



HAL
open science

Handedness in monkeys reflects hemispheric specialization within the central sulcus. An in vivo MRI study in right- and left-handed olive baboons

Konstantina Margiotoudi, Damien Marie, Nicolas Claidière, Olivier Coulon, Muriel Roth, Bruno Nazarian, Romain Lacoste, William D. Hopkins, Sandra Molesti, Pauline Fresnais, et al.

► To cite this version:

Konstantina Margiotoudi, Damien Marie, Nicolas Claidière, Olivier Coulon, Muriel Roth, et al.. Handedness in monkeys reflects hemispheric specialization within the central sulcus. An in vivo MRI study in right- and left-handed olive baboons. *Cortex*, 2019, 118, pp.203-211. <10.1016/j.cortex.2019.01.001>. <hal-02104937>

HAL Id: hal-02104937

<https://hal.science/hal-02104937v1>

Submitted on 26 Nov 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.



Distributed under a Creative Commons CC BY-NC-ND 4.0 - Attribution - Non-commercial use - No Derivative Works - International License

Handedness in monkeys reflects hemispheric specialization within the central sulcus. An *in vivo* MRI study in right- and left-handed olive baboons

Konstantina Margiotoudi^{1,2}, Damien Marie^{1,2}, Nicolas Claidière^{1,2}, Olivier Coulon³, Muriel Roth³, Bruno Nazarian³, Romain Lacoste², William D. Hopkins^{4,5}, Sandra Molesti², Pauline Fresnais^{1,2}, Jean-Luc Anton³, & Adrien Meguerditchian^{1,2,4*}

¹Laboratoire de Psychologie Cognitive, UMR7290, Université Aix-Marseille/CNRS, 13331 Marseille, France

²Station de Primatologie, UPS846, CNRS, 13790 Rousset, France

³Institut des Neurosciences de la Timone, Centre IRMF, UMR7289, Université Aix-Marseille/CNRS, 13005 Marseille, France

⁴Brain & Language Research Institute, Institute Language, Communication and the Brain, Université Aix-Marseille, CNRS, 13604 Aix-en-Provence, France.

⁵University of Texas MD Anderson Cancer Center, Bastrop, TX 78602, USA.

* Corresponding author : adrien.meguerditchian@univ-amu.fr

Abstract

Handedness, one of the most prominent expressions of laterality, has been historically considered unique to human. This noteworthy feature relates to contralateral inter-hemispheric asymmetries in the motor hand area following the mid-portion of the central sulcus. However, within an evolutionary approach, it remains debatable whether hand preferences in nonhuman primates are associated with similar patterns of hemispheric specialization. In the present study conducted in Old world monkeys, we investigate anatomical asymmetries of the central sulcus in a sample of 86 olive baboons (*Papio anubis*) from *in vivo* T1 anatomical magnetic resonance images (MRI). Out of this sample, 35 individuals were classified as right-handed and 28 as left-handed according to their hand use responses elicited by a bimanual coordinated tube task. Here we report that the direction and

degree of hand preference (left or right) as measured by this manual task relates and correlates to contralateral hemispheric sulcus depth asymmetry, within a mid-portion of the central sulcus. This neuroanatomical manifestation of handedness in baboons located in a region, which may correspond to the motor hand area, questions the phylogenetic origins of human handedness that may date back to their common ancestor, 25-40 millions years ago.

Keywords: central sulcus; baboons; asymmetries; hemispheric specialization; handedness

Introduction

A prominent feature of the human brain is its hemispheric specialization. Hemispheric specialization refers to the functional lateralization of the brain for a particular cognitive process, as well as to interhemispheric anatomical asymmetries for specific structures. In humans, handedness is one the most well-known behavioral manifestations of such a hemispheric specialization and shows a predominance of right-handed individuals in all cultures (Annett, 1985; Marchant et al., 1995). Handedness was historically considered to be associated with hemispheric specialization for language (Knecht, 2000). Nevertheless, it turned out that both right-handed and left-handed individuals present similar pattern of left-lateralization for language, indicating that handedness might involve its own lateralized brain network which might be independent from language hemispheric specialization (Mazoyer et al 2014, Tzourio-Mazoyer et al 2015). In fact, an anatomical inter-hemispheric asymmetry was found in the primary motor cortex along the central sulcus (CS) in the hemisphere contralateral to the preferred hand of the individuals (Hammond, 2002). The CS is one of the primary sulci developed in the brain (Chi et al., 1977). The CS lies along the primary motor and the primary sensory cortex, where topographic sensory and motor representations of human body parts are organized (Penfield and Boldrey, 1937). Within this topographic

organization, a morphological landmark of hand and finger representations has been documented across the dorsal-ventral plane of the CS, known as KNOB or motor hand area (Yousry et al., 1997).

Functional imaging studies have shown that the motor hand area corresponds to the location of hand, finger, and wrist movements (Boling, et al., 1999; Coulon et al., 2011). KNOB is shaped by the primary motor cortex displacing part of the CS due to the existence of a “pli de passage” known as the “pli de passage fronto-parietal moyen” (PPFM). PPFM connects the pre to the post central gyri (Alkadhi and Koliass, 2004) and forms an epsilon or omega-like shape (Yousry et al., 1997). In addition, this portion of the CS that delimits the motor hand area is deeper in the hemisphere contralateral to the preferred hand of the individual (Amunts et al., 2000; Foundas et al., 1998). In other words, handedness in humans seems to reflect neuroanatomical asymmetry in this region.

Within an evolutionary framework, such hemispheric specialization patterns, including both, handedness and language, have been historically considered unique to human evolution (Crow, 2004; Warren, 1980). However, this view has been challenged by a large body of evidence showing brain and behavioral asymmetries in many vertebrates including nonhuman primates (Marie et al. 2018; Rogers et al., 2013). Nevertheless, the question whether handedness is human-specific in terms of population-level laterality remains unclear. This question has been addressed both by paleoanthropological research (e.g., hand paintings, tool making and skeletal asymmetries, reviewed in Cashmore et al., 2008; Uomini, 2009) and by ethological research on our phylogenetically close primate relatives such as great apes and monkeys (Fagot and Vauclair, 1991; Ward and Hopkins, 1993; Hopkins, 1996; McGrew and Marchant, 1997). Some authors support the view of a continuity on handedness based on the increased number of studies showing population-level right-handedness mostly in terrestrial nonhuman primates (e.g., baboons, gorillas, chimpanzees) especially on complex manual

tasks such as tool use (Lonsdorf et al., 2005; Hopkins et al., 2009), bimanual coordinated action (Vauclair et al., 2005; Zhao et al., 2016; Molesti et al., 2016), and gestures (Meguerditchian and Vauclair, 2006; Meguerditchian et al., 2011; Prieur et al., 2017).

One complementary way of addressing the question of phylogenetic continuity among species concerning handedness is to investigate, not population-level asymmetry but rather the brain correlates of handedness in primates. In nonhuman primates, brain imaging studies have confirmed in great apes - but not in monkeys (Hopkins et al., 2014) - the presence of morphological KNOB landmark along the CS, which corresponds to the motor hand area as, described above in humans (Hopkins and Cantalupo, 2004; Hopkins et al., 2014). In the few studies conducted in chimpanzees, it has been shown that hemispheric structural asymmetries of this region along the central sulcus are associated to contralateral hand preferences for a bimanual coordinated task (Hopkins et al., 2004; Dadda et al., 2006; Hopkins et al., 2010a) as well as on tool-use (Hopkins et al., 2017). These findings indicate that, similarly to humans, handedness in chimpanzees is also represented in the KNOB region, which is assumed to be associated to the motor hand area in chimpanzees.

Despite the absence of a morphological KNOB landmark in Old and New World monkeys, finger and hand neuronal representations have been documented along the primary motor cortex by electrophysiological studies (Asanuma and Rossen, 1972; Waters et al., 1990). Because of the absence of the KNOB (Hopkins et al., 2014), whether this delimitation of the motor hand area in monkeys shows any inter-hemispheric anatomical asymmetries in relation to handedness, as was found for the KNOB area in chimpanzees, remains unclear. In other words, does the continuity between humans and chimpanzees concerning handedness representation in the primary motor cortex extend to more distant primate relatives such as Old World or New World monkeys? In fact, there is some evidence for neuroanatomical correlates of hand preferences within the motor cortex in New world monkeys including

squirrel and capuchin monkeys (Nudo et al., 1992; Philips and Sherwood, 2005). For instance, deeper right central sulcus was found for left-handed capuchin monkeys for bimanual coordination (Philips and Sherwood, 2005) and tool-use (Phillips and Thompson, 2013).

In respect to Old World monkeys, despite the absence of KNOB (Hopkins et al., 2014), baboons seem to constitute a particularly interesting model for studying brain correlates of handedness. Indeed, baboons have been found to show robust and consistent patterns of population level-right handedness for bimanual coordinated actions (Vauclair et al., 2005; Molesti et al., 2016). Interestingly, this right-hand bias in baboons was similar to the one observed in terrestrial great apes such as chimpanzees, gorillas and adult bonobos (Meguerditchian et al., 2013). Moreover, among Old World monkeys (Rogers et al., 2010), baboons have the largest brains (Leigh, 2004) and higher degree of folding i.e. gyrification, including all the primary sulci such as the CS (Kochunov et al., 2010; Love et al., 2016).

In the present study, we further question the evolutionary continuity for hemispheric specialization among primates in investigating brain anatomical correlates of handedness in baboons. For this purpose, we examine anatomical asymmetries of depth across the whole CS in 86 baboons (*Papio Anubis*) from *in vivo* anatomical magnetic resonance imaging (MRI) scans. Moreover, we explore the effect of hand preferences – previously assessed in those subjects for bimanual coordination actions (i.e. tube task) - on depth asymmetries all along the CS. Indeed, the tube task has been shown to be the most relevant task to assess and compare hand preference in non-human primates (Westergaard et al., 1997; Spinozzi et al., 1998; Hopkins et al., 2003; Meguerditchian et al., 2013), including baboons (Vauclair et al., 2005; Molesti et al., 2016).

Based on the current knowledge on handedness and neuroanatomical asymmetries along the CS depth in humans (e.g., Amunts 1996) and in nonhuman primates (Hopkins and Cantalupo, 2004; Dadda et al., 2006), in the present study, we expected a larger depth of the

CS at the hemisphere contralateral to the preferred hand of the individuals and at the mid-ventral topographic representation of the motor hand area (Waters et al., 1990).

Methods

Subjects

Magnetic resonance images were collected in 86 baboons (56 females and 30 males). The subjects were aged from 2,5 to 26,5 years (mean of 12.0 ± 6.0 S.E.) and, to our knowledge, did not display neurological antecedents or brain abnormalities. Out of this sample, hand preferences were documented in 74 baboons that were previously assessed by a bimanual coordinated task (i.e. TUBE task: Vauclair et al., 2005; Molesti et al., 2016). All baboons are housed in social groups at the Station de Primatologie CNRS (UPS 846, Rousset, France) and have free access to outdoor areas connected to indoor areas. Enclosures are enriched by wooden platforms and vertical structures. Baboons are fed four times a day with monkey pellets, seed mixture, fresh vegetables and fruits. Water is available ad libitum. The experimental procedure complied with the current French laws and the European directive 86/609/CEE and has been approved by the ethic committee of Provence (Agreement number for conducting experiments on vertebrate animals at the Station de Primatologie CNRS: D130877).

MRI Image acquisition

From December 2012 to January 2015, in vivo imaging was performed with a 3T imager MEDSPEC 30/80 ADVANCE (Bruker) located at the Marseille Functional MRI Center (Institut de Neurosciences de la Timone). Whole brain anatomical MRI data were acquired using a Rapid-Biomed surface antenna on top of the head for reception. High-resolution structural T1-weighted images were obtained thanks to two MPRAGE sequences depending

on acquisition, namely female/young male (TR: 9.4 ms; TE: 4.3 ms; flip angle: 30°; inversion time: 800 ms; field of view : 108x108x108 mm ; isotropic voxel size: 0.6 mm³) or adult male (same parameters except for field of view : 126x126x126 mm, and isotropic voxel size : 0.7 mm³). For each MRI session, premedication was released with an intramuscular injection of ketamine (10 mg/kg) at the Station de Primatologie and subjects remained immobilized during their transportation to the MRI center. Once arrived at the MRI center, the focal subject was further immobilized with an intramuscular injection of tiletamine and zolazepam (Zoletil™, 7 mg/kg) and acepromazine (Calmivet™, 0,2–0,5 mg/kg). The latter injection was needed to provoke a myorelaxation and avoid snoring or motions. Finally anesthesia was maintained during the whole experiment thanks to a drip irrigation setup including tiletamine, zolazepam (Zoletil™, 4mg/kg/h) and NaCl (0,9% of 4ml/kg/h). Cardiovascular and respiratory functions were monitored respectively with a SpO₂ device placed on the lower lip and with a respiratory belt (mechanical captor). Each subject was placed in ventral decubitus position in the MRI scanner and the head of the subject was maintained using foam positioners, cushions and Velcro strips in order to obtain a straight position of the head and reduce potential motion occurrences. At the end of the MRI session, baboons were returned in their social group at the Station de Primatologie.

Image processing

Images were first denoised using the Spatial Adaptive Nonlocal Means filter (SANLM) and skull stripped with the freely distributed Multi Atlas Skull Stripping software (MASS,<http://www.cbica.upenn.edu/sbia/software/MASS/index.html>).

Finally, intensity inhomogeneities were corrected in the skull stripped images using the N4 algorithm (for an extensive description of the methods our previous study, Love et al., 2016). After this step we imported images in BrainVISA 4.4.0 (BV) (<http://brainvisa.info>, Mangin et

al., 2004), a sulcus-based morphometry software that allows the quantification of depth of the cortical sulci. The pipeline process of the BV Morphologist tool was used in order to extract successfully the sulci from the cortex after a series of steps. During the whole pipeline procedure some manual tuning was necessary in order for the pipeline to meet specificities of the baboons' brain anatomy. Firstly, at the pipeline procedure the anterior and posterior commissures are selected manually at the point where they intersect with the mid-sagittal slice. After this step spatial inhomogeneities of the signal intensities across the brain are corrected by applying a spatial smoothed bias field. Then, the signal histogram and mathematic morphology was computed in order to acquire a binary mask of the brain. The computed brain mask was divided into left, right hemisphere and cerebellum. Once the brain mask is divided, a negative mold of the white matter is computed where the outside boundary of the mold is a 5 mm morphological closing of the masked hemisphere, which fills up the fold. This mold is later skeletonized in order to detect the cortical folding of the brain.

Sulci parameterization

Once the cortical folding is constructed, the CS was manually labeled on a 3D visualization interface using the Anatomist toolbox included in BrainVISA. After that we extracted the sulcus depth (mm) and profile with the process of sulcus parameterization (Coulon et al., 2006). This process extracts depth values for each sulcus at each hemisphere, after an x-y coordinated system is being applied on the mesh of the sulcus. This coordinated system is extended across the length of the sulcus from position $y=1$ to $y=100$ and from the brain envelope $x=1$ to the fundus of each sulcus $x=100$. This system indicates the positions of each sulcus's relative to its depth (x-coordinate) and its position along the sulcus between the dorsal and the ventral extremities (y-coordinate). The depth is calculated on 100 positions as the length of $x=1$ to $x=100$ positions on the y-iso-coordinate from positions $y=1$ through

y=100 (Coulon et al., 2006). The sulcus profile allows the visualization of the bending pattern of the CS across the dorsal to ventral direction (Cykowski et al., 2008) (see supplementary material, Figure S1).

Central sulcus asymmetry depth measures

First, among the 100 positions of the sulcus, we excluded from our analysis the 14 first and last portions of the two extreme portions of the sulcus, in accordance to previous studies (McKay et al., 2013; Hopkins et al., 2017). Indeed it has been described that the CS branches with the Sylvian fissure and the interhemispheric fissures resulting in spikes in the depth measurements at the extreme positions (McKay et al., 2013). Secondly, for each CS position from positions 14 to positions 85, we calculated for each subject, the asymmetry quotient (AQ) based on the following formula: $AQ = (R-L)/[(R+L)*0.5]$, with R and L represent depth values for the right and left hemisphere correspondingly (Cantalupo et al., 2003; Hopkins et al., 2010a). Positive AQ values indicate rightward asymmetry, whereas negative AQ values indicate leftward asymmetry.

Behavioral Measures

Hand preferences in baboons for coordinated bimanual actions were assessed by using the tube task (Fig. 1). The tube task data were collected across several sessions between 2004 and 2015. During this task a pipe is given to social groups of baboons. Peanut butter is smeared about 4 cm into both edges of the pipe. The focal subject is holding the pipe with the one hand and extracts the peanut butter with the other hand. Each time one of the focal subjects was putting its finger into the tube and was bringing it to its mouth, we counted as one response for individual hand preference (Vauclair et al., 2005; Molesti et al., 2016). In case a subject has been assessed in multiple sessions within 2004-2015, the final classification as right or

left handed was selected based on the session with the most observations.

For classifying the subjects as significantly left-handed and right-handed, z-score was calculated on the basis of the total number of right and left hand responses for each individual (z values $z \geq 1.96$ indicates right-handedness, $z \leq -1.96$ left-handedness, $-1.96 < z < 1.96$ ambidextrousness). Based on such criteria, among the 86 baboons, 35 subjects were classified as right-handed, 28 as left-handed, 11 as ambidextrous and 12 as undetermined because of lack of hand use data.

The handedness index (HI), or degree of individual manual asymmetry, was calculated based on the formula $(\#R - \#L) / (\#R + \#L)$, with #R indicating right hand responses and #L for left hand responses. The HI values vary between -1 and +1 with positive values indicating right hand preference and negative values indicating left hand preference. Absolute values of the HI indicated the strength of the manual asymmetry.

Data analysis

To determine the effect of handedness on brain asymmetry along the CS, we first evaluated the observed difference in mean AQ score between the right- and left-handed groups of baboons using a t-test (two sided, uncorrected) for each position from positions 14 to positions 85. Next, in order to address the correction of multiple t-test comparisons and to determine whether the location of the AQ differences (if any) is robust, we used a non-parametric permutation-based approach. Permutation test was used to determine if the observed t-values fell within the range of what would have been observed by chance if there was no spatial organization. For each permutation, we randomly changed the position of the AQ score of each baboon and recalculated the t-values. This procedure allowed us to maintain the characteristics of each individual (the values of the AQ remained the same for each individual) while at the same time modifying the spatial organization (the position of the AQ

values changed). This permutation procedure generates the true distribution of t-values under the assumption of no spatial organization. If the observed t-values fall outside the 95% confidence interval of the distribution, it can be concluded that the observed difference in AQ score is not within the normal range of variation observed in the rest of the data.

Last, we performed a linear correlation between (1) the Handedness Index (HI) values calculated from the 74 individuals (including the 28 left-handed, the 35 right-handed and the 11 ambiguously handed individuals) and (2) the AQ depth values of those 74 baboons calculated from the continuous depths positions of the sulcus for which significant difference in AQ score (if any) is detected by t-test comparison between the right- and left-handed groups.

Results

According to the mean depth values and profiles plotted across all the positions from 0 (dorso-) to 100 (ventral) of the CS (see Fig. S1 in the supplementary materials), no difference was observed on the profile and depth curves between right and left hemisphere. The CS depth curve from 0-100 positions did not draw any omega or epsilon-like motor hand area shape comparable to the one observed in humans and great apes (Hopkins et al., 2014).

Out of the 100 positions of CS, only 6 continuous positions revealed significant contralateral difference of depth asymmetry between the left-handed and right-handed groups according to unpaired *t-test* (two sided, uncorrected). These significant consecutive positions include position 56 (2.02, $p = 0.047$), position 57 (2.15, $p = 0.036$), position 58 (2.37, $p = 0.021$), position 59 (2.50, $p = 0.015$), position 60 (2.69, $p = 0.009$) and position 61 (2.10, $p = 0.039$). Specifically, in these 6 positions located in the mid-ventral portion of the CS (labelled as “MH” for “Motor Hand area”), the preferred hand showed CS depth asymmetry in the contralateral hemisphere: Whereas left-handed showed CS depth asymmetry toward the right-

hemisphere, right-handed subjects showed CS depth asymmetry toward the left-hemisphere. In contrast, any other positions showed no significant difference on the depth AQ values for the two groups of handedness (Fig. 2). According to permutation test for correction, the observed t-values at positions 56, 57, 58, 59, 60 and 61 fall outside the 95% confidence interval of the distribution, indicating that observed differences in AQ scores at those positions between left-handed and right-handed are not within the normal range of variation observed in the rest of the data (see Fig. S2 in the supplementary materials).

Finally, there was significant negative correlation between individual AQ depth values at this MH segment and individual hand preference's degree (HI) : $r(74) = -0.316$; $p = 0,0061$ (i.e. stronger the hand preference is for one hand, deeper is the CS asymmetry at the MH segment in the contralateral hemisphere) (Fig. 3). The AQ score per subject representing the depth asymmetry of the whole MH segment was calculated from the sum of the CS depths from positions 56 to 61 in the left hemisphere and the sum of CS depths from position 56 to 61 in the right hemisphere .

Discussion

We found, in the largest sample size ever investigated in nonhuman primates, a clear association in both direction and degree between hand preferences for bimanual tube coordination and neuroanatomical depth asymmetries at a specific portion of the CS in the contralateral hemisphere.

In addition, with respect to the depth patterns of the CS, we confirmed the absence of a clear omega or epsilon-like motor hand area comparable to the one observed in humans and great apes (Hopkins et al., 2014). The absence of this omega or epsilon-like motor hand area might also be related to the lower degree of gyrification of the monkeys' brains in comparison to the brains of humans and great apes (Zilles et al., 1989).

Interestingly, the specific portion of the CS (labelled as “MH”) which was associated with hand preference was localized at the mid-ventral portion of the CS. This MH portion of the CS seems to correspond to the topographic representation of the hand and finger representations along the primary motor cortex in baboons based on electrophysiological data in the same species (Waters et al., 1990). Additional electrophysiological studies in Old World monkeys such as macaques reported consistent location for the motor hand area (e.g., Schaffelhofer et al. 2015), indicating that hand region in monkeys might be located much more ventrally along the CS than in humans. In other words, even with the absence of a clear anatomical landmark of a motor hand area, we were able to show difference in CS depth asymmetries between right-handed and left-handed subjects at the portion where hand and finger representations are likely present, similarly to the asymmetries reported previously in humans and in great apes along the motor hand area (Amunts et al., 2000; Hopkins and Cantalupo, 2004). Moreover, histological studies in post-mortem chimpanzees’ brains showed that microstructural asymmetry in this region within the primary motor cortex predict handedness (Sherwood et al., 2007). Thus, it cannot be excluded that the baboons’ neuroanatomical correlates of handedness found in this region might be related to histological asymmetry at the neuronal level.

The present result is in clear congruency with similar findings in humans (Amunts et al., 1996) and chimpanzees (Hopkins and Cantalupo, 2004), where the motor hand area of the CS is deeper at the hemisphere contralateral to the preferred hand of the individuals (i.e. right-handed individuals have a deeper leftward CS asymmetry at the MH portion of the sulcus *versus* left-handed individuals have a deeper rightward CS asymmetry at the same portion). In capuchin monkeys, a New World monkey species, two studies revealed a contralateral depth CS asymmetry only for left-handed individuals and not for right-handed (i.e. Phillips and Sherwood, 2005; Phillips and Thompson, 2013). Perhaps the limitations of these latter results

on generalizations at a population-level might be due to their small sample size compared to the present study. Some difference must also be noted between baboons and humans concerning CS depth asymmetry. Whereas in the Amunts et al.'s (1996) study in humans, contralateral anatomical CS asymmetry was found more prominent in right-handers than in left-handers, we found that left-handed baboons were more strongly asymmetrical in the CS than the right-handed subjects, suggesting a potential difference of hand direction effect on the degree of CS asymmetry between the two species. Nevertheless, as mentioned above in both baboons and humans, left- and right-handed are essentially mirror symmetrical in their contralateral direction of CS depth asymmetry within the CS. The consistency of the present findings with previous research in humans gives credits for the continuity hypothesis of handedness represented at the primary motor cortex of our distant relatives.

In addition, handedness and interhemispheric depth of CS asymmetries in baboons might be related not only at a qualitative level but also at a quantitative level as well. In fact, interhemispheric asymmetry of CS depth related to handedness was confirmed by the significant negative correlation of AQ depth values at the mid-ventral CS portion with the Handedness Index (HI) values of the individuals. Based on this correlation, individuals with a higher degree of hand preference have larger CS asymmetries in the hemisphere contralateral to their preferred hand.

One issue raised in this study is whether bimanual coordinated behaviors in baboons would similarly stimulate cortical activation in the contralateral MH segment (mid-ventral CS portion) instead of simply being linked to variation in neuroanatomy. Although no functional neuroimaging data are available for handedness in baboons at the present time, one functional brain imaging study published in another primate species, the chimpanzee, using positron emission tomography (PET) suggests that such a hypothesis would be supported. A study on grasping in chimpanzees has demonstrated that the neuroanatomical landmark of the motor

hand area (KNOB) overlaps with the functional maps generated by PET analysis indicating that neuroanatomical asymmetry of the brain might predict functional asymmetry in chimpanzees (Hopkins et al., 2010b). Regarding the present finding in baboons, we propose the hypothesis that the neuroanatomical correlates of handedness found within the CS might be related to functional contralateral activation in this region. Further neurofunctional studies in baboons would be needed to address this hypothesis.

To sum up, the findings assemble empirical evidence on the assumption of evolutionary continuities between neuroanatomical asymmetries and behavior, as has been previously addressed by Hopkins (2013). The riddle regarding the evolutionary continuity of handedness, seems almost to be solved based on the present evidence reflecting handedness and neuroanatomical correlates in an Old World monkey. Such representation of handedness in the monkey brain clearly supports the idea that hand preferences in baboons is a robust phenomenon. As reported in previous studies, bimanual coordinated behaviors in baboons as expressed in manipulating the tube task elicit not only consistent predominance of right-handedness across independent groups but also stable patterns of individual hand preferences across time (Molesti et al. 2016). According to the present study, those individual hand preferences in baboons seem clearly related to hemispheric specialization of the brain. Nonhuman primates offer thus a compelling model for the evolution of human handedness contrary to what has been previously suggested by some authors (McGrew & Marchant, 1997). Consistency about contralateral neuroanatomical correlates of handedness between humans, great apes, and monkeys suggest that such a handedness feature might be well spread across primate evolution and might be inherited from their common ancestor back to 25-40 million years ago.

References

- Alkadhi, H., & Kollias, S. S. (2004). Pli de passage fronto-parietal moyen of Broca separates the motor homunculus. *American Journal of Neuroradiology*, 25(5), 809-812.
- Amunts, K., Schlaug, G., Schleicher, A., Steinmetz, H., Dabringhaus, A., Roland, P. E., & Zilles, K. (1996). Asymmetry in the human motor cortex and handedness. *Neuroimage*, 4(3), 216-222.
- Amunts, K., Jäncke, L., Mohlberg, H., Steinmetz, H., & Zilles, K. (2000). Interhemispheric asymmetry of the human motor cortex related to handedness and gender. *Neuropsychologia*, 38(3), 304-312.
- Annett, M. (1985). *Left, right, hand and brain: The right shift theory*. Psychology Press.
- Asanuma, H., & Rosén, I. (1972). Functional role of afferent inputs to the monkey motor cortex. *Brain research*, 40(1), 3-5.
- Boling, W., Olivier, A., Bittar, R. G., & Reutens, D. (1999). Localization of hand motor activation in Broca's pli de passage moyen. *Journal of neurosurgery*, 91(6), 903-910.
- Cantalupo, C., Pilcher, D. L., & Hopkins, W. D. (2003). Are planum temporale and sylvian fissure asymmetries directly related?: A MRI study in great apes. *Neuropsychologia*, 41(14), 1975-1981.
- Cashmore, L., Uomini, N., & Chapelain, A. (2008). The evolution of handedness in humans and great apes: a review and current issues. *Journal of anthropological sciences*, 86, 7-35.
- Chi, J. G., Dooling, E. C., & Gilles, F. H. (1977). Gyral development of the human brain. *Annals of neurology*, 1(1), 86-93.
- Corballis, M. C. (1991). *The lopsided ape: Evolution of the generative mind*. Oxford University Press.
- Coulon, O., Clouchoux, C., Operto, G., Dauchot, K., Sirigu, A., & Anton, J.-L. (2006). *Cortical localization via surface parametrization : a sulcus-based approach*, Communication at the 12th Human Brain Mapping (OHBM) conference, Florence, Italy.
- Coulon, O., Pizzagall, F., Operto, G., Auzias, G., Delon-Martin, C., & Dojat, M. (2011). Two new stable anatomical landmarks on the Central Sulcus: Definition, automatic detection, and their relationship with primary motor functions of the hand. *Conference Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2011*, 7795-7798. doi:10.1109/iembs.2011.6091921
- Crow, T. (2004). Directional asymmetry is the key to the origin of modern Homo sapiens (the Broca-Annett axiom): A reply to Rogers' review of The Speciation of Modern Homo Sapiens. *Laterality: asymmetries of body, brain and cognition*, 9(2), 233-242.

- Cykowski, M. D., Coulon, O., Kochunov, P. V., Amunts, K., Lancaster, J. L., Laird, A. R., Glahn, C.D., Fox, P. T. (2008). The central sulcus: an observer-independent characterization of sulcal landmarks and depth asymmetry. *Cerebral Cortex*, 18(9), 1999-2009.
- Dadda, M., Cantalupo, C., & Hopkins, W. D. (2006). Further evidence of an association between handedness and neuroanatomical asymmetries in the primary motor cortex of chimpanzees (*Pan troglodytes*). *Neuropsychologia*, 44(12), 2582-2586.
- Fagot, J., & Vauclair, J. (1991). Manual laterality in nonhuman primates: a distinction between handedness and manual specialization. *Psychological bulletin*, 109(1), 76.
- Foundas, A. L., Eure, K. F., Luevano, L. F., & Weinberger, D. R. (1998). MRI asymmetries of Broca's area: the pars triangularis and pars opercularis. *Brain and language*, 64(3), 282-296.
- Hammond, G. (2002). Correlates of human handedness in primary motor cortex: A review and hypothesis. *Neuroscience & Biobehavioral Reviews*, 26, 285-292.
- Hopkins, W. D. (1996). Chimpanzee handedness revisited: 55 years since Finch (1941). *Psychonomic Bulletin & Review*, 3(4), 449-457.
- Hopkins, W. D., Stoinski, T. S., Lukas, K. E., Ross, S. R., & Wesley, M. J. (2003). Comparative assessment of handedness for a coordinated bimanual task in chimpanzees (*Pan troglodytes*), gorillas (*Gorilla gorilla*) and orangutans (*Pongo pygmaeus*). *Journal of Comparative Psychology*, 117(3), 302.
- Hopkins, W. D., & Cantalupo, C. (2004). Handedness in chimpanzees (*Pan troglodytes*) is associated with asymmetries of the primary motor cortex but not with homologous language areas. *Behavioral neuroscience*, 118(6), 1176.
- Hopkins, W., Russell, J., Schaeffer, J., Gardner, M., & Schapiro, S. (2009). Handedness for tool use in captive chimpanzees (*Pan troglodytes*): Sex differences, performance, heritability and comparison to the wild. *Behaviour*, 146(11), 1463-1483.
- Hopkins, W. D., Coulon, O., & Mangin, J. F. (2010a). Observer-independent characterization of sulcal landmarks and depth asymmetry in the central sulcus of the chimpanzee brain. *Neuroscience*, 171(2), 544-551.
- Hopkins, W. D., Tagliabata, J. P., Russell, J. L., Nir, T. M., & Schaeffer, J. (2010b). Cortical representation of lateralized grasping in chimpanzees (*Pan troglodytes*): a combined MRI and PET study. *PLoS One*, 5(10), e13383.
- Hopkins, W. D. (2013). Neuroanatomical asymmetries and handedness in chimpanzees (*Pan troglodytes*): a case for continuity in the evolution of hemispheric specialization. *Annals of the New York Academy of Sciences*, 1288(1), 17-35.
- Hopkins, W. D., Meguerditchian, A., Coulon, O., Bogart, S., Mangin, J. F., Sherwood, C. C., Grabowski, M.W., Bennett, A.J., Pierre, P.J., Fears, S. & Woods, R. (2014). Evolution of the central sulcus morphology in primates. *Brain, behavior and evolution*, 84(1), 19-30.

Hopkins, W. D., Coulon, O., Meguerditchian, A., Autrey, M., Davidek, K., Mahovetz, L., ... & Schapiro, S. J. (2017). Genetic Factors and Orofacial Motor Learning Selectively Influence Variability in Central Sulcus Morphology in Chimpanzees (*Pan troglodytes*). *Journal of Neuroscience*, 37(22), 5475-5483.

Knecht, S., Dräger, B., Deppe, M., Bobe, L., Lohmann, H., Flöel, A., ... & Henningsen, H. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain*, 123(12), 2512-2518.

Kochunov, P., Glahn, D. C., Fox, P. T., Lancaster, J. L., Saleem, K., Shelledy, W., Zilles, K., Thompson, P. M., Coulon, O., Mangin, J. F., & Blangero, J. (2010). Genetics of primary cerebral gyrication: heritability of length, depth and area of primary sulci in an extended pedigree of *Papio baboons*. *Neuroimage*, 53(3), 1126-1134.

Leigh, S. R. (2004). Brain growth, life history, and cognition in primate and human evolution. *American journal of primatology*, 62(3), 139-164.

Lonsdorf, E. V., Hopkins, W. D. (2005). Wild chimpanzees show population level handedness for tool use. *Proceedings of the National Academy of Sciences*, 102, 12634–12638.

Love, S. A., Marie, D., Roth, M., Lacoste, R., Nazarian, B., Bertello, A., Coulon, O., Anton, J.-L., & Meguerditchian, A. (2016). The average baboon brain: MRI templates and tissue probability maps from 89 individuals. *NeuroImage*, 132, 526-533.

Mangin, J. F., Rivière, D., Cachia, A., Duchesnay, E., Cointepas, Y., Papadopoulos-Orfanos, D., Collins, D.L., Evans, A.C. and Régis, J. (2004). Object-based morphometry of the cerebral cortex. *Medical Imaging, IEEE Transactions on*, 23(8), 968-982.

Marchant, L. F., McGrew, W. C., & Eibl-Eibesfeldt, I. (1995). Is human handedness universal? Ethological analyses from three traditional cultures. *Ethology*, 101(3), 239-258.

Marie, D., Roth, M., Lacoste, R., Nazarian, B., Bertello, A., Anton, J. L., ... & Meguerditchian, A. (2018). Left Brain Asymmetry of the Planum Temporale in a Nonhominid Primate: Redefining the Origin of Brain Specialization for Language. *Cerebral Cortex*, 28, 1808-1815..

Mazoyer, B., Zago, L., Jobard, G., Crivello, F., Joliot, M., Perchey, G., ... & Tzourio-Mazoyer, N. (2014). Gaussian mixture modeling of hemispheric lateralization for language in a large sample of healthy individuals balanced for handedness. *PLoS One*, 9(6), e101165.

McGrew, W. C., & Marchant, L. F. (1997). On the other hand: current issues in and meta-analysis of the behavioral laterality of hand function in nonhuman primates. *American Journal of Physical Anthropology*, 104(s 25), 201-232.

McKay, D. R., Kochunov, P., Cykowski, M. D., Kent, J. W., Laird, A. R., Lancaster, J. L., ... & Fox, P. T. (2013). Sulcal depth-position profile Is a genetically mediated neuroscientific trait: description and characterization in the central sulcus. *Journal of Neuroscience*, 33(39), 15618-15625.

- Meguerditchian, A., & Vauclair, J. (2006). Baboons communicate with their right hand. *Behavioural brain research*, *171*(1), 170-174.
- Meguerditchian, A., Molesti, S., & Vauclair, J. (2011). Right-handedness predominance in 162 baboons (*Papio anubis*) for gestural communication: Consistency across time and groups. *Behavioral neuroscience*, *125*(4), 653.
- Meguerditchian, A., Vauclair, J., & Hopkins, W. D. (2013). On the origins of human handedness and language: a comparative review of hand preferences for bimanual coordinated actions and gestural communication in nonhuman primates. *Developmental psychobiology*, *55*(6), 637-650.
- Molesti, S., Vauclair, J., & Meguerditchian, A. (2016). Hand preferences for unimanual and bimanual coordinated actions in olive baboons (*Papio anubis*): Consistency over time and across populations. *Journal of Comparative Psychology*, *130*(4), 341.
- Nudo, R. J., Jenkins, W. M., Merzenich, M. M., Prejean, T., & Grenda, R. (1992). Neurophysiological correlates of hand preference in primary motor cortex of adult squirrel monkeys. *The Journal of Neuroscience*, *12*, 2918-2947.
- Penfield, W., & Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain: A journal of neurology*.
- Phillips, K. A., & Sherwood, C. C. (2005). Primary motor cortex asymmetry is correlated with handedness in capuchin monkeys (*Cebus apella*). *Behavioral Neuroscience*, *119*(6), 1701.
- Phillips, K. A., & Thompson, C. R. (2013). Hand preference for tool-use in capuchin monkeys (*Cebus apella*) is associated with asymmetry of the primary motor cortex. *American journal of primatology*, *75*(5), 435-440.
- Prieur, J., Pika, S., Barbu, S., & Blois-Heulin, C. (2017). Intraspecific gestural laterality in chimpanzees and gorillas and the impact of social propensities. *Brain research*, *1670*, 52-67.
- Rogers, J., Kochunov, P., Zilles, K., Shelledy, W., Lancaster, J., Thompson, P., Duggirala, R., Blangero, J., Fox, P. T., & Glahn, D.C. (2010). On the genetic architecture of cortical folding and brain volume in primates. *Neuroimage*, *53*(3), 1103-1108.
- Rogers, L. J., Vallortigara, G., & Andrew, R. J. (2013). *Divided brains: the biology and behaviour of brain asymmetries*. Cambridge University Press.
- Schaffelhofer, S., Agudelo-Toro, A., & Scherberger, H. (2015). Decoding a wide range of hand configurations from macaque motor, premotor and parietal cortices. *The Journal of Neuroscience*, *35*(3), 1068-1081.
- Sherwood, C. C., Wahl, E., Erwin, J. M., Hof, P. R., & Hopkins, W. D. (2007). Histological asymmetries of primary motor cortex predicts handedness in chimpanzees (*Pan troglodytes*). *Journal of Comparative Neurology*, *503*, 525-537.

- Spinozzi, G., Castorina, M. G., & Truppa, V. (1998). Hand preferences in unimanual and coordinated-bimanual tasks by tufted capuchin monkeys (*Cebus apella*). *Journal of Comparative Psychology*, *112*(2), 183.
- Tzourio-Mazoyer, N., Marie, D., Zago, L., Jobard, G., Percey, G., Leroux, G., ... & Mazoyer, B. (2015). Heschl's gyrification pattern is related to speech-listening hemispheric lateralization: fMRI investigation in 281 healthy volunteers. *Brain Structure and Function*, *220*(3), 1585-1599.
- Uomini, N. T. (2009). The prehistory of handedness: archaeological data and comparative ethology. *Journal of Human Evolution*, *57*(4), 411-419.
- Vauclair, J., Meguerditchian, A., & Hopkins, W. D. (2005). Hand preferences for unimanual and coordinated bimanual tasks in baboons (*Papio anubis*). *Cognitive Brain Research*, *25*(1), 210-216.
- Ward, J. P., & Hopkins, W. D. (Eds.). (1993). *Primate laterality: Current behavioral evidence of primate asymmetries*. Springer Science & Business Media.
- Warren, J. M. (1980). Handedness and laterality in humans and other animals. *Physiological psychology*, *8*(3), 351-359.
- Waters, R. S., Samulack, D. D., Dykes, R. W., & McKinley, P. A. (1990). Topographic organization of baboon primary motor cortex: face, hand, forelimb, and shoulder representation. *Somatosensory & motor research*, *7*(4), 485-514.
- Westergaard, G. C., Champoux, M., & Suomi, S. J. (1997). Hand Preference in Infant Rhesus Macaques (*Macaca Mulatta*). *Child Development*, 387-393.
- Yousry, T. A., Schmid, U. D., Alkadhi, H., Schmidt, D., Peraud, A., Buettner, A., & Winkler, P. (1997). Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. *Brain*, *120*(1), 141-157.
- Zhao, D., Wang, Y., & Wei, X. (2016). Hand preference during bimanual coordinated task in northern pig-tailed macaques *Macaca leonina*. *Current Zoology*, *62*(4), 385-391.
- Zilles, K., Armstrong, E., Moser, K. H., Schleicher, A., & Stephan, H. (1989). Gyrification in the cerebral cortex of primates. *Brain, Behavior and Evolution*, *34*(3), 143-150.

Figure legends

Fig. 1. Picture of an adult male olive baboon performing the bimanual coordinated tube task.



Fig. 2. a) 3-D representation of a baboon's right hemisphere of a baboon. b) 3-D representation of Central Sulcus (CS). c) Depth CS Asymmetry (Mean Asymmetry

Quotient values $AQ \pm SE$) from posterior to anterior CS positions (14-85) in left-handed *versus* right-handed groups of baboons. Positive AQ values indicate rightward hemispheric asymmetry, negative AQ values leftward hemispheric asymmetry. Highlighted in purple the MH region from position 56 to position 61 of the CS where difference of depth asymmetry (Mean AQ values) was significant between the right-handed and the left-handed baboons' groups. * $p < 0.05$.

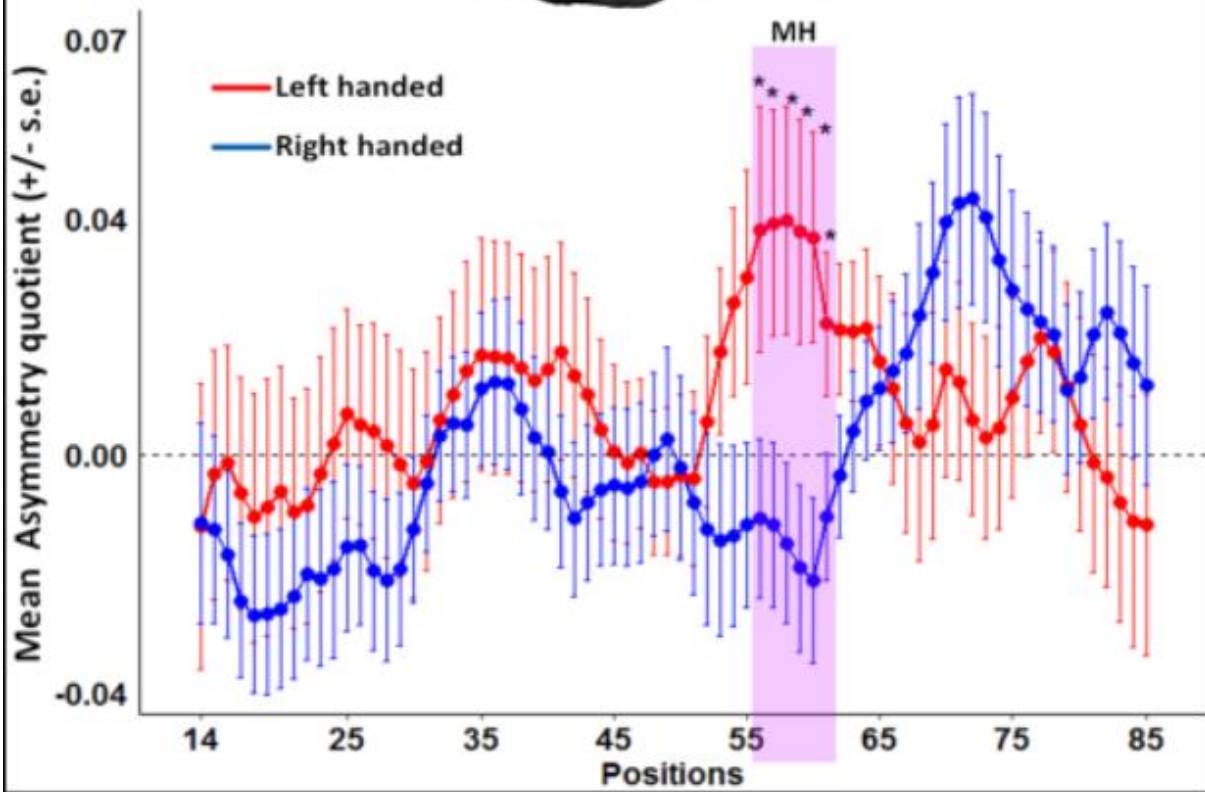
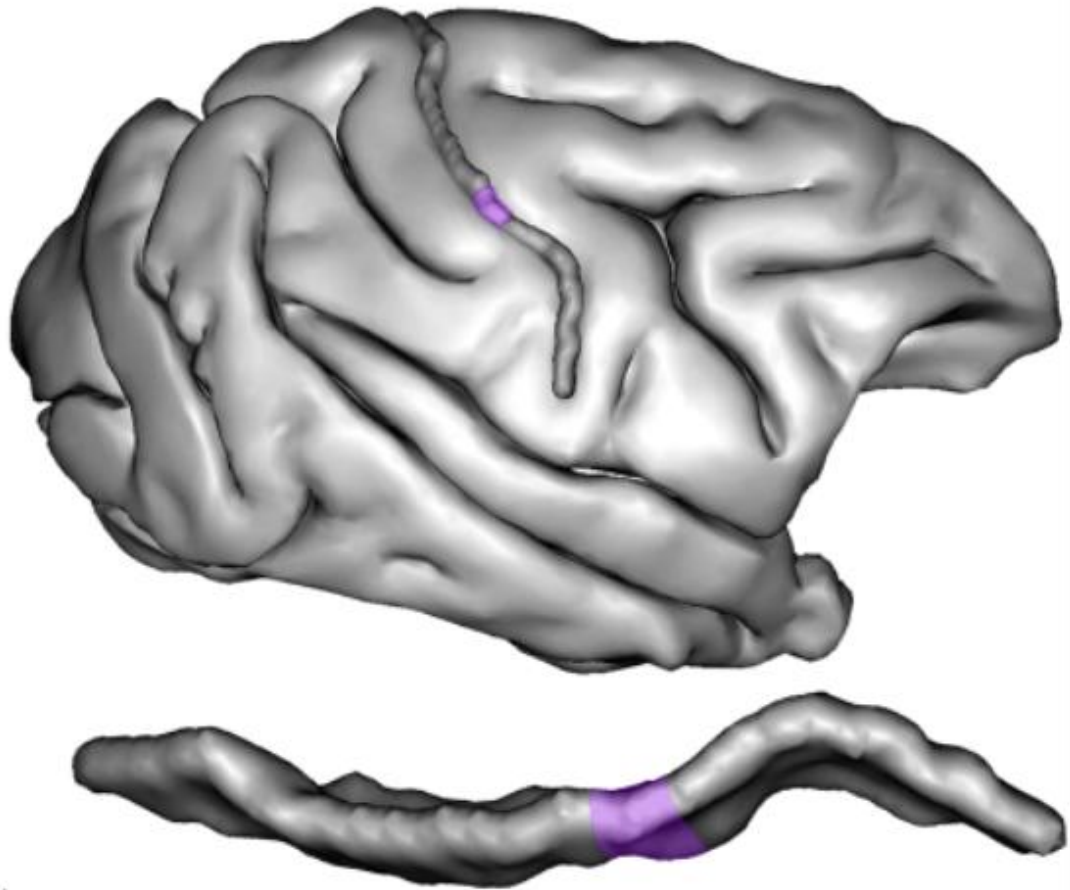
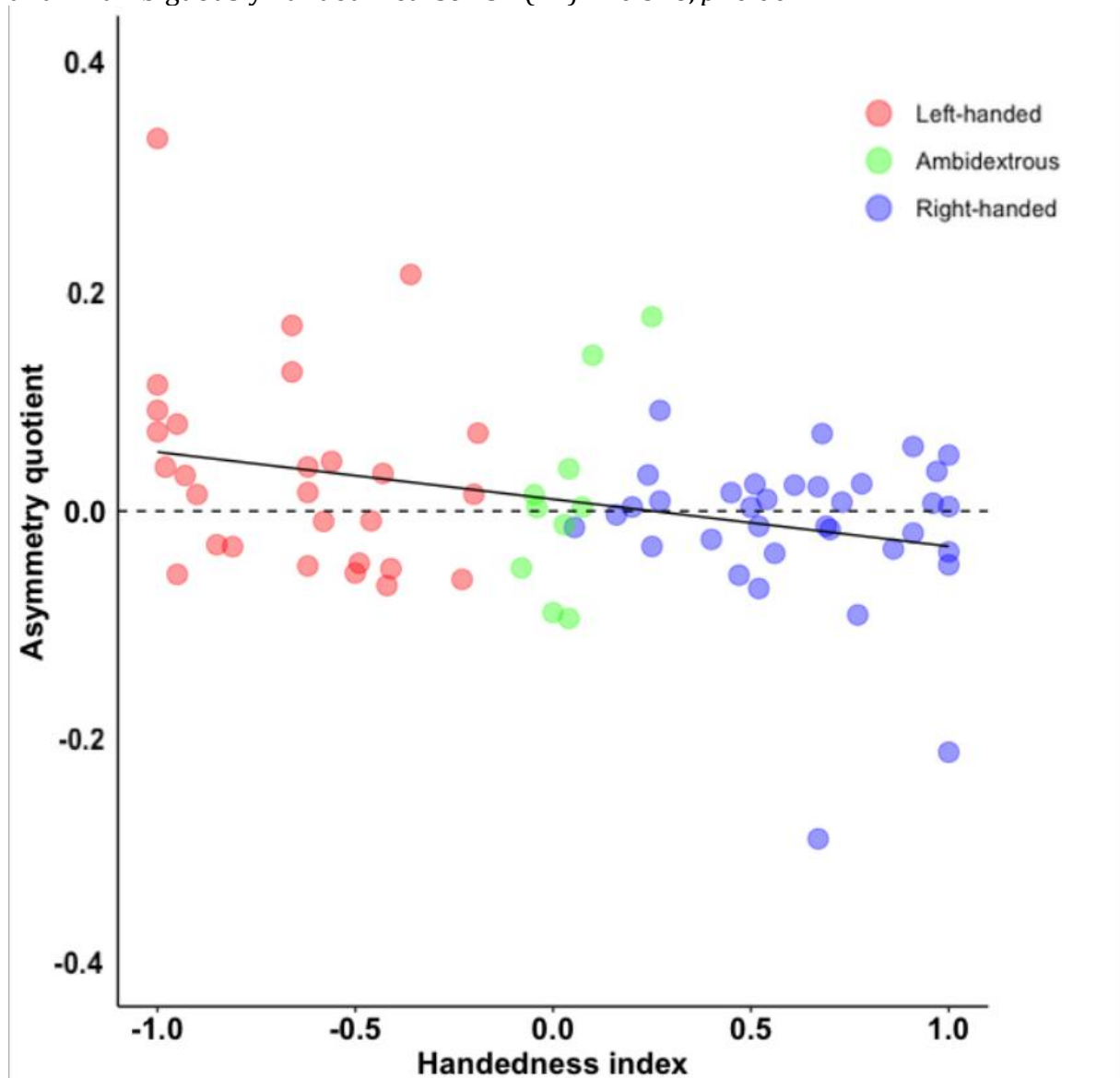


Fig. 3. Individual AQ depth values for MH segment (i.e., 56-61 positions) plotted with individual Handedness Index (HI) values in 74 baboons: 35 right-handed, 28 left-handed and 11 ambiguously handed. Pearson's $r(74) = -0.316, p < 0.007$.



Acknowledgments

The project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme grant agreement No 716931 (716931 - *GESTIMAGE - ERC-2016-STG*, P.I. Adrien Meguerditchian), from the French "Agence Nationale de la Recherche" (ANR-12-PDOC-0014-01, LangPrimate Project, P.I. Adrien Meguerditchian) as well as from grants ANR-16-CONV-0002 (ILCB), ANR-11-LABX-0036 (BLRI) and ANR-11-IDEX-0001-02 (A*MIDEX).

We are very grateful to the Station de Primatologie CNRS, particularly the animal care staff and technicians, Jean-Noël Benoit, Jean-Christophe Marin, Valérie Moulin, Fidji and Richard Francioly, Laurence Boes, Célia Sarradin, Brigitte Rimbaud, Sébastien Guiol, Georges Di Grandi but also the vet Alice Bertello for their critical involvement in this project, Ivan Balansard, Sandrine Melot-Dusseau, Laura Desmis, Frédéric Lombardo and Colette Pourpe for additional assistance.

Conflict of Interest:
None declared.