Neuroscience Research 122 (2017) 25–34

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.elsevier.com/locate/neures

Elucidation of developmental patterns of marmoset corpus callosum through a comparative MRI in marmosets, chimpanzees, and humans

Tomoko Sakai[a,b,c,d,*], Yuji Komaki[b,e], Junichi Hata[b,e,f], Junko Okahara[b,e,f], Norio Okahara[b,e], Takashi Inoue[b,e], Akichika Mikami[c,g], Mie Matsui[h], Kenichi Oishi[a], Erika Sasaki[e,f,i,**], Hideyuki Okano[b,f,***]

[a] The Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA
[b] Department of Physiology, Keio University School of Medicine, Tokyo 160-8582, Japan
[c] Primate Research Institute, Kyoto University, Inuyama, Aichi 484-8506, Japan
[d] Japan Society for the Promotion of Science, Tokyo 102-0083, Japan
[e] Central Institute for Experimental Animals, 3-25-12 Tonomachi, Kawasaki, Kanagawa 210-0821, Japan
[f] RIKEN Brain Science Institute, Laboratory for Marmoset Neural Architecture, Wako, Saitama 351-0198, Japan
[g] Faculty of Nursing and Rehabilitation, Chubu Gakuin University, Seki, Gifu 504-0837, Japan
[h] Department of Cognitive Science, Institute of Liberal Arts and Science, Kanazawa University, Ishikawa 920-1192, Japan
[i] Advanced Research Center, Keio University, Shinjuku-ku, Tokyo 160-8582, Japan

ARTICLE INFO

Article history:
Received 13 February 2017
Received in revised form 2 April 2017
Accepted 3 April 2017
Available online 9 April 2017

Keywords:
Corpus callosum
Brain development
Brain evolution
Magnetic resonance imaging
Marmosets
Chimpanzees
Humans

ABSTRACT

The corpus callosum (CC) is present in all primate brains and is the major white matter tract connecting the cerebral hemispheres for integration of sensory, motor and higher-order cognitive information. The midsagittal area of the CC has frequently been used as a sensitive biomarker of brain development. Although the marmoset has been considered as an alternative non-human primate model for neuroscience research, the developmental patterns of the CC have not been explored. The present longitudinal study of magnetic resonance imaging demonstrated that marmosets show a rapid increase of CC during infancy, followed by a slow increase during the juvenile stage, as observed in chimpanzees and humans. Marmosets also show a tendency toward a greater increase in CC during late infancy and the juvenile stage, as observed in humans, but not in chimpanzees. However, several differences between marmosets and humans were identified. There was a tendency toward a greater maturation of the human CC during early infancy. Furthermore, there was a tendency toward a greater increase during late infancy and the juvenile stage in marmosets, compared to that observed in chimpanzees and humans. These differences in the developmental trajectories of the CC may be related to evolutional changes in social behavior.

1. Introduction

Elucidating the differences between phylogenetic and ontogenetic patterns underlying brain structure in humans (*Homo sapiens*) and non-human primates is important for understanding unique social behaviors and cognition as well as brain mechanisms in human evolution. These biological insights will provide important clues for clarifying the mechanisms underlying neurodevelopmental and psychiatric disorders such as autism disorder, attention deficit hyperactivity disorder, and schizophrenia.

Recently, an arboreal New World primate species native to the Atlantic coastal forests of Brazil, the common marmoset (*Callithrix jacchus*), has been anticipated to become an important non-human primate model of human behavior, including its dysfunction in neurodevelopmental and psychiatric disorders (see more detail in (Miller et al., 2016; Okano et al., 2016)). The fundamental reasons for using a marmoset model rather than the other non-human primate models are as follows: (i) Like humans, but unlike many other non-human primates, the marmoset lives in family groups (Tardif et al., 2003) and shows alloparental care, i.e., care provided by

* Corresponding author at: The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, 210 Traylor building, 720 Rutland AvenueBaltimore, MD 21205, USA.
** Corresponding author at: Central Institute for Experimental Animals, Kawasaki, Kanagawa 210-0821, Japan.
*** Corresponding author at: Department of Physiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan.
E-mail addresses: sakai.tomoko.5w@gmail.com, tsakai3@jhmi.edu, sakai@z3.keio.jp (T. Sakai), esasaki@ciea.or.jp (E. Sasaki), hidokano@a2.keio.jp (H. Okano).

http://dx.doi.org/10.1016/j.neures.2017.04.001
0168-0102/

non-mother family members (Fernandez-Duque et al., 2009); (ii) the marmoset has unique vocal communications with social context (Pistorio et al., 2006); (iii) the marmoset can be handled with comparative ease owing to its small adult body size (350–450 g) (Hearn, 1983), which makes this non-human primate perhaps the least expensive primate model to maintain in a biomedical laboratory; (iv) the marmoset has a strong reproductive efficiency: it matures by 18 months to two years of age, and produces the next generation of offspring by three years of age; (v) the marmoset can be genetically modified and manipulated by genetic engineering, which makes it possible to generate models of human disease in a non-human primate (Sasaki et al., 2009; Sato et al., 2016).

However, whether ontogenetic development differs between the brains of marmosets and humans remains unclear, because the developmental trajectory of the brain has not been explored in marmosets. To address this lack of information and obtain empirical evidence that the marmoset is useful as a non-human primate model to understand the brain mechanism underlying human neurodevelopmental and psychiatric disorders, we started to track the developmental patterns of the brain in growing common marmosets using high resonance magnetic imaging in 2014 as part of a Japanese brain mapping project (Brain/MINDS; http://brainminds.jp/en/).

In the present study, we focused on the developmental pattern of the corpus callosum (CC) of the marmoset brain. The CC is the major commissural white matter bundle that connects the left and right cerebral hemispheres and provides interhemispheric integration, which is related to sensory, motor, and higher-order cognitive functions (Pandya and Seltzer, 1986; Tomasch, 1954). The CC is present in all primates and has evolved with the neocortex (Kappers et al., 1936; Rapoport, 1990). The midsagittal area of the CC has commonly been used as a sensitive marker of brain development in basic and clinical neuroscience studies (Giedd et al., 1999; Keshavan et al., 2002; LaMantia and Rakic, 1990a; Pujol et al., 1993; Rakic and Yakovlev, 1968), since this area is related to the number of axons traversing the CC (Aboitiz et al., 1992; Evangelou et al., 2000; Hasan et al., 2008; Highley et al., 1999; Wahl et al., 2007).

In humans, the midsagittal CC area increases rapidly during the first two to three years of life (Faria et al., 2010; Tanaka-Arakawa et al., 2015) and continues to increase slowly during the juvenile stage, adolescence (Allen et al., 1991a; Giedd et al., 1999; Keshavan et al., 2002; Lenroot et al., 2007; Pujol et al., 1993; Tanaka-Arakawa et al., 2015), and young adulthood until the third decade of life (Clarke et al., 1989; Prendergast et al., 2015; Pujol et al., 1993; Rakic and Yakovlev, 1968).

Like humans, the development of the CC area in chimpanzees is characterized by a rapid increase during infancy, followed by gradual increase during juvenile stage (Sakai et al., submitted).

To investigate the developmental changes of the marmoset CC, we longitudinally quantified the midsagittal CC area in growing common marmosets during infancy and the juvenile stage and compared these results with previously recorded data from chimpanzees and humans.

2. Materials and methods

2.1. Participants

2.1.1. Marmosets

Sixteen marmosets (seven males and nine females), whose ages ranged from 0.9 to 12.7 months were longitudinally (Table S1). In addition, eight adult marmosets were cross-sectionally evaluated as references (Table S1). Adult marmoset characteristics were as follows: mean (s.d.) age, 6.24 (0.30) years; female/male ratio, 50 percent male. All subjects lived within a family consisting of a breeding pair and two or three litters of their offspring at the Central Institute for Experimental Animals (CIEA). The treatment of the marmosets was in accordance with the 2013 and 2016 version of the Guidelines for the Care and Use of Laboratory Primates issued by the CIEA. All care and experimental protocols were approved by the Institutional Animal Care and Use Committee of the CIEA (approval number: 14040A, 16017A).

Table 1
Distribution of scan availability in marmosets.

Infancy-juvenile period (Longitudinal scan, n = 16)		Adult period (Cross-sectional scan, n = 8)	
Number of scans	n	Number of scans	n
1 scan	2	1 scan	8
2 scans	3	2 scans	0
3 scans	9	3 scans	0
4 scans	1	4 scans	0
5 scans	1	5 scans	0

2.1.2. Chimpanzees

We used part of the previously published numerical dataset from a chimpanzee longitudinal MRI study about midsagittal CC areas. Four chimpanzees (1 male, 3 females), whose ages ranged from 1.8 months to 6 years (see details in Sakai et al., submitted data; these data were presented as an abstract at the 38th Annual Meeting of the Japan Neuroscience Society in 2015) were analyzed (Table S1). The comparison with chimpanzee adult CC areas was based on the data from 10 adult chimpanzees which served as controls (see details in Sakai et al., submitted data). Adult participant characteristics were as follows: mean (s.d.) age, 31.2 (5.8) years; female/male ratio, 30 percent male (Table S1). All subjects lived within a social group of 14 individuals in an indoor-outdoor enclosure at the Primate Research Institute, Kyoto University (KUPRI) (Matsuzawa et al., 2006; Matsuzawa, 2007). The treatment of the chimpanzees was in accordance with the 2002 and 2010 version of the Guidelines for the Care and Use of Laboratory Primates issued by KUPRI. All care and experimental protocols were approved by the Animal Welfare and Animal Care Committee of the KUPRI.

2.1.3. Humans

We used part of the previously published numerical dataset from a human cross-sectional MRI study about midsagittal CC areas. Seventy-two healthy children (40 males, 32 females), whose ages ranged from one month to 10.5 years (see details in (Tanaka-Arakawa et al., 2015)) were analyzed (Table S1). The comparison with human adult CC areas was based on the data from 14 healthy adults who served as controls (Tanaka-Arakawa et al., 2015). Adult participant characteristics were as follows: mean (s.d.) age, 19.9 (1.9) years; female/male ratio, 50 percent male. All parents and adult participants gave written informed consent for participation after the nature and possible consequences of the study were explained (Table S1). All the protocols of the study were approved by the Committee on Medical Ethics of Toyama University (#165).

2.2. Image acquisition

2.2.1. Marmosets

Three-dimensional, high-resolution T1-weighted, whole-brain images were acquired with a 7 T MR imager (Biospec 70/16; Bruker Biospin) equipped with actively shielded gradients that had a maximum strength of 700 mT/m. The inner diameter of the integrated transmitting and receiving coil was 62 mm. At least 1 scan was obtained from each of 16 marmosets. Of these, 14 had at least 2 scans, 11 had at least 3 scans, 2 had at least 4 scans and 2 had 5 scans, acquired at approximately regular intervals (Table 1). The marmosets were anesthetized with ketamine (30 mg/kg) and xylazine