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FRONT MATTER

Title

- Neurodevelopmental timing and socio-cognitive development in a prosocial cooperatively breeding primate (*Callithrix jacchus*)
- Neural and cognitive development in the common marmoset

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Abstract

Primate brain development is shaped by inputs received during critical periods. These inputs differ between independent and cooperative breeders: in cooperative breeders infants interact with multiple caregivers. We study how the neurodevelopmental timing of the cooperatively breeding common marmoset maps onto behavioral milestones. To obtain structure-function co-constructions we combine behavioral, neuroimaging (anatomical and functional) and neural tracing experiments. We find that brain areas critically involved in observing conspecifics interacting: (i) develop in clusters; (ii) have prolonged developmental trajectories; (iii) differentiate during the period of negotiations between immatures and multiple caregivers; (iv) do not share stronger connectivity than with other regions. The developmental timing of social brain areas correlates with social and behavioral milestones in marmosets and, as in humans, extends into adulthood. This rich social input is likely critical for the emergence of their strong socio-cognitive skills. Since humans are cooperative breeders too, these findings have strong implications for the evolution of human social cognition.

Teaser

In common marmosets, brain regions implicated in processing social interactions develop slowly, until early adulthood.

MAIN TEXT

Introduction

Strong social cognition and prosociality are, from a very young age, hallmarks of the human mind compared to the closest living relatives, the non-human great apes (1). Due to our peculiar life-history, characterized by early weaning and extensive allomaternal care starting from very early in infancy, human development is embedded in a world filled with other individuals, including parents, siblings, and other family members. Thus, this is the context in which human toddlers' strong social cognition and prosociality develops (2). It is this same period that is also the most important for the formation of the neural bases of higher-order social, emotional and communicative functions (3). Not surprisingly then, several independent lines of evidence, spanning neuroscience, pediatrics, primatology and psychiatry point to the fundamental role that the relative timing of brain development and social interactions have for the acquisition of social cognition and prosocial behaviors (4).

During ontogeny, total brain volume increases until reaching its adult levels. This volumetric increase is the product of gray matter volume increase until a peak value is reached in childhood, after which it decreases concurrently with synaptic pruning and white matter volumetric increase (5). Additionally, the ontogenetic trajectories of cerebral gray matter are heterochronous, such that both maximum gray matter volume and gray matter reduction rate vary across brain regions. The importance of the temporal patterns of brain development in shaping the adult phenotype become apparent, for example, in the case of autism spectrum disorder (ASD). Indeed, deviations from the normal range of developmental timing of the cortex can profoundly impact socio-cognitive skills and are one of the main factors linked to the occurrence of autism spectrum disorder (3). Specifically, several studies have found that early brain overgrowth during the first years of life strongly correlates with ASD (e.g. (6)) and a meta-analysis of all published MRI data by 2005 revealed that the period of greatest brain enlargement in autism is during early childhood rather than xx as in neurotypicals (7), with about a 10% volume increase compared to controls during the first year of life. Hence, individuals affected by ASD present an accelerated early-life brain growth and achieve a final brain volume that is not different from that of controls, but they achieve it earlier than controls. Indeed, recent work with human brain organoids has confirmed the accelerated maturation of the cortex in the ASD phenotype, especially interneurons (8, 9)[EG1]. Consequently, given this accelerated early-life brain development, fewer social inputs are available during the period when gray matter volume reduces to adult size and differentiates via experience-dependent pruning. Accelerated development of functional connectivity between certain brain areas (e.g. amygdala-prefrontal cortex) can also be a consequence of early life stress, which in turn can cause adverse physiological conditions such as increased anxiety and cortisol levels (10). Unfortunately, so far nothing is known regarding the impact of changes in brain developmental timing within non-human species. That is, we don't know whether within a given non-human species, alterations in ontogenetic trajectories of the brain have an impact on the adult behavioral phenotype. However, comparative studies across species with different ontogenetic trajectories and social behaviors can help us shed light on the relationship between the two.

The importance of social inputs occurring during prolonged brain maturation and slow developmental pace has also been highlighted in the context of human evolutionary studies. The significant brain growth and development occurring postnatally in humans arguably allows the

brain to be influenced by the social environment outside of the uterus to a greater extent than that seen in other great apes (11), who are not cooperative breeders (12). Hawkes and Finlay (2018) show that in addition to weaning our infants earlier than expected (based on allometric scaling with other life-history variables), human neonates have an especially delayed neural development, which is likely correlated with the energetic trade-offs stemming from the large size and high caloric demand of our brain (14). Additionally, we observe that in humans, compared to other great apes, myelination is much prolonged and continues well into adulthood (15).

Common marmosets (*Callithrix jacchus*) are cooperatively breeding platyrrhine monkeys. Like humans, but unlike other great apes (12), they rely on extensive allomaternal care and share many life-history traits (e.g. short interbirth intervals and a hiatus between menarche and first reproduction) with humans (16). They also show remarkable prosociality (4, 15, much more than great apes: 16) and strong socio-cognitive abilities, which have been argued to correlate with cooperative breeding (19, 20). However, the neurobiological features underlying the socio-cognitive abilities promoting prosocial behavior are poorly understood. Moreover, experimental research has shown that in common marmosets (hereafter: marmosets) there is a critical period for the development of social behaviors (21); although the relationship between developmental timing of the brain and these early-life social interactions is poorly understood.

Given these similarities with humans, marmosets are becoming an ever-more important model in neuroscience (22–25), and particularly in research investigating the neurobiological and neurodevelopmental bases of social cognition. As in humans, immature marmosets are surrounded and cared for by multiple caregivers from the first day on. The entire family is typically present during birth and oxytocin levels increase not only in mothers, but in all group members (26). Group members contribute significantly to carrying the infants and once infants start eating solid food, frequently share food with them. After a peak provisioning period, adults are increasingly less willing to share food with them (27–29). During this period, intense and noisy negotiations over food are frequent, with immatures babbling and begging and adults eventually giving in – or not. Intriguingly, when doing so, immatures appear to take into account how willing individual adults are to share and will insist in more and longer attempts with adults who are generally less likely to refuse them. Soon after, immatures not only have to compete for attention and food with their twin sibling, but also with the next offspring that are born far before they themselves are independent because, like in humans, marmosets are weaned early and mothers have their next offspring soon after (30). By now, the immatures still have not reached puberty; this only happens shortly before yet another set of younger siblings is born. Typically with these new arrivals the immatures start to act as helpers themselves, and thus face the developmental task of switching from being a recipient of help to becoming a provider of help and prosocial acts (31). This is thus the developmental context in which marmoset socio-cognitive skills develop.

The goal of this study is to map these behavioral milestones specific to a cooperatively breeding primate to its region-specific brain development to better understand the social interactions in which infants engage during the differentiation period of brain regions selectively implicated in processing social stimuli. Our working hypothesis is that, like in humans, social interactions with several caregivers during this critical period profoundly contribute to the co-construction of the marmoset brain, the maturation of socially-related associative areas and, therefore, the emergence of prosocial behaviors. For that purpose, we sought to determine whether there is a relationship

between the temporal profile of the developing marmoset brain and the early-life social interactions which may help explain their sophisticated socio-cognitive skills at adulthood.

To compare the timing of brain development to that of these behavioral milestones and developmental tasks of attaining nutritional independence, we focused on brain regions that in adult marmosets are selectively activated by the observation of social interactions between conspecifics, but not by multiple, but independently behaving marmosets, as identified by Cléry and colleagues (2021). We tested whether these brain regions share similar developmental trajectories based on the developmental patterns of regional gray matter volume. To potentially reveal a coordinated ontogenetic profile underlying the “tuning” of the social brain in marmosets, we then compared these neurodevelopmental patterns to longitudinal data of infant negotiations with caregivers in relation to food (as measured by the frequency of food begging). Finally, since it is known that brain regions whose activations correlate with performance on a given task strengthen and get fine-tuned with age (33, 34) we assessed whether there is stronger connectedness between areas that develop according to similar developmental trajectories and share similar response to social interaction stimuli.

We thus combined several types of previously-published data from marmosets in order to provide a unified picture of structural brain development alongside the development of social interactions between infants and multiple caregivers necessary to ensure survival (infant provisioning). These included structural magnetic resonance data (sMRI) of gray matter (GM) of 53 cortical areas and 16 subcortical nuclei acquired from a developmental cohort (aged 13 to 104 weeks) of 41 male and female marmosets (35) (for these data only summary statistics had been previously published, while here we accessed and analyzed the entire dataset); functional magnetic resonance data (fMRI) mapping the brain areas activated by the observation of social interactions in marmosets (32); food sharing interactions in five family groups of marmosets including a total of 26 adults and 14 immatures (from 1 to 60 weeks of age, (27)), and cellular-resolution data of corticocortical connectivity in marmosets obtained via 143 retrograde tracer injections in 52 young adult marmosets of both sexes (36).

Overall, we make the following predictions:

- P1: cortical regions that show significantly stronger activation during the observation of social interactions (32) share similar structural neurodevelopmental profiles, which are distinct from those regions showing significantly stronger activation during the observation of non-social activities.
- P2: specifically, the different neurodevelopmental profiles are determined by the fact that brain regions (both cortical and subcortical) showing a significantly stronger activation during the observation of social interactions exhibit a protracted development, reaching their adult volume later than the other regions.
- P3: the developmental trajectory of infant negotiations with caregivers in relation to food (as measured by the frequency of food begging) is more similar to that of brain regions responding more strongly to the observation of social interactions than to the other regions.
- P4: functional connectivity is stronger between regions with similar developmental timing and response strength to the observation of either social or non-social behaviors, and weaker between regions with different developmental timing and response strength.

Results

Overall, our results support our predictions and show that: (i) brain areas that respond significantly more strongly to visual stimuli of social interactions present similar developmental trajectories and thus belong to the same clusters to the exclusion of regions that respond more strongly to visual stimuli of individuals acting alone; that (ii) social clusters have an extended developmental trajectory, reaching adult-like volumes later and after a period of plateau; and that (iii) the ontogenetic trajectory of food negotiations matches quite well that of “social” brain regions. However, we did not find support for stronger corticocortical connections between areas with stronger responses to visual stimuli of social interactions: social regions did not appear to form a strongly connected network.

P1 – do ‘social’ areas share similar trajectories?

There is a biunivocal correspondence between those brain regions that were differentially activated (as measured via fMRI) by either social interactions or solitary behaviors (Fig. 1A) and neurodevelopmental clusters (Fig. 1B). Specifically, social interactions activated regions fell into three developmental clusters; cortical areas 1 and 2, 3a, 4ab, 6DC and 8C cluster together; areas 14C, 25, 46D and 9 belong to another cluster; areas 10, 45, 47L and the preisocortical motor region belong to yet another cluster. Conversely, the seven cortical areas that responded more strongly to the observation of solitary behaviors, fell into the other three of the six developmental clusters: visual areas 1, 2 and 6 form one cluster; visual areas 3 and 4 form another cluster; and temporal area TE1/2 and the ventral temporal lobe form another cluster. As per our prediction, a given developmental cluster contains areas responding more strongly only to one of the two conditions.

P2 – do “social” areas have protracted developmental?

The results of the Bonferroni-corrected pairwise t-tests for each of the four neurodevelopmental milestones and three ranges (Table 1, Fig. 2) indicate that the age at the fastest rate of gray volume decline is the only milestone that differs significantly between regions that respond more strongly to visual stimuli of social interaction vs. solitary behaviors. Moreover, it is the temporal range between the age at maximum gray volume and the age at fastest rate of gray volume decline that distinguishes regions with differing activation to the two types of stimuli. The duration of the volumetric “plateau”, measured as time from the age at maximum volume to the age at which there is the first descending inflexion point (Fig. S1 and S2) differs significantly ($p=0.011$) between brain areas that respond more strongly to visual stimuli of social interactions than to those of solitary behavior. The ontogenetic trajectory of the 10 regions that don’t differ in response to both stimuli of social interaction and non-social activities are shown in Fig. S3. These regions are located in the temporal, parietal, and orbitofrontal cortex, which are known to be implicated in both social perception and socioemotional action.

P3 - are regional trajectories of “social” brain areas similar to those of social feeding behaviors?

The results of the comparisons between developmental trajectories of brain regions and food proactively shared or begged support our prediction. The age at fastest decline is much later for the proportion of food begged (58 weeks) than for the proportion of proactively shared food (25 weeks). Moreover, the range between the peak and the age at fastest decline is also larger for the proportion of food begged (31 weeks) than for the proportion of food shared (17 weeks). The ontogenetic trajectory of food begging parallels that of the brain regions with stronger activation in response to visual stimuli of social interactions, while that of proactively shared food parallels that of the brain regions with stronger activation in response to stimuli of solitary behaviors (Fig.

S4, Table 2). The ontogenetic trajectories of the two patterns of food provisioning (proactively sharing and begging) parallel those of brain regions (respectively, non-social and social) but anticipate them (Fig. 2).

P4 – do regions with similar GM developmental profiles and fMRI response to stimuli of social interactions have stronger functional connectivity?

Our results (Table 3) indicate that connectivity strength is significantly different (and greater) between those regions that both respond more strongly to non-social stimuli, rather than between those responding more strongly to social stimuli. The regions that respond more strongly to non-social stimuli are also the ones with faster developmental trajectories, which cluster in groups 1, 3 and 6. The results when the same analysis is performed on regions grouped by developmental cluster, rather than in response to different stimuli, are reported in the supplementary materials (Table S1, Fig. S5). Models with *Source_to_Target* as additive term had lower AIC scores than the corresponding model with *Source_to_Target* as interaction term, indicating that source to target alters the slope of the relationship between fraction of extrinsic labeled neurons and age at maximum rate of volumetric decline of the region. The results of the two models with additive term (Tables S2 and S3) indicate that there is a weak correlation between similarity in developmental timing and connectivity strength (for both models: $R^2 = 0.2$; $p < 0.0001$). We used the Akaike Information Criterion (AIC) (37) to compare the two models, and the one having as response variable the absolute difference in age at maximum rate of volume decline is the best one. Finally, in both models, the intercept is significantly different ($p < 0.0001$) only between regions that both respond more strongly to non-social stimuli, thus confirming the results of the Wilcoxon-rank sum tests (Fig. S6).

Discussion

Our findings reveal that those brain regions more strongly activated when observing social interactions between conspecifics than conspecifics engaging in non-social activities have ontogenetic trajectories that differ from those regions that are not more strongly activated (P1), indicating that developmental timing and function are correlated in marmosets. Specifically, while the various brain regions do not differ significantly with respect to the age at which they reach their maximum GM volume, those involved in processing social interactions maintain the maximum volume significantly longer, before decreasing in size and reaching their adult value (P2). Since GM volumetric decline is a consequence of synaptic pruning and intra-cortical myelination (38), it functionally corresponds to a decrease in developmental plasticity.

Social regions thus remain plastic for longer during ontogeny. Of all the regions analyzed, the one with the latest peak in volumetric decline and therefore most prolonged plasticity is the basolateral nucleus of the amygdala. This nucleus is implicated in encoding emotional events with reference to their particular sensory-specific features (39) and has undergone convergent evolution in its volumetric patterns in cooperatively breeding species including marmosets and humans (40). The slowest developing cortical area is 46D. It is located in the dorsolateral prefrontal cortex, together with areas A10 and A9, which are also slow in developing and respond more strongly to social stimuli. In humans, the dorsolateral prefrontal cortex has been shown to be implicated in theory of mind (41) and in the suppression of selfish behaviors (42). The next slowest developing brain region is A14C, located in the ventromedial prefrontal cortex together with areas 45, 47L and the preisocortical motor region (ProM). A14C is also known to be heavily implicated in social

cognition (43), including joint attention (44), facial emotion recognition, theory-of-mind ability and processing self-relevant information in humans (45). Interestingly, a longitudinal study in humans affected by ASD has shown that differential activation during a temporal discontinuing task in the ventromedial prefrontal cortex, including A14C, and cerebellum in these individuals was associated with abnormal functional brain maturation (46). In addition, there is a decrease in effective connectivity from the temporal pole (another late-maturing brain region) to the ventromedial prefrontal cortex, and overall lower activation in the latter in ASD (47).

Our findings on regional developmental timing in marmosets are similar to those recently described in humans (5). Both species have similar temporal ranges, in relation to developmental milestone, in the ages at which the different regions reach their maximum volume (2 to 10 years in humans; roughly corresponding to the 22 to 77 weeks in marmosets) (48). The same study on humans also highlighted an important similarity to our findings in marmosets: primary sensory regions showed earlier post-peak declines, whereas fronto-temporal association cortical areas showed later post-peak declines.

It is during the period of peak provisioning by non-maternal family members that gray matter volume is dramatically increasing (Fig. 3), potentially highlighting the fundamental role played by food sharing in providing the nutritional and energetic needs of the developing brain.

The ontogenetic trajectory of regions more strongly activated by the observation of social interactions resembles that of food begging (which is inherently socially interactive), but not of proactively shared food, which does not require active communicative participation from the side of the infant (P3). The proportion of proactively shared food peaks at 8 weeks of age (ranging from week 7-20), a time during which breeders and alloparental caregivers share more than 50% of the food items. Conversely, infant begging peaks at 27 weeks of age, with values remaining high (above 50%) until 50 weeks. Infant begging is a form of interaction and communication that requires an active participation of the infant (unlike proactive sharing), who must learn to engage and elicit care most efficiently from a plurality of individuals (parents and helpers). Anticipating the current motivation and intention of these individuals and adjusting their own solicitation behavior accordingly are important means by which immatures can reach high efficiency in achieving their goal.

Research on humans has shown that the elicitation of care from non-maternal caregivers entails the mobilization of more regulatory efforts than during the interactions with mothers (49). Furthermore, comparative work on primates (50) indicates that in species practicing alloparental care there is greater control of the facial musculature and facial expressions, which facilitate non-vocal communication between infants and caregivers. These findings align well with recent work (51, 52) that used fMRI to identify face-selective patches in the marmoset brain and found differential activation in subcortical regions and in the anterior cingulate and lateral prefrontal cortices while animals viewed socially relevant videos of marmoset faces. This differential activation was observed in many of the brain regions that are also the slowest to reach the age at maximum volume decline, such as the amygdala (102 weeks of age), the cerebellum (92.6 weeks), A32 (82.5 weeks) and A8 (70.1 weeks) which are located in the anterior cingulate, and A47L (68.3 weeks) which is located in the lateral prefrontal cortex. This combined evidence suggests that facial expressions are not only important for infant-alloparent communication, but that the brain regions employed to process these expressions have a prolonged plasticity compared to other brain

regions (average age at fastest decline across all regions is 65.1 weeks), and that this prolonged ontogenetic trajectory maps onto that of infant-caregiver interactions in relation to food begging.

Limitations of this study are mainly regarding sample sizes. First, while the fMRI data used in our work (32) represents the most cutting-edge development and updated data of this type for marmosets, it is nevertheless collected on a small sample of subjects: three adult marmosets (one female, two males). However, other recent work (52, 53) on marmosets employing fMRI to differentiate brain regions that are activated by visual stimuli depicting an intact action vs. its phase-scrambled version corroborate and replicate the results obtained by Cléry and colleagues (32). Further work with an increased number of individuals representing several age groups would provide a valuable validation of our results and the possibility to assess how the structural development and the functional response of brain regions responding more actively to stimuli of social interactions map onto each other. Furthermore, due to slight differences in the parcellation of the cortical areas between the structural MRI and the functional MRI data (e.g. area 19 in sMRI data and area 19M in fMRI data), it was only possible to match 32 regions. Greater homology in the parcellation used would allow for an increased sample size in regions for which structural and functional data is both available. Importantly, the connectivity data used for this study, although representing the most extensive anatomical collection, it is clearly insufficient. A recent study focusing on nine prefrontal subregions provide an alternative dataset in which, additionally, inputs and outputs have been analyzed separately (Watakabe et al Neuron 2023). Furthermore, as suggested by accelerated maturation of specific neuronal subsets in ASD (Paulsen et al Cell 2022), it would be essential for future experiments to gain access to connectivity patterns of precise cell types in NHPs as previously reported in rodents (Ährlund-Richter et al Nat Neurosci 2019). Ultimately, studies such as this one would benefit tremendously from collecting all the different types of data (neuroanatomical, functional and behavioral) from the same individuals. This is largely limited by the different research questions that are motivating each lab to collect a specific type of data, and by the facilities available to each lab. Ideally, future research could consider conducting longitudinal studies in which behavioral, anatomical and physiological measures are acquired for animals living in as “natural-like” conditions as possible.

Despite the above limitations, several lines of evidence highlight the distinct developmental trajectories of brain regions that display a significantly stronger response to visually presented social interactions compared to those of individuals acting alone. Specifically, regions implicated in the evaluation of social interactions have prolonged neurodevelopmental time periods. Furthermore, we show that this same neurodevelopmental trajectory mirrors, with a temporal shift of about 20 weeks, that of infant food begging, a form of care elicitation and infant-adult interaction that is necessary to ensure infant survival in cooperatively breeding species. More broadly, our results are in line with recent work (54) showing that in marmosets the critical period for the acquisition of cognitive control is between 39 and 65 weeks of age, falling within the temporal period from age at maximum total GM volume and the age at fastest GM volume decline (Fig. 3). This temporal range is also the one during which individuals transition from being a recipient of help to becoming a helper (31), which arguably requires inhibitory control (i.e. to share rather than consume food items) (55). Our results are further supported by previous findings (56) showing that, in marmosets, family size has an effect on the age at which brain regions mature, with individuals belonging to larger families (and therefore having to integrate a larger number of different social interactions) having protracted neurodevelopment compared to those living in smaller families. This could be explained by the need to become helpers earlier on, if no older

sibling are present, however further research taking into account not only family size but social roles within the family group are necessary to better understand the mechanism at play.

Finally, our current work underscores the striking similarity in the relationship between brain developmental patterns and behavioral milestones in marmosets and humans (Fig. 3). In both species, perhaps because of the short interbirth intervals, immatures become helpers and become physiologically capable of reproduction while GMV volumes are still drastically changing, and even before GMV reaches its maximum rate of decline. Additionally, both species experience a hiatus between the onset of puberty and the age at which first reproduction actually occurs. This is likely because prior social experience with being a helper is necessary to carry out a successful reproductive event. Indeed, reproduction in callitrichids often fails if individuals have not been helpers first (57).

Phenotypic convergences between distantly related species as a consequence of changes in developmental timing are all but surprising. Indeed, across mammals, both allomaternal behavior and developmental timing are phylogenetically labile compared to most other traits (58, 59). Hence, heterochrony (i.e. a difference in the timing, rate, or duration of a developmental process) can likely cause the phenotypic convergence observed in marmosets and humans, two species whose evolutionary trajectories diverged ~42MYA (60) but that in many life-history aspects resemble each other more than each one resembles its sister taxon. Moreover, it is known that small differences in timing can result in large phenotypic changes, such that, for example, heterochronic divergence can cause paedomorphosis (i.e. the retention of an ancestral juvenile trait into adulthood) due to neoteny (61). Hence, changes in the timing of life history events, in relation to the relatively phylogenetically conserved neurodevelopmental schedule (62) can cause convergence in the adult phenotype. Future comparative studies of the neurodevelopmental and behavioral trajectories of independently-breeding, closely related taxa are the next fundamental step to effectively understand how the interplay between anatomical and behavioral timing shapes prosocial behavior. Additionally, data including non-primate cooperative breeders and independently-breeding taxa has the potential to further corroborate the evolutionary convergence between protracted neurodevelopment, breeding system and social behaviors.

While life-history and cognitive convergences between humans and marmosets have been abundantly documented, here we provide the first comparative evidence of what is potentially the developmental trajectory underlying the emergence of the adult phenotype (i.e. we address the mechanistic and ontogenetic aspect of the question, *sensu* Tinbergen (63)). We argue that it is a delayed and prolonged brain development occurring during a time in which infants actively engage in social interactions and negotiations that allows for the emergence of prosociality: the brain needs time with alloparents and selective pressures to interact with them, in order to be tuned towards prosociality. Our results further support the notion that marmoset is an appropriate model to investigate the neurobiological underpinnings of human prosociality.

Materials and Methods

Experimental Design

Cortical and subcortical structural developmental data

The data were collected in 41 male and female animals aged between 13 and 104 weeks, with each animal scanned at least twice using a Bruker PharmaScan 47/16 MRI system (Bruker, Inc.,

Ettlingen, Germany). Temporal milestones describing the structural developmental trajectories of the 69 brain regions considered have already been published (35). The data include 53 cortical areas and 16 subcortical nuclei. In the present work we accessed non-published, GM region-specific volumetric data, compiled across individuals using cubic spline models, following (35). Since both hemispheric asymmetry and sexual dimorphism were tested for and excluded (35) we use pooled male and female right and left hemisphere values.

Functional magnetic resonance (fMRI) data

These data were obtained from a published source (32) and were acquired on male and female adult awake marmosets. Each animal was recorded while presented with video stimuli of social interactions (playing, grooming etc.) and non-social behaviors (eating, foraging, etc.), as well as to the scrambled versions of the same videos (four conditions in total). For each monkey, all four conditions were analyzed and compared, revealing the brain regions that show significantly stronger activation while observing the social condition comparing to all other three conditions (32). These areas have been coded as “social” in our dataset. The areas showing instead a significantly stronger activation during the observation of non-social behaviors have been coded as “non-social” and all others as “neither” (Data S1).

Provisioning data

Infant provisioning patterns were recorded in five family groups, including a total of 14 immatures (aged 1 to 60 weeks) and 26 adults, representing both male and female breeders, and male and female helpers (older siblings) (27). Once a food item was given to an individual, it was recorded whether each food item was shared with the infant proactively, was shared with the infant in response to infant’s begging, or was refused to a begging infant. Hence, sharing could be either proactive, facilitated or resisted, while the response to begging could be either refusing or sharing. The total proportion of food proactively shared and begged was then compiled across infants and family groups for each point in time, providing a developmental trajectory of both (Data S2). The trajectories of proactive, facilitated and resisted sharing are very similar among each other (27). Conversely, the proportion of refused food increased as the one of shared food decreased. The trajectory of food begging reflects the complex negotiation dynamic that goes from helplessly receiving, to increasingly more interacting with caregivers in order to elicit a desired outcome (food). These interactions and negotiations with multiple caregivers are a behavioral peculiarity of cooperatively breeding animals (such as humans and marmosets) which entail infant provisioning by a variety of individuals as a consequence, also, of prolonged post-weaning dependence (16).

Corticocortical connectivity data

These data have been published in an open-access form (36) and are available on the following web platform: <https://www.marmosetbrain.org>. We used the full extrinsic fraction of labeled neurons (FLNe) connectivity matrix which was obtained via 143 retrograde tracer injections in 52 young adult marmosets of both sexes. The matrix reports the results of injections centered in 55 target areas of the marmoset cortex, including subdivisions of prefrontal, premotor, superior temporal, parietal, and occipital complexes. The data represents the weighed and directed connectivity matrix based on the results of injections of monosynaptic retrograde fluorescent tracer injections. The rows and columns of the matrix represent individual cortical areas. The targets are the injected areas while the sources indicate the areas in which the projections originate. The intrinsic connections are excluded from our analysis.

Statistical Analysis

P1 – do ‘social’ areas share similar trajectories?

To obtain a finite number of meaningfully different developmental trajectories of the cortical areas, we followed Sawiak and colleagues (2018) and identified six clusters: the visual and cingulate cluster; the somatomotor cluster; the auditory-visual cluster; the orbitofrontal, dorsolateral and ventromedial prefrontal cluster; the ventrolateral prefrontal cortex (PFC), polar, operculum and insula cluster; the lateral and inferior temporal lobe cluster. Increasing cluster numbers resulted in the further subdivision of the prefrontal cortex, which is the area presenting the largest heterogeneity of developmental trajectories. We then matched the sMRI and fMRI data, which resulted in 32 regions for which we had both types of data (Data S1). Of these 32 regions, 15 respond more strongly to social interaction stimuli; 7 to stimuli of individuals acting alone; 10 respond with non-significantly different strength to both types of stimuli. The clusterization of regions based on their developmental trajectory, combined with the matching of the sMRI and fMRI data, allowed us to test whether regions with similar response to social or non-social visual stimuli present similar developmental trajectories (i.e. belong to same developmental clusters), and therefore whether developmental timing and socio-cognitive function are correlated. Subcortical nuclei are excluded from this clusterization.

P2 – do “social” areas have protracted development?

To quantify and compare the developmental timing of the different regions we defined four different milestones: A) the age at maximum volume; B) the age at the first descending inflexion point (the first local maxima of the first derivative); C) the age at maximum rate of volume decline; D) the age at the last ascending inflexion point (the last local minima of the first derivative). Three of these milestones (A, B and C) are standard ones that have been previously used (e.g. Sawiak et al., 2018), while we decided to introduce a novel one (D) to capture the decrease in rate of decline visible towards the end of the trajectories. For a visual representation and example of the four milestones, see Fig. S1 and Fig. S2. Using these four milestones we defined three temporal ranges: age at maximum volume to age at first descending inflexion point (A to B); age at maximum volume to age at fastest decline (A to C); age at maximum volume to age at the last ascending inflexion point (A to D). Finally, we proceeded to compute Bonferroni-corrected pairwise t-test for each of the four milestones and three ranges, to assess whether they were significantly different between “social” and “non-social” regions.

P3 - are regional trajectories of “social” brain areas similar to social feeding behaviors?

Based on the results of the analyses carried out to verify P2, we selected the milestones and ranges that distinguish the developmental trajectories of social regions from non-social ones and computed them also for the developmental trajectories of proactive food sharing and food begging. We then compared the values (in weeks) obtained for the provisioning data to those of the neurodevelopmental trajectories to test our prediction that interindividual negotiations (such as those occurring when infants beg caregivers for food) follow a similar developmental pattern to that of social brain regions.

P4 – do regions with similar GM developmental profiles and fMRI response to stimuli of social interactions have stronger functional connectivity?

First, we matched the corticocortical connectivity data with the GM neurodevelopmental data, which resulted in a dataset of 1400 connections encompassing 28 target and 51 source regions (Data S3). We also matched the connectivity data with the fMRI data and included only the connections for which fMRI data is present for both the target and the source. This resulted in 494 connections between 19 target and 27 source regions (Data S4). To test whether connection strength differs between regions with similar response to social or non-social visual stimuli we performed Wilcoxon-rank sum tests and adjusted the results for multiple-hypothesis testing. We used non-parametric tests because of the non-normal distribution of the data. We also performed the same tests on the data grouped according to the six developmental clusters. To test whether there is a correlation between developmental timing and connection strength across regions, for each connection we computed the average age at peak rate of volume decline between the source and target region, and the absolute difference in age at peak rate of volume decline between the source and target region. We then built four models with fraction of extrinsic labeled neurons (FLNe) as response variable and either average age at peak rate of volume decline (*avg_age_max_rate*) or absolute difference in age at peak rate of volume decline (*d_age_max_rate*) as explanatory variables, and fMRI response type in source and target regions as either: i) additive variable: $lm1 = FLNe \sim avg_age_max_rate + Source_to_Target$ and $lm2 = FLNe \sim d_age_max_rate + Source_to_Target$ or ii) interaction term: $lm3 = FLNe \sim avg_age_max_rate * Source_to_Target$ and $lm2 = FLNe \sim d_age_max_rate * Source_to_Target$. We compared each pair of models (with *Source_to_Target* as either additive or interaction term) using AIC (37).

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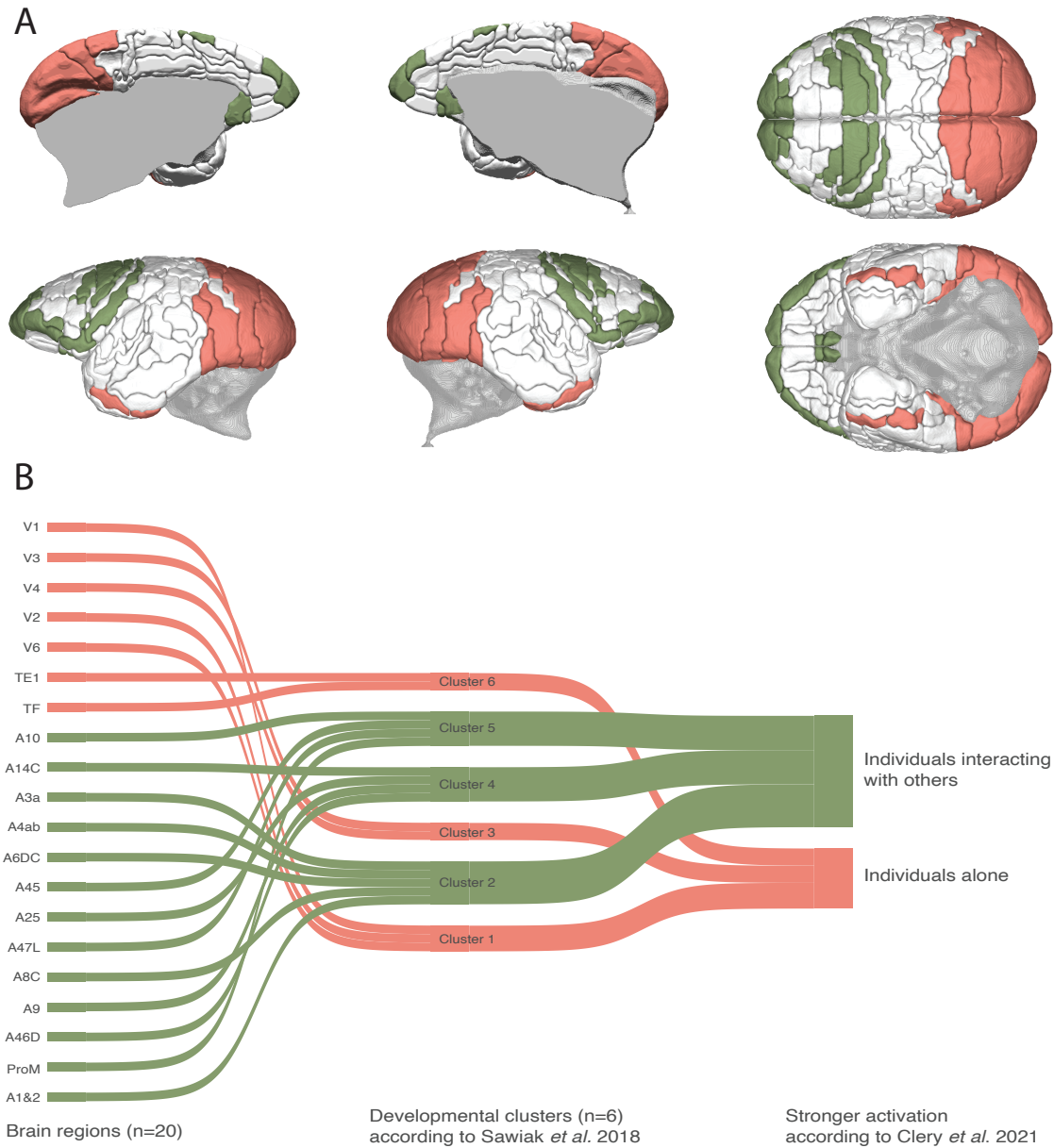


Fig. 1. Developmental clusters of the cortical regions analyzed. **A:** Location of the 20 cortical brain regions that are significantly more active (fMRI data) when observing individuals interacting with conspecifics (green), or individuals acting alone (pink). From top left moving clockwise: medial views of the left and right hemispheres, superior view, inferior view, lateral views of the right and left hemispheres. **B:** Sankey diagram of these same brain regions and their relationship to the six cortical clusters reported in Sawiak *et al.* (35): the visual and cingulate cluster (1); the somatomotor cluster (2); the auditory-visual cluster (3); the orbitofrontal, dorsolateral and ventromedial prefrontal cluster (4); the ventrolateral prefrontal cortex (PFC), polar, operculum and insula cluster (5); the lateral and inferior temporal lobe cluster (6).

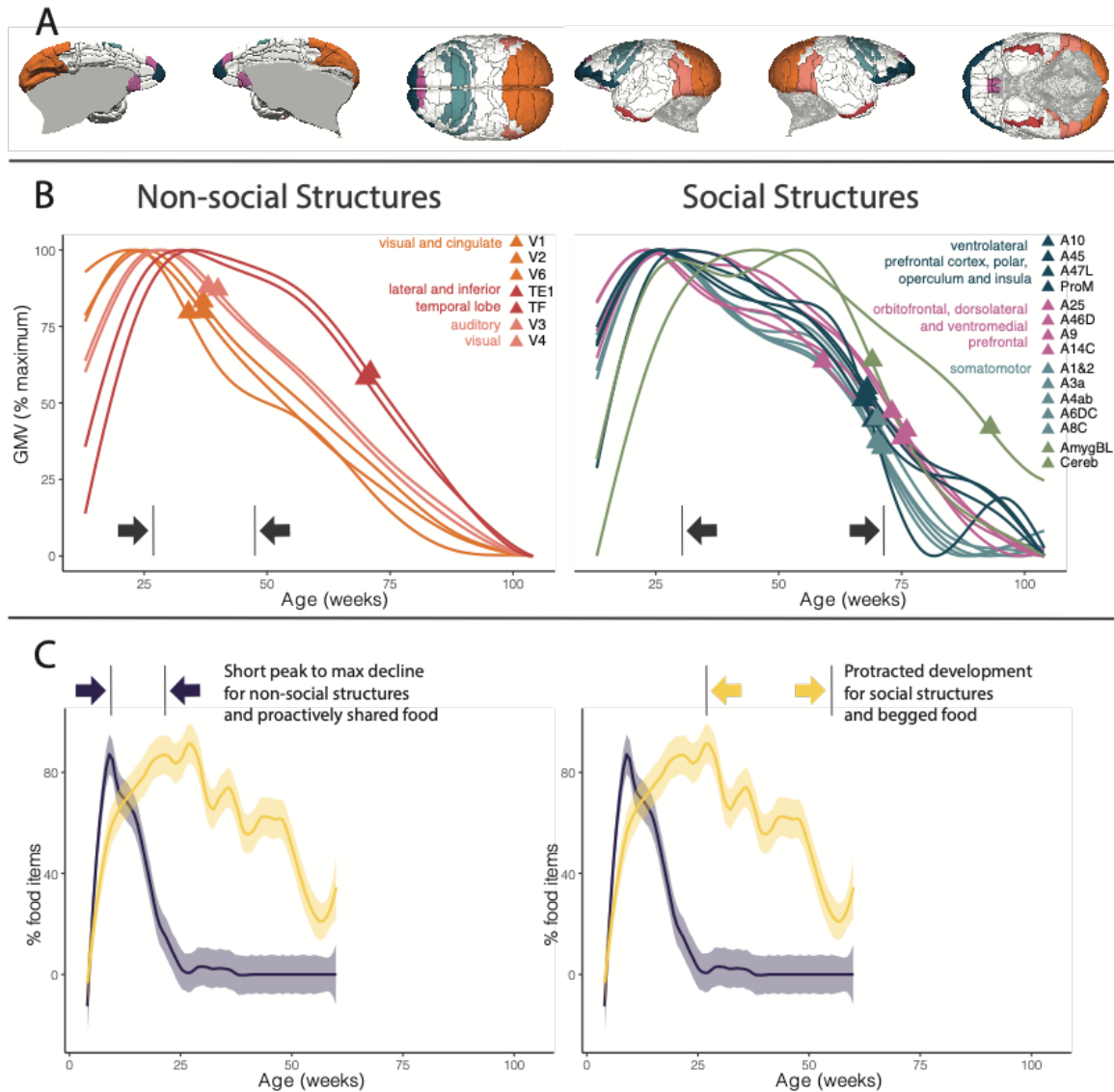


Fig. 2. Developmental trajectories of infant-caregiver interactions and of all brain regions analyzed. **A:** Location of the 20 cortical regions analyzed. Colors represent developmental clusters and match the colors in panel B. **B:** Developmental profiles of the "non-social" (left) and "social" (right) regions. The triangle is placed on point C (age fastest rate of decline). The colors represent the six developmental clusters of cortical regions, while the sub-cortical regions (basolateral nucleus of the amygdala and cerebellum) are represented in green. The x-axis represents time (expressed in weeks from birth), while the y-axis represents relative volume (absolute values are not reported graphically as there is tremendous variance between regions and would therefore be difficult to visualize all together). **C:** In blue, the proportion of food that is proactively shared, in yellow the proportion of trials for which infant begging occurs (regardless of the outcome of begging), the shaded areas indicate the 95% C.I. The ranges reported in the four plots indicate the time between developmental milestones A (maximum value) and C (maximum rate of decline).

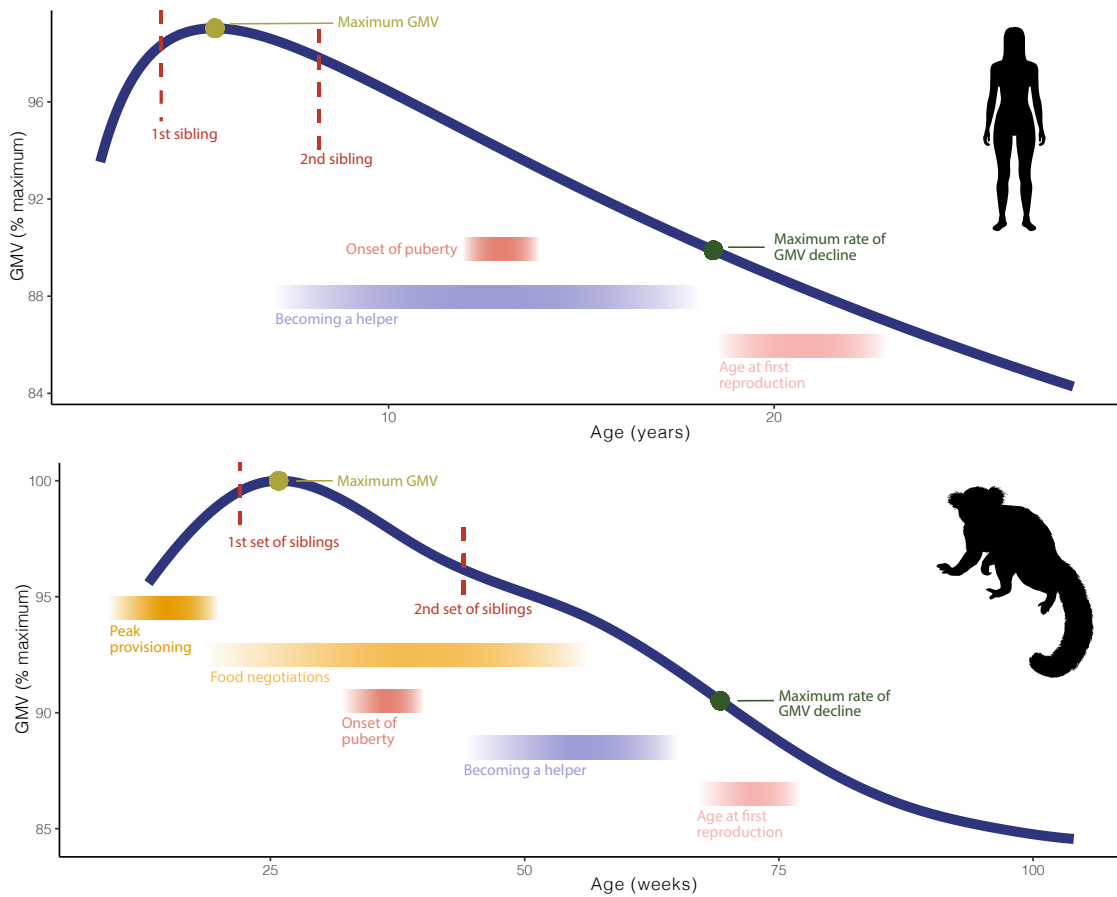


Fig. 3. Behavioral milestones and ontogenetic trajectories of gray matter volume in humans and common marmosets. Comparison between cortical gray matter volume (GMV) trajectories and behavioral and developmental milestones in humans (top) and common marmosets (bottom). Comparative GMV data for humans is from Bethlehem et al., 2022. Data for behavioral and developmental milestones for humans refer to hunter-gatherer populations and are compiled from several sources (64–66). Behavioral and developmental data for marmosets are obtained from the following sources: (27, 30).

Table 1. Differences in developmental timing between regions. Results of Bonferroni-corrected pairwise t-tests comparing milestone and ranges between brain regions that have significantly stronger activation in response to either social or non-social stimuli. Bolded results are significant at $p < 0.05$.

Regions	Variable	p-value
Social vs non-social	A (Age at max volume)	0.6168
Social vs all	A (Age at max volume)	0.4966
Non-social vs all	A (Age at max volume)	0.7575
Social vs non-social	B (Age at first descending inflexion point)	0.43
Social vs all	B (Age at first descending inflexion point)	0.6364
Non-social vs all	B (Age at first descending inflexion point)	0.2415
Social vs non-social	C (Age at fastest rate of volume decline)	0.0015
Social vs all	C (Age at fastest rate of volume decline)	0.0008
Non-social vs all	C (Age at fastest rate of volume decline)	0.0214
Social vs non-social	D (Age at last ascending inflexion point)	0.46
Social vs all	D (Age at last ascending inflexion point)	0.1522
Non-social vs all	D (Age at last ascending inflexion point)	0.1366
Social vs non-social	A to B (Age at max volume to age at first descending inflexion point)	0.011
Social vs all	A to B (Age at max volume to age at first descending inflexion point)	0.188
Non-social vs all	A to B (Age at max volume to age at first descending inflexion point)	0.1064
Social vs non-social	A to C (Age at max volume to age fastest decline)	0.0016
Social vs all	A to C (Age at max volume to age fastest decline)	0.0007
Non-social vs all	A to C (Age at max volume to age fastest decline)	0.0063
Social vs non-social	A to D (Age at max volume to age at last ascending inflexion point)	0.011
Social vs all	A to D (Age at max volume to age at last ascending inflexion point)	0.2394
Non-social vs all	A to D (Age at max volume to age at last ascending inflexion point)	0.1065

Table 2. Ages for the different milestones of neurodevelopment and behaviors. For the ontogenetic trajectories of brain regions average values and standard deviations are reported, while for the ontogenetic trajectories of food sharing the single value is reported (all values are in weeks).

Variable	Average / *Value	
	(weeks)	SD
C Social regions	71.3	7
C Non-Social regions	46.7	16.3
C Proportion begged	*58	
C proportion proactively shared	*25	
A to C Social regions	42.2	8.25
A to C Non-Social regions	19	12.3
A to C Proportion begged	*31	
A to C proportion proactively shared	*17	

Table 3. Connectivity strength between different regions. Results of the pairwise Wilcoxon-rank sum tests (p-values are corrected for multiple hypothesis testing) on the connectivity strength between brain regions with different activation strength to different types of stimuli. Values reported as 0 are < 0.00000001 .

	Neither to Neither	Neither to Nonsocial	Neither to Social	Nonsocial to Neither	Nonsocial to Nonsocial	Nonsocial to Social	Social to Neither	Social to Nonsocial
Neither to Nonsocial	1	NA	NA	NA	NA	NA	NA	NA
Neither to Social	0.44866	1	NA	NA	NA	NA	NA	NA
Nonsocial to Neither	0.70614	1	1	NA	NA	NA	NA	NA
Nonsocial to Nonsocial	0.01302	0.00104	0.00007	0.00072	NA	NA	NA	NA
Nonsocial to Social	0.00001	0.00286	0.00045	0.00503	0	NA	NA	NA
Social to Neither	1	1	1	1	0.00049	0.00001	NA	NA
Social to Nonsocial	0.00155	0.44866	0.37016	0.70293	0	0.44866	0.00695	NA
Social to Social	1	1	1	1	0.00093	0.00049	1	0.21406

Supplementary Materials for

Neurodevelopmental timing and socio-cognitive development in a prosocial cooperatively breeding primate (*Callithrix jacchus*).

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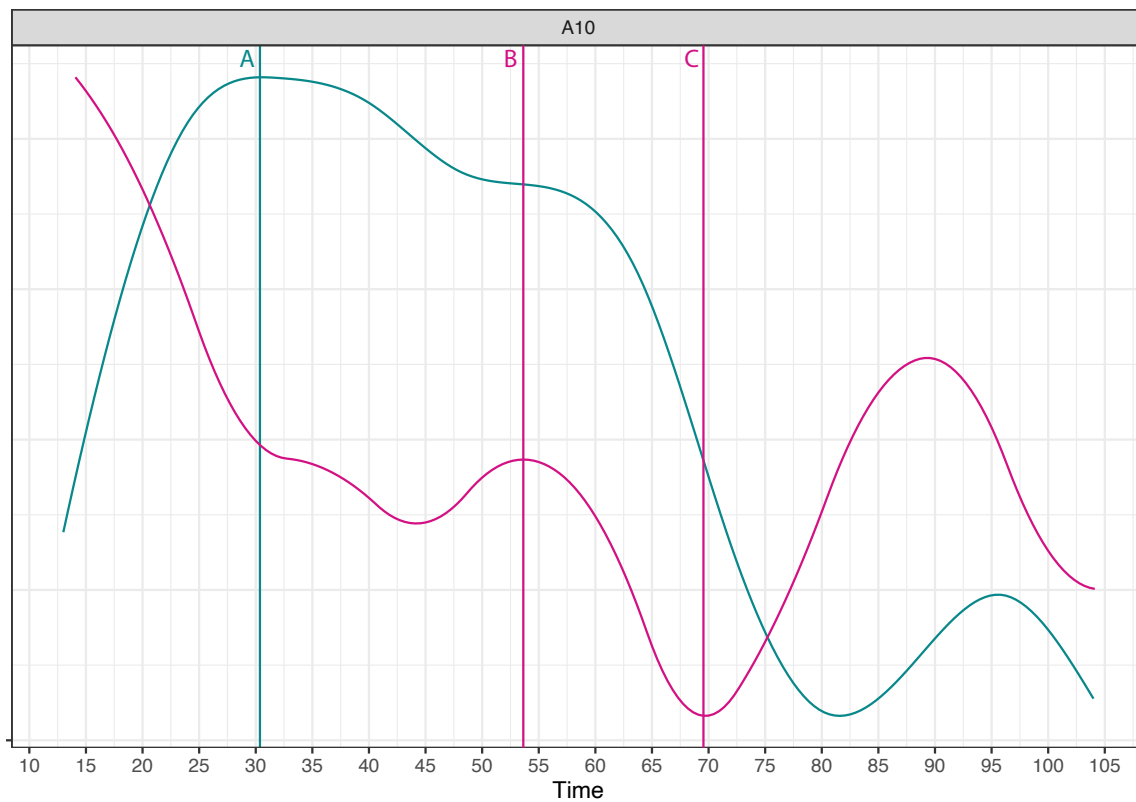
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This PDF file includes:

Figs. S1 to S5
Tables S1 to S2
Legends for Data S1 to S4

Other Supplementary Materials for this manuscript include the following:

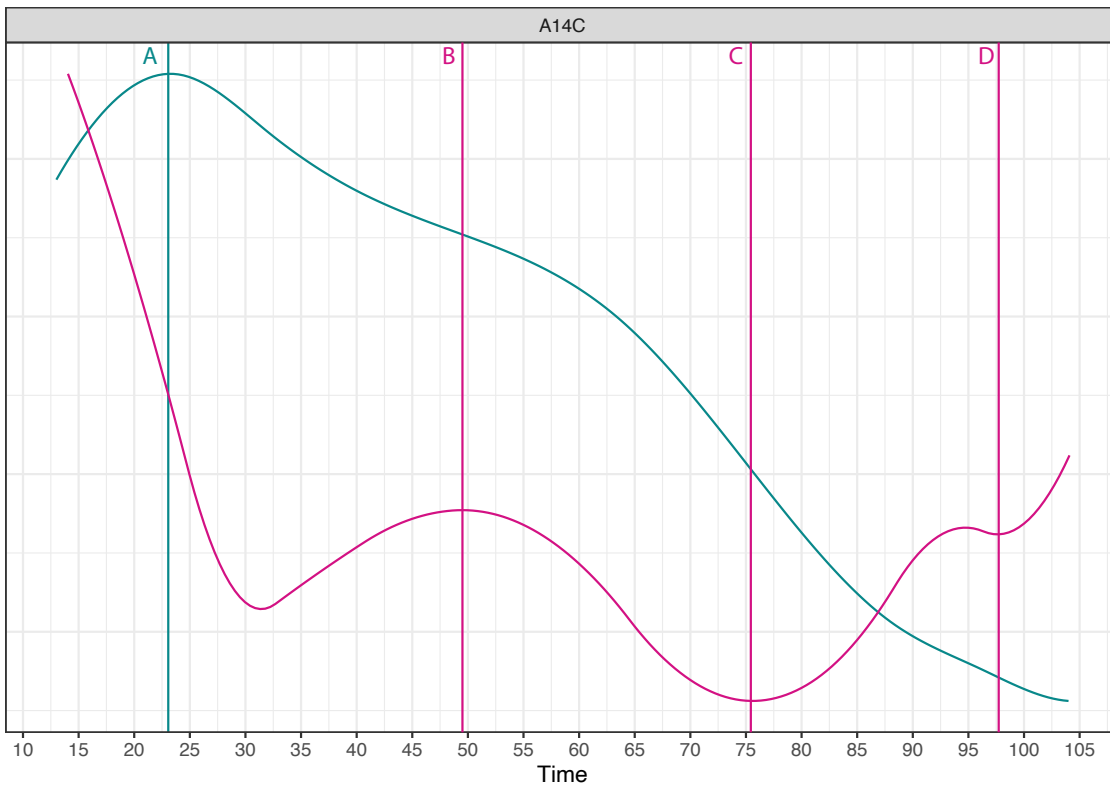
Data S1 to S4



29

30 **Fig. S1.**

31 Definition of developmental milestones A, B and C exemplified on region A10. Green: volume
 32 changes over time. Pink: First derivative of green curve. Y-axis is different for the pink and green
 33 curves, but not relevant here. A = age at maximum volume; B = Age at first descending inflexion
 34 point (the first local maxima of the first derivative); C = age at maximum rate of decline (global
 35 minima of the first derivative).
 36



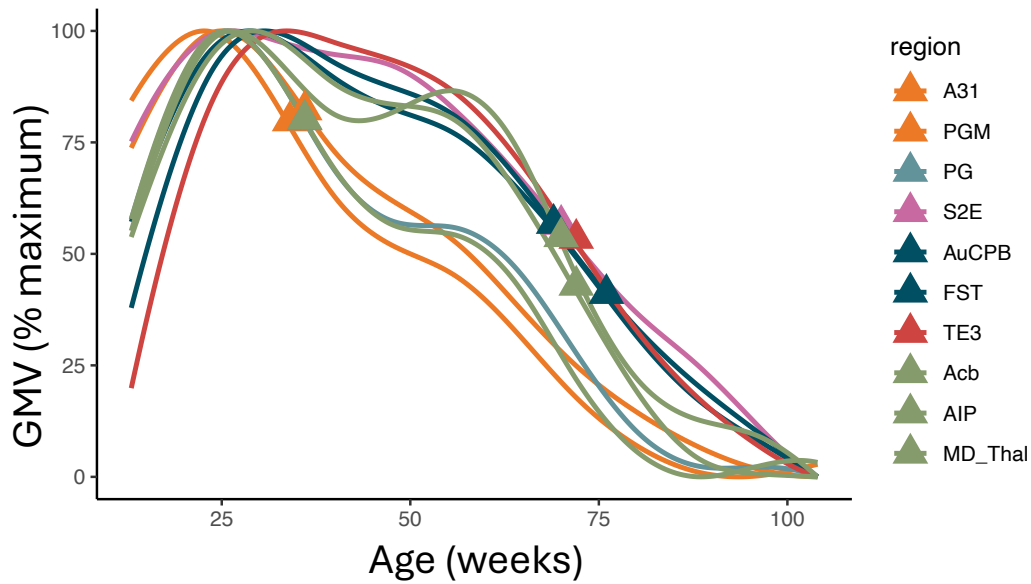
37

38 **Fig. S2.**

39 Definition of developmental milestones A, B, C and D exemplified on region A14C. Green:
 40 volume changes over time. Pink: First derivative of green curve. Y-axis is different for the pink
 41 and green curves, but not relevant here. A = age at maximum volume; B = Age at first descending
 42 inflexion point (the first local maxima of the first derivative); C = age at maximum rate of decline
 43 (global minima of the first derivative); D = age at last local minima of the first derivative.

44

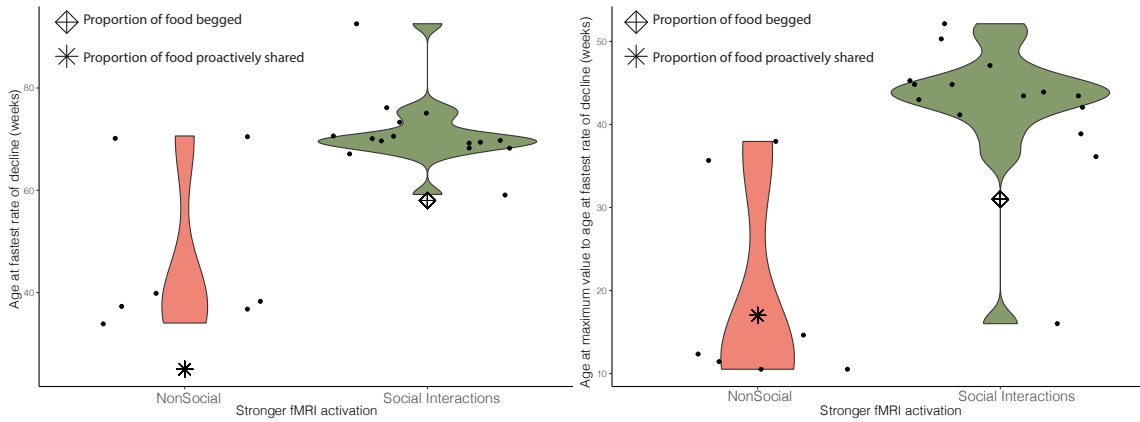
45



46

47 **Fig. S3.**

48 Developmental profiles of the regions in which the fMRI response is not significantly different
 49 between “social” and “non-social” stimuli. The triangle is placed on point C (age fastest rate of
 50 decline). The colors (same as in Fig. 2) represent the six developmental clusters of cortical
 51 regions (orange: visual and cingulate; light blue: somatomotor; pink: orbitofrontal, dorsolateral
 52 and ventromedial prefrontal; dark blue: ventrolateral prefrontal cortex, polar, operculum and
 53 insula; red: lateral and inferior temporal lobe), while the sub-cortical regions (basolateral nucleus
 54 of the amygdala and cerebellum) are represented in green. The x-axis represents time (expressed
 55 in weeks from birth), while the y-axis represents relative volume (absolute values are not reported
 56 graphically as there is tremendous variance between regions and would therefore be difficult to
 57 visualize all together).
 58



59

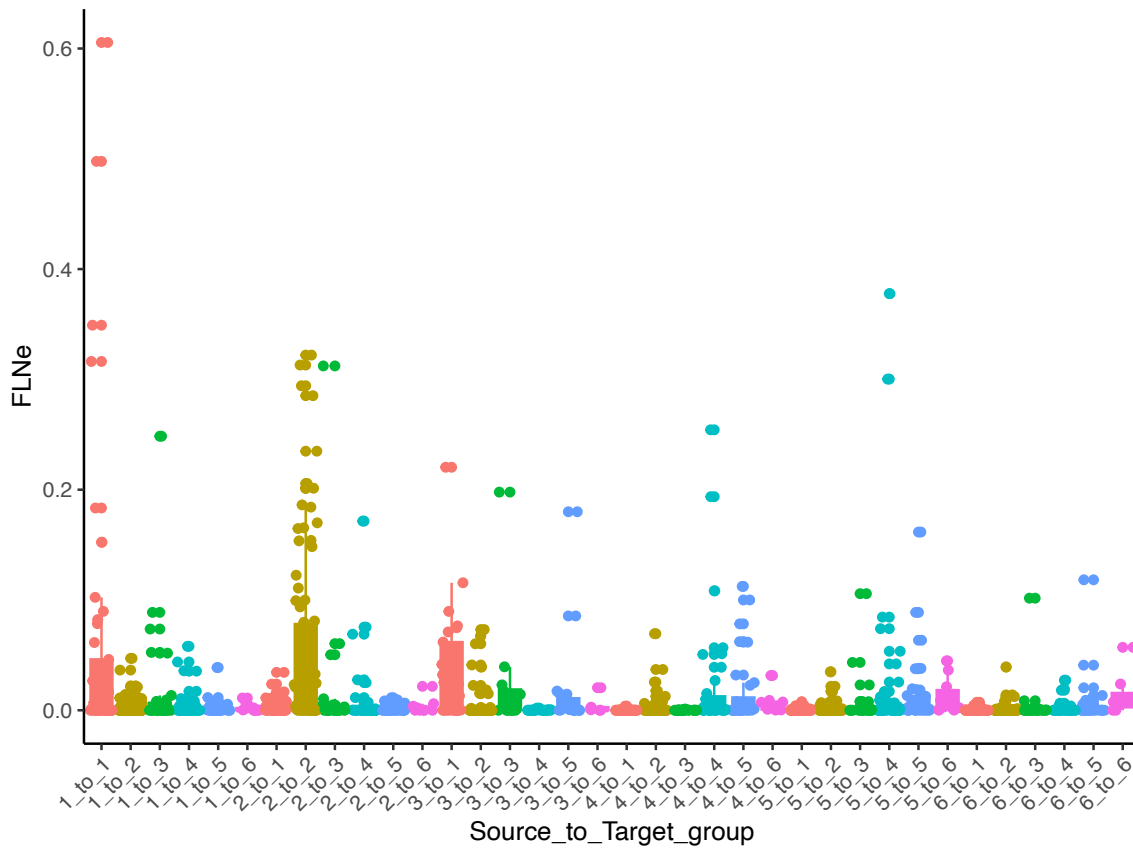
60 **Fig. S4.**

61 For social regions (i.e. those activated when observing social interactions, green), the fastest
 62 decline of gray matter volume occurs later than for non-social regions (left), and the plateau from
 63 the maximum value to the fastest decline is longer (right). These same milestones and ranges are
 64 also shown for the ontogenetic trajectories of proactive food sharing (star) and food begging and
 65 negotiation (diamond). Individual dots represent individual brain regions.

66

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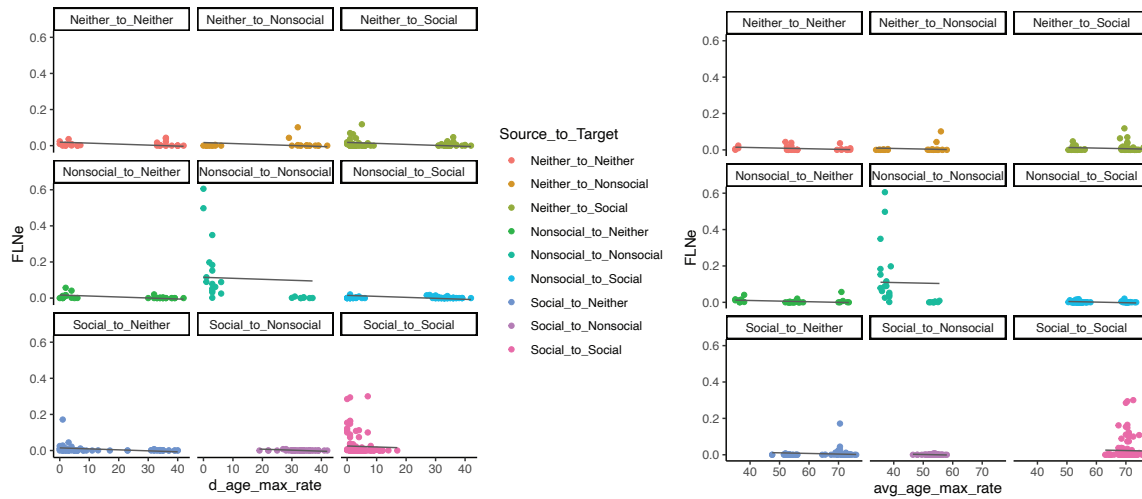


69

70 **Fig. S5.**

71 Fraction of extrinsic labeled neurons (FLN2) colored according to the developmental cluster of
 72 the target regions: the visual and cingulate cluster (1); the somatomotor cluster (2); the auditory-
 73 visual cluster (3); the orbitofrontal, dorsolateral and ventromedial prefrontal cluster (4); the
 74 ventrolateral prefrontal cortex (PFC), polar, operculum and insula cluster (5); the lateral and
 75 inferior temporal lobe cluster (6). For the names of each region pertaining to each cluster see
 76 Figure 1 and Data S1.

77



78

79 **Fig. S6.**

80 Plots showing the correlation between fraction of extrinsic labeled neurons (FLNe) and two
 81 different measures of similarity in developmental timing (expressed in weeks). Left: absolute
 82 difference in the age at which the maximum rate of GM volumetric decline is reached. Right:
 83 average age at which the maximum rate of GM volumetric decline is reached. The regression
 84 lines are those for $FLNe \sim d_age_max_rate + Source_to_Target$ (left) and $FLNe \sim avg_age_max_rate +$
 85 $Source_to_Target$ (right). In both models, the intercepts are significantly different only for non-
 86 social to non-social regions. The overall R-squared is 0.2 for both models.

87

88

89 **Table S1.**90 Results of the $FLNe \sim d_age_max_rate + Source_to_Target$ model.

term	estimate	std.error	statistic	p.value
(Intercept)	0.019	0.009	2.102	0.036
Connectivity_S\$d_age_max_rate	-0.001	0.000	-3.338	0.001
Connectivity_S\$Source_to_TargetNeither_to_Nonsocial	-0.002	0.012	-0.184	0.854
Connectivity_S\$Source_to_TargetNeither_to_Social	-0.001	0.010	-0.140	0.889
Connectivity_S\$Source_to_TargetNonsocial_to_Neither	-0.002	0.012	-0.214	0.831
Connectivity_S\$Source_to_TargetNonsocial_to_Nonsocial	0.096	0.013	7.461	0.000
Connectivity_S\$Source_to_TargetNonsocial_to_Social	-0.004	0.010	-0.433	0.665
Connectivity_S\$Source_to_TargetSocial_to_Neither	-0.005	0.010	-0.461	0.645
Connectivity_S\$Source_to_TargetSocial_to_Nonsocial	-0.001	0.011	-0.096	0.924
Connectivity_S\$Source_to_TargetSocial_to_Social	0.006	0.010	0.574	0.566

91
92

93 **Table S2.**
 94 Results of the $FLNe \sim avg_age_max_rate + Source_to_Target$ model.
 95

term	estimate	std.error	statistic	p.value
(Intercept)	0.027	0.018	1.500	0.134
Connectivity_S\$avg_age_max_rate	0.000	0.000	-1.240	0.215
Connectivity_S\$Source_to_TargetNeither_to_Nonsocial	-0.005	0.013	-0.405	0.686
Connectivity_S\$Source_to_TargetNeither_to_Social	0.004	0.010	0.350	0.727
Connectivity_S\$Source_to_TargetNonsocial_to_Neither	-0.003	0.012	-0.255	0.799
Connectivity_S\$Source_to_TargetNonsocial_to_Nonsocial	0.096	0.013	7.123	0.000
Connectivity_S\$Source_to_TargetNonsocial_to_Social	-0.005	0.010	-0.493	0.622
Connectivity_S\$Source_to_TargetSocial_to_Neither	0.001	0.011	0.087	0.930
Connectivity_S\$Source_to_TargetSocial_to_Nonsocial	-0.008	0.011	-0.750	0.454
Connectivity_S\$Source_to_TargetSocial_to_Social	0.020	0.010	1.972	0.049

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99 **Data S1 (separate file).** List of brain regions included in Sawiak et al. (35) and Cléry et al (32).
100 For each brain region, if available, we also report the developmental cluster and fMRI response to
101 the different conditions analyzed.

102 **Data S2 (separate file).** Provisioning and infant begging ontogenetic data (from weeks 4 to 60 of
103 age). As reported in Guerriero-Martins et al. (27), values for each category (proactively shared,
104 facilitated, resisted, begged, shared, refused) are reported as percentages. Shared is the sum of
105 proactive, facilitated and resisted; begged is the sum of facilitated, resisted and refused.

106 **Data S3 (separate file).** Corticocortical connectivity strength (36) for regions for which GMV
107 neurodevelopmental data is also present in both target and source regions. This results a dataset of
108 1400 connections encompassing 28 target and 51 source regions. For each of the two regions in
109 each connection we also report: the developmental cluster (see methods section of main manuscript
110 file), the age at maximum rate of volume decline and the age at maximum volume. Finally, we also
111 report the difference (between the regions forming each connection) in age at maximum volume
112 and age at maximum rate of volume decline.

113 **Data S4 (separate file).** Corticocortical connectivity strength (36) for regions for which fMRI
114 response data to the different types of social stimuli is also present in both target and source regions.
115 This results a dataset of 494 connections between 19 target and 27 source regions. For each of the
116 two regions in each connection we also report: the fMRI response type (see methods section of
117 main manuscript file), the developmental cluster, the age at maximum rate of volume decline and
118 the age at maximum volume. Finally, we also report the difference (between the regions forming
119 each connection) in age at maximum volume and age at maximum rate of volume decline.

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