; Rilling et al., 2007; Hutchison et al.,

2011; Hutchinson and Everling, 2012]. These studies have described between 8 and 11 circuits that appeared consistent with what its know about neurobiological systems and with what we found in this study. Although the methods of identification and the nomenclature for naming them have been different, similar anatomical patterns have been detected through temporal correlations. The correlated areas suggest that many elements of the resting state may be conserved across primate species and even other mammals [Damoiseaux et al., 2006; Vincent et al., 2007; Kannurpatti et al., 2008; Pawela et al., 2008; Hutchison et al., 2011; Hutchinson and Everling, 2012; Barks et al., 2015; Wu et al., 2016]. Interestingly, recent works have argued that resting-state activity may underlie rudimentary brain functioning, showing that several brain regions can be tonically active at rest, maximizing the efficiency of information transfer while preserving a low physical

connection cost [Bullmore and Sporns, 2009; Hutchinson and Everling, 2012]. This could have been essential for survival in a socioecological context like that shared by the first primates more than 100 million years ago [Allman, 1999; Sporns, 2010].

Since the default mode network was the first intrinsic network to be described, it has been studied in the greatest detail. However, many studies on humans and non-human primates have also identified executive function networks in resting-state data, and although, as it was mentioned earlier, identification methods and the nomenclature for labeling them vary, similarity in the functional connectivity can be detected in these studies [Damoiseaux et al., 2006; Vincent et al., 2007; Hutchison et al., 2011; Hutchinson and Everling, 2012]. Nevertheless, many of the structures we find in the WM network are limbic. We consider that since the concept, characterization, and delimitation of the limbic system has been controversial throughout history [LeDoux, 1991; Kötter and Meyer, 1992; Roxo et al., 2011], it does not seem appropriate to use this term to label the network. In any case, we found the proposal for labeling the networks of Hutchison et al. [2011] and Ghahremani et al. [2017] to be closer to what was found in this research. However, we decided to call the network WM because the regional activation studies show that WM tasks in monkeys are associated with these areas [Owen, 1997, 2000; Inoue et al., 2004; D'Esposito and Postle, 2015]. At the same time, many of these areas are also involved in EC, episodic processing, declarative memory, and the phonological loop [Baddeley, 2000, 2003], so we cannot claim they are specifically implicated in WM, and in fact, they often overlap with other functions.

In this context, the objective was to identify the neural correlates of the WM and EC networks and to highlight regional similarities with other primates. The main difference found between the executive networks (EC and WM) is that in *Ateles*, they are separated into two components, whereas in the human group studied, they appear as a single network, which concurs with what is reported in other research [Damoiseaux et al., 2006 (Fig. 1j)]. Moreover, in humans there is an area, not observed in the spider monkey, which are the central regions, mainly motor areas, on the dorsolateral side of the hemisphere. This, on the one hand, reflects the fact that although the brains are comparable, there are substantial neuroanatomical differences in keeping with the evolutionary history of each species. This lack of connectivity in *Ateles* between the networks may suggest an incipient homology [Laubichler, 2000], as has been pro-

posed with other networks such as the ventral salience subnetwork in macaques [Touroutoglou et al., 2012]. Nevertheless in *Ateles*, components of the WM-EC were found extending into the hypothalamus and the olfactory areas. The active voxels in spider monkeys corresponded to olfactory areas, the preoptic-hypothalamic areas, and the septal area, as well as the frontopolar and hippocampal areas (Fig. 3, 4).

Data published on macaques by Vincent et al. [2007] and Hutchison et al. [2010, 2011] and on marmosets by Ghahremani et al. [2017] do not specifically mention EC-WM networks. They refer to the frontal and frontoparietal network, which consists of regions known to be involved in EC and WM functions [Koshino et al., 2014], where strong similarities were observed in *Ateles* in the regions associated with EC, particularly in the frontopolar area and the medial PFC [Hutchison et al., 2011 (Fig. 1e); Hutchinson and Everling, 2012 (Fig. 2: executive network)]. However, if the frontoparietal networks are compared in the resting state as described by Hutchison et al. [2010, 2011] in macaques with what we found in our study, similarities were seen in the components reported but that in *Ateles*, there is a greater correlation in the frontomedial structures of the brain, such as the cingulate gyrus.

These results suggest that the WM network in spider monkeys, as well as humans and macaques, could be integrating different types of information (e.g., verbal, spatial, and olfactory), and confirm the evidence from neurophysiological findings in monkeys showing simultaneous connectivity of different areas of the brain in the resting state, which compromise WM [Napier and Napier, 1985; Jonides et al., 1993; Courtney et al., 1997].

The size of networks, when considering either number of voxels or percentage of brain volume, showed a tendency to be larger in humans when compared to *Ateles*. This was so in the two networks on which this work is focused (WM and EC). These differences never achieved statistical significance, but were in concordance with previous reports on nonhuman primates [Hutchison et al., 2011; Hutchinson and Everling, 2012].

WM was addressed by subdividing it into verbal, spatial, and olfactory, since in the species studied these are the most relevant modalities, while in humans it is verbal and visual [Paulesu et al., 1993; Ungerleider et al., 1998].

Verbal WM

Ateles has a frontal lobe with a simpler, smaller configuration, almost exclusively limited to the straight gyrus, olfactory sulcus, olfactory bulb, and olfactory tract.

However, as in humans, voxels are seen to be associated with verbal WM in the anterior frontal cortex [Ungerleider et al., 1998; Raichle et al., 2001; Damoiseaux et al., 2006; Rottschy et al., 2012] (Fig. 3). The anterior frontal cortex, and specifically Brodmann area 10 in humans, has been implicated with WM and branching operations, in which subjects maintain a primary goal in WM while at the same time processing tasks related to a secondary goal in tasks with a high audio-verbal demand (Fig. 2) [Petrides et al., 1993; Ungerleider et al., 1998; Koechlin et al., 1999]. This approach makes us wonder whether there might be a behavioral correlate derived from an anatomical feature similar to that of humans, such as area 10, and whether it is present in *Ateles*.

The vocal communication system in *Ateles* can provide the receiver with information on the identity of the sender and their location, as well as the type of meeting (agonistic or affiliative interactions) [Chapman et al., 1989]. Obviously, although members of the genus *Ateles* do not have a recognizable interindividual communication system that is as diversified as that of humans, they do have a relatively sophisticated communication system that adequately serves their needs and perhaps beyond.

Spatial WM

In humans, the mid-ventrolateral and mid-dorsolateral areas of the PFC may be activated in WM tasks involving spatial localization [Petrides et al., 1993; Courtney et al., 1997; Koechlin et al., 1999]. Although these analyses have mainly been conducted in cognitive tasks where subjects are conscious and locations have been previously learned [Petrides et al., 1993; Koechlin et al., 1999], resting-state studies also support this statement, showing correlation in the lateral parts of the prefrontal regions.

Research on chimpanzees' resting-state brain activity [Rilling et al., 2007; Barks et al., 2015] also shows activity in the lateral PFC and suggests that this could indicate that, like humans, chimpanzees (and probably *Ateles*) are not restricted to thinking about what can be directly perceived in the environment, and may instead generate internal thoughts when perceptual input is temporarily absent [Rilling et al., 2007; Barks et al., 2015]. This would involve maintaining visual representations of possible movements, coupled with an awareness of the flow of information in and out of memory [Napier and Napier, 1985; Dubreuil et al., 2015]. The neuronal correlate shows that in *Ateles*, as in other primates as macaques, representations of WM are necessary for selecting the appropriate action, depending on the contingencies of the moment

[Jonides et al., 1993; Goldman-Rakic, 1995; Rilling et al., 2007; Barks et al., 2015]. This pattern of brain activity could reflect the maintenance of relevant information before motor action, in other words, retrospective sensorial information is maintained until the motor response is performed [Wang, 2001].

At the same time, connectivity patterns were observed in the *Ateles* group in the dorsolateral PFC in the EC network, although in the WM only a medial and orbital correlation is seen (Fig. 1, EC and WM, 3, 4). Various electrophysiological studies on macaques and humans state that the dorsolateral PFC has extremely important functions such as coding, scanning, and manipulating information, especially during delayed recognition tasks [e.g., Funahashi et al., 1993; Goldman-Rakic, 1988; Pessoa et al., 2002; Sakai et al., 2002]. On the other hand, fMRI findings agree that sustained neural activity during tasks with delay periods involving the WM is not only observed in the dorsolateral PFC, but is also present in the posterior parietal cortex, temporal inferior cortex, and premotor cortex [Niendam et al., 2012]. According to this approach, dorsolateral PFC related to EC would be responsible for the strategic processes (coding) required to maintain an amount of information that would otherwise saturate WM [Rypma and D'Esposito, 1999]. However, it has been reported that in the absence of tasks (resting state), there is a significant reduction in regional cerebral blood flow to the dorsolateral PFC [Niendam et al., 2012]. This would coincide with the article by Damoiseaux et al. [2006] on resting states in humans, which describes frontal parietal networks associated with WM, while the dorsolateral PFC region is not observed as part of these networks, which would coincide with our results.

Olfactory Information

Our results showed that, as part of the WM network, spider monkeys displayed connectivity in the olfactory areas, including the olfactory cortex, the entorhinal cortex, and the olfactory bulb. These areas were interconnected with the amygdala, gustatory cortices, temporal cortex, lateral PFC, and anterior cingulate, as well as the ventral striatum, mesencephalic structures, and hypothalamus [Fletcher and Henson, 2001; Chico-Ponce de León et al., 2009; McCabe et al., 2010].

Correlation of the olfactory areas supports the assumption of high olfactory performance for this species [Fletcher and Henson, 2001; Laska et al., 2003]. This adaptation of the sensory system speaks to the behavioral importance of olfactory memory for these primates,

which is crucial in their natural setting [Fletcher and Henson, 2001; Hernandez Salazar et al., 2003; Laska et al., 2006]. In this respect, we assume that the intense correlation of the amygdala in *Ateles* is involved in the formation of emotional experiences associated with olfactory as well as auditory and visual memories, since it is crucial to create memories of stimuli that contribute to their survival. This is probably related to the amygdala, meaning a more emotional tone, as has also been reported in chimpanzees, suggesting a greater representation of emotional states than thoughts [Rilling et al., 2007].

Executive Control

As noted in the introduction, EC has received special attention, because it serves as an attention controller that allocates and organizes attentional resources for cognitive tasks [Baddeley, 1996; Engle and Kane, 2004]. It has therefore been suggested that WM has an EC component distributed in the brain areas mentioned earlier, which works at the same time as certain cortical regions in any of the various sensitive sensory modalities, which interact through attention processes [Ericsson and Kintsch, 1995; Baddeley, 1996; Smith and Jonides, 1999; Bunge et al., 2000; Carpenter et al., 2000; Baddeley, 2003; Engle and Kane, 2004; Inoue and Matsuzawa, 2007; Botvinick et al., 2009; Carruthers, 2013]. It has been found that WM for different information domains (e.g., audio and visual) recruit different networks [Carpenter, 1976]. However, for the EC in correlation with the WM, some authors use the concept of the central executive and include brain areas not restricted to the PFC and anterior cingulate [Carpenter, 1976; Baddeley, 1996; Smith and Jonides, 1999; Carpenter et al., 2000].

The EC network of spider monkeys shows connectivity in the frontal cortex and the hemispheric medial areas: paracentral area, anterior and middle cingulate gyrus. At the back of the brain, it moves towards the parietal areas. As mentioned earlier, unlike humans, *Ateles* have a small frontal lobe [McCabe et al., 2010], meaning that EC correlation in the PFC is barely visible. Some authors have observed a more widespread distribution to other cortical areas [Smith and Jonides, 1999; Carpenter et al., 2000]. Significant areas include the medial parts, covering regions II and III of the corpus callosum, the septal area, and the central cingulate. In its medial region and septum, the corpus callosum has a high level of connectivity. These structures correspond to regions primarily connecting motor and somatosensory cortices. An important factor observed in humans and macaques in this regard is that WM is closely linked to motor processes, such as ex-

aptation mechanisms that model the expected actions. Accordingly, this mechanism probably developed for on-line motor control [Gould and Vrba, 1982; Goldman-Rakic, 1988; Baddeley, 2003] by storing motor activity programs as experiences of past responses [Baddeley, 2003]. It is therefore possible that this arrangement is part of this primate's adaptations for efficient life in the three layer [Rosenberger and Strier, 1989; Jeannerod, 2006].

At the same time, it is important to note the high degree of correlation, in the analysis, between components for the paracentral region and the dorsal edge of the corresponding hemisphere, associated with the tail (Fig. 3). The cortical representation of the tail is much more extensive than in other species, occupying the areas mentioned [Pubols and Pubols, 1971; Groves, 2001] and showing finer motor activity, with a greater number of sensory nerve endings in neotropical primates [Pubols and Pubols, 1971; Rosenberger and Strier, 1989; Groves, 2001]. This not only indicates the important role it plays in locomotion, posture, and contact with other individuals [Laska and Tutsch, 2000; Laska and Seibt, 2002], but also the burden of tasks and motor planning in which it may be involved, by aligning with the afferent sensory representations and supporting representations in the WM involving this fifth limb. In humans and chimpanzees, this could be the equivalent of the cortical representation of fine motor skills in tasks involving the precision grip and manipulation of objects, which were so important in the process of humanization. Anatomically speaking, however, the tail region of the spider monkey is equivalent to the sensitive motor area of the hip and lower limbs in humans [Rosenberger and Strier, 1989].

Finally, spider monkeys displayed a fission-fusion social system, in which group size is adjusted according to the availability and distribution of resources [Boyer et al., 2006; Aureli et al., 2008; Aureli and Schaffner, 2008]. Accordingly, large home ranges are required to meet their nutritional requirements, compared to other sympatric primates such as *Alouatta* [Crockett and Eisenberg, 1987; Ramos-Fernández et al., 2006], which involves continuous recognition of their environment and their conspecifics. It has therefore been said that the fission-fusion dynamic creates particular conditions for social interaction, meaning that the action of these selection pressures was probably important in the enhancement of certain cognitive abilities as WM [Ramos-Fernández et al., 2006; Aureli et al., 2008; Aureli and Schaffner, 2008].

Conclusions

In the last decade, there has been a great deal of interest in the functional networks in resting-state conditions, and in this regard animal studies, although still incipient, are fundamental instruments that have contributed to the understanding of the neural bases underlying the evolution and function of this system. Together with the study of WM and EC networks, they can provide basic information for the investigation of neurological disorders associated with memory, as seen in neurodegenerative diseases, drug abuse, and psychiatric disorders. Re-evaluation of neurodegenerative diseases and psychiatric disorders from an evolutionary perspective would generate insights into our comprehension, and open a new line of research unveiling the biological mechanisms and thereby prevention and treatments [Nesse, 2002; Yamaguchi et al., 2015].

Overall, our research provides a novel contribution to the wider understanding of the evolution of WM and what we know of it in New World primates, by providing evidence of the neuroanatomical basis of WM in the spider monkey. Studying spider monkeys may provide additional insight into olfactory areas associated with WM and EC evolution. Therefore, there is a need for more comparative studies that will enable us to review the conceptual and experimental bases that have guided research on WM mechanisms in animals, in the light of techniques such as the one presented.

The main results of the present study can be summarized as follows: (1) Neural correlates associated with a network of WM and EC in the spider monkey were identified. (2) The executive WM network in *Ateles* is separated into two components, which may suggest an incipient homology in this monkey.

Limitations of the Present Study

It is important to note that the results and conclusions of this study must be regarded with caution. This argument is based on the fact that only a small sample of animals was used. Also, due to the computing and software limitations that exist when analyzing animal models, the analysis was not as strong as it is in similar studies on humans. Available commercial software for brain imaging analysis is usually developed for studies on humans rather than animals. This is particularly the case when the animals studied are rarely used in research. That is the case here, at least when comparing *Ateles* studies with the number of published papers using mice or rats for example. As no brain template for this monkey existed, thorough image preprocessing steps normally used in human studies were not performed. One

of the consequences could be the absence of a language network in the animal study. There was a network candidate, but it did not include large areas of auditory cortex and as a result was left out of the study. Nevertheless, when comparing the *Ateles* and human results from this work with those of previously published papers, a high level of reproducibility as well as logic in the results can be seen to have been achieved. Therefore, the authors believe that even with the constraints of the study, results are reliable and of relevance to the field.

The existence of significant individual differences associated with age, sex, the environment, etc. has been widely discussed. Comparative performance cannot be predicted of the sample with respect to these variables. Nevertheless, although this study is based on a small sample, the results provide significant information on the regions associated with WM, EC, and behavioral specialization in spider monkeys.

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Statement of Ethics

For the animal study, research was performed according to the international principles for the ethical treatment of nonhuman primates: the Weatherall Report for the use of nonhuman primates in research, the ARRIVE Guidelines, the American Society of Primatologists protocols, and the Official Mexican Norm NOM-062-ZOO-1999. For the human study, all ethical permissions were granted by the hospital, and data protection laws were strictly followed for the use of this information in this study. The participants signed a written informed consent form that was approved by the Medical Research Ethics Committee of the hospital. The Ethical Research Committee of the Ramón de la Fuente National Institute of Psychiatry, Mexico City, Mexico granted the necessary ethical approval for this study under project number 109147, supported by the National Council for Science and Technology of Mexico.

Disclosure Statement

The authors declare no conflict of interest.

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References

- Allman J. *Evolving Brains*. New York: Scientific American Library; 1999.
- Amici F, Aureli F, Call J. Fission-fusion dynamics, behavioral flexibility, and inhibitory control in primates. *Curr Biol*. 2008 Sep;18(18):1415–9.
- Amici F, Aureli F, Call J. Monkeys and apes: are their cognitive skills really so different? *Am J Phys Anthropol*. 2010 Oct;143(2):188–97.
- Aureli F, Schaffner C. Social Interactions, social relationships and the social system of spider monkeys. In: Campbell CJ, editor. *Spider monkeys: Behavior, ecology and evolution of the genus Ateles*. Cambridge: Cambridge University Press; 2008. p. 236–65.
- Aureli F, Schaffner C, Boesch C, Bearder S, Call J, Chapman C, et al. Fission-fusion dynamics: new research frameworks. *Curr Anthropol*. 2008;49(4):627–54.
- Baddeley A. *Working Memory. Oxford Psychology Series*. Oxford: Clarendon Press; 1986.
- Baddeley A. Exploring the central executive. *Q J Exp Psychol A*. 1996;49(1):5–28.
- Baddeley A. The episodic buffer: a new component of working memory? *Trends Cogn Sci*. 2000 Nov;4(11):417–23.
- Baddeley A. Working memory: looking back and looking forward. *Nat Rev Neurosci*. 2003 Oct;4(10):829–39.
- Barks SK, Parr LA, Rilling JK. The default mode network in chimpanzees (Pan troglodytes) is similar to that of humans. *Cereb Cortex*. 2015 Feb;25(2):538–44.
- Beckmann CF, DeLuca M, Devlin JT, Smith SM. Investigations into resting-state connectivity using independent component analysis. *Philos Trans R Soc Lond B Biol Sci*. 2005 May;360(1457):1001–13.
- Biswal B, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med*. 1995 Oct;34(4):537–41.
- Bonnefond M, Kastner S, Jensen O. Communication between Brain areas based on nested oscillations. *eNeuro*. 2017 Mar;4(2):1–14.
- Botvinick MM, Wang J, Cowan E, Roy S, Bastian C, Patrick Mayo J, et al. An analysis of immediate serial recall performance in a macaque. *Anim Cogn*. 2009 Sep;12(5):671–8.
- Boyer D, Ramos-Fernández G, Miramontes O, Mateos JL, Cocho G, Larralde H, et al. Scale-free foraging by primates emerges from their interaction with a complex environment. *Proc Biol Sci*. 2006 Jul;273(1595):1743–50.
- Bullmore E, Sporns O. Complex brain networks: graph theoretical analysis of structural and functional systems. *Nat Rev Neurosci*. 2009 Mar;10(3):186–98.
- Bunge SA, Klingberg T, Jacobsen RB, Gabrieli JD. A resource model of the neural basis of executive working memory. *Proc Natl Acad Sci USA*. 2000 Mar;97(7):3573–8.
- Cabral J, Hugues E, Sporns O, Deco G. Role of local network oscillations in resting-state functional connectivity. *Neuroimage*. 2011 Jul;57(1):130–9.
- Carpenter M. *Human neuroanatomy*. Baltimore: Williams and Wilkins; 1976.
- Carpenter PA, Just MA, Reichle ED. Working memory and executive function: evidence from neuroimaging. *Curr Opin Neurobiol*. 2000 Apr;10(2):195–9.
- Carruthers P. Evolution of working memory. *Proc Natl Acad Sci USA*. 2013 Jun;110 Suppl 2:10371–8.
- Chapman C, Fedigan LM, Fedigan L, Chapman L. Post-weaning resource competition and sex in spider monkeys. *Oikos*. 1989;54(3):315–9.
- Chico-Ponce de León F, Platas-Neri D, Muñoz-Delgado J, Santillán-Doherty AM, Arenas-Rosas RV, Trejo D, et al. Cerebral anatomy of the spider monkey Ateles geoffroyi studied using magnetic resonance imaging. First report: a comparative study with the human brain Homo sapiens. *Rev Cienc Salud*. 2009;7(1):10–27.
- Courtney SM, Ungerleider LG, Keil K, Haxby JV. Transient and sustained activity in a distributed neural system for human working memory. *Nature*. 1997 Apr;386(6625):608–11.
- Cowan N. What are the differences between long-term, short-term, and working memory? *Prog Brain Res*. 2008;169:323–38.
- Crockett C, Eisenberg J. Howlers: variations in group size and demography. In: Smuts BB, Cheney DL, Seyfarth RM, Wrangham RW, Struhsaker TT, editors. *Primates Societies*. Chicago, London: The University of Chicago Press; 1987. p. 54–68.
- Curtis CE, D'Esposito M. Persistent activity in the prefrontal cortex during working memory. *Trends Cogn Sci*. 2003 Sep;7(9):415–23.
- de Celis Alonso B, Hidalgo Tobón S, Dies Suarez P, García Flores J, de Celis Carrillo B, Baragán Pérez E. A multi-methodological MR resting state network analysis to assess the changes in brain physiology of children with ADHD. *PLoS One*. 2014 Jun;9(6):e99119.
- D'Esposito M, Postle BR. The cognitive neuroscience of working memory. *Annu Rev Psychol*. 2015 Jan;66(1):115–42.
- Damoiseaux JS, Rombouts SA, Barkhof F, Scheltens P, Stam CJ, Smith SM, et al. Consistent resting-state networks across healthy subjects. *Proc Natl Acad Sci USA*. 2006 Sep;103(37):13848–53.
- Dubreuil C, Notman H, Pavelka M. Sex differences in the use of whinny vocalizations in spider monkeys (Ateles geoffroyi). *Int J Primatol*. 2015;36(2):412–28.
- Emrich SM, Riggall AC, Larocque JJ, Postle BR. Distributed patterns of activity in sensory cortex reflect the precision of multiple items maintained in visual short-term memory. *J Neurosci*. 2013 Apr;33(15):6516–23.
- Engle R, Kane M. Executive attention, working memory capacity, and a two-factor of cognitive control. In: Ross B, editor. *The Psychology of Learning and Motivation*. New York: Elsevier; 2004. p. 145–99.
- Ericsson KA, Kintsch W. Long-term working memory. *Psychol Rev*. 1995 Apr;102(2):211–45.
- Fletcher PC, Henson RN. Frontal lobes and human memory: insights from functional neuroimaging. *Brain*. 2001 May;124(Pt 5):849–81.
- Fox MD, Greicius M. Clinical applications of resting state functional connectivity. *Front Syst Neurosci*. 2010 Jun;4:19.
- Funahashi S, Chafee MV, Goldman-Rakic PS. Prefrontal neuronal activity in rhesus monkeys performing a delayed anti-saccade task. *Nature*. 1993 Oct;365(6448):753–6.
- Ghahremani M, Hutchison RM, Menon RS, Everling S. Frontoparietal functional connectivity in the common marmoset. *Cereb Cortex*. 2017 Aug;27(8):3890–905.
- Goldman-Rakic PS. Topography of cognition: parallel distributed networks in primate association cortex. *Annu Rev Neurosci*. 1988;11(1):137–56.
- Goldman-Rakic PS. Cellular basis of working memory. *Neuron*. 1995 Mar;14(3):477–85.
- Gould SJ, Vrba ES. Exaptation a missing term in the science of form. *Paleobiology*. 1982;8(01):4–15.
- Greicius MD, Krasnow B, Reiss AL, Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proc Natl Acad Sci USA*. 2003 Jan;100(1):253–8.
- Groves CP. *Primate Taxonomy*. Washington (D.C.): Smithsonian Institution Press; 2001.
- Hampson M, Peterson BS, Skudlarski P, Gatenby JC, Gore JC. Detection of functional connectivity using temporal correlations in MR images. *Hum Brain Mapp*. 2002 Apr;15(4):247–62.
- Harrison SA, Tong F. Decoding reveals the contents of visual working memory in early visual areas. *Nature*. 2009 Apr;458(7238):632–5.
- Hernandez Salazar LT, Laska M, Rodriguez Luna E. Olfactory sensitivity for aliphatic esters in spider monkeys (Ateles geoffroyi). *Behav Neurosci*. 2003 Dec;117(6):1142–9.
- Horwitz B. The elusive concept of brain connectivity. *Neuroimage*. 2003 Jun;19(2 Pt 1):466–70.

- Hutchinson R, Everling S. Monkey in the middle: why non-human primates are needed to bridge the gap in resting state investigation. *Front Neuroanat*. 2012;6(29):1–19.
- Hutchison RM, Leung LS, Mirsattari SM, Gati JS, Menon RS, Everling S. Resting-state networks in the macaque at 7 T. *Neuroimage*. 2011 Jun; 56(3):1546–55.
- Hutchison RM, Mirsattari SM, Jones CK, Gati JS, Leung LS. Functional networks in the anesthetized rat brain revealed by independent component analysis of resting-state fMRI. *J Neurophysiol*. 2010 Jun;103(6):3398–406.
- Inoue M, Mikami A, Ando I, Tsukada H. Functional brain mapping of the macaque related to spatial working memory as revealed by PET. *Cereb Cortex*. 2004 Jan;14(1):106–19.
- Inoue S, Matsuzawa T. Working memory of numerals in chimpanzees. *Curr Biol*. 2007 Dec; 17(23):R1004–5.
- Jeanerod M. *Motor Cognition*. Oxford: Oxford Univ Press; 2006. <https://doi.org/10.1093/acprof:oso/9780198569657.001.0001>.
- Jonides J, Smith EE, Koeppel RA, Awh E, Minoshima S, Mintun MA. Spatial working memory in humans as revealed by PET. *Nature*. 1993 Jun;363(6430):623–5.
- Just MA, Carpenter PA. A capacity theory of comprehension: individual differences in working memory. *Psychol Rev*. 1992 Jan;99(1):122–49.
- Kannurpatti SS, Biswal BB, Kim YR, Rosen BR. Spatio-temporal characteristics of low-frequency BOLD signal fluctuations in isoflurane-anesthetized rat brain. *Neuroimage*. 2008 May;40(4):1738–47.
- Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J. The role of the anterior prefrontal cortex in human cognition. *Nature*. 1999 May; 399(6732):148–51.
- Kojima T, Onoe H, Hikosaka K, Tsutsui K, Tsukada H, Watanabe M. Default mode of brain activity demonstrated by positron emission tomography imaging in awake monkeys: higher rest-related than working memory-related activity in medial cortical areas. *J Neurosci*. 2009 Nov;29(46):14463–71.
- Koshino H, Minamoto T, Yaoi K, Osaka M, Osaka N. Coactivation of the Default Mode Network regions and Working Memory Network regions during task preparation. *Sci Rep*. 2014 Aug;4(1):5954.
- Kötter R, Meyer N. The limbic system: a review of its empirical foundation. *Behav Brain Res*. 1992 Dec;52(2):105–27.
- Laska M, Rivas Bautista RM, Hernandez Salazar LT. Olfactory sensitivity for aliphatic alcohols and aldehydes in spider monkeys (*Ateles geoffroyi*). *Am J Phys Anthropol*. 2006 Jan; 129(1):112–20.
- Laska M, Salazar LT, Luna ER. Successful acquisition of an olfactory discrimination paradigm by spider monkeys, *Ateles geoffroyi*. *Physiol Behav*. 2003 Feb;78(2):321–9.
- Laska M, Seibt A. Olfactory sensitivity for aliphatic esters in squirrel monkeys and pigtail macaques. *Behav Brain Res*. 2002 Aug;134(1–2): 165–74.
- Laska M, Tutsch M. Laterality of tail resting posture in three species of New World primates. *Neuropsychologia*. 2000;38(7):1040–6.
- Laubichler M. Homology in Development and the Development of the Homology Concept. *Integr Comp Biol*. 2000;40(5):777–88.
- LeDoux J. Emotion and the limbic system concept. *Concepts Neurosci*. 1991;2:169–99.
- Lee SH, Kravitz DJ, Baker CI. Goal-dependent dissociation of visual and prefrontal cortices during working memory. *Nat Neurosci*. 2013 Aug;16(8):997–9.
- McCabe DP, Roediger HL 3rd, McDaniel MA, Balota DA, Hambrick DZ. The relationship between working memory capacity and executive functioning: evidence for a common executive attention construct. *Neuropsychology*. 2010 Mar;24(2):222–43.
- Napier J, Napier P. *The Natural History of the Primates*. Cambridge: The MIT Press; 1985.
- Nesse RM. Evolutionary biology: a basic science for psychiatry. *World Psychiatry*. 2002 Feb; 1(1):7–9.
- Niendam TA, Laird AR, Ray KL, Dean YM, Glahn DC, Carter CS. Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cogn Affect Behav Neurosci*. 2012 Jun;12(2):241–68.
- Osaka M, Osaka N, Kondo H, Morishita M, Fukuyama H, Aso T, et al. The neural basis of individual differences in working memory capacity: an fMRI study. *Neuroimage*. 2003 Mar;18(3):789–97.
- Owen AM. The functional organization of working memory processes within human lateral frontal cortex: the contribution of functional neuroimaging. *Eur J Neurosci*. 1997 Jul;9(7): 1329–39.
- Owen AM. The role of the lateral frontal cortex in mnemonic processing: the contribution of functional neuroimaging. *Exp Brain Res*. 2000 Jul;133(1):33–43.
- Pasternak T, Greenlee MW. Working memory in primate sensory systems. *Nat Rev Neurosci*. 2005 Feb;6(2):97–107.
- Paulesu E, Frith CD, Frackowiak RS. The neural correlates of the verbal component of working memory. *Nature*. 1993 Mar;362(6418): 342–5.
- Pawela CP, Biswal BB, Cho YR, Kao DS, Li R, Jones SR, et al. Resting-state functional connectivity of the rat brain. *Magn Reson Med*. 2008 May;59(5):1021–9.
- Pessoa L, Gutiérrez E, Bandettini P, Ungerleider L. Neural correlates of visual working memory: fMRI amplitude predicts task performance. *Neuron*. 2002 Aug;35(5):975–87.
- Petrides M, Alivisatos B, Meyer E, Evans AC. Functional activation of the human frontal cortex during the performance of verbal working memory tasks. *Proc Natl Acad Sci USA*. 1993 Feb;90(3):878–82.
- Platas-Neri D, Hidalgo-Tobón S, de Celis Alonso B, de León FC, Muñoz-Delgado J, Phillips KA. Tractography of the spider monkey (*Ateles geoffroyi*) corpus callosum using diffusion tensor magnetic resonance imaging. *PLoS One*. 2015 Feb;10(2):e0117367.
- Proal E, Alvarez-Segura M, de la Iglesia-Vayá M, Martí-Bonmati L, Castellanos FX. Actividad funcional cerebral en estado de reposo: Redes en conexión. *Rev Neurol*. 2011 Mar;52(0 1): S3–10.
- Pubols BH Jr, Pubols LM. Somatotopic organization of spider monkey somatic sensory cerebral cortex. *J Comp Neurol*. 1971 Jan;141(1): 63–75.
- Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci USA*. 2001 Jan;98(2):676–82.
- Ramos-Fernández G, Boyer D, Gómez V. A complex social structure with fission-fusion properties can emerge from a simple foraging model. *Behav Ecol Sociobiol*. 2006;60(4):536–49.
- Rilling JK, Barks SK, Parr LA, Preuss TM, Faber TL, Pagnoni G, et al. A comparison of resting-state brain activity in humans and chimpanzees. *Proc Natl Acad Sci USA*. 2007 Oct; 104(43):17146–51.
- Rosenberger AL, Strier KB. Adaptive radiation of the ateline primates. *J Hum Evol*. 1989;18(7): 717–50.
- Rottschy C, Langner R, Dogan I, Reetz K, Laird AR, Schulz JB, et al. Modelling neural correlates of working memory: a coordinate-based meta-analysis. *Neuroimage*. 2012 Mar;60(1): 830–46.
- Roxo MR, Franceschini PR, Zubaran C, Kleber FD, Sander JW. The limbic system conception and its historical evolution. *ScientificWorldJournal*. 2011;11:2428–41.
- Rypma B, D'Esposito M. The roles of prefrontal brain regions in components of working memory: effects of memory load and individual differences. *Proc Natl Acad Sci USA*. 1999 May;96(11):6558–63.
- Sakai K, Rowe JB, Passingham RE. Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nat Neurosci*. 2002 May;5(5):479–84.
- Schöpf V, Kassess CH, Lanzenberger R, Fischmeister F, Windischberger C, Moser E. Fully exploratory network ICA (FENICA) on resting-state fMRI data. *J Neurosci Methods*. 2010 Oct;192(2):207–13.
- Smith EE, Jonides J. Storage and executive processes in the frontal lobes. *Science*. 1999 Mar; 283(5408):1657–61.

- Sporns O. [Networks of the Brain](#). Cambridge: The MIT Press; 2010. <https://doi.org/10.7551/mitpress/8476.001.0001>.
- Sreenivasan KK, Vytlačil J, D'Esposito M. Distributed and dynamic storage of working memory stimulus information in extrastriate cortex. [J Cogn Neurosci](#). 2014 May;26(5):1141–53.
- Touroutoglou A, Hollenbeck M, Dickerson BC, Feldman Barrett L. Dissociable large-scale networks anchored in the right anterior insula subserve affective experience and attention. [Neuroimage](#). 2012 May;60(4):1947–58.
- Ungerleider LG, Courtney SM, Haxby JV. A neural system for human visual working memory. [Proc Natl Acad Sci USA](#). 1998 Feb;95(3):883–90.
- Vincent JL, Patel GH, Fox MD, Snyder AZ, Baker JT, Van Essen DC, et al. Intrinsic functional architecture in the anaesthetized monkey brain. [Nature](#). 2007 May;447(7140):83–6.
- Wang XJ. Synaptic reverberation underlying mnemonic persistent activity. [Trends Neurosci](#). 2001 Aug;24(8):455–63.
- Wu TL, Mishra A, Wang F, Yang PF, Gore JC, Chen LM. Effects of isoflurane anesthesia on resting-state fMRI signals and functional connectivity within primary somatosensory cortex of monkeys. [Brain Behav](#). 2016 Oct;6(12):e00591.
- Yamaguchi Y, Lee YA, Goto Y. Dopamine in socioecological and evolutionary perspectives: implications for psychiatric disorders. [Front Neurosci](#). 2015 Jun;9:219.
- Zhao F, Zhao T, Zhou L, Wu Q, Hu X. BOLD study of stimulation-induced neural activity and resting-state connectivity in medetomidine-sedated rat. [Neuroimage](#). 2008 Jan;39(1):248–60.