Orbital prefrontal cortex volume predicts social network size: an imaging study of individual differences in humans

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The social brain hypothesis, an explanation for the unusually large brains of primates, posits that the size of social group typical of a species is directly related to the volume of its neocortex. To test whether this hypothesis also applies at the within-species level, we applied the Cavalieri method of stereology in conjunction with point counting on magnetic resonance images to determine the volume of prefrontal cortex (PFC) subfields, including dorsal and orbital regions. Path analysis in a sample of 40 healthy adult humans revealed a significant linear relationship between orbital (but not dorsal) PFC volume and the size of subjects’ social networks that was mediated by individual intentionality (mentalizing) competences. The results support the social brain hypothesis by indicating a relationship between PFC volume and social network size that applies within species, and, more importantly, indicates that the relationship is mediated by social cognitive skills.

Keywords: MRI; prefrontal cortex; stereology; social network

1. INTRODUCTION

Primates have larger brains relative to body size than all other vertebrates [1] and it is now widely accepted that the best functional predictor of relative brain size in non-human primates is social group size [2]. This relationship, according to the ‘social brain hypothesis’ [3,4], is founded on the premise that maintaining cohesion and stability through time in the kinds of bonded social groups characteristic of primates is cognitively very demanding [5–8]. However, among primates, differences in brain size do not reflect proportional increases in all brain regions; instead, the size of the neocortex accounts for most of the deviation from overall trend lines [9]. Neocortex size rather than total brain size—or the volume of any other brain region—yields the best correlation with social group size across a wide range of primate species [7]. More importantly, there is evidence to suggest that an increasingly better fit is obtained if the more posterior regions of the neocortex (e.g. the visual areas) are excluded from the analysis (neocortex minus primary visual cortex [10]; prefrontal cortex only [11]). The underlying assumption is that the neocortex provides the computational power to manage the complex web of social relationships needed to give a social group its cohesion and stability through time.

While the social brain hypothesis has been tested in some considerable detail with comparative data across a wide range of primate species [8,11–14], the possibility that it might also apply within species has never been seriously considered. However, at least within humans, there is considerable individual variation in social network size [15,16] and there is evidence to suggest that this variance correlates with competence in the kinds of social cognitive abilities (usually known as ‘theory of mind’ or ‘mentalizing’ [17–20]) that are thought to underpin human sociality [21]. (The terms ‘mentalizing’ and ‘intentionality’ are used interchangeably and refer to the ability to assess the intentions and mental states of others.) In addition, recent magnetic resonance imaging (MRI) studies have shown that various indices of social engagement (including number of Facebook friends) correlate with grey matter volume in the amygdala [22] and the classic theory of mind areas in the temporal and frontal lobes [23,24]. In a previous MRI-based study, we were able to show that individual differences in intentionality competence correlate with differences in the volume of the orbital prefrontal cortex (PFC) [25]. Collectively, these studies suggest that there should be a three-way correlation between social network size, intentionality competence and PFC volume. We test this hypothesis here by applying the Cavalieri method of stereology in combination with point counting on structural $T_1$-weighted MR images from a sample of 40 human subjects.

In this analysis, we focus on the PFC for two reasons. First, the PFC is associated with many cognitive functions that are crucial for social interaction, including social information processing [26,27], planning [28], working
memory [29], aspects of language and symbolic behaviour [30–32], and attention [33]. Second, neuroimaging studies have identified areas within the PFC as being central to social cognitive processing, including mentalizing (notably the ventromedial PFC [25,34–38]). This does not exclude the possibility that other regions (especially in the temporal lobe) may also be involved, but we emphasize the PFC simply because it provides a simple yet particularly relevant test case for an analysis that is very time-consuming to do. We used the Cavalieri method in combination with point counting to estimate the volume of four subfields of the PFC (i.e. dorsal and orbital prefrontal regions in each of the two hemispheres). The procedure used to estimate PFC subfields has been repeatedly used [25,39,40] and has been shown to have high test–retest reliability. The logic of the social brain hypothesis is that neural volume determines social cognitive competences, and that it is these in turn that determine social network size. As we have already shown that the first step in this sequence holds [25], we use path analysis on the same sample of subjects to determine whether this relationship extends to social network size as well in a three-step causal model, and then whether the relationship between brain region volume and network size is direct (brain volume and intentionality competences independently influence network size) or indirect (brain volume determines intentionality competence, and these in turn determine network size). The social brain hypothesis implicitly assumes the second.

2. MATERIAL AND METHODS

(a) Participants

The original cohort comprised 42 subjects with no history of neurological illness. However, two subjects were subsequently removed due to excessive head movement during MR data acquisition, making an examined cohort of 40 subjects aged 25.47, s.d. = 2.87; 23 females: mean age = 25.78, s.d. = 7.83). All participants gave written informed consent. This is the same cohort of subjects as that used by Lewis et al. [24].

(b) Social network size

Prior to scanning, participants were asked to complete a version of the social network questionnaire designed by Stillier & Dunbar [21] to capture the size of the inner layers of an individual’s social network (following [15,41]). This involved listing the initials of everyone the participant had personal contact with or communicated with over the previous 7 days, excluding professional contacts (doctor, shopkeepers and teachers) unless the contact could explicitly be considered a genuine social interaction. This has previously been shown to be a reliable way of estimating the size of the inner layers (referred to as clique and sympathy group size) of social networks and has been used in several published studies [15,16,41]. The layers of the social network have been found to scale with each other on a consistent ratio [15,16], such that an index of any one layer in the network is a reasonable estimator for the network as a whole. Intentionality competence scores for the subjects are taken from Powell et al. [25]; details outlining the approach used to assess intentionality competence and calculate intentionality score are given therein.

(c) Magnetic resonance image acquisition and analysis

MRI data were acquired using a Siemens Trio 3.0 T whole-body MRI system, with an eight-channel head coil. High-resolution anatomical whole-brain images were obtained using a T1-weighted three-dimensional gradient-echo (i.e. 3D modified driven equilibrium Fourier transform) pulse sequence, with the following parameters acquired in the sagittal plane: T1 = 100, TR = 7.92, TE = 2.48, FOV = 224 × 256, matrix 256 × 256 × 256 mm3 pixels, flip angle 16°. These structural MR images were used for deriving volume estimates of prefrontal subfields. After MR acquisition, datasets were imported into BrainVoyager software for re-alignment (www.Brainvoyager.com, Brain Innovation, Maastricht, The Netherlands), which required reformattting the image and orienting it to a standardized sagittal plane orthogonal to the bicommissural plane. Details of the reformattting procedure are described elsewhere [39,42].

(d) Parcellation of prefrontal cortex anatomical subfields

The protocol used to demarcate the PFC into anatomically defined subfields is based on the previously established methodology developed by Howard et al. [39]; this involves dividing the right and left PFC into dorsolateral (DL), dorso medial (DM), orbitolateral (OL) and orbitomedial (OM) regions, yielding a total of eight PFC subfields. The bicommissural plane was used to delineate orbital and dorsal subfields. Demarcation of medial from lateral regions used the first axial slice superior to the olfactory sulcus. The genu of the corpus callosum, viewed at sagittal midline, formed the posterior boundary of the DL and DM regions. These provided fixed boundaries, which were marked with editing tools in BrainVoyager software. The posterior boundary of the orbital subfield was visualized by the rater during point counting. For complete details of the demarcation procedure, refer to earlier studies [25,39]. Based on the reviewed evidence on the role of the PFC in social information processing, this study examined both the neocortex volume (grey matter) and white matter volume as a combined volume within the PFC. Whole hemisphere volume was calculated to correct for the effect of relative volume in the model.

(e) Cavalieri method

Following parcellation of PFC anatomical subfields, MR images were imported into Easymeasure software [43,44] for point counting and volume estimation. The technique provides mathematically unbiased volume estimators for which their precision can be computed by applying an error-prediction formula [45–49]. Therefore, volume estimates with comparable levels of precision may be derived for different anatomical structures (see Baddeley & Jensen [50] and references therein). A description of the principles and application of this method to PFC have been reported previously [39]. The technique involves exhaustively ‘sectioning’ (non-invasively) the structure of interest with a series of parallel planes a fixed distance apart, with the first section at a uniform random position within the sectioning interval. A grid of test points for point counting is overlaid with uniform random position and isotropic orientation on every alternate section, beginning randomly on either the first or second section on successive subjects. A grid size of 6 × 6 pixels unit area (36 mm2 area per point) was used for DL and DM subfields, and a grid size of 4 × 4 pixels unit area (16 mm2) was used for OL and OM regions. Shape coefficients were applied to estimate the corresponding...
coefficients of error; the estimated shape coefficients for DL, DM, OL and OM were 5.65, 5.99, 5.48 and 5.19, respectively. For whole hemisphere volume, a larger grid of test points (i.e. 8 × 8 pixels = 64 mm² area per point) on every fifth slice was chosen to accommodate the larger volume of interest and reduce labour intensity during point counting.

The reproducibility and repeatability of the method was assessed by Howard et al. [39] and Cowell et al. [40] across healthy and clinical samples, yielding acceptable limits for total and regional prefrontal volume. For instance, predicted coefficients of error of the volume estimator, based on our data from individual volume estimates, were less than 5 per cent, and regional subfield volume estimates for PFC derived from point-counting methods showed satisfactory 95 per cent limits of agreement between raters (reproducibility between raters) and within rater (repeatability by the same rater). Intraclass correlation coefficients ranged from 0.92 to 0.95 between raters and from 0.93 to 0.99 within rater.

Volume estimates for orbital and dorsal PFC were obtained as the sum of the volumes of the lateral and medial subfields for each hemisphere.

(f) Statistical analysis
Path analysis was performed to test the association between network size, intentional competence, orbital PFC volume and dorsal PFC volume. To do this, two linear regression models were performed. In the first model, network size was the outcome variable, and predictor variables were intentional-ity score, orbital PFC volume and dorsal PFC volume. In the second model, intentionality score was the outcome variable, and the predictor variables were orbital PFC volume and dorsal PFC volume. Total hemisphere volume was included in the linear regression models, both when group size was the outcome variable and when intentional-ity was the outcome variable. Hemisphere volume was not significantly associated with either intentional-ity (coefficient = −0.24, p = 0.2) or clique size (coefficient = −0.068, p = 0.7). These results are therefore not included in the path analysis.

3. RESULTS
Descriptive statistics for the main variables used in the analysis (separated by gender) are summarized in table 1. The mean number of contacts (22.65 ± 11.7 s.d.) is within the range of variation reported in previous studies for the sympathy group layer [21,51]. It is likely that the relatively large number of contacts in the present dataset reflects both the way the social contacts questionnaire was phrased and the fact that the sample consists largely of students (who are likely to have an unusually active social life). As in previous studies [21,51], women have larger networks (mean =25.5 ± 13.5 s.d.) than men (mean = 18.8 ± 7.7 s.d.), though the difference is not statistically significant in the present case, albeit close to the boundary (since equality of variance did not hold, the Welch approximation to degrees of freedom was used: t½ = 1.98, p = 0.06, 95%CI: −0.2, 13.5).

We used path analysis to explore the most likely causal relationship between the network size, intentional-ity and PFC volume (figure 1). The results confirm that orbital PFC volume is the best predictor of network size, with this relationship being mediated via intentional-ity competence. Dorsal PFC was not significantly related to network size (or intentional-ity competence). The partial correlation between orbital PFC volume and network size is not significant (p = 0.09), and the slope is negative, indicating that PFC volume does not itself influence network size directly but rather is explicitly mediated via intentional-ity competence, as predicted by the social brain hypothesis. To check for a possible effect of gender on the results, we fitted a multiple linear regression model with network size as the outcome variable, and gender, intentional-ity, orbital PFC volume, dorsal PFC volume and interaction terms involving gender, brain region and intentional-ity as predictor variables: there was no significant effect for gender or either interaction term (p > 0.05), indicating that the main relationship between orbital volume, intentional competence and network size is independent of gender.

Table 1. Mean (± s.d.) for key variables for the total sample and separated by gender.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 40)</th>
<th>Males (n = 17)</th>
<th>Females (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>network size</td>
<td>22.7 (± 11.7)</td>
<td>18.8 (± 7.7)</td>
<td>25.5 (± 13.5)</td>
</tr>
<tr>
<td>age</td>
<td>25.7 (± 6.2)</td>
<td>25.5 (± 2.9)</td>
<td>25.8 (± 7.8)</td>
</tr>
<tr>
<td>orbital PFC volume (cm³)</td>
<td>51.6 (± 10.8)</td>
<td>54.8 (± 11.7)</td>
<td>49.4 (± 9.8)</td>
</tr>
<tr>
<td>dorsal PFC volume (cm³)</td>
<td>109.0 (± 16.1)</td>
<td>110.0 (± 19.5)</td>
<td>108.3 (± 13.6)</td>
</tr>
<tr>
<td>total brain volume (cm³)</td>
<td>970.8 (± 107.6)</td>
<td>1042.7 (± 79.0)</td>
<td>917.7 (± 95.1)</td>
</tr>
</tbody>
</table>

Figure 1. Path analysis of the causal relationships between the main prefrontal cortex (PFC) divisions, intentional competences and network size. The numbers on each arrow indicate the slope standardized coefficients obtained from the linear regression models and in parentheses the correlations.
4. DISCUSSION

Orbital PFC volume was significantly correlated with the number of weekly social contacts that an individual had, with this relationship being mediated by mentalizing (i.e. intentionality) competence. The results of this study add important support to the social brain hypothesis by demonstrating that the relationship between brain size and social group size applies not just between species, but even at the level of the individual within species: those individuals with larger orbital PFC have a greater number of weekly (i.e. regular) social contacts (an index of the size of their entire social network). Enlarged frontal lobes, such as are found in humans, are of relatively recent evolutionary origin [8]. More importantly, however, our results confirm an explicit assumption of the social brain hypothesis: that this relationship is mediated by social cognitive abilities. This thus adds an important rider to how we formulate the social brain hypothesis by reminding us that it is not simply a direct causal relationship between brain volume and social group size.

Previous studies have shown an effect of gender on measures of network (or social group) size [14,21,41]. However, the present study did not, although the gender difference in network size is close to the boundary of significance ($p = 0.06$) when no other factors were taken into account. While our result should not, perhaps, preclude the possibility of a gender effect with a larger sample, the existence of such an effect does not obviate the fact that there is a generic relationship between social network size and PFC volume that applies across both genders (as was also the case in all the cited studies).

The neuropsychological literature suggests a functional distinction between dorsal PFC, which mediates higher-order cognitive functions, and orbital PFC, which is implicated in mood, affective behaviour and social aspects of cognition [52]. This functional division is supported by findings from individuals with dorsolateral PFC lesions, who have been reported to have poorer performance on various subtasks of standardized intelligence tests, as well as deficits in memory, including the Wisconsin Card Sorting Task, and the formation and modification of abstract concepts [53–55]. In contrast, damage to orbital PFC typically leads to impulsive aggressive behaviour [56], as well as impairments of social cognition [57] and risk judgement [58,59]. In healthy adults, the orbitomedial PFC is involved in a range of functions, including affect [60] and olfaction [61]. Our previous study using the same sample of subjects [25] demonstrated a relationship between intentionality capacity (a social cognitive competence) and orbital PFC volume, but no association between short-term memory capacity and orbital PFC volume, suggesting that orbital PFC may be particularly important for high-order social cognition (i.e. orders of intentionality greater than conventional theory of mind).

A previous neuroimaging study reported a relationship between an index of sociality and the volume of the corticobasal complex of the amygdala [22], a subcortical unit known to be correlated with sociality in primates [62], but not between sociality and hippocampus volume. This study did not explicitly test for a relationship with neocortex volume, though weak correlations (uncorrected at $p = 0.05$) were reported from an exploratory analysis of cortical thickness (as opposed to cortical unit volume) in three selected cortical regions of interest (subgenual anterior cingulate cortex, caudal superior frontal gyrus, caudal inferior temporal gyrus), none of which overlap with PFC. Unlike the other two units of the amygdala, the corticobasal complex has a direct neural connection to the orbitofrontal cortex, although this may have more to do with inhibition of amygdala emotional responses by the orbitofrontal cortex [63,64]. Similarly, using voxel-based morphometry (VBM), Kanai et al. [23] reported correlations between several indirect indices of online and offline social network size and the volumes of the amygdala and two temporal lobe regions known to be associated with theory of mind competence (temporo-parietal junction and superior temporal sulcus), but did not explicitly test for PFC associations. However, just such a relationship has in fact been demonstrated using VBM [24]. Similar findings relating individual differences in both social group size and social rank to the volumes of subregions of the frontal and temporal lobes have recently been reported for macaques [65], suggesting that these relationships may apply widely across the primates. Our analyses extend these findings by demonstrating that these relationships are in fact explicitly mediated by social cognitive competences (in the case of humans at least, intentionality competence). We argue, and our path analysis convincingly demonstrates, that the causal logic involved is that network size is ultimately determined by social cognitive competences, and that these in turn are underpinned by the amount of neural matter that can be brought to bear on the computational demands involved (reflected here in the volume of key PFC brain regions). Our results thus establish the important point (so far missing in all discussions of the social brain hypothesis) that cognition mediates the relationship between brain volume and social group/network size. As with other imaging studies [22–24], our study is neutral as to the formal causal direction of the relationship between PFC volume and social network size. Since it is known that the speed with which children acquire theory of mind is determined by the size of their sibship [66,67], it is possible that the (developmental) causal arrow runs from network size via intentionality competences to PFC volume. Whether (and to what extent) PFC places direct constraints on network size will ultimately require longitudinal studies to determine.

Overall, these studies support both the claim that sociality is cognitively demanding and the claim that the evolution of brain size has been influenced by these demands (see also [6]). Our study specifically adds to this body of literature by demonstrating that social network size (a direct measure of sociality) is related to an increase in relative orbital PFC volume. Understanding the association between increased brain volume and domains of sociality, such as social network size, brings us some way towards understanding the mechanisms that have contributed to the enhanced brain volume of our species.

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