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Correlation between corpus callosum shape and cognitive performance in healthy young adults

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Abstract Corpus callosum (CC) might be related to cognitive performance because of its role in interhemispheric communication. Previous research has focused mainly on volumetric analyses of the CC, yielding contradictory results to some extent. Shape is an approach that integrates and extends the data obtained with the volumetric methodology. Here, we analyze the relationships between midsagittal CC shape variation and several cognitive measures. 2D coordinates from 102 MRI-scanned young adult human CCs were superimposed through a Procrustes approach. The residual variation was regressed onto 21 cognitive measures completed by the participants. Most of these measures (including general intelligence, working memory, executive functioning, and mental speed) were unrelated to midsagittal CC morphology. However, attentional control did show consistent and significant correlations with CC shape variation. Slower responses in attentional control were systematically associated with more curved and thinner CC, with consequent rotation of the splenium and the genu. Although the magnitude of the correlations suggests a small relationship of midsagittal CC geometry and attention, the results provide

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interesting clues regarding the links between brain anatomical configuration and human cognitive function.

Introduction

The corpus callosum (CC) is the largest white matter structure in the human brain. It connects the two hemispheres and it is topographically organized, binding homologous areas for visual, motor, somatosensory, and auditory information (Huang et al. 2005). Further, the human brain is highly lateralized, allowing a great hemispheric specialization (Springer and Deutsch 2001).

In this regard, it has been postulated that it is more efficient for information to be processed by a single hemisphere if the task is simple, whereas for complex tasks the use of both hemispheres may improve processing because it facilitates parallel processing (Banich and Brown 2000). Hence, it has been suggested that total or partial size of the CC might improve cognition. However, another view postulates that a smaller CC would represent a brain relying less on interhemispheric communication and, hence, a more lateralized/specialized brain with better performance (Allin et al. 2007; Hutchinson et al. 2009). Nevertheless, the available findings are not conclusive. Several studies support the view that a larger CC, either total or partial, provides greater processing power (Luders et al. 2007a) whereas other studies have found negative correlations between cognitive function and total or partial size of the CC (Allin et al. 2007; Ganjavi et al. 2011; Hutchinson et al. 2009). Still other reports find no relationships (Haier et al. 2004). The high variability among

analyzed samples, mostly composed by developmental and clinical populations, might account for these inconsistencies.

The referred studies have focused on the size of the CC, either total or partitioned, which probably reflects variations in the absolute or relative number of small-diameter (slow conducting) fibers crossing the hemispheres (Aboitiz et al. 1992). The analysis of its shape is a different approach. Shape is defined by the geometrical relationships within a group of elements, in terms of their spatial organization. The shape of brain structures results from the integration between the development of neural functions and structural adjustments (Bruner 2007; Richtsmeier et al. 2006). The final form is constrained by topological and functional relationships linking volume, surface distribution, folding patterns, tissue thickness, and cellular organization, among others (Hilgetag and Barbas 2006; Hofman 1989). Therefore, shape analysis can override some limitations of volumetric studies, comprising the latter variable as well as a plethora of other factors likely affecting its morphology, extending beyond the exploratory power of volumetric methodology in search of variations in anatomical configurations. Accordingly, the final shape of the CC might be constrained by a number of functional factors, and hence express significant variations in the configuration and arrangements of these commissural fibers regardless of total or partial size values, which, in turn, may be related to cognitive performance. Further, the shape of the CC might also be constrained by peculiarities in structural and spatial configurations of other neighboring structures, and hence provide interesting clues on possible anatomical patterns likely related to cognitive performance. Although there are several techniques for analyzing the shape of biological structures, Procrustes analysis, and coordinate-based morphometrics are particularly relevant in this regard (Bookstein 1991, 1997, 2003; Gower and Dijksterhuis 2004; Mardia and Dryden 1998).

Several studies support the potential interest of studying the shape of the CC in relation to cognition. Using other approaches, such as high-resolution changes in callosal thickness, Luders et al. (2007a, 2011) have reported sizeable relationships between CC morphology and intelligence in both children and adults. This has also been the case when the same methods have been applied to clinical populations, such as William's syndrome, schizophrenia, depression, or bipolar disorders (Luders et al. 2007b; Walterfang et al. 2008, 2009a, b). More complex measures of callosal thickness with 3D tools have also generated interesting results in dyslexia and autism (Casanova et al. 2010; Elnakib et al. 2011). Further, simpler measures of CC shape, such as callosal bending angle based on its two endpoints relative to the midpoint (Walterfang et al. 2008, 2009a, b) or ocular inspection of CC shape (Luders et al. 2007b) have been also successfully employed in clinical

populations. Procrustes and coordinate-based morphometrics methodology of the CC would extend and complement these explorations. However, the application of this technique for studying CC shape has been very scarce and limited to clinical populations, such as schizophrenic patients (reviewed in Bookstein 2003) or adults with neuropsychological deficits after fetal alcohol exposure (Bookstein et al. 2001, 2002). The application of Procrustes analysis and coordinate-based morphometrics in normal adult populations, studying the relationship between CC shape and a broad set of intellectual and cognitive measurements, is missing. This is a necessary step for surpassing the inherent limitations in generalizing inferences from small and clinical samples to the population (Shallice 1998). The present study is intended to fill this gap.

Recently, the normal variation of the CC midsagittal section has been described and quantified by means of shape analysis through Procrustes and geometric morphometrics (Bruner et al. 2012). The morphology of the corpus callosum displays high levels of variability, possibly because of different and independent factors influencing its anatomy along the outline. Differences between males and females are subtle and mostly due to allometric effects; the large variability at the individual level makes such differences generally negligible. This indicates that studying CC morphology in relation to cognition as a function of gender would introduce a clear confound with allometric factors and, hence, gender will be disregarded as a variable of interest in the present study. Here, we analyze the correlation between the morphological variation of the CC at its midsagittal section and scores associated with a comprehensive set of cognitive measures tapping fluid, crystallized, and spatial intelligence, along with working memory, executive function, controlled attention, and mental speed. This set of cognitive variables has been studied in relation to variation in midsagittal brain surface shape (cortical profile) and spatial position of a number of subcortical structures in the same sample, revealing small but consistent relationships between overall brain morphology and mental speed (Bruner et al. 2011). The present approach extends this previous study exploring in detail the shape of one of the subcortical structures—the CC—whose position was significantly involved in the overall morphological brain pattern related to cognition.

Materials and methods

Sample

The sample used in this study was previously analyzed and described in Bruner et al. (2011). It was composed by 102 participants (52 females), with ages between 18 and

27 years (mean age = 19.9, SD = 1.6). According to a standardized questionnaire, none of them had medical illness, brain injury, or a psychiatric history. All participants were university psychology undergraduates, their native language was Spanish, and gave written informed consent prior to the study. The study conforms with the Declaration of Helsinki and was approved by the ethics committee of the Universidad Autónoma de Madrid.

Morphometrics

A 3.0-T GE scanner (HD×, 14× with 16 channels; amplitude 50 mT/m; slew rate 150 mT/m ms), equipped with a standard birdcage head coil, was used for magnetic resonance imaging. High-resolution whole brain images (exact voxel size = 0.469 × 0.469 × 1 mm) were acquired from each participant using a T1-weighted three-dimensional 3DSPGR sequence (30 axial adjacent slices, 512 × 512 pixel matrix per slice, TR = 11.2 ms, TE = 2.21 ms, measurement time = 21 min). The obtained resolution is well beyond the scale of the expected morphological differences in the corpus callosum geometry, so that biases associated with submillimetric imaging artifacts (e.g., partial volume effects) can be excluded. Images were rotated and aligned to attain the same orientation as the ICBM template using the display function from SPM 8 (Wellcome Trust Centre for Neuroimaging). After orientating the specimen along the midsagittal axis, the most midsagittal slice was selected by using anatomical references as the *falx cerebri* and the thalamic structures.

In order to investigate the shape of the CC, a geometrical model including 2 landmarks and 50 equally spaced semi-landmarks was chosen (Fig. 1). Landmarks represent the centre of the genu and the splenium, respectively, while semi-landmarks where drawn on the sagittal contour of the CC starting from the posterior tip of genu. Coordinate data were sampled by using TPSdig2 (Rohlf 2005). Shape variation was investigated through geometric morphometrics (Zelditch et al. 2004). Coordinates were registered with Procrustes superimposition, by translation to a common centroid, scaling to unitary size, and rotation according to a least-square approach (Bookstein 1991). Semi-landmarks were further adjusted through minimization of the bending energy values, as suggested for the outlines like the CC profile (Bookstein 1997; Gunz et al. 2005). Procrustes approach minimizes the difference between individuals, normalizing position, scale, and rotation of a set of coordinates according to a quantitative criterion. After superimposition, residual differences are used in standard multivariate regression, by using shape variables as dependent variables and psychometric scores as independent variables (Monteiro 1999). The correlation vector can be used to visualize the spatial changes associated with the
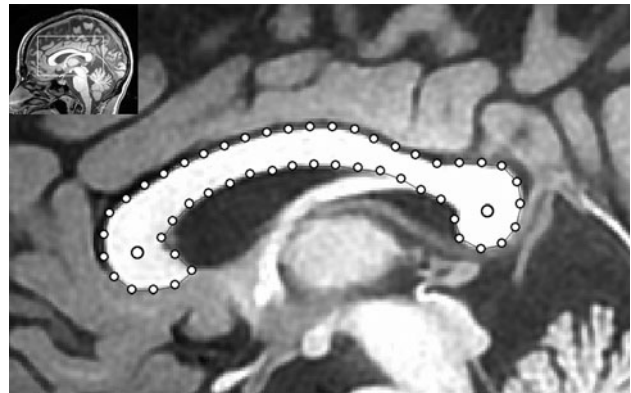
Fig. 1 The morphology of the corpus callosum was modeled by using the centre of the genu, the centre of the splenium, and 50 equally spaced semi-landmarks to delineate the profile

covariation patterns, by coordinate displacements or through interpolant functions like the thin-plate spline (Bookstein 1989).

Procrustes residuals were regressed onto psychometric scores from different cognitive tests through multivariate and partial-least square (Rohlf and Corti 2000) regressions. The former regression was used for analyzing the relationships between shape and each cognitive score separately, while the latter approach was used to analyze the overall correlation between CC shape and groups of cognitive variables. Multivariate analyses were performed with MorphoJ 1.02d (Klingenberg 2011). Basic statistics were computed using PAST 1.91 (Hammer et al. 2001). Centroid size, calculated as the square root of the sum of squared distances of all the landmarks from their centroid, was also regressed onto psychometric scores to evaluate the relationship between cognitive performance and CC cross-sectional size. Given the exploratory nature of the present study, conservative methods to adjust *p* values for the number of comparisons performed were considered inappropriate.

Cognitive measures

A total of 21 specific measures and seven composite scores were considered. Each composite score was calculated as the mean of 3 specific measures. Composite variables represent general psychological constructs of interest and are based on three different specific measures to override possible task-related specific factors. Extensive details on tests and tasks used here can be seen in Colom et al. (2008, 2009), which can be summarized as follows. The composite variable *Fluid intelligence* (Gf) is measured by the Advanced Progressive Matrices (APM; Raven et al. 1998) test, the inductive reasoning subtest (PMA-R) from the Primary Mental Abilities battery (PMA; Thurstone 1938), and the abstract reasoning subtest (DAT-AR) from the

Differential Aptitude Test battery (DAT; Bennett et al. 1990). The APM comprises a 3 × 3 matrix figure with the lower right hand entry missing; participants must choose one of eight alternatives completing the matrix. PMA-R comprises letters' series; the rule underlying a given sequence must be extracted to select one from six alternatives. DAT-AR is similar to PMA-R, but comprising series of abstract figures. A second composite variable, *Crystallized intelligence* (Gc), is measured by the verbal reasoning (DAT-VR) and numerical reasoning (DAT-NR) subtests from the DAT battery, along with the vocabulary subtest (PMA-V) from the PMA battery. The DAT-VR comprises sentences stated as analogies in which the first and the last words are missing; participants must choose one of five word-pairs alternatives completing each sentence. The DAT-NR is similar but comprising quantitative reasoning problems. The PMA-V is a synonym test in which the meaning of four alternative words must be evaluated against a given word. The composite variable *Spatial intelligence* (Gv) is measured by the spatial relations subtest (DAT-SR) from the DAT battery, the mental rotation subtest (PMA-S) from the PMA battery, and the rotation of the solid figures test (SOD, Yela 1969). The DAT-SR is a mental folding test in which the items contain an unfolded figure and four folded alternatives; participants must choose the folded figure matching the unfolded one. In PMA-S, each item contains a model figure and six alternatives of which several are correct rotated versions whereas the remaining are mirror imaged. In SOD, the participant must evaluate which of five alternatives can be rotated within a 3D space to fit a model figure. A further variable, general intelligence or *g* is the average of Gf, Gc, and Gv.

The composite variable Working memory (WM) is measured by the reading span (RSPA; after Kane et al. 2004), computation span (CSP; Ackerman et al. 2002), and dot matrix tasks (DMAT, after Miyake et al. 2001). In RSPA participants verify which discrete sentences, presented in a sequence, do or do not make sense; each sentence is presented together a to-be remembered capital letter and at the end of a given set of sentence-letter pairs, participants have to recall, in their correct serial order, each letter from the set. CSP is similar to RSP but sentences are replaced by math equations and the capital letters by numbers. In DMAT, the mechanism is similar, but verification is about matrix equations and a dot location in a 5 × 5 matrix must be retained.

Executive functioning (EF) is the composite variable measured by the 2-Back (after Hockey and Geffen 2004), letter memory (LMEM; after Miyake et al. 2000, and keep-track (KTR; after Miyake et al. 2000) tasks. In the 2-Back task, upper and lower case letters are presented in one of eight locations around the center of the screen; the participant has to respond which letter was presented in the

same spatial location two positions back in the sequence relative to a target letter. In LMEM, long sequences of letters appear and the participant must recall, after each letter, the last four letters appeared so far. In the KTR, the task consists of remembering the last item presented in each of six target categories (odd, even, vowel, consonant, lowercase pairs of letters, and uppercase pairs of letters) and then write down the items at the end of the trial.

The composite variable Mental speed (MS) is measured by verbal (VSP), numerical (NSP), and spatial (SSP) simple recognition tasks (Colom et al. 2008), which consist of verifying, as fast and accurately as possible, if a given test stimulus (letters, digits, or arrows in different orientations, respectively) was presented in a small sized memory test.

Finally, Attentional control (ATT) is measured by the verbal (VATT) and numerical (NATT) versions of the Flanker Task (Eriksen and Eriksen 1974) along with the Simon Task (SATT, Simon 1969). In these tasks, a stimulus (letter, number, or arrow, respectively) is surrounded by stimuli that could be compatible or incompatible (i.e., vowel vs. consonant; odd vs. even; left vs. right).

Results

Centroid size was not correlated with any cognitive measure (all r below 0.15; p always >0.1). Table 1 shows the percentage of CC shape variation explained by each psychological variable (significance values are also reported). Among the composite scores only attention (ATT) shows a significant correlation with overall morphological variation ($p = 0.007$; explained variance = 3.1 %; Fig. 2a). This result would remain significant with $p < 0.05$ if Bonferroni correction were applied at this level of analyses. The pattern involved antero-posterior compression and rotation of the genu, as well as rotation of the splenium, a pattern associated with thinner and more curved CC with consequent flexion of the extremes (Fig. 2b). A partial-least square regression of shape against the three ATT measures shows a first latent vector which is statistically significant ($p = 0.01$; Fig. 3, top), associated with the same pattern described for the regression of shape onto ATT. The deformation along the correlation vector shows an association between increasing ATT values and a morphological pattern characterized by flexion of splenium and genu and thinning of the CC main body. The two specimens at the extreme of this trajectory (Fig. 3, bottom) are representative of this pattern evidencing, as ATT variables increase, thinning and increasing curvature of the CC. This pattern can be confirmed and strengthen by averaging the ten individuals with the extreme negative values and the ten individuals showing the extreme positive values, using

Table 1 Means (SD) and correlations between psychometric scores and CC shape variation (explained variance, % VAR and p value)

	Specific variables	Mean[a] (SD)	% VAR	p		Composite variables	Mean[a] (SD)	% VAR	p
					g	General intelligence ([Gf + Gc + Gv]/3)	17.71 (4.59)	0.72	0.622
APM	Adv. progressive matrices	11.84 (2.36)	0.53	0.797	Gf	Fluid intelligence	16.24 (3.45)	0.54	0.790
PMA-R	Inductive reasoning	19.47 (4.49)	0.61	0.719					
DAT-AR	Abstract reasoning	14.43 (3.52)	0.82	0.539					
DAT-VR	Verbal reasoning	13.64 (3.00)	0.62	0.713	Gc	Crystallized intelligence	19.42 (4.26)	0.58	0.750
DAT-NR	Numerical reasoning	11.95 (3.23)	0.59	0.745					
PMA-V	Vocabulary test	32.69 (6.57)	1.02	0.383					
DAT-SR	Spatial relations	15.95 (4.79)	0.36	0.938	Gv	Spatial intelligence	17.49 (6.08)	0.51	0.817
PMA-S	Spatial rotation	27.53 (9.66)	0.89	0.481					
SOD	Rotation of solid figures	9.00 (3.89)	0.74	0.588					
RSPA	Reading span	98.07 (6.57)	0.91	0.459	WM	Working memory	70.90 (8.11)	0.86	0.503
CSPA	Computation span	59.36 (12.8)	0.45	0.872					
DMAT	Dot matrix	55.28 (4.90)	0.87	0.487					
2-Back	2-back	16.45 (5.51)	0.77	0.585	EF	Executive functioning	16.91 (4.46)	1.52	0.152
LMEM	Letter memory	17.51 (3.38)	1.24	0.254					
KTR	Keep track	16.79 (4.51)	1.32	0.218					
VSP	Verbal speed	636.48 (172.3)	2.20	0.042	MS	Mental speed	723.96 (205.8)	1.16	0.301
NSP	Numerical speed	903.46 (288.1)	0.83	0.521					
SSP	Spatial speed	631.94 (157.0)	1.04	0.368					
VATT	Verbal attention	558.26 (71.7)	2.16	0.041	ATT	Attentional control	549.95 (72.55)	3.08	0.007
NATT	Numerical attention	608.45 (85.9)	2.38	0.025					
SATT	Spatial attention	483.16 (60.0)	2.30	0.036					

[a] All measures in total number of correct responses except MS and ATT specific and composite variables, in milliseconds

tpsSuper 1.14 (Rohlf 2004) to compute average shapes (Fig. 4). Increasing ATT therefore is associated with thinner and more curved CC. This pattern is also associated with a patent enlargement of the septum pellucidum.

Among the specific scores, only the three ATT variables (verbal, numerical, and spatial) plus verbal speed show a significant correlation with shape (Verbal attention: $p = 0.04$, explained variance = 2.2 %; numerical attention: $p = 0.02$, e.v. = 2.4 %; spatial attention: $p = 0.04$, e.v. = 2.3 %; verbal speed: $p = 0.04$, e.v. = 2.2 %; Fig. 5). These results hold significant only without alpha correction for multiple comparisons. Though some subjects might appear as outliers in the correlation plots—of, e.g., NATT or VSP—, they all are within the normal ranges of variation in these cognitive scores (Colom et al. 2008, 2009) while not departing from the covariation patterns expressed by the rest of the sample.

Discussion

Beginning with the predicted relationships between brain structures geometry and neural organization, the present study quantified the degree of correlation between midsagittal corpus callosum (CC) shape variation and cognitive performance. We found no correlation between CC shape variation and most of the cognitive scores, except for those associated with overall attentional control and verbal speed.

Therefore, the first result concerns the lack of evidence for association between midsagittal CC shape and several relevant cognitive factors, like general intelligence, working memory, or executive functioning. It appears of interest to point out that, during maturation, the correlations between cognition and CC shape using the callosal thickness approach have been seen to shift their sign, from mostly negative in childhood and adolescence (Luders et al. 2011) to positive in adulthood (Luders et al. 2007a). Similar findings have been reported for other brain structural measures such as cortical thickness (Shaw et al. 2006). Considering that our sample was composed of young adults, it seems admissible that these might represent an intermediate stage in the dynamic relationships between CC shape and cognition and, hence, a main finding is the lack of significant associations. Although this is an interesting possibility, it is constrained by the fact that our results cannot be directly compared to those using the callosal thickness approach.

Fig. 2 **a** Correlation between attentional control (values standardized to mean = 100 and SD = 15) and the shape regression scores from multivariate regression; **b** thin-plate spline deformation grid and vectors showing the geometrical changes associated with attentional control increase
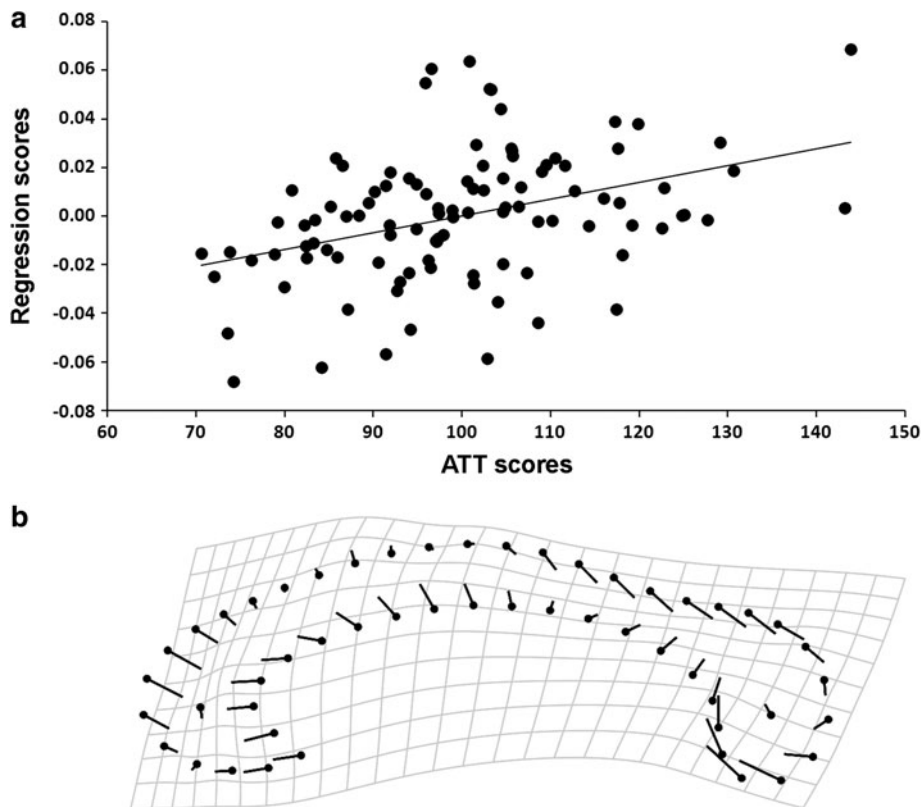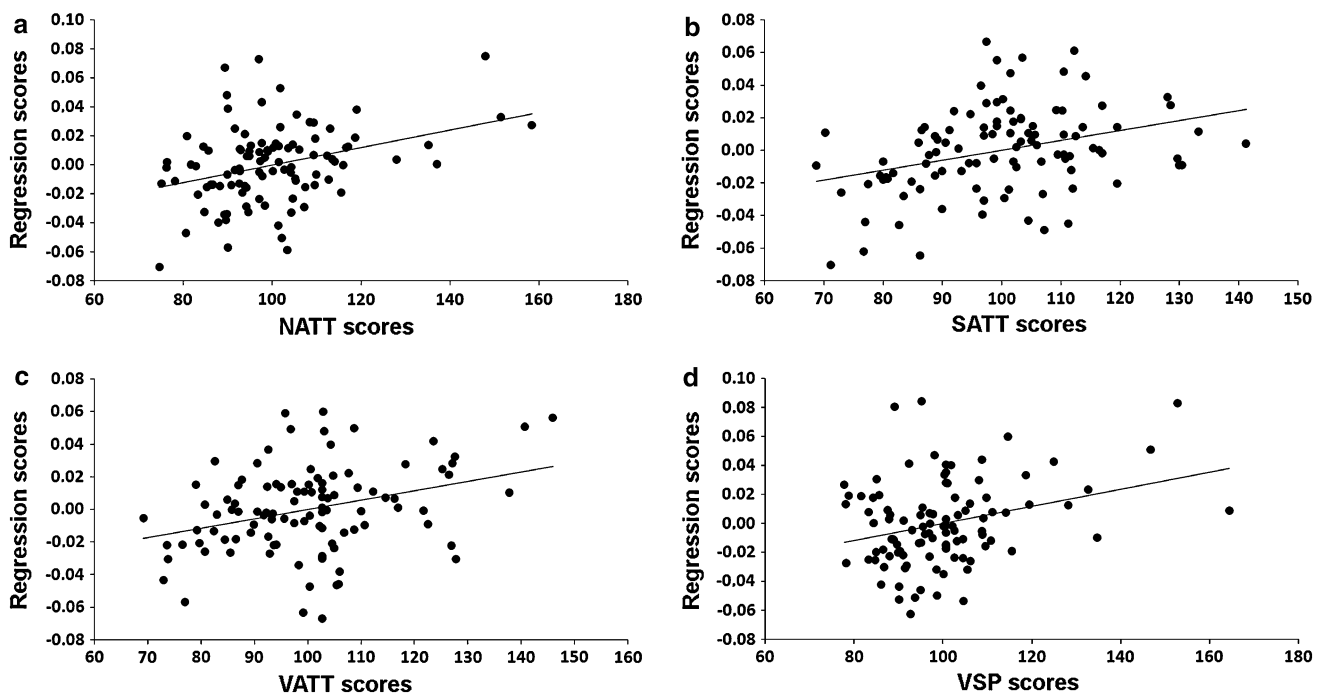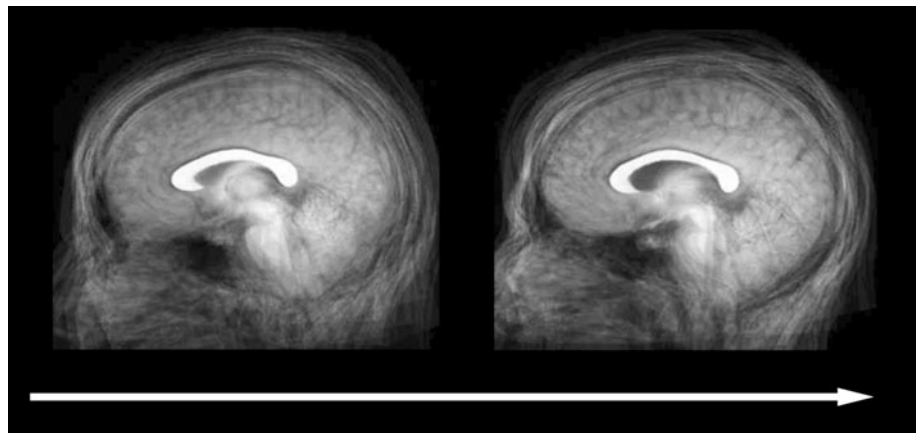

Fig. 3 Correlation between shape variation and the three specific attentional control variables (numerical, spatial, verbal) after PLS-regression. The MRI sections show extreme individuals. The shape deformation associated with this correlation is the same showed for attentional control (Fig. 2), and the two extreme individuals are representative of the changes associated with the corpus callosum morphology, from lowest (*left*) to highest (*right*) attentional score values
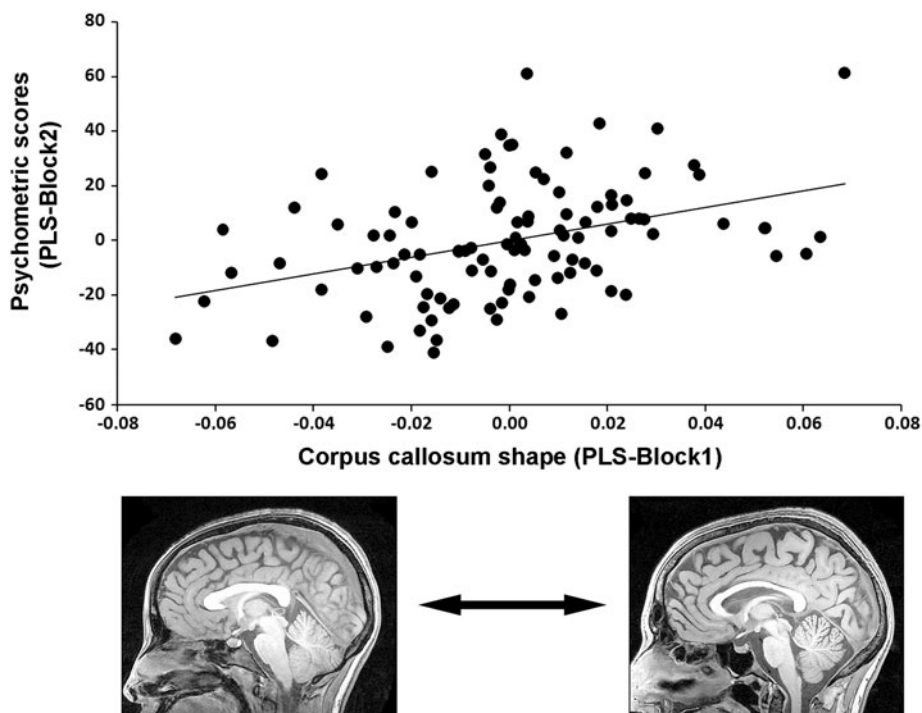
Nevertheless, all the attentional control tasks showed a small but significant correlation with CC shape. It is important to underscore that this finding cannot be attributed to collinearity issues affecting the specific attention measures. At the behavioral level, verbal, numerical, and spatial attention correlated from a minimum of 0.31 to a maximum of 0.62. Hence, although the percentage of variance explained by the correlation between attention and

Fig. 5 Correlation between verbal speed, numerical, spatial, and verbal attentional control (values standardized to mean = 100 and SD = 15) and the shape regression scores from multivariate regression

CC morphology is low, the fact that all variables associated with attentional control display a comparable relationship with CC morphology deserves scrutiny. CC shape changes accounted for between 2.2 and 2.4 % of the performance in these attention tasks (3.1 % when they are considered together as a composite score). Accordingly, the present data support a small but significant relationship between midsagittal CC morphology and attentional control, regardless of task content domain (verbal, numerical, or spatial). In this regard, it can also be considered that the data concerning each specific domain were significant only without adjusting p values for multiple comparisons, whereas the data relative to the composite variable still held significant after applying these methods. Even if the

determination coefficients were low, the consistency of these correlations deserves consideration as a noteworthy biological signal. Increase of the ATT values (i.e., slower responses) is associated with more curved and thinner CC, with consequent rotation of the splenium and the genu. This variation is also associated with enlargement of the septum pellucidum. Actually, the CC and the septum pellucidum are structurally and functionally related in terms of morphogenesis: the latter is attached to the former, and both share a common embryogenetic process (Born et al. 2004).

Attentional control implies selectively attending to certain stimuli while ignoring (or inhibiting) others (Posner and Rothbart 1998). From this perspective, the control of

attention involves executive function (i.e., executive inhibition, Miyake et al. 2000). However, with the exception of verbal speed, all the other cognitive factors—including the executive updating factor—were unrelated to CC shape. It is interesting to note that our executive factor was defined by updating measures closely related to working memory (n back, keep track, and letter memory), whereas the attention factor was defined by speeded responses in situations of stimulus incompatibility, that is, speed in tackling attentional conflicts. This suggests that CC shape would be related mainly with this inhibition component of executive function. Indeed, the relevance of processing speed in our data could explain the isolated correlation of CC shape with verbal speed, and accordingly this might be considered a derived result. In this regard, it is interesting to note that in our previous analyses correlating midsagittal overall brain shape and cognitive variables (Bruner et al. 2011) low but systematic results primarily related to mental speed (verbal, numerical, and spatial) were found. Moreover, the lack of associations between brain shape and most of the cognitive variables was also a key finding. Therefore, whereas the morphology of brain structures has been mostly unrelated to cognitive function in our present and previous studies, processing speed emerges as a subtle but systematic exception. However, there might be a plus in the attention factor when the CC is concerned because the medium collinearity values for processing speed ranged from 0.29 to 0.54, and then comparable to attention measures, but only the latter show systematic correlations with CC shape.

In the analyses reported here, slower responses in attentional control tasks and verbal speed are associated with thinner and more curved CC, with rotation of the splenium and the genu. Using a Procrustes analysis, Huang et al. (2005) reported that CC areas with the highest interindividual shape variability correspond to the genu and splenium, and this is replicated by Bruner et al. (2012). It is also of interest that studies using a volumetric approach and reporting changes in the CC related to cognitive performance find these changes mainly in the genu and splenium and specifically in clinical and developmental populations (Allin et al. 2007; Hutchinson et al. 2009). Several studies have actually reported abnormalities in the CC in clinical populations in which attentional control processes are particularly and significantly affected, as in attention-deficit hyperactivity disorders (Giedd et al. 2001; Luders et al. 2009; Rüsch et al. 2007). Noticeably, in the Luders et al. (2009) study the genu and the splenium were importantly affected. Moreover, schizophrenia, which specifically involves deficits in attentional control processes (Luck and Gold 2008), has been seen to display CC shape abnormalities (Bookstein 2003). Furthermore, schizophrenia has been also related to an enlargement of the septum pellucidum (Davidson et al. 2012). The configuration in our data adds to the extant literature by relating a particular morphology of the CC with a specific set of cognitive features (attentional control tasks plus verbal speed) in young adults. The morphological pattern associated with variation in these scores is not related to the size of the cross-section. Cognitive scores do not show any correlation with CC size variation, and the pattern itself is different from the allometric changes already described by using the same landmark configuration (Bruner et al. 2012).

Two main complementary possibilities might account for our data. One is that CC shape variations related to attentional control are reflecting 'intrinsic' factors, or factors specifically related with the spatial distribution and arrangement of the fibers connecting distant cortical areas across the CC. In this regard, Huang et al. (2005) report a partition of connectivity in the CC using tractography according to which our two major loci of shape variation correspond to fibers connecting orbitofrontal and frontal areas (antero-posterior compression with rotation of the genu) as well as those connecting mainly the occipital lobes (rotation of the splenium), though some temporal and parietal connections might also be included. The implication of frontal areas of the brain, including the orbitofrontal cortex, and areas of the dorsolateral prefrontal cortex in inhibition processes, shifting processes, and dual-task coordination has been reported in several studies (for an extensive review, see Collette and Van der Linden 2002). Interestingly, the occipital lobes also appear importantly involved in these functions (Collette and Van der Linden 2002). If the data reported here relate with intrinsic factors of the CC, they would suggest that performance in attentional control tasks appears related to morphological changes in the configuration and arrangement of the nerves crossing the CC at points related with interhemispheric transmission of information between frontal and occipital regions, two cortical areas essential for these functions.

In their review, Collette and Van der Linden (2002) also show that the participation of those regions involves either hemisphere, though the left occipital appears somewhat more engaged than its right counterpart. In conjunction with our results, all these evidences would seemingly indicate that, to the extent that our data are explained by intrinsic factors, executive inhibition processes or attentional control may make an important use of callosal transmission. Thereafter, the dependency of a task on either callosal transmission or on hemispheric specialization might not be a linear function of its complexity, as discussed at the introduction. Instead, tasks' specific requirements may be the relevant factor.

The other possibility is that our CC morphological changes may be associated with influences of different

'extrinsic' factors, i.e., factors related with variations in the structural and spatial configurations of neighboring structures. Indeed, the CC contacts many cortical and subcortical structures likely influencing its shape according to different functional and structural variables. On a larger evolutionary scale, the position of the corpus callosum is influenced by cranial base flexion (Bruner and Jeffery 2007), and during morphogenesis the splenium is likely to be influenced by tensions and constraints exerted by the tentorium cerebelli (Bruner et al. 2012). Apart from such biomechanical influences, differential volumetric expansion/reduction of adjacent neural areas may also have secondary consequences on CC morphology. Interestingly, several of the structures that might directly or indirectly affect CC shape display abnormalities in attention-deficit hyperactivity disorders, such as the basal ganglia, the cerebellum, or the cerebral ventricles (Giedd et al. 2001; Verkhlyutov et al. 2010). In addition, patients with schizophrenia consistently present alterations in the cerebral ventricles—including the third ventricle, directly contacting the CC—, the thalamus, the striatum, and the internal capsule (Bornstein et al. 1992; Horga et al. 2011). As reviewed above, both disorders specifically affecting attentional control processes also display abnormal CCs. Direct neuro-functional evidence is needed to elucidate the amount of contribution of each of the two possibilities discussed here to our data, and a combination of both cannot be ruled out at present.

The exploratory analysis performed here is limited to the cognitive variables explored, their relationships with CC shape as approached through Procrustes and coordinate-based morphometrics, and to young adults. The number of cognitive variables analyzed, even if ample and comprehensive, by no means exhausts the range of cognitive variables encompassed by complex human cognition. In addition, other approaches to CC shape have been able to find a number of relationships between CC changes and cognitive variables in both healthy and clinical populations, as reviewed above. Extending the variables and methodology used here in future studies, as well as the age ranges of the samples studied, would noticeably improve and complete the picture on the relationships between CC morphology and cognition.

In summary, here we reported results supporting systematic relationships between CC shape and speeded cognitive inhibitory functions in healthy young adult subjects. However, morphometric modeling must be interpreted as an exploratory tool, and direct interpretation of these shape patterns is suggestive, needing the support of neuro-functional evidence (with, e.g., currently available diffusion tractography). If these correlations support a biological relationship between CC shape and cognition, the low determination coefficients nonetheless evidence a large

individual component. Even so, the presence of this morphological signal must be taken into consideration for providing new clues in assessing hypotheses regarding human brain anatomy and function.

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