ACC Sulcal Patterns and their Modulation on Cognitive Control Efficiency across Lifespan:

A Neuroanatomical Study on Bilinguals and Monolinguals

Nicola Del Maschio[1], Simone Sulpizio[1], Davide Fedeli[1], Keerthi Ramanujan[2], Guosheng Ding[3], Brendan S. Weekes [2,4], Arnaud Cachia[5,6,7,8], Jubin Abutalebi[1]

[1] *Centre for Neurolinguistics and Psycholinguistics, University Vita-Salute San Raffaele, Milano, Italy*

[2] *Department of Speech and Hearing Sciences, University of Hong Kong, Hong Kong*

[3] *State Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University, Beijing, China*

[4] *School of Psychological Sciences, Faculty of Dentistry, Medicine and Health Sciences, University of Melbourne, Parkville, Australia*

[5] *Laboratory for the Psychology of Child Development and Education, Sorbonne, CNRS UMR8240, Paris, France*

[6] *Paris Descartes University, Sorbonne Paris Cité, Paris, France*

[7] *Institut Universitaire de France, Paris, France*

[8] *Imaging biomarkers for brain developement and disorders, Ste Anne hospital, INSERM UMR894, Paris, France*

Corresponding author:

Prof. Jubin Abutalebi
Vita-Salute San Raffaele University,
Via Olgettina, 58 – 20132 Milan, Italy
email: abutalebi.jubin@hsr.it

Abstract

The anterior cingulate cortex (ACC) is a key structure implicated in the regulation of cognitive control (CC). Previous studies suggest that variability in the ACC sulcal pattern – a neurodevelopmental marker unaffected by maturation or plasticity after birth – is associated with intersubject differences in CC performance. Here, we investigated whether bilingual experience modulates the effects of ACC sulcal variability on CC performance across the lifespan. Using structural MRI, we first established the distribution of the ACC sulcal patterns in a large sample of healthy individuals (*N*=270) differing on gender and ethnicity. Second, a participants' subsample (*N*=157) was selected to test whether CC performance was differentially affected by ACC sulcation in bilinguals and monolinguals across age. A prevalent leftward asymmetry unaffected by gender or ethnicity was reported. Sulcal variability in the ACC predicted CC performance differently in bilinguals and monolinguals, with a reversed pattern of structure-function relationship: asymmetrical versus symmetrical ACC sulcal patterns were associated with a performance advantage in monolinguals and a performance detriment to bilinguals and vice versa. Altogether, these findings provide novel insights on the dynamic interplay between early neurodevelopment, environmental background and cognitive efficiency across age.

***Keywords*:** anterior cingulate cortex (ACC), bilingualism, cognitive control, paracingulate sulcus (PCS).

Introduction

The ability to optimize behaviour when confronted with changing environmental demands is essential to everyday life. The dorsal anterior cingulate cortex (ACC), located bilaterally in the medial frontal lobes, is a key structure implicated in the regulation of attention and cognitive control (CC) (Botvinick et al. 2001; Petersen and Posner 2012; Yeung 2013). The considerable heterogeneity of the ACC in terms of connectivity, cytology and receptor organization (Devinsky et al. 1995; Palomero−Gallagher et al. 2008) is paired with an extensive inter- and intra-individual variability in gyral and sulcal architecture (Vogt and Palomero-Gallagher 2012). Increasing evidence shows that individual differences in ACC sulcal pattern are related to functional consequences across a range of executive cognitive tasks both in healthy and clinical populations (Yücel et al. 2003a; Fornito et al. 2004; Buda et al. 2011; Cachia et al. 2014). In this study, we investigate whether ACC sulcal patterns predict CC performance differently when the sample has variable linguistic experience, *i.e.* when participants use one versus multiple languages across the lifespan.

Anatomical magnetic resonance imaging (MRI) investigations of healthy participants show that individual variation in CC is correlated with differences in ACC structure as indexed by measures of local cortical thickness (Westlye et al. 2011), cortical surface area (Fjell et al. 2012) and regional gray matter volume (Takeuchi et al. 2012). In clinical studies, structural abnormalities of the ACC have been reported in disorders associated with CC deficits such as schizophrenia (Fornito et al. 2009), attention deficit hyperactivity disorder (ADHD) (Dickstein et al. 2006) and obsessive-compulsive disorder (OCD) (Fitzgerald et al. 2005). The contribution of ACC morphology to CC skills has been recently investigated by parameterizing variability in ACC sulcation (Huster et al. 2011; Borst et al. 2014; Cachia et al. 2014), which is primarily assessed by quantifying the occurrence and extension of the paracingulate sulcus (PCS), a secondary sulcus that runs dorsal and parallel to the cingulate sulcus (CS) on the medial surface of the ACC (Ono et al.

1990; Paus et al. 1996; Vogt and Palomero-Gallagher 2012). Differently from quantitative measures of cortex structure (e.g. cortical thickness, surface area or gyrification index), the ACC sulcal pattern is a neurodevelopmental marker determined *in utero* (Chi et al. 1977; Welker 1990; Mangin et al. 2010) and largely unaffected by brain maturation (Cachia et al. 2016; Tissier et al. 2018) or environmentally-induced neuroplastic changes (Sun et al. 2012). While primary sulci (e.g. CS) emerge early during fetal development and are present in all individuals with stable characteristic locations and orientations, secondary and tertiary sulci (e.g. PCS) begin to appear much later during gestation (in the 2nd-3rd trimester) in approximately half of all neonates, thus providing a clue to the study of individual differences in brain-behaviour relationships (Chi et al. 1977; Armstrong et al. 1995). The occurrence of the PCS is the primary basis for identifying two types of ACC sulcation: a 'single' type (CS only) and a 'double parallel' type (CS and additional PCS) (Ono et al. 1990). The double parallel type is present in 30-60% of normal individuals (Paus et al. 1996; Yücel et al. 2001) with greater prevalence in the left hemisphere (e.g. Paus et al. 1996; Yücel et al. 2001; Leonard et al. 2009), thereby yielding a leftward asymmetry population bias. Although the specific factors mediating the development of the PCS and its asymmetry are still unclear, evidence suggests that individuals with asymmetrical ACC sulcal patterns as compared to those with symmetrical patterns exhibit a performance advantage across several higher-order functions that draw on CC, such as reality monitoring (Whittle et al. 2009; Buda et al. 2011), inhibitory control (Huster et al. 2009; Cachia et al. 2014; Borst et al. 2014; Tissier et al. 2018) and verbal and spatial working memory (Fornito et al. 2004). The functional significance of individual differences in ACC sulcation has also been reported in clinical studies, where abnormal occurrence and/or morphology of the PCS have been linked to CC impairment in patients with full-blown schizophrenia (Yücel et al. 2002; Fornito et al. 2006; Garrison et al. 2015) as well as in individuals at-risk of developing schizophrenia symptoms (Yücel et al. 2003b).

A critical issue that has only begun to be inquired is the interaction between ACC sulcal anatomy and experience-related variables on CC efficiency. In a recent exploratory study, Cachia et al. (2017) contrasted the effect of the ACC sulcal pattern on the conflict resolution abilities of individuals from different linguistic environments, *i.e.* a bilinguals and monolinguals. Bilingual speakers heavily rely on CC functions to coordinate between languages and avoid cross-linguistic interference (Abutalebi and Green 2007). Neuroimaging evidence has shown that the extended use of such functions has structural and functional consequences in regions of the neural network that serves CC, including the dorsal ACC (e.g. Abutalebi et al. 2012; Abutalebi et al. 2015; De Baene et al. 2015). A number of studies report an association between bilingualism-induced neuroplastic changes in the CC network and better performance of bilinguals versus monolinguals on CC tasks, with a higher proportion of statistically significant benefits in seniors than young adults (Bialystok et al. 2012; Valian 2015; Bialystok et al. 2016). Recently, Cachia et al. (2017) found that the CC performance of bilinguals and monolinguals measured with the Flanker Task (Fan et al. 2005) was differentially affected by interindividual variation in ACC folding, with asymmetrical versus symmetrical ACC sulcal patterns associated with a performance advantage in monolinguals and a performance detriment to bilinguals and vice versa. These findings suggest that long-term exposure to a second language may overcome the established effects of early neurodevelopmental constraints on CC performance. Despite the limitation of a relatively small sample size (17 bilinguals, 14 monolinguals, all females), the study provided a novel insight into the influence of neuroanatomical markers fixed prenatally and environment on behaviour.

The present study aims to contribute to the current debate on the relationship between early neurodevelopment, environmental factors and cognitive function by moving the investigation in two directions. First, we provide a comprehensive account of the distributional characteristics of the PCS in a large sample of healthy individuals ($N = 270$) who differ in gender and ethnicity. This group-distribution analysis makes possible~~allows~~ to investigate the effects of biologically determined factors such as gender and ethnicity on the sulcal anatomy of the ACC. Second, we investigate the long-term contribution of the inter- and intra-individual variability of the PCS to CC across age, and the extent to which this contribution may vary according to experiential factors such as living in a bilingual environment and speaking more than one language. To reach this goal, we selected a participants' subsample ($N = 157$) to test whether a classic in-lab executive measure of CC – *i.e.*, the Flanker Task (Fan et al. 2005) – is differentially modulated by the characteristics of the PCS in bilingual and monolingual speakers. The sulcal variability of the ACC was assessed with a categorical method that is sensitive to variations in the prevalence of the PCS within and across hemispheres. Specifically, ~~two anatomical measures are adopted:~~

~~(1)~~ a ~~measure of the occurrence of the PCS in each hemisphere (with the ACC sulcal type categorized as 'single' or 'double parallel');~~

~~(2) A~~ measure of ~~the distribution of the PCS across hemispheres, *i.e.* a measure of~~ PCS asymmetry was adopted (with the ACC sulcal pattern categorized as: 'single/single', 'double parallel/double parallel', 'double parallel/single' and 'single/double parallel').

~~With respect to the occurrence of the PCS in each hemisphere, we predict a significant laterality effect driven by greater occurrence of the PCSs on the left versus right hemisphere based on previous reports (e.g. Paus et al. 1996; Yücel et al. 2001; Wei et al. 2017). With respect to the distribution of the PCS across hemispheres,~~ B~~b~~ased on previous accounts (e.g. Paus et al. 1996; Yücel et al. 2001) we expect a significant effect of ACC sulcal pattern driven by a prevalence of leftward PCS asymmetry. As the available evidence is respectively mixed (Ide et al. 1999; Yücel et al. 2001; Leonard et al. 2009) or insufficient (Wei et al. 2017), we do not have specific predictions for the effects of gender and ethnicity on ACC sulcal variability. On the other hand, consistent with findings from studies in monolinguals using conflict-related tasks such as the Stroop and the Flanker (e.g. Huster et al. 2009; Borst et al. 2014; Cachia et al. 2017), we predict monolinguals' performance to be shaped by ACC sulcal pattern, with leftward PCS asymmetry associated with a performance advantage as compared to the other patterns of ACC sulcation. It is also possible that the variable effects of ACC sulcation on CC will be different in young and older participants, due to specific patterns of interaction between sulcation pattern and cognitive function as age increases and executive attention declines. However, to our knowledge this is the first study to explore the impact of ACC sulcal patterns on the executive processing of participants ranging from early adulthood to old age (age range = 18 to 67 years). Finally, based on the findings from Cachia et al. (2017), we expect a significant difference in CC performance between bilingual and monolingual groups as a function of ACC sulcal pattern variability.

Materials and Methods

Participants

Two hundred seventy-five (N = 275) right-handed adults with no history of neurological or psychiatric condition were initially included in the study. Five participants were excluded from subsequent analyses because of ambiguous ACC sulcation in one or both hemispheres. The final sample comprised 270 participants (mean age = 36.4±18.7; range = 18:75) differing on gender (152 F, 118 M), ethnicity (Caucasian = 130; South Asian = 43; East Asian = 97) and linguistic profile (bilingual = 155; monolingual = 115). Educational history was reported for all participants (years of education: 15.4±3.1; 5:26).

Mini Mental State Examination (MMSE) (Cockrell and Folstein 2002) was used to evaluate cognitive state for the participants over 50 years of age (N = 102) (inclusion threshold: ≥27 raw score). Mean raw score was 28.3±1.6 and no participant was excluded due to clinical signs of cognitive impairment.

The age of acquisition (AoA) and proficiency of the second language (L2) were recorded for all bilinguals (overall AoA = 7.2±7.8; 1:41; Caucasian AoA: 5.6±4; : South Asian AoA: 5.4±3.9; East Asian AoA: 7.7±8.9; overall proficiency (%) = 85±12; Caucasian proficiency: 90±6; South

Asian proficiency: 93±4; East Asian proficiency: 88±6). L2 proficiency was established with a 30-item picture naming task using coloured pictures from a revised version of the Snodgrass and Vanderwart picture set (Snodgrass and Vanderwart 1980) suitably modified for cultural familiarity and the different L2s spoken (see Abutalebi et al. 2014).

The study was conducted with ethical approval from the Human Research Ethics Committees of the Universities, Centres or Institutes involved, *i.e.* the Vita-Salute San Raffaele University (Milan, Italy), the University of Hong Kong (HKSAR), the National Brain Research Center (Manesar, India) and the Beijing Normal University (China). Written informed consent was obtained from all participants.

<Insert Table 1 about here>

MRI Acquisition and Analysis

Individual T1-weighted MR images (N = 275) were used for determining the ACC sulcal pattern of each participant. MPRAGE (Magnetization prepared Rapid Gradient Echo) images were acquired for 242 subjects in a 3T Achieva Philips MR scanner (Philips Medical Systems, Best, Netherlands) at The University of Hong Kong (HKSAR), National Brain Research Center (Manesar, India) and Vita-Salute San Raffaele University (Milan, Italy) using identical exam cards with the following parameters: repetition time (TR)=8.03 ms, echo time (TE)=4.1 ms; flip angle=8°, field of view (FOV)=250 x 250, matrix=256, number of slices=150, voxel size=1.0×1.0×1.0 mm. MPRAGE images for additional 33 subjects were acquired with a 3T Siemens Trio Scanner at Beijing Normal University with the following parameters: TR=2530 ms, TE=3.39 ms, flip angle=7°, FOV=256x 256, matrix=256×256, number of slices=128, voxel size=1.33×1.0×1.0 mm. All T1 images were visually inspected for the presence of any artefacts and no participant was discarded due to this reason. To overcome the potential bias from the sulcus shape deformations induced by the warping process, neither linear nor non-linear spatial normalization to a common space (e.g. MNI or Talairach space) was applied to MRIs. The origin was set on all images to match the bicommissural line (AC-PC). All images were anonymised; labelling of ACC sulcal pattern in each hemisphere, based on the prevalence and morphology of the PCS, was carried out independently by two authors blind to participants' age, gender, ethnicity and language group.

PCS Measurement and ACC Classification

Following Garrison's PCS measurement protocol (Garrison 2017), first reported in Garrison et al. (2015), all T1 data were imported into MANGO (Multi-image Analysis GUI, v 4.0, http://ric.uthscsa.edu/mango/mango.html, The University of Texas Health Science Center) and the cingulate sulcus (CS) was identified at 4mm laterally from the midline (x=0) on either hemisphere. The PCS was identified as the sulcus running dorsal and predominantly parallel to the CS and being clearly visible for at least four slices from the midline. At x=4mm, the anterior limit of the PCS was identified as the point at which the sulcus begins to move posteriorly from an imaginary line perpendicular to the AC-PC line and starts to run parallel to the CS. The PCS was measured from this point onwards using MANGO's 'Trace Line' function. The measurement, incorporating both visual classification and automated components, was carried out by two blind raters. Disagreement among raters on PCS identification was resolved by a third blind rater. Five participants (*i.e.*, < 2% of the whole dataset) had ambiguous ACC sulcation in one or both hemispheres, which rendered PCS identification particularly difficult (see Leonard et al. 2009 for discussion). Since ambiguity persisted after general inter-rater discussion, those five participants were discarded from the dataset and not included in subsequent analyses. Inter-rater agreement for the remaining 270 cases was above 95%. ~~; unagreed cases were discussed and eventually resolved.~~

The PCS was categorized as either ‘present’ (≥20mm) or ‘absent’ (≤19mm) following Ono’s nomenclature (Ono et al. 1990) as in our previous study with bilinguals (Cachia et al. 2017). When the PCS was discontinuous, sulcus elements were included in the measurement only when interruptions or gaps were ≤19mm (Yücel et al. 2001; Garrison et al. 2015; Cachia et al. 2017). This binary classification was adopted since the occurrence of the PCS has been found to be stable with age (Clark et al. 2010; Cachia et al. 2016). Quantitative measures of ACC sulcal morphology such as sulcal width, depth or length were not included in the analyses since these cortical features vary with age (Kochunov et al. 2005; Clark et al. 2010; Cachia et al. 2016), especially in multimodal areas such as the cingulate cortex (Kochunov et al. 2005; Li et al. 2011), which indicates that they can be modified both by brain maturation and environmentally-induced plasticity.

Based on the occurrence of the PCS in each hemisphere, the ACC sulcal type was categorized as ‘single’ (*i.e.* CS only) or ‘double parallel’ (*i.e.* CS and additional PCS). An asymmetry index based on this classification was used to assess the interhemispheric distribution of the PCS in each brain: A = ‘single/single’ (*i.e.* CS only in both hemispheres); B =‘double parallel/double parallel’ (*i.e.* CS and additional PCS in both hemispheres); C = ‘double parallel/single’ (*i.e.* leftward PCS asymmetry); D = ‘single/double parallel’ (*i.e.*, rightward PCS asymmetry) (see Fig. 1).

<Insert Fig. 1 about here>

Behavioral Assessment

One hundred fifty-seven (N = 157) right-handed adults performed a revised version of the Flanker Task (Fan et al. 2002, 2005). Among them, ninety-four participants were monolinguals and sixty-three were bilinguals. Participants were instructed to press the left or the right button of a mouse as quickly as possible depending on whether the target, a central arrow presented foveally on a computer screen for 1700 ms, pointed to left or right, respectively. Targets were presented in congruent, incongruent or neutral conditions, *i.e.* with additional arrows flanked to the same direction as the target (→→→→→), with additional arrows flanked to the opposite direction of the target (←←→←←) or with additional neutral lines (-- -- → -- --). Whereas the neutral lines surrounding the target typically bias neither the correct nor the incorrect response, the incongruent flankers represent conflicting information with the correct response and are generally associated with decline in performance, *i.e*. lower accuracy and increasing response time (RT). By contrast, congruent flankers favor the correct response and are generally associated with better performance, *i.e*. higher accuracy and lower RTs. Our key behavioral contrast was between RTs on incongruent and congruent trials, *i.e*. the 'conflict' effect on decision time (Fan et al. 2002). Congruent, incongruent and neutral trials (64 for each condition; overall = 192) were presented in a pseudo-randomized order. Prior to the experiment, participants had a practice run consisting of 24 pseudo-randomized trials. Stimulus presentation and data collection were controlled using Presentation software system v.18 (www.neurobs.com).

Statistical Analyses

Statistical ~~Two types of~~ analys~~e~~is were run to (1) explore the distribution of the ACC sulcal pattern (*ACC sulcal pattern distribution*) and (2) investigate its effects on CC performance (*Effects of ACC sulcal pattern on cognitive control*). All analyses were performed using R (R Core Team 2016, https://www.r-project.org/).

ACC sulcal pattern distribution. An ~~Two distinct~~ ordinal logistic regression model~~s~~ was~~ere~~ run to explore the prevalence of the PCS ~~within and~~ across hemispheres in a large sample of healthy individuals (N = 270) differing on gender and ethnicity.

~~The first model had ACC sulcal type ('single' vs. 'double parallel') as dependent variable and Gender ('male' vs. 'female'; reference level = male), Ethnicity ('Caucasian' vs. 'South Asian' vs. 'East Asian'; reference level = Caucasian) and Hemisphere ('left' vs. 'right'; reference level = left) as predictors. To account for the multiple observations for each subject, a mixed-effects model was run with by-subjects intercept as random factor (e.g. Baayen et al. 2008). The model was fitted using the *lmer* function (lmerTest package; Kuznetsova et al. 2013).~~

The ~~second~~ model had ACC sulcal pattern ('single/single', 'double parallel/double parallel', 'leftward PCS asymmetry', 'rightward PCS asymmetry') as dependent variable and Gender ('male' vs. 'female'; reference level = male) and Ethnicity ('Caucasian' vs. 'South Asian' vs. 'East Asian'; reference level = Caucasian) as predictors. The model was run with the Mass package.

Effects of ACC sulcal pattern on cognitive control. We used a participants' subsample (*N* = 157) to assess whether CC performance was differentially modulated by the ACC sulcal pattern distribution in bilingual (*N* = 63) and monolingual speakers (*N* = 94). To reach this goal, we ran ~~two distinc~~a ~~t~~ linear mixed-effects model~~s~~.

The ~~first~~ model was run using participants' RTs on the Flanker task as dependent variable and Flanker condition ('congruent' vs. 'incongruent'; reference level = congruent), ACC sulcal pattern ('single/single' vs. 'double parallel/double parallel' vs. 'leftward PCS asymmetry' vs. 'rightward PCS asymmetry'; reference level = 'single/single') ~~ACC sulcal type ('single' vs. 'double parallel'; reference level = single)~~, ~~Hemisphere ('left' vs. 'right'; reference level = left),~~ Language group ('monolingual' vs. 'bilingual'; reference level = monolingual) and Age (as a continuous variable) as predictors. The model also included participants' Gender, Education (in years) and Native language as covariates (which allowed to control for potentially confounding variables), as well as by-participants random intercepts for the random part of the model.

~~A second model identical to the first was run with ACC sulcal pattern ('single/single' vs. 'double parallel/double parallel' vs. 'leftward PCS asymmetry' vs. 'rightward PCS asymmetry';~~

~~reference level = 'single/single') instead of ACC sulcal type as predictor (the model did not include Hemisphere as a factor).~~ The~~Both~~ model~~s~~ was~~ere~~ fitted using the *lmer* function~~.~~ (lmer Test package; Kuznetsova et al. 2013).

Results

ACC sulcal pattern distribution. Tables 2 and 3 report absolute numbers and proportions of ACC sulcal ~~types and~~ patterns within and across hemispheres. Of note, the ACC sulcal pattern distribution was not affected by Language Group (β = -0.50, st. err. = .27, t = -1.8, p = .07) or Language Group x Hemisphere interaction (β = .06, st. err. = .36, t = .17, p >.8).

~~The model for ACC sulcal type showed a significant effect of Hemisphere (β = -.50, st. err. = .17, z = -2.85, p =.004) driven by a larger presence of the 'double parallel' type of ACC sulcation in the left hemisphere. No effects of Gender (β = -0.06 , st. err. = .18, z < 1, p >.7) or Ethnicity (East Asian: β =-.20 , st. err. =.20, t =-1.04, p >.2; South Asian: β =.21, st. err. =.26, z <1, p >.4) reached significance.~~

The model for ACC sulcal pattern showed no significant effects either of Gender (β = -0.09, st. err. = 0.16, t < 1, p >.5) or Ethnicity (East Asian: β = -0.16, st. err. = .17, t = -1.53, p >.3; South Asian: β = 0.16, st. err. = .22, t = 1.02, p >.4).

<Insert Table 2 about here>

<Insert Table 3 about here>

Effects of ACC sulcal pattern on cognitive control. ~~The model for the effect of ACC sulcal type on Flanker RTs showed a main effect of Age (β = 4.39, st. err. = 0.65, t = 6.74, p <.001) and three significant interactions: (1) a two-way Flanker condition x Age interaction (β = 1.88, st. err. = 0.34, t = 5.41, p <.001) indicating that the conflict resolution skills of participants decrease with age, with~~

~~the larger slowdown for incongruent trials; (2) a two-way Language group x Age interaction (β = -1.98, st. err. = 0.87, t = -2.26, p =.02) showing that task performance decline with increasing age is larger in monolingual than bilingual speakers; (3) a three-way Flanker condition x Age x ACC sulcal type interaction (β = -1.10, st. err. = 0.47, t = -2.32, p =.02) indicating that the age-related effect of Flanker increases more in participants with a 'single' type of ACC sulcation in each hemisphere (*i.e.* a bilateral absence of the PCS) than in those with other types of ACC sulcation (all ts < 1.8, ps >.07) (see Fig. 2a). No other effect reached significance.~~

The model for the effect of ACC sulcal pattern on Flanker RTs showed a main effect of Age (β = 3.65, st. err. = 1.12, t = 3.11, p =.002) and two-way interactions between Flanker condition and Age (β = 2.29, st. err. = 0.31, t = 7.21, p <.001), Flanker condition and Language group (β = 56.39, st. err. = 20.31, t = 2.77, p =.005) and Flanker condition and ACC sulcal pattern (β = 49.48, st. err. = 20.65, t = 2.39, p =.01). Three higher order interactions were also significant: (1) A Flanker condition x Age x Language group interaction (β = -1.28, st. err. = 0.41, t = -3.12, p =.001) showing that while monolinguals outperform bilinguals at a young age, CC decline is larger in monolinguals as age increases (see Fig. 3); (2) A Flanker condition x Age x ACC sulcal pattern interaction (β = -1.46, st. err. = 0.43, t = -3.34, p =.008) indicating that the Flanker effect is larger in older than younger participants and its increase is maximal with 'single/single' patterns of ACC sulcation (*i.e.*, when the PCS is absent in both hemispheres (see Fig. 2~~b~~); (3) A Flanker condition x Language group x ACC sulcal pattern interaction (β = -50.89, st. err. = 25.55, t = -1.99, p =.04) showing that while asymmetrical patterns of ACC sulcation contribute to greater CC efficiency in monolinguals, a reversed pattern of structure-function relationship is found in bilinguals, *i.e.* symmetrical patterns are associated with superior performance in bilinguals (see Fig. 4). No other effect reached significance (all ts < 1.8, ps > .06).

<Insert Fig. 2 ~~(a,b)~~ about here>

<Insert Fig. 3 about here>

<Insert Fig. 4 about here>

Discussion

The purpose of the present study was twofold: (1) to provide a distributional account of the ACC sulcal patterns in a large sample of healthy individuals differing on gender and ethnicity; (2) to test whether prenatal neurodevelopmental mechanisms modulate the effects of different environmental backgrounds (*i.e.* bilingualism versus monolingualism) on CC performance.

ACC sulcal pattern distribution

A 'double parallel' type of ACC sulcation was detected in 49.44% of our sample irrespective of hemisphere, in line with previous findings according to which the 'double parallel' sulcal type is present in 30-60% of the normal population (e.g. Paus et al. 1996; Yücel et al. 2001). Resulting from neurodevelopmental processes starting as early as 10 weeks of fetal life (White et al. 2010), the ACC sulcal pattern is a qualitative feature of cortex anatomy which is stable from childhood to adulthood irrespective of brain maturation and environmental factors (Sun et al. 2012; Cachia et al. 2016). The distribution of the ACC sulcal pattern was significantly affected by hemispheric laterality, with the 'double parallel' type more frequently present than absent on the left hemisphere and more frequently absent than present on the right (see Table 2). This leftward bias largely confirms previous data from post-mortem studies of healthy brain specimens (Ide et al. 1999) and structural MRI investigations of intact living brains (Paus 1996; Yücel et al. 2001; Fornito et al. 2004; Huster et al. 2007; Leonard et al. 2009; Wei et al. 2017). Remarkably, prior work on psychiatric populations with CC deficits failed to report comparable laterality effects, showing a reduced degree of leftward PCS asymmetry in patients versus healthy controls (Yücel et al. 2002, 2003a; Le Provost et al. 2003; Marquardt et al. 2002; Fujiwara et al. 2007) and a reduced PCS extent in hallucinating patients versus non-hallucinating patients and healthy controls (Garrison et al. 2015).

When we tested the effects of gender and ethnicity on ACC folding, we found that these variables had no significant impact on the distributional characteristics of the ACC sulcal pattern, nor on the presence of a leftward bias in our sample.

With respect to gender membership, the incidence rates (%) of 'single' and 'double parallel' types of ACC sulcation in the left and right hemispheres were balanced between groups (see Table 2), with higher proportions of bilateral presence of the PCS and rightward PCS asymmetry in males versus females and higher proportions of bilateral absence of the PCS and leftward PCS asymmetry in females versus males, although differences did not reach statistical significance (see Table 3). Some previous studies failed to detect gender-related effects on ACC sulcation (e.g. Ide et al. 1999; Wei et al. 2017), whereas others reported greater leftward PCS asymmetry in males versus females (Yücel et al. 2001; Whittle et al. 2009; Clark et al. 2010) or in females versus males (Leonard et al. 2009). These inconsistencies are reflected in morphometric analyses of global (*i.e.* whole-brain) and localized (*i.e.* lobe-wise) effects of sexual dimorphism on the convolutional properties of the cerebral cortex (Zilles et al. 1988; Luders et al. 2004; Im et al. 2008; Toro et al. 2008). It should be further noted that a few studies found an interaction between gender and handedness, with right handed males and left handed females showing greater prevalence of leftward PCS asymmetry than left handed males and right handed females (Huster et al. 2007; Wei et al. 2017). As our participants were all right handers, we were unable to test whether hand preference interacted with gender membership in modulating ACC sulcation.

With respect to ethnicity, the 'double parallel' type of ACC sulcation was more frequently lateralized to the left versus right hemisphere in all ethnic groups (*i.e.* Caucasian, East Asian and South Asian), with a proportionally higher occurrence of 'double parallel' (on the left) and 'single' type (on the right) of ACC sulcation in East Asians compared to the other groups, although differences did not reach statistical significance (see Table 2). A higher proportion of bilateral presence of the PCS and a lower proportion of bilateral absence of the PCS were also reported for the same group when compared to the others (see Table 3). Previous morphometric studies have reported global and regional differences in brain structure between Caucasian and Eastern populations such as Chinese, Koreans and Japanese (Lee et al. 2005; Tang et al. 2010; Uchiyama et al. 2013; Rao et al. 2017), which has led to the development of brain atlases specific to ethnicity (e.g. Chinese: Tang et al. 2010; Japanese: Uchiyama et al. 2013). To our knowledge, Wei et al. (2017) is the only study that explored whether ethnicity interferes with ACC sulcation by contrasting Caucasian (German and Belgian) and East Asian (Chinese) participants. In line with our results, no significant differences in ACC folding were reported as a function of ethnic group membership.

Effects of ACC sulcal pattern on cognitive control

Performance on the Flanker decreased with age, consistent with previous evidence linking normal aging with a deterioration of the executive attention networks (e.g. West 1996; Mahoney et al. 2010; Zhou et al. 2011). A significant interaction between Flanker performance, age and language group indicated that, although monolinguals outperformed bilinguals at a young age, bilinguals were more resistant to cognitive decline in terms of overall task performance *(i.e.* global RTs across congruent and incongruent conditions) and conflict experience (*i.e.* RT difference between incongruent and congruent conditions) (see Fig. 3). Earlier studies investigating the cognitive effects of bilingualism in young and older populations have provided mixed results (Hilchey and Klein 2011; Paap et al. 2015), eliciting an ongoing debate on the potential benefits of multiple language use across the lifespan (de Bruin et al. 2015; Valian 2015; Bialystok et al. 2016). Drawing on relatively large language-group sizes, our findings suggest that sustained forms of cognitive stimulation such as lifelong bilingualism may contribute to postpone cognitive aging, thus acting as a cognitive reserve (Bialystok et al. 2008; Salvatierra and Rosselli 2011; Abutalebi et al., 2015; Abutalebi and Green, 2016). Our current findings showing that task performance declines with increasing age is larger in monolingual than bilingual speakers are even more relevant when considering that our subjects have different ethnicities and cultural backgrounds (Europe, India, China and Hong Kong).

Independent of language group membership, the participants' performance was modulated by individual differences in ACC morphology, with a larger decline of overall task performance in participants with rightward PCS asymmetry and a larger increase of conflict experience in participants with a bilateral absence of the PCS. Moreover, as compared to the other patterns of ACC sulcation, leftward PCS asymmetry contributed to faster RTs on both conditions of the Flanker at an old age and to a conflict experience that was consistent from early to older adulthood (see Fig. 2b). In previous studies using conflict monitoring tasks such as the Stroop and the Flanker, a bilateral absence of the PCS and a leftward PCS asymmetry have been associated – respectively – with a detriment to performance and with a performance advantage both in children (Borst et al. 2014; Cachia et al. 2014) and young adults (e.g. Huster et al. 2009; Buda et al. 2011; Cachia et al. 2017). When the behavioural effects of leftward and rightward asymmetry patterns were directly compared on tasks tapping CC processes, leftward asymmetry was consistently associated with a superior performance in terms of RT scores and/or accuracy rates (Fornito et al. 2004; Whittle et al. 2009; Buda et al. 2011). Our findings expand previous evidence and identify the distribution of the ACC sulcal pattern as a key predictor of executive behaviour across the lifespan. The degree of regional fissurization of the cerebral cortex is known to be related with variations in local cytoarchitecture (Vogt et al. 1995; Paus et al. 1996) and intra- and inter-regional axonal connectivity (Welker 1990; Hilgetag and Barbas 2005; Toro and Burnod 2005). Variability in the sulcal anatomy of the ACC could thus lead to differences in CC performance through changes in connectivity between the cingulate area and other regions of the CC network such as adjacent portions of the prefrontal cortex (Vogt et al. 1995; Van Essen 1997; Koski and Paus 2000; Cachia et al. 2014). In particular, as CC tasks are thought to be largely reliant on left hemispheric processing (e.g. Langdon and Warrington 2000; Brown et al. 2001; Chokron et al. 2003), the association between higher CC efficiency and leftward PCS asymmetry might result from enhanced cingulo-frontal connectivity in the left hemisphere (Fornito et al. 2004; Cachia et al. 2014). Conversely, the bilateral absence of the PCS as well as its right-lateralization should lead to a more effortful processing resulting in poorer CC performance. Further research utilizing both structural and functional imaging methods is needed to confirm this interpretation.

Of particular interest, as indexed by the significant interaction between Flanker, ACC sulcal pattern and language group, the functional consequences of ACC sulcal variability were differentially modulated by participants' linguistic background. Specifically, a reversed pattern of structure-function relationship between ACC morphology and CC performance was reported for bilingual and monolingual speakers: asymmetrical versus symmetrical sulcal patterns were associated with a performance advantage in monolinguals and a performance detriment to bilinguals and vice versa (see Fig. 4). Using a different set of analyses on a much larger independent sample, this finding extends the results of the previous exploratory study by Cachia and colleagues (2017) and attests the dynamic interplay between fetal stages of brain development, environmental background and cognitive functions. We posit that the long-term exposure to a second language may overcome the known correlation between leftward PCS asymmetry and better conflict resolution capacity, pointing to a compensatory effect of bilingualism over early and invariant neurodevelopmental factors. In particular, it is tempting to speculate that bilinguals rely more heavily on a bilateral recruitment of the CC network as compared to monolinguals, with a greater contribution of interhemispheric activity to executive functioning, which could explain the positive association between performance efficiency and ACC symmetrical patterns, as brain structural symmetry is thought to imply greater cross-hemispheric communication fostered by contralateral projections through the hemispheric commissures (Rosen et al. 1989; Luders et al. 2003). Evidence in support of this hypothesis comes from functional MRI investigations reporting a bilateral recruitment of the ACC in bilinguals engaged in non-verbal executive tasks (Abutalebi et al. 2012; De Baene et al. 2015) as well as from diffusion tensor imaging (DTI) studies showing increased fractional anisotropy (FA) values in the bilateral genu of the corpus callosum as a result of second language training (Schlegel et al. 2012) and second language immersion (Pliatsikas et al. 2015). Similar results were reported by Singh et al. (2018) showing increased radial diffusivity bilaterally in the forceps minor for bilinguals as opposed to monolinguals.

In conclusion, our results suggest that the ACC sulcal pattern – a stable morphological feature of cortical anatomy determined *in utero* and not affected by gender or ethnicity – is differentially associated with the CC abilities of bilingual and monolingual individuals across age. Altogether, our findings add a new piece of critical information to the neuroscience of bilingualism and provide novel evidence on the dynamic interplay between early neurodevelopment, environmental background and cognitive processing across the lifespan.

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Table 1. Languages spoken by monolingual (N =115) and bilingual participants (N = 155)

Mono	Mandarin	Italian					
N	33	84					
Bil (L1)	Cantonese	Hindi	Dutch	Italian	German	Ladin	Ladin
N	64	44	20	9	16	5	5
Bil (L2)	English	English	English	German	Italian	German	Italian
N	64	44	20	9	16	1	4

Table 2. Distribution of the Anterior Cingulate Cortex (ACC) sulcal type in a large sample (*N* = 270) of healthy individuals differing on gender and ethnicity. Two types of ACC sulcation were identified based on the occurrence of the paracingulate sulcus (PCS) in each hemisphere (0 = 'single' type, *i.e.* cingulate sulcus only; 1 = 'double parallel' type, *i.e.* cingulate sulcus and additional PCS). Incidence rates (%) are calculated within groups and reported in brackets.

	Hemisphere		Gender				Ethnicity					
			M		F		Caucasian		East Asian		South Asian	
	Left	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*
0	120	153	55	68	65	85	58	71	44	62	18	20
1	150 (56.17)	117 (43.33)	63 (55.75)	50 (42.37)	87 (56.49)	67 (44.07)	72 (54.96)	59 (45.38)	53 (60.22)	35 (36.08)	25 (58.13)	23 (53.48)

Table 3. Distribution of the Anterior Cingulate Cortex (ACC) sulcal pattern in a large sample (N = 270) of healthy individuals differing on gender and ethnicity. An asymmetry index based on the 'single'/'double parallel' type classification was used to assess the distribution of the PCS across the two hemispheres (0 = 'single/single', *i.e.* cingulate sulcus only in both hemispheres; 1 = 'double parallel/double parallel', *i.e.* cingulate sulcus and additional PCS in both hemispheres; 2 = 'double parallel/single, *i.e.* leftward PCS asymmetry; 3 = 'single/double parallel, *i.e.* rightward PCS asymmetry). Incidence rates (%) are calculated within groups and reported in brackets.

		GENDER		ETHNICITY		
	OVERALL	M	F	Caucasian	East Asian	South Asian
0	48 (17.77)	17 (14.40)	31 (20.39)	26 (20.0)	11 (11.34)	11 (25.58)
1	72 (26.66)	38 (32.20)	34 (22.36)	32 (24.61)	33 (34.02)	7 (16.27)
2	81 (30.0)	30 (25.42)	51 (33.55)	39 (30.0)	29 (29.89)	13 (30.23)
3	69 (25.55)	33 (27.96)	36 (23.68)	33 (25.38)	24 (24.74)	12 (27.90)