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Structural correlates of spoken language abilities: a surface-based region-of interest morphometry study

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Abstract

Brain structure can predict many aspects of human behavior, though the extent of this relationship in healthy adults, particularly for language-related skills, remains largely unknown. The objective of the present study was to explore this relation using magnetic resonance imaging (MRI) on a group of 21 healthy young adults who completed two language tasks: 1) semantic fluency and 2) sentence generation. For each region of interest, cortical thickness, surface area, and volume were calculated. The results show that verbal fluency scores correlated mainly with measures of brain morphology in the left inferior frontal cortex and bilateral insula. Sentence generation scores correlated with structure of the left inferior parietal and right inferior frontal regions. These results reveal that the anatomy of several structures in frontal and parietal lobes is associated with spoken language performance. The presence of both negative and positive correlations highlights the complex relation between brain and language.

Keywords

Surface-based morphometry; Neuroanatomy; Speech production; Magnetic resonance imaging; Cerebral cortex; Gray matter; Language; Sentence generation; Verbal fluency

1. Introduction

Language is a multifaceted faculty that we use every day to comprehend and communicate complex ideas and emotions. Functional magnetic resonance imaging (fMRI) studies have shown that a distributed network of cortical and subcortical regions is used to accomplish even the simplest language tasks, which demonstrates that the complexity of the language

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system translates into a complex neural architecture (for a review, see for example Indefrey & Levelt, 2004; Price, 2010). While the relation between brain functioning and language processes has been studied in some detail, little is known about the relation between brain anatomy and language skills. Interestingly, if the results of functional and structural imaging are sometimes convergent, suggesting a close relationship between brain structure and function (Maguire et al., 2000; Richardson, Thomas, Filippi, Harth, & Price, 2010), structural imaging studies can also offer novel insights by identifying regions not typically identified using fMRI.

One of the most widely studied aspects of human brain anatomy is cortical thickness (CT), which can be assessed using magnetic resonance imaging (MRI). The human cerebral cortex is composed of highly folded horizontal layers of neurons; the thickness of this neuronal sheet varies across brain regions and individuals, and ranges from 1 to 4.5 mm, with an average of approximately 2.5 mm (Zilles, 1990). Changes in CT are of great interest in both normal brain maturation and aging as well as in a variety of neurodegenerative and psychiatric disorders (Fischl & Dale, 2000). Recent neuroimaging studies have revealed that differences in gray matter architecture are also associated with differences in performance in healthy adults in a number of cognitive and motor tasks (Kanai & Rees, 2011; May & Gaser, 2006; Tomassini et al., 2011). For example, positive correlations have been found between GM architecture and proficiency in sports, in regions involved in motor planning, execution and learning including the bilateral inferior frontal (IFG) and mid-temporal gyrus, left precentral and middle frontal gyri (MFG), cerebellum, as well as regions involved in visual and spatial association processes such as the left inferior parietal (IPL), left superior temporal sulcus and right parahippocampal gyrus (Di Paola, Caltagirone, & Petrosini, 2013; Draganski et al., 2004; Jacini et al., 2009; Wei, Zhang, Jiang, & Luo, 2011).

However, only a limited number of studies have used structural MRI to study language skills, including vocabulary acquisition (Lee et al., 2007), second language proficiency (Hosoda, Tanaka, Nariai, Honda, & Hanakawa, 2013; Mechelli et al., 2004), and speech perception and production (Bilodeau-Mercure, Lortie, Sato, Guitton, & Tremblay, 2014; Grogan, Green, Ali, Crinion, & Price, 2009; Tremblay, Dick, & Small, 2013). The study of spoken language production is complex because it depends upon a very large number of sensorimotor and cognitive processes. To express conceptual ideas, word forms must first be retrieved, converted into a phonological code, sequenced and articulated, while unintended words need to be suppressed and the output need to be monitored (see for example Guenther, Ghosh, & Tourville, 2006; Price, 2010 for a review). Commensurate with this complex picture, fMRI studies of speech production have identified a large number of regions involved in producing language including the cerebellum, M1, the basal ganglia, IFG and MFG, the inferior parietal lobe, the prefrontal cortex, and the superior and middle temporal gyri (e.g. Adank, 2012; Blank, Scott, Murphy, Warburton, & Wise, 2002; Bohland, Bullock, & Guenther, 2010; Bohland & Guenther, 2006; Ghosh, Tourville, & Guenther, 2008; Peeva et al., 2010; Riecker et al., 2005; Riecker, Wildgruber, Dogil, Grodd, & Ackermann, 2002; Tremblay & Gracco, 2009, 2010; Tremblay & Small, 2011b; Turkeltaub, Eden, Jones, & Zeffiro, 2002; Whitney et al., 2009; Wildgruber, Ackermann, & Grodd, 2001; Wise, Greene, Büchel, & Scott, 1999). The functional importance of anatomical

variations within these regions, however, is largely unknown, and so is their importance for the different cognitive and motor stages of spoken language production.

Because most studies of language production have relied preferentially on voxel-based morphometry (VBM) (Amici et al., 2007; Beal, Gracco, Brettschneider, Kroll, & De Nil, 2013; Golestani & Pallier, 2007; Grogan et al., 2009; Mechelli et al., 2004; Zhu, Zhang, & Qiu, 2013) and no study has examined how other morphometric measures (cortical volume (VOL) and surface area (SA)) are associated with language abilities in healthy adults, the main objective of this study was to explore the relation between brain morphometry and language performance using two classic language production tasks (sentence generation task and semantic fluency) in healthy adults using surface-based morphometry (SBM). In SBM, morphometric measures are derived from geometric models of the cortical surface from which different metrics like CT, VOL or SA of brain regions at a subvoxel level resolution can be extracted (Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999). In the present study, CT, VOL, and SA measures were computed and correlated with performance in these tasks, which involve different sets of processes. In the verbal fluency task, word retrieval is usually driven by association chains between clusters of words belonging to semantic subcategories. For example, for the category “animals”, people often begin with animals considered as pets and when this subcategory is exhausted, they switch to a different subcategory (Katzev, Tuscher, Hennig, Weiller, & Kaller, 2013; Wechsler-Kashi, Schwartz, & Cleary, 2014). Sentence generation, in contrast, involves a different series of cognitive stages that include object recognition, lexical retrieval of the element presented in the picture, access to the phonological word form, syntactic planning (DeLeon et al., 2007; Wechsler-Kashi et al., 2014). Because of these differences, we hypothesized that performance on the two language tasks would be correlated with distinct brain regions. For example, damage to the anterior insula (AI) has been associated with fluency and articulatory impairments (Baldo, Wilkins, Ogar, Willock, & Dronkers, 2011; Dronkers, 1996). The structure of the AI could then correlate with the performance on the semantic fluency task. Because the sentence generation task relies on the recognition of object pictures, performance on this task should instead correlate with the structure of regions involved in visual processing located in the inferior parietal lobe (Culham & Kanwisher, 2001). Several fMRI studies have also shown that manipulating response selection during word production modulates the pre-SMA, the inferior frontal gyrus (IFG), and the ventral premotor (PM) cortex (F. X. Alario, H. Chainay, S. Lehericy, & L. Cohen, 2006; Crosson et al., 2001; Nagel, Schumacher, Goebel, & D’Esposito, 2008; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997; Thompson-Schill, D’Esposito, & Kan, 1999; Thompson-Schill et al., 1998; Tremblay & Gracco, 2009; Tremblay & Gracco, 2006; J. X. Zhang, Feng, Fox, Gao, & Tan, 2004). In view of these results, we were interested in examining if the structure of these regions would show a stronger relation to verbal fluency than to sentence generation due to the high demand on selection imposed by the fluency task.

2. Methods

2.1 Participants

21 right-handed adults (10 males, mean 25 ± 4.4 years, range 20–36 years), with a mean education level of 15.4 years (range = 12–22 years) participated in the experiment. The study sample consisted of Caucasian (85.7%), African American (9.5%) and Hispanic participants (4.7%). All participants were native speakers of standard American English and had normal pure tone thresholds and normal speech recognition scores (92.3% accuracy on the Northwestern University auditory test number 6). Participants were recruited through the student email address list at The University of Chicago. The study was approved by the Institutional Review Board for the Division of Biological Sciences at The University of Chicago.

2.2 Image acquisition

T1-weighted brain images were acquired on a 3T General Electric (Milwaukee, WI) Signa HDx MRI scanner. The structural images included 166 slices (TR = 5.7 ms, TE = 2.036 ms, FoV = 240 mm, flip angle = 12° , matrix = $256\text{mm} \times 256\text{mm}$, 166 slices, $1\text{mm} \times 1\text{mm} \times 1\text{mm}$, no gap). The images were acquired as part of a larger project that also included BOLD fMRI. The BOLD fMRI results have been reported elsewhere and will not be discussed in this article (Argyropoulos, Tremblay, & Small, 2013; Tremblay & Small, 2011a, 2011c).

2.2 Image analysis

CT, SA, VOL and subcortical volumetric brain measures were computed with the FreeSurfer image analysis suite, which is well documented and freely available for download online (<http://surfer.nmr.mgh.harvard.edu/>) (Dale et al., 1999; Fischl et al., 1999; Fischl et al., 2004). First, a surface representation of each participant's anatomy was created by inflating each hemisphere of the anatomical volumes to a surface representation. The resulting surface representation was aligned to a template of average curvature. These surface representations were obtained by submitting each participant's MRI to a series of steps that included: (1) motion correction and affine transformation to Talairach space, (2) intensity normalization, (3) removal of non-brain voxels, (4) segmentation of GM, white matter (WM) and cerebrospinal fluid, and, finally (5) tessellation of the GM/WM boundary, and automated topology correction. At each step, the results were visually inspected and manual interventions were performed when required to correct topological defects. The surface representations were then parcellated into 17 anatomical regions of interest per hemisphere using an automated parcellation scheme (Desikan et al., 2006; Fischl et al., 2004). This automated parcellation scheme relies on a probabilistic algorithm that incorporates the anatomical convention of Duvernoy (Duvernoy, 1991). The anatomical accuracy of this method is high and approaches the accuracy of manual parcellations (Desikan et al., 2006; Fischl et al., 2002; Fischl et al., 2004). The ROIs were selected based on a review of the literature, and included 1) IFG pars triangularis, 2) IFG pars orbitalis, 3) IFG pars opercularis, 4) Inferior frontal sulcus, 5) MFG, 6) middle frontal sulcus, 7) inferior precentral gyrus, 8) pre-SMA, 9) Superior parietal lobule, 10) angular gyrus, 11) supramarginal gyrus (SMG), 12) posterior middle temporal gyrus, 13) temporal pole, 14) lateral posterior superior temporal gyrus, 15) lateral anterior superior temporal gyrus 16)

Planum temporal, 17) AI (including the short gyrus, long gyrus and the anterior circular sulcus). The anatomical location of the ROIs is represented in Figure 1. For each ROI, CT, SA and VOL were calculated. CT was estimated by computing the shortest distance between each point on the white/gray surface and the pial surface, and conversely, between each point on the pial surface and the white/gray surface. At each location, CT was set to the average of the two values. To calculate SA, a triangular tessellation was used to generate the surface of the white/gray frontier. The generated surface (white matter surface) is then smoothed to reduce metric distortions. The VOL at each vertex is defined as the area multiplied by the thickness. The volume of a region is therefore obtained by adding up the volume of each vertex contained in each individual region.

2.3 Experimental procedure

A category fluency task was used to evaluate the capacity to spontaneously generate words. Participants were instructed to name as many animals and vegetables as possible during one minute, in two distinct trials. Participants' responses were recorded and stored to disk for offline analysis. A research assistant naïve to the purpose of the study transcribed all the responses. The total number of correct words generated in both categories was used as the measure of overall fluency. Participants underwent the fluency task immediately prior to the MRI session.

The ability to generate short sentence was evaluated in the scanner with a sentence generation task. During this task, participants were presented a set of 40 pictures of objects, and asked to generate, for each picture, a short sentence action and an object sentence describing the picture. The same pictures were presented in two different blocks, one for each answer type condition (object or action sentence) to prevent a task switching effect on performance. Each block contained 40 experimental trials. Each trial consisted in the presentation of a picture during 1.5, s followed by the presentation of a Go cue, after 500ms. Once the cue was presented, participants had 4.5s to generate the sentence. Experimental tasks preceding this one, involving hearing or repeating short sentences, were explicitly designed to take advantage of structural priming (Bock, 1986, 1990) and thus served as an answer model for the participants in the generation task. For more information regarding the tasks, see (Tremblay & Small, 2011a). Participants' responses were recorded and stored to disk for offline analysis. The responses for two participants could not be analyzed due to technical difficulty with the recordings. A research assistant naïve to the purpose of the study transcribed the responses for the remaining 19 participants, and for each sentence, assessed accuracy (whether the answer conformed to task instructions) and grammaticality (whether the sentence was correctly formed). The percentage of correct answers across all experimental conditions was computed.

2.4 Brain/behaviour analyses

First, the normality assumption for the two language measures (fluency, generation) was tested with the Shapiro-Wilk test, which reported *p*-values of 0.431 and 0.346 for sentence generation and verbal fluency respectively (i.e. no violation). Next, a total of 204 partial Pearson's correlation analyses were computed, at the group level, to test for a linear relationship between each morphometric measure (CT, VOL and SA) and scores on the two

language tasks (verbal fluency, sentence generation). A supplementary analysis of the effect of sex on is available as supplementary material. To account for global individual differences in brain size, total GM volume, total surface area and mean thickness of each hemisphere were included as covariate for the correlation between language performance and VOL, SA and CT, respectively. To address the issue of multiple hypothesis testing, correlations were divided into 12 subsets (families) based on the morphometric measure, hemispheric location and language task. The null hypotheses of each family were individually tested and resulting *p* values were corrected using the false discovery rate (FDR) method (Benjamini & Hochberg, 1995). The FDR method attempts to assign an adjusted *p*-value to each test by controlling for the number of false discoveries. The correction consists in ranking the raw *p*-values within a family in ascending order and applying the formula $[p\text{-value} * (m/j)]$ where *m* is the total number of test within the family and *j* the respective rank of each raw *p*-value. The statistical decision is made on the resulting *p* value without changing the statistical threshold of .05. In the present study we report the 95 and 99% confidence intervals (CIs), the raw *p* value for each correlation, as well as the corrected *p* value in Table 1.

3. Results

3.1 Behavioural Data

The scores on the verbal fluency task ranged from 26.5 to 59 words, with a mean of 39.7 ± 9.6 words. The accuracy in the sentence generation task ranged from 67.5 to 100 %, with a mean accuracy of 86.4 ± 7.9 %. The generated sentences had an average length or 4.48 ± 0.18 words.

3.2 Correlations between verbal fluency and brain morphometry

The structure of several frontal, insular and parietal regions (the complete list is provided in Table 1 and represented in Figure 2a) correlated with the ability to spontaneously name items of a specific category as evaluated by the verbal fluency task.

In the left hemisphere, fluency scores correlated negatively with CT of the orbital part of the IFG ($r = -0.64$, $p = 0.002$, *corr. p* = 0.042) and the inferior frontal sulcus ($r = -0.53$, $p = 0.016$, *corr. p* = 0.133), and positively with CT of the superior parietal lobule ($r = 0.49$, $p = 0.027$, *corr. p* = 0.154). Significant correlations were found between verbal fluency and the VOL of the anterior insula ($r = -0.49$, $p = 0.03$, *corr. p* = 0.517) and the triangular part of the IFG ($r = 0.45$, $p = 0.048$, *corr. p* = 0.408). Verbal fluency scores also correlated negatively with SA of the anterior insula ($r = -0.49$, $p = 0.029$, *corr. p* = 0.497) and inferior precentral gyrus ($r = -0.46$, $p = 0.039$, *corr. p* = 0.332), and positively with SA of the triangular part of the IFG ($r = 0.46$, $p = 0.043$, *corr. p* = 0.243). In the right hemisphere, fluency scores negatively correlated negatively with CT of the anterior insula ($r = -.495$, $p = 0.026$, *corr. p* = 0.477). A subset of these results is illustrated in Figure 3 and 4.

3.3 Correlations between sentence generation and brain morphometry

The ability to generate sentences, as evaluated by the sentence generation task, was associated with the anatomy of parietal and frontal regions (see Table 1 and Figure 2b). In

the left hemisphere, a negative correlation was found between generation scores and CT of the SMG ($r = -0.52$, $p = 0.028$, *corr. p* = 0.477). In the right hemisphere, sentence generation scores correlated negatively with the CT of the triangular part of the IFG ($r = -0.51$, $p = 0.033$, *corr. p* = 0.278).

4. Discussion

The aim of this study was to examine the relation between brain morphometry and performance on two classic measures of expressive language in a group of young healthy right-handed adults. The current findings demonstrate that inter-individual differences in the structure of several cortical regions correlate with measures of expressive language. First, this study highlights the presence of task-related differences in the relationship between brain morphometry and spoken language skills. Second, our results reveal that CT of several regions correlated with language performance, and that the direction of the relationship between brain anatomy and language skills is spatially heterogeneous and differs as a function of the specific morphometric measure (CT, SA, VOL), suggesting that more is not always better. These findings are discussed in the following paragraphs. It should be noted that only one correlation (CT in IFG pars orbitalis and fluency) survived FDR correction for multiple comparisons. This was not unexpected due to the relatively high number of bilateral ROIs (17), the use of 2 tasks and 3 morphometric measures, and the overly conservative aspect of FDR corrections. The results should nevertheless be interpreted with some caution.

4.1 Verbal fluency vs. sentence generation scores

As expected, for the verbal fluency task, significant correlations were found with the inferior precentral gyrus and several areas of the left IFG, including the pars orbitalis, pars triangularis and inferior frontal sulcus. These results are consistent with fMRI studies that reported increased activation in these regions during language production tasks with high demands on lexical retrieval/selection supporting the notion of a role for the IFG in semantic retrieval (F.X. Alario, H. Chainay, S. Lehericy, & L. Cohen, 2006; Amunts et al., 2004; Basho, Palmer, Rubio, Wulfeck, & Müller, 2007; Buckner, Raichle, & Petersen, 1995; Fu et al., 2002; Thompson-Schill, Aguirre, D'Esposito, & Farah, 1999; Thompson-Schill et al., 1997; Thompson-Schill et al., 1998; Tremblay & Gracco, 2006).

Another important finding is that of significant correlations between fluency scores and the bilateral AI. The insular cortex, and particularly its anterior part, is known for being activated across a wide variety of cognitive, linguistic and sensorimotor tasks suggesting that it may have a general role in attention and task level control (Nelson et al., 2010), both of which are necessary to produce fluent spoken language. This interpretation is consistent with Golestani and Pallier (2007) who found that participants who were better at producing foreign speech sounds had a higher density of white matter in the left AI. Moreover, Eickhoff, Heim, Zilles, and Amunts (2009) recently suggested that the left AI is part of a network with the cerebellum, basal ganglia and cortical motor system involved in speech preparation and execution. Aging studies have shown that decline in speech skills are accompanied by functional and anatomical changes in the AI (Bilodeau-Mercure et al., 2014; Tremblay et al., 2013). In a study combining post-mortem blunt dissections of a

healthy 90 year old woman and diffusion tractography of a healthy young adult, Catani et al. (2012) found that the AI connects directly, through U shaped tracts, to the triangular and orbital parts of the IFG, two regions that we also found to be significantly associated to verbal fluency in the present study.

Fluency scores also correlated with the left superior parietal lobule. This high order associative region is involved in several cognitive processes including task switching, visual attention and working memory (Behrmann, Geng, & Shomstein, 2004; Sohn, Ursu, Anderson, Stenger, & Carter, 2000). Results from a diffusion tensor imaging study by Kamali, Flanders, Brody, Hunter, and Hasan (2014) have recently shown, for the first time, a connection between the superior parietal lobule and several regions involved in the production of spoken language, including the superior temporal gyrus, the SMA, and the dorsomedial premotor cortex through white matter fiber bundles of the superior longitudinal fasciculus, implicating this region in the neural network that supports language functions (Kamali, Flanders, et al., 2014; Kamali, Sair, Radmanesh, & Hasan, 2014). The superior parietal lobule could support the retrieval of category-related items by improving an individual's capacity to organize his search within a given semantic cluster with strong visual features. For example, for the cluster "vegetables", a participant could attempt to imagine his last visit to the supermarket vegetable aisle or recall which vegetables he uses when cooking (Gruenewald & Lockhead, 1980). Parietal regions could be recruited and stimulate visual imagery, enhancing the ability to efficiently find category-related items and, therefore, increase performance on the fluency task.

Compared to the verbal fluency scores, the sentence generation scores correlated with distinct brain regions, localized in the parietal and frontal lobes. Of interest is the correlation found with the left SMG. Consistent with this finding, Lee et al. (2007) found a correlation between the grey matter density in the posterior SMG of adolescents and performance on a vocabulary knowledge test, but no correlation was found with verbal fluency. Although the posterior SMG is not typically activated in functional imaging studies of word processing, it is surrounded by the anterior SMG and angular gyri, which are activated during phonological and semantic association tasks respectively (Demonet et al., 1992; Devlin, Matthews, & Rushworth, 2003; Mummery, Patterson, Hodges, & Price, 1998; Price, Moore, Humphreys, & Wise, 1997). The posterior SMG could then be involved in linking phonological and semantic aspects of words during vocabulary acquisition throughout adolescence and, at latter stages, to play a role in accessing the phonological representation of existing words (Gathercole, 2006). In the context of a task in which participants must quickly process the semantic aspects evoked by a visually presented picture, and access the phonological form of the corresponding words, the correlation between the left SMG and performance on the sentence generation task is consistent with existing literature suggesting that this region supports phonological access during speech production.

In the right hemisphere, scores on the generation task also correlated with the triangular part of the IFG. According to the literature, the right IFG is involved in executive control during tasks requiring generation or inhibition of motor responses (Go/no-go) (Aron, Robbins, & Poldrack, 2014; Levy & Wagner, 2011). Results from a study of response inhibition by Hampshire, Chamberlain, Monti, Duncan, and Owen (2010) have also shown that the right

IFG is active following the presentation of important visual cues, whether or not a response is required. These IFG results are of interest in understanding the role of the right IFG during the sentence generation task that was used in the present study. Indeed, here sentence generation began with the presentation of a picture whose visual features had to be quickly identified. Then, during response production, participants had to select one feature to describe and inhibit other related features. Hence, it is possible that the relationship that was found between the right IFG and the sentence generation scores could be related to the response inhibition component of the task, though additional studies are needed to further explore this interpretation.

In summary, performance on the verbal fluency task correlated particularly with the structure of the left IFG, left inferior precentral gyrus, left superior parietal lobule and bilateral insular regions whereas performance on the sentence generation task correlated with the structure of the left inferior parietal and right IFG. These differences could reflect the use of distinct core linguistic or cognitive processes, with semantic fluency perhaps requiring a higher attentional level to switch between semantic subcategories and monitor responses to avoid repetitions, while sentence generation would depend on the rapid recognition of relevant semantic aspects evoked by a picture and the associations with their phonological representations.

4.2 Direction of correlations between cortical thickness, surface and volume

Voxel-based morphometry (VBM) has traditionally been used to examine brain/behaviour correlations. VBM provides information regarding the GM volume and concentration of a given cerebral region (Ashburner & Friston, 2000; Whitwell, 2009). One limitation of VBM is that results reflect both differences in GM, SA or CT (Greve et al., 2013). To account for this limitation, we decided to use surface-based morphometry instead of VBM. In SBM, morphometric measures are derived from geometric models of the cortical surface from which different metrics like CT, VOL or SA of brain regions at a subvoxel level resolution can be extracted and interpreted separately, (Dale et al., 1999; Fischl et al., 1999).

A surprising finding was the difference in the direction of the relationship between CT, SA and VOL on both language tasks. With the exception of CT in the superior parietal lobule, CT was negatively correlated with performance on the verbal fluency and sentence generation tasks, meaning that a thinner cortex was associated with a better performance. For SA, two correlations were negative and one was positive with the fluency task suggesting that a smaller cortical surface tends to be associated with a better performance. For VOL, a negative correlation was found between the left AI and verbal fluency, whereas the correlation was positive between the performance on the verbal fluency task and the left triangular part of the IFG. At first, these results can seem counter-intuitive, as a few previous studies of language abilities have reported positive correlations between performance on language tasks and grey matter density or volume (Grogan et al., 2009; H. Zhang et al., 2013). However, our results are supported by a study from Porter, Collins, Muetzel, Lim, and Luciana (2011) who found significant negative correlations between performance on a verbal fluency task (COWAT) and CT in regions including the bilateral superior and middle temporal gyrus, left SMG and angular gyrus, left pars opercularis,

In one region however, we did find a positive relation between CT and language skills. Indeed, for the superior parietal lobule, CT correlated positively with the performance on the verbal fluency task. For this region a thicker cortex was associated with a better performance. We hypothesized that the superior parietal lobule could stimulate visual imagery and therefore enhance one's ability to find category related items with prominent visual characteristics. However, if this is the case and if a thinner cortex is associated with a better performance, a negative correlation should have been observed. A possible explanation is that CT in this region is indeed associated with functions such as visual and spatial attention shifts however, instead of promoting within cluster search during the fluency task, superior parietal lobule activity could interfere with the high level of focused attention required during the task. Therefore, a thinner CT in this region (or a more efficient superior parietal lobe) could be associated with predominant visual attention, which could prejudice one's ability to ignore surrounding stimuli and process the fluency task.

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Herskovits, 2011; Libero, DeRamus, Deshpande, & Kana, 2014). However, because most longitudinal study have focused on CT (Shaw et al., 2008), it is not clear whether the correlations between SA and language abilities can be explained by genetic influence in critical periods of early development or not. Nevertheless, including a measure of cortical SA in morphometric studies might provide new insights regarding brain/behavior relationships and may be a valuable complement to the information provided by CT.

Finally, because surface-based morphometric methods allow subdivision of VOL into its two main constituents, CT (distance between the boundary of GM/WM division and GM/pial surface) and SA (total area of the surface encompassing a brain region), which are globally and regionally independent, VOL interpretation is more complex (Libero et al., 2014; Panizzon et al., 2009; Winkler et al., 2010). In a twin study on the genetic relationships between CT and SA, Panizzon et al. (2009) found that these two metrics are influenced by different genetic sources. Moreover, CT and SA have distinct trajectories of anatomical changes that are influenced by several factors such as sex and developmental stage (Raznahan et al., 2011). It is interesting to note that in the present study, the two regions in which VOL correlated with fluency scores, there was also a correlation between fluency scores and SA, in the same direction (positive or negative). Thus, correlations between the VOL of a specific region and performance on the verbal fluency task that were found in the present study might be explained, at least in part, by a stronger impact of SA (rather than CT) on the relation between regional VOL and fluency. This result is in accordance with growing literature supporting the idea that VOL is driven by SA (Im et al., 2008; Pakkenberg & Gundersen, 1997; Panizzon et al., 2009; Rakic, 1988, 2004; Squeglia, Jacobus, Sorg, Jernigan, & Tapert, 2013). Therefore, using a composite measure of cortical anatomy like VOL instead of the variables constituting it may not be the optimal morphometric measure to use to study brain/behaviour relationships, though this needs to be further examined.

5. Conclusion

In conclusion, the present findings provide important insights into the relationship between brain structure and spoken language production. Performance on the sentence generation and semantic fluency tasks were associated with different brain regions, suggesting that they relied, at least partly, on different cognitive and sensorimotor abilities. Moreover, by looking at CT, SA and VOL, we found different patterns of correlation that might reflect different neuronal plastic changes occurring through maturation and experience. Our results therefore offer a comprehensive portrait of the relation between brain morphometry and performance in two expressive language tasks. More studies are needed to replicate our findings (most of which did not survive FDR correction) using larger sample sizes to increase power, and improve our understanding of the cellular mechanisms (synaptic pruning, increase in myelination or experience-dependent cortical plasticity) underlying brain-behaviour relationships.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

1. Verbal fluency performance correlates with the anatomy of the IFG and insula
2. Sentence generation correlates with the anatomy of parietal and prefrontal regions
3. Cortical thickness is negatively correlated with spoken language production skills
4. Cortical surface is correlated with language production skills
5. Cortical volume positively and negatively correlated with language production skills

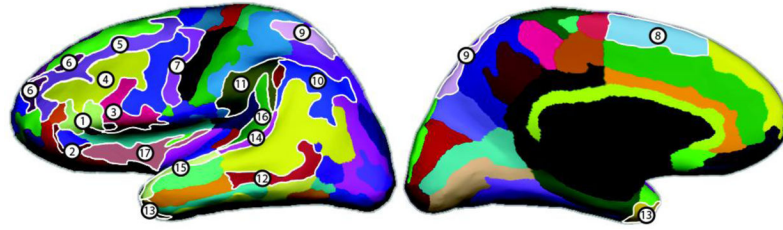


Figure 1. Localisation of cortical regions of interest (ROIs) on an inflated brain

ROIs were bilateral and only the left hemisphere is shown to avoid redundancy. Legend: 1) IFG pars triangularis, 2) IFG pars orbitalis, 3) IFG pars opercularis, 4) IFG sulcus, 5) middle frontal gyrus, 6) middle frontal sulcus, 7) inferior precentral gyrus, 8) pre-supplementary motor area, 9) Superior parietal lobule, 10) angular gyrus, 11) supramarginal gyrus, 12) posterior middle temporal gyrus, 13) temporal pole, 14) lateral posterior superior temporal gyrus, 15) lateral anterior superior temporal gyrus 16) Planum temporal, 17) anterior insula

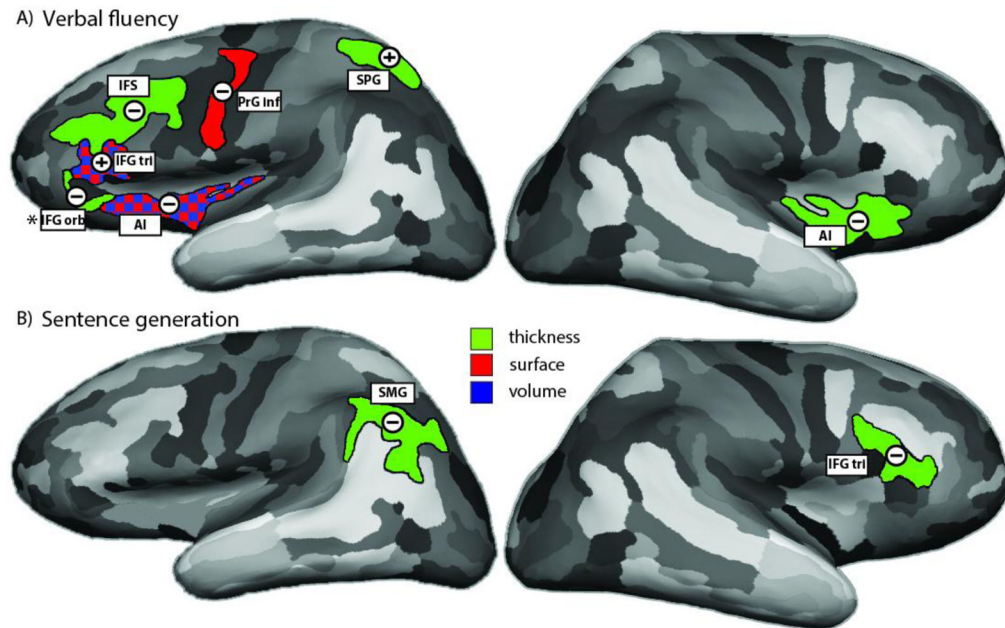


Figure 2. Localisation of significant correlations between cortical thickness, surface and volume, and verbal fluency and sentence generation scores

A) significant correlation between verbal fluency scores and the 3 morphometric measures.

B) significant correlation between sentence generation scores and the 3 morphometric measures.

In the figure, correlations between CT, SA and VOL and the two language tasks are represented in green, red and blue respectively. a checked font means that a region correlates with more than one morphometric measure. The left hemisphere is on the right.

Legend: AI = anterior insula; IFG orb = inferior frontal gyrus orbital part; IFG tri = inferior frontal gyrus triangular part; IFS = inferior frontal sulcus; PrG inf = inferior precentral gyrus; SMG = supramarginal gyrus; SPG = superior parietal lobule. An asterisk (*) indicates a correlation that remained significant after FDR correction.

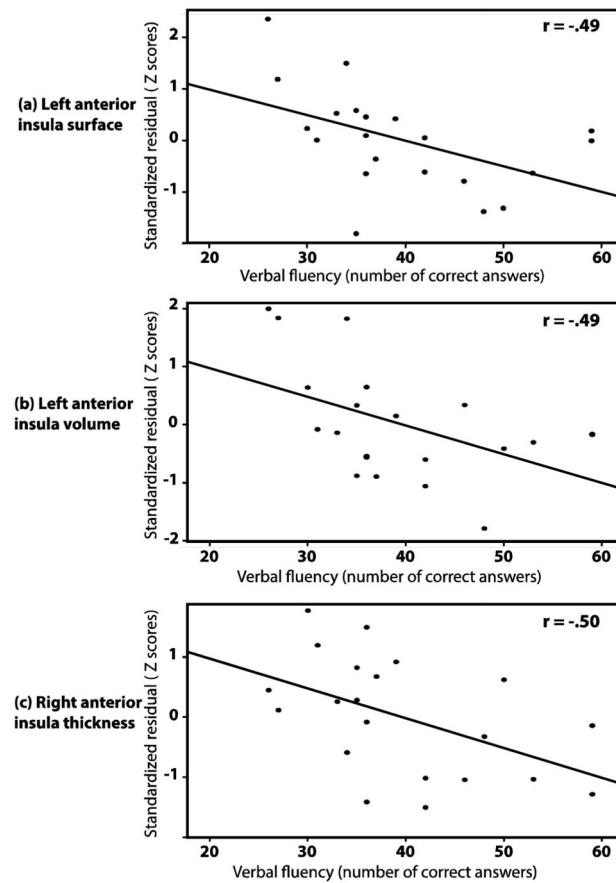
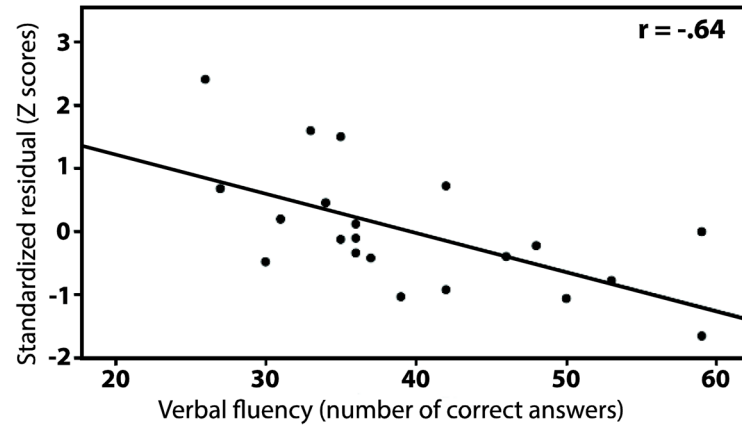


Figure 3. Correlation between verbal fluency scores

and a) standardized residuals of the left anterior insula surface area regressed by left total gray matter surface area; b) standardized residuals of the left anterior insula volume regressed by left total gray matter volume; c) standardized residuals of the right anterior insula thickness regressed by left mean thickness.

Left anterior IFG pars orbital cortical thickness**Figure 4.**

Correlation between verbal fluency scores and standardized residuals of the left inferior frontal gyrus pars orbitalis cortical thickness regressed by left mean cortical thickness.

Table 1
Correlations between brain structure and language scores (bold CI values indicates significance)

Anatomic region	Hemisphere	Measure	r	95 % confidence interval		99% confidence interval		p value	FDR corrected p value
Verbal fluency									
Inferior frontal gyrus orbital part	Left	Thickness	-0.638	-0.838	-0.285	-0.876	-0.147	0.002	0.042
Inferior frontal sulcus	Left	Thickness	-0.533	-0.784	-0.132	-0.834	0.012	0.016	0.133
Superior parietal gyrus	Left	Thickness	0.493	0.078	0.762	-0.067	0.816	0.027	0.154
Anterior insula	Left	Surface area	-0.487	-0.759	-0.071	-0.814	0.074	0.029	0.497
Inferior frontal gyrus triangular part	Left	Surface area	0.457	0.032	0.742	-0.113	0.8	0.043	0.243
Inferior precentral gyrus	Left	Surface area	-0.465	-0.746	-0.042	-0.804	0.103	0.039	0.332
Anterior insula	Left	Volume	-0.485	-0.757	-0.068	-0.813	0.077	0.030	0.517
Inferior frontal gyrus triangular part	Left	Volume	0.447	0.019	0.736	-0.125	0.796	0.048	0.408
Anterior insula	Right	Thickness	-0.495	-0.763	-0.081	-0.817	0.064	0.026	0.450
Sentence generation									
Supramarginal gyrus	Left	Thickness	-0.517	-0.786	-0.083	-0.838	0.071	0.028	0.477
Inferior frontal gyrus triangular part	Right	Thickness	-0.505	-0.78	-0.066	-0.833	0.087	0.033	0.278