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Selective increase of cortical thickness in high-performing elderly—structural indices of optimal cognitive aging

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The aim of this study was to identify cortical areas important for optimal cognitive aging. 74 participants (20–88 years) went through neuropsychological tests and two MR sessions. The sample was split into two age groups. In each, every participant was classified as "high" or "average" on fluid ability tests and on neuropsychological tests related to executive function. The groups were compared with regard to thickness on a point-by-point basis across the entire cortical mantle. The old high fluid performers had thicker cortex than the average performers in large areas of cortex, while there was minimal difference between the groups of high vs. average executive function. Furthermore, the old group with high fluid function had thicker cortex than the young participants in the posterior cingulate and adjacent areas. Further analyses showed that the latter was a result of a complex aging pattern, differing between the two performance groups, with decades of cortical thickening and subsequent thinning.

Keywords: Aging; Cingulate gyrus; Cognition; Fluid function; Executive function; Cortical thickness

How is optimal cognitive aging characterized neuroanatomically? While most people experience some decline of cognitive functions with increasing age, others are able to maintain a very high level of intellectual function throughout the entire life span. The mechanisms causing this wide array of individual cognitive differences in aging are largely unknown, but one would expect neural, perhaps volumetrically detectable, correlates. High function may be upheld into old age by preservation of the original neuronal circuits. In this case, optimal aging is a matter of being as similar as possible to younger persons. Alternatively, recruitment of alternative neuroanatomical structures during cognitive processing may help keep up a high level of function, even when the primary areas responsible for that function have begun to deteriorate. A potential neuroanatomical correlate of the latter may be thickening of specific cortical areas.

This article focuses on the importance of cortical thickness for optimal cognitive aging.

The rationale for relating volumetric measures to cognitive function is that (1) there is considerable individual variation in the volume of brain structures and (2) larger volume may be associated with higher cognitive capacity. The exact reason for such a relationship is unknown, but candidate explanations involve number of neurons or synaptic connections, degree of complex circuitry, dendritic expansion, myelin thickness, metabolic efficiency, efficient neurotransmitter production, release and reuptake, and brain reserve capacity (Deary and Caryl, 1997). However, even though a relationship between general intellectual ability and total brain volume is established (for a review, see Vernon et al., 2000), more specific relationships have been harder to demonstrate. Van Petten et al. (2004) gave an overview of 11 studies of healthy participants (including Baare et al., 1999; Gunning-Dixon and Raz, 2003; Gur et al., 1998; Hanninen et al., 1997; MacLullich et al., 2002; Raz et al., 1993, 1998; Salat et al., 2002; Sanfilipo et al., 2002; Schretlen et al., 2000; Sowell et al., 2001) and concluded that it has been difficult to establish robust relationships between neuropsychological functioning and gross morphometric characteristics. All these studies included measures of frontal volume, but with the exception of Salat et al. (2002) and Van Petten et al. (2004), either rather gross or restricted measures have been used (e.g. the entire frontal lobe or dorsolateral prefrontal gray volume).

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Still, some relationships have been identified. Schretlen et al. (2000) showed that perceptual comparison speed, executive ability, and frontal lobe volume each made significant contributions to fluid intelligence, indicating that the processing speed and frontal-executive theories of cognitive aging complement one another. However, diverse results have been reported. Salat et al. (2002) found that greater orbital prefrontal volume selectively predicted worse working memory performance in older adults. One reason for the discrepant findings may be the use of predefined regions of interests (ROIs). This may pose two opposite problems. Less refined volumetric measures can reduce the possibility of identifying robust relationships since the functional organization of the frontal lobe is extremely complex and specialized. On the other hand, the use of predefined restricted ROIs may also lead to omission of important information since we do not know the exact localization of complex cognitive functions. An approach less constrained by predefined neuroanatomical borders may be more suitable for exploring the relationship between morphometric properties and cognitive function. Thus, a point-by-point strategy may be more sensitive and less biased. This was employed in the present study, where thickness was compared for groups of interest at each vertex across the entire cortical mantle.

The present paper seeks to relate two broad domains of cognitive function to cortical thickness. The first domain is 'fluid' abilities, a type of intelligence that is applied to novel problems and is relatively independent of educational and cultural influences. In this paper, fluid abilities refer to scores on psychometric tests related to visuo-constructive abilities (block design) and visual reasoning (matrices). These two tests have the highest *g*-loading in the WAIS-R battery (Deary, 2001). The other domain is termed 'executive', or somewhat inaccurately, 'frontal' abilities. Normal aging is known to lead to a reduction of the cortical volume or thickness of the frontal lobes (Salat et al., 1999a,b; Tisserand et al., 2002; Raz et al., 2004). This selective loss is taken to support the view that 'executive' or 'frontal' abilities decline relatively more with increasing age than other cognitive functions (e.g. West, 1996; West and Bell, 1997; Chao and Knight, 1997; Lowe and Rabbitt, 1997). However, the distinction between 'executive' vs. 'fluid' tests is not uncomplicated (Rabbitt, 1997). Still, there is evidence in favor of a conceptual distinction. For instance, Lowe and Rabbitt (1997) found that age-related variance on executive tasks remained after controlling for speed and intelligence. Such evidence, combined with scientific interest in the role of the frontal cortex in cognitive aging, justifies a study of the relationship between the different functions and brain characteristics.

The following questions were investigated:

(1) Can structural cortical characteristics explain why some elderly show superior cognitive function? A general linear model (GLM) approach was employed contrasting the cortical thickness at each vertex of groups of old participants with high versus average functioning with regard to both fluid and executive abilities, respectively (see Materials and methods).

(2) If cortical thickness can contribute to explain the difference between high and average functioning old groups, the following needs to be put to the test: does optimal aging only require preservation of cortical volume or does it call for changes in brain morphometry, such as thickening in certain parts of the cortex? If elderly uphold cognitive function mainly by preserving cortical thickness, we will expect to see differences between high and average performers in areas where cortical thickness is known to decrease with age. If, however, optimal cognitive aging is characterized by actual change, we may see thickening of selective cortical areas with age. Cortical areas less prone to age reductions will be neuroanatomical candidates for possible thickening. Based on previous research using a point-by-point approach (Salat et al., 2004), areas where thickening may occur include the temporal lobe and medial structures such as the cingulate cortex. If the old high performers have thicker cortex than the young (superior or average performers) in specific areas, this implies actual changes, and similar thickening in the old average performers is not to be expected. However, if the only difference between the old and the young participants is that the old have thinner cortex but to varying degrees according to level of function, then limitation of cortical decrement seems to be the more important mechanism in optimal cognitive aging.

Materials and methods

Sample

Table 1 summarizes the sample, consisting of 74 volunteers (41 F/33 M) between 20 and 88 years. The participants were community dwellers recruited among employees from a local hospital, or through charity organizations, activity centers for the elderly, and newspaper ads. They were screened by interview for diseases and traumas known to affect CNS functioning, and criteria for exclusion were neurological conditions or use of medication known to influence central nervous system functioning (for more specific exclusion criteria, see Walhovd and Fjell, 2002). All participants were required to not use a hearing aid and have normal or corrected to normal vision. They were given a moderate sum of money to refund possible costs related to their participation. All were examined with the Norwegian version of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). Participants with an IQ score of below 85 were excluded. Table 1 summarizes the characteristics of the total sample and the sample divided into two age groups by the median age.

Neuropsychological tests

The frontal lobes, or circuits involving parts of the frontal cortex, support a number of human higher-order cognitive

Table 1
Sample characteristic

	Young (n = 35)		Old (n = 39)		Total (n = 74)	
	M	SD	*M*	SD	*M*	SD
Age	35.5	12.5	70.7	7.0	52.6	20.4
Education	15.8	2.4	14.6	3.0	15.2	2.8
IQ	114.2	8.3	113.3	12.2	113.8	10.3
Beck DI	2.1	2.6	6.0	3.3	4.2	3.5
MMS	29.1	0.8	28.6	1.1	28.8	1.0

For the Beck Depression Inventory (Beck DI), we have data from only 66 of the 74 participants. t test showed that no significant differences between the groups existed for education (t = 1.862, df = 67.28, n.s.) and IQ (t = 0.338, df = 72, n.s.), while significant differences in mean score of MMS (t = 2.473, df = 2.47, $P < 0.05$) and Beck DI (t = −5.13, df = 62.55, $P < 0.05$) existed in the two age groups. In addition, IQ did not correlate with age (r = −0.03, n.s.).

functions, including regulation of behavior and cognition, response monitoring and inhibition, and working memory and attention (e.g. Balota et al., 2000; Damasio, 1994; Luria, 1980; West and Baylis, 1998). These functions are distinguished from more general fluid abilities by their neuroanatomical and behavioral correlates. Evidence for the frontal basis of these abilities comes from behavioral patient studies (Bryan and Luszcz, 2000; Stuss et al., 2001) and brain imaging studies (Bush et al., 2000; Chao and Knight, 1997). However, involvement of other cortical and subcortical structures are also critical in performing such tasks (see, for example, Alexander et al., 1986; Rubin, 1999). In the present study, a battery of five clinically validated tests related to executive function was employed, in addition to two tests of fluid cognitive function (tests with high loadings on fluid intelligence). The tests used in the present study are well-validated neuropsychological instruments, described in depth elsewhere, e.g. Lezak (1995) and Spreen and Strauss (1991). Here, they will only be described briefly.

Tests of neuropsychological fluid function

Block design and matrix reasoning from the WASI battery are fluid measures known to be less influenced by cultural experiences but dramatically affected by age (Woodruff-Pak, 1997). Block design involves copying small geometric designs with four or nine plastic cubes while viewing a constructed model or a picture within a specified time limit. Matrix reasoning requires the participant to complete logical arrangements of designs with missing parts, multiple choice.

Tests of executive function

Five tests assumed related to executive functions were used.

Stroop test (MacLeod, 1991). The version of the test employed in this study consists of three conditions. The simple tasks require the participant to name the ink color of rows of colored circles and to read color words (Stroop 1 and 2, respectively). The complex task (Stroop 3) requires the participant to name the ink of words that are color-incongruent (that is, the word meanings and ink colors mismatch, e.g. the word *blue* printed in yellow ink). Much literature links performance on the Stroop test to the function of the prefrontal cortex in both aging and neurological conditions (West and Bell, 1997; Brown and Marsden, 1998; Rafal and Henik, 1994).

Trail Making Test part A and B. TMT-A consists of consecutively numbered circles arranged randomly on a sheet of paper, and the participant is required to draw a line between the circles in ascending order as quickly as possible. In TMT-B, half the numbers are replaced with letters, and the task is to connect each number with a letter and each letter with a number (1–A–2–B–3–C etc.). TMT-B is a commonly used test of prefrontal function (Rasmusson et al., 1998; Lezak, 1995) and is considered a measure of the ability to flexibly shift the course of an ongoing activity.

Digit span Backward (Wechsler, 1981) requires the participant to mentally reverse an orally presented string of digits. This involves double tracking in that both the memory and the reversing operations must proceed simultaneously. Performance depends upon working memory and cognitive regulation and manipulation to a stronger degree than in the forward span task. It is thus assumed that the test depends more on frontal structures than its forward counterpart.

Corsi Block Tapping Test (CBTT) consists of nine black 1 ½ in. cubes fastened in a random order to a black surface, and the participant is required to repeat a tapping pattern tapped by the examiner. This test is one of the most commonly used tests of non-verbal short-term memory in clinical neuropsychology.

Controlled Word Association test is a measure of a person's ability to make verbal associations to specified letters (here: F, A, and S) within a time limit of 1 min per letter. COWAT is regarded a measure of frontal function since frontal lesions generally result in reduced scores, and the task tends to involve bilateral frontal and temporal lobe activation. Studies have indicated a relationship with tests like oral spelling, digit span, Stroop, and mental calculations (Boone et al., 1998; Lezak, 1995).

For Stroop 3 and TMT-B, the influence from the simple conditions (Stroop 1, TMT-A) was regressed out, and all analyses were performed on the residuals, removing the effect of lower-order cognitive functions like motor speed, visual search, and color naming. Each participant's score on the five tests was then converted to t scores (mean of 50, standard deviation (SD) of 10) based on the mean and the SD of the sample (i.e. not age-corrected), and a composite score was calculated as the mean of the t scores. Inter-item reliability analysis of the 5 measures yielded a Cronbach's alpha of 0.61, indicating substantial overlap, and also non-shared variance between the different variables. Since exclusion of any of the variables would not have lead to an increase in the alpha, all were included. This composite score will be referred to as 'executive function'. Following the same procedure, a composite score based on the two WASI performance subtests (block design, matrix reasoning) was calculated, and this will be referred to as 'fluid function'.

MRI scanning and volumetric analyses

A Siemens Symphony Quantum 1.5 T MR scanner with a conventional head coil was used. The pulse sequences used for morphometric analysis were: two 3D magnetization prepared gradient echo (MP-RAGE), T1-weighted sequences in succession (TR/TE/TI/FA = 2730 ms/4 ms/1000 ms/7°, matrix = 192 × 256, FOV = 256 mm), with a scan time of 8.5 min per volume. Each volume consisted of 128 sagittal slices with slice thickness = 1.33 mm and in-plane pixel size of 1 mm × 1 mm. The image files in DICOM format were transferred to a Linux workstation for morphometric analysis.

The automated procedures for volumetric measurement of the entire cortical mantle are described by Salat et al. (2004). Cortical thickness measurements were obtained by reconstructing representations of the gray/white matter boundary (Dale and Sereno, 1993; Dale et al., 1999) and the cortical surface and then calculating the distance between those surfaces at each point across the cortical mantle. This method uses both intensity and continuity information from the entire 3D MR volume in segmentation and deformation procedures to construct representations of cortical thickness. The maps are created using spatial intensity gradients across tissue classes and are therefore not simply reliant on absolute signal intensity. The maps produced are not restricted to the voxel resolution of the original data and thus are capable of detecting submillimeter differences between groups (Fischl and Dale, 2000). Thickness measures may be mapped on the 'inflated' surface of each participant's reconstructed brain (Dale and Sereno, 1993; Fischl et al., 1999), allowing visualization of data across the entire cortical surface without interference from cortical folding. Maps were smoothed

using a circularly symmetric Gaussian kernel across the surface with a standard deviation of 12.6 mm and averaged across participants using a non-rigid high-dimensional spherical averaging method to align cortical folding patterns (Fischl et al., 1999). This procedure provides accurate matching of morphologically homologous cortical locations among participants on the basis of each individual's anatomy while minimizing metric distortion, resulting in a mean measure of cortical thickness for each group at each point on the reconstructed surface. The gray/white matter boundaries are illustrated in Fig. 1. Statistical comparisons of global data and surface maps were generated by computing a general linear model of the effects of each variable on thickness at each vertex. Instead of using a corrected P value threshold, a scale with the actual P values is displayed in the figures. Since group comparisons are done, the number of participants in each group is limited, and a harsh criterion for multiple comparisons may be too conservative.

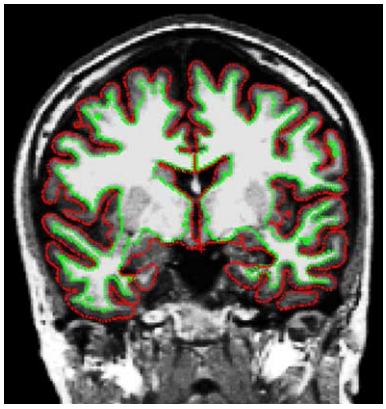

Fig. 1. Gray matter segmentation. White and gray matter boundaries in the T1 volume of a young woman. Gray matter is represented by the area between the red and the green line.

Results

High vs. average fluid function old groups

The different function groups were distinguished by dividing the sample at the median score (Fig. 2). The high and the average fluid groups had a mean age of 67.4 years 71.9 years, respectively (t = 1.85, df = 37, n.s.), a statistically equal gender distribution (t = −1.785, df = 37, n.s.), and the respective fluid t scores were 50.3 (SD = 2.8) and 38.1 (SD = 4.9) (t = −9.1, df = 37, P < 0.0001). Even though the age difference between the groups was statistically insignificant, age was included in the GLM as a regressor to ensure that differences between groups were not due to age. The IQ means of the high and average functioning groups were 121.8 (SD = 8.6) and 104.6 (SD = 9.6), respectively. The GLMs comparing the high functioning with the average functioning old group showed differences in a variety of cortical areas, especially in the right hemisphere. The results are displayed in Fig. 3. All significant differences indicated thicker cortex for the high relative to the average functioning group. The largest difference between the groups was found in posterior parts of the cingulate gyrus in right hemisphere. Furthermore, some frontal and prefrontal areas differed between the groups in both hemispheres, as well as the medial structure and the gyrus of the cingulate isthmus.

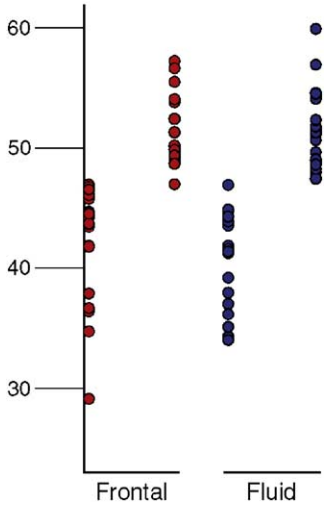

Fig. 2. Distribution of high and average old cognitive performers. The scatterplots show the t scores of the high and the average old fluid and frontal performers. A median split was used to divide the participants into high and average functioning groups. The t scores are based on the mean and standard deviation of the test scores of the sample itself. Thus, the scores are not corrected for age and cannot be related to the population mean. However, full-scale IQ (WASI) was above 100 (the population mean) for both groups.

High vs. average executive function old groups

The group with high versus average executive function had a mean age of 69.1 years and 70.1 years respectively (t = 0.04, df = 37, n.s.) and an equal gender distribution (t = −0.791, df = 37, n.s.). The respective executive t scores were 51.5 (SD = 2.8) and 42.2 (SD = 4.9) (t = −7.3, df = 37, P < 0.0001). Of the 39 old participants, 25 got the same classification on both domains, while 14 changed. As evident from Fig. 4, apart from a tendency towards thicker cortex in a small part of the right frontal middle gyrus in the high performers, there is essentially no difference between the high executive performers and those with average scores.

Old high and average performers compared to young

Since the cortical differences between the fluid groups were much larger than the differences between the executive groups, further analyses were restricted to fluid function only. By GLM, the high functioning old group was compared to young participants (mean age 33.7 years), who on average had higher fluid function (old high mean = 50.3, SD = 3.8, young mean = 56.3; SD = 5.9, t = 4.058, df = 53, P < 0.0001). The young group had thicker cortex in most areas. However, the old high performers showed thicker cortex in certain restricted areas, mainly in the posterior half of the right cingulate gyrus and in a small area of the left subcallosal gyrus. To rule out the possibility that this distinguishes high from average performers at any age, the high and the average young group were compared. No significant differences in these areas were identified. The results are illustrated in Figs. 5 and 6.

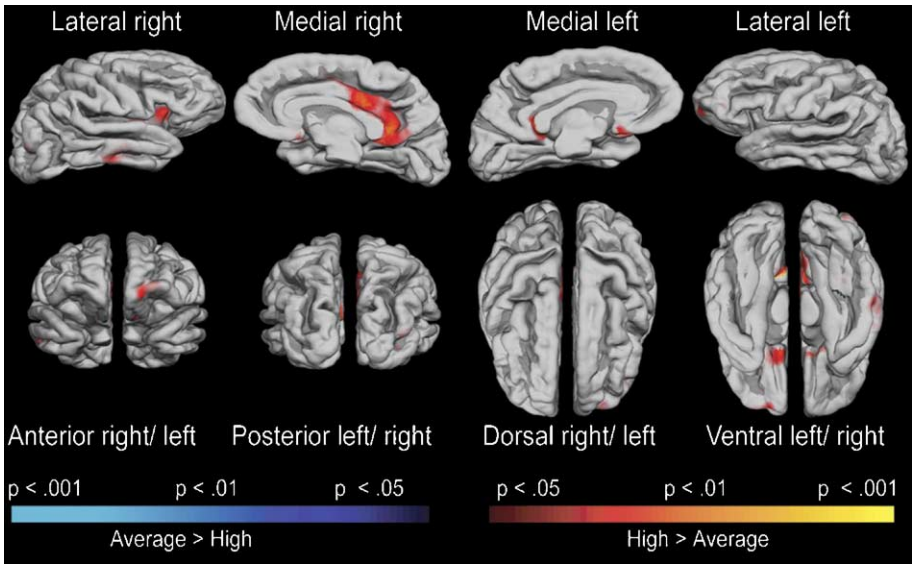

Fig. 3. Fluid function and cortical thickness. The cortical thickness of old participants with high and normal function on the two performance (fluid) tests of WASI was compared by general linear modeling (different onset, same slope, assumed) across the entire cortical mantle. Red and yellow indicate areas of thicker cortex for the high functioning group. In the right hemisphere, the main differences were found in temporal middle gyrus and temporal inferior gyrus, gyrus cuneus, the gyrus and sulcus of the insula, gyrus rectus, the gyrus of the cingulate isthmus, and the posterior cingulate gyrus. In the left hemisphere, no effects were identified in gyrus cuneus, insula, posterior cingulate gyrus, and temporal inferior and middle gyrus. Effects found in left but not in right hemisphere included fronto-marginal gyrus, orbital gyrus, and subcallosal gyrus.

Next, the average functioning old group was compared to the young, and the results showed differences in the form of thicker cortex of the young group throughout most of the cortical mantle. Generally, the differences were larger in the right than in the left hemisphere. The thickening of the right cingulate cortex was not seen for the average functioning group of elderly. The results are illustrated in Fig. 7. Scatterplots illustrating the individual data points for four selected vertexes on the surface of the cortex are presented in Fig. 8.

Based on the results from the GLMs, posterior cingulate was chosen as an area deserving further exploration. Regression analyses were performed for the high and the average functioning parts of the sample separately (young and old pooled together) to investigate whether the age slope of the two function groups differed. Regression analyses with cortical thickness at a point of the posterior cingulate as the dependent variable, and age and age square as independent variables, showed that, for the high functioning group, there was indeed a non-linear relationship (all beta's are standardized: $y = 0.32 \times \text{age}\ (P < 0.01) - 0.28 \times \text{age}^2\ (P < 0.01)$, $F = 8.178\ (P < 0.001)$, $R^2 = 0.32$), indicating a prolonged thickening prior to a later decline, while the same prolonged thickening was not observed for the average functioning group ($y = 0.15 \times \text{age}$ (n.s.) $- 0.17 \times \text{age}^2$ (n.s.), $F = 1.618$ (n.s.), $R^2 = 0.09$) (Fig. 9). For the other three points picked for further investigation, within the insula, inferior temporal gyrus, and occipital gyrus, no non-linear effects were observed (for all age2 values, $P > 0.30$).

Discussion

Cortical correlates of optimal aging

The present data indicate that cortical thickness is related to superior fluid cognitive function in higher age. Since no corresponding group differences were identified in young groups of high vs. average fluid ability, the observed effects are likely not only due to characteristics that are observable early in life. Similar

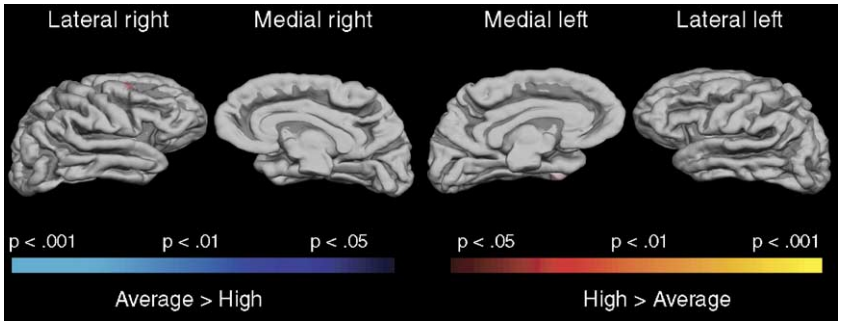

Fig. 4. Executive function and cortical thickness. The cortical thickness of old participants with high and normal function on a battery of neuropsychological tests of executive functioning was compared by general linear modeling (different onset, same slope, assumed) across the entire cortical mantle. Red and yellow indicate areas of thicker cortex for the high functioning group.

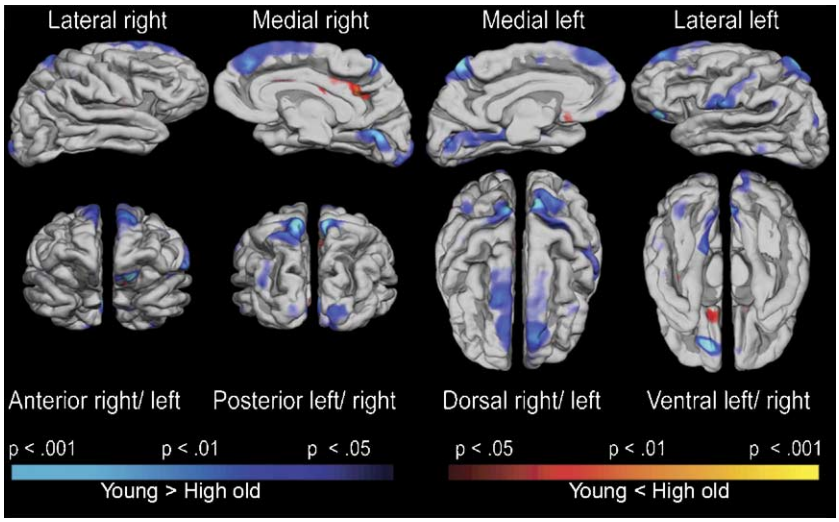

Fig. 5. High-performing elderly and young participants. The cortical thickness of old participants with high function on the two performance (fluid) tests of WASI was compared by general linear modeling (different onset, same slope, assumed) across the entire cortical mantle to the group of younger participants. Red and yellow indicate areas of thicker cortex for the high functioning old group, blue indicates thicker cortex for the young group. Differences were identified in several areas, mainly the parietal superior gyrus, the inferior angular part of parietal gyrus, frontal superior gyrus, the temporal medial lingual part of the occipital gyrus, the occipital pole, and gyrus precuneus, mainly anterior sections, in both hemispheres, in addition to the precentral and postcentral gyri and the orbital gyrus in the left hemisphere. However, in the right hemisphere, the high functioning old participants exhibited thickening of the posterior half of the cingulate gyrus, and in the left, the same phenomenon was demonstrated in a small area of the subcallosal gyrus.

differences in cortical thickness were not found for groups of high vs. average executive abilities. Therefore, we will focus on fluid abilities here. Furthermore, there was a tendency for stronger relationships in the right hemisphere, which was not surprising since the fluid tests consist of visuospatial material (Prabhakaran et al., 1997). Thus, in the following, we will concentrate on discussing these right hemisphere effects. The superior and average functioning old groups differed in the right middle and inferior temporal gyrus (Broadman's areas [BA] 21 and 20, respectively). These brain structures are involved in several complex cognitive tasks (Cabeza and Nyberg, 2000). For instance, functional studies indicate a role for the inferior temporal gyrus in visual perception (Ishai et al., 1999; Herath et al., 2001) and syllogistic reasoning (Goel et al., 2004). It is unreasonable to expect a strict anatomical correspondence between the results from structural and functional imaging studies, but the abovementioned functions have some resemblance with the visuo-constructive and visual reasoning task used in the present study.

Furthermore, and somewhat more surprising, significant differences were found in large sections of the posterior cingulate gyrus (BA 29, 30, 23, 31), the isthmus of the cingulate gyrus (BA 26), and the adjacent gyrus cuneus (BA 18, 19). Gyrus cuneus is part of the visual association cortex, and functional brain imaging has demonstrated involvement of the cingulate gyrus in many higher order cognitive functions. Both the anterior and posterior cingulate have been implicated in tasks involving integration of complex relations among stimuli (Kroger et al., 2002). Posner and Petersen (1990) suggested that the cingulate is part of an executive attention system needed when a supervisory mechanism is required to resolve a cognitive conflict. Such situations may generally involve high task demands, including planning and decision making, error monitoring and correction, and novel and not well-learned responses. These functions partly overlap with the requirements involved in the fluid tests in the present study. Furthermore, the posterior cingulate has been found to be a part of a neural network involved in relational reasoning, also including the secondary

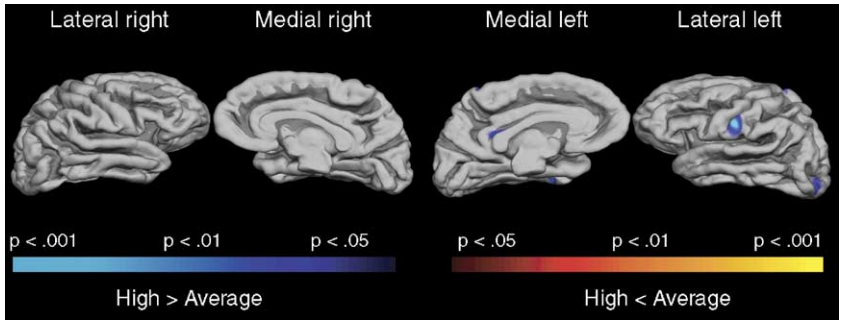

Fig. 6. High- versus average-performing young participants. The cortical thickness of young participants with high function on the two performance (fluid) tests of WASI was compared by general linear modeling (different onset, same slope, assumed) across the entire cortical mantle to a group of young average-performing participants. Blue indicates areas of thicker cortex for the high functioning group. Differences were found in left hemisphere postcentral gyrus and the occipital pole.

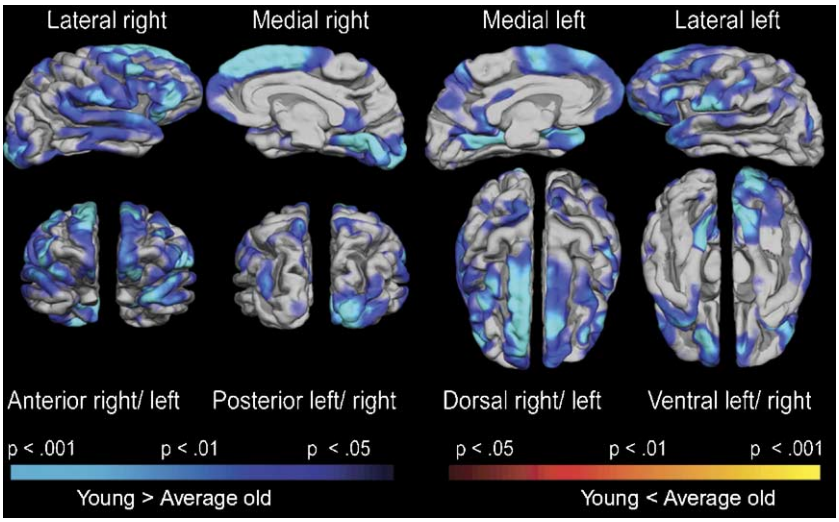

Fig. 7. Average-performing elderly and young participants. The cortical thickness of old participants with average function on the two performance (fluid) tests of WASI was compared by general linear modeling (different onset, same slope, assumed) across the entire cortical mantle to the group of younger participants. Red and yellow indicate areas of thicker cortex for the average-functioning old group, blue indicates thicker cortex for the young group. Differences in the form of thicker cortex of the young group were found throughout most of the cortical mantle, both laterally and medially, in the frontal (including the middle and superior frontal gyri, rectus gyrus, fronto-marginal, frontal inferior opercular, frontal inferior triangular, transverse frontopolar, and orbital gyri), temporal (including the temporal middle gyrus, the temporal pole gyrus, inferior posterior parts, and the superior lateral aspect of the temporal gyrus and temporal superior planum polar gyrus), and occipital (including occipital pole gryus, the middle occipital gyrus, and the occipital inferior gyrus) lobes, in addition to areas in the parietal lobes, as lateral sections of the precentral gyrus and lateral and medial sections of postcentral gyrus, paracentral gyrus, gyri cuneus and precuneus, parietal superior gyrus and the inferior supramarginal part of the parietal gyrus, the cingulate isthmus gyrus and posterior parts of the cingulate gyrus, and ventral part of gyrus cuneus.

visual cortex and the medial anterior frontal cortex (Ruff et al., 2003).

The main focus of cognitive research has been on the anterior part of the cingulate cortex (BA 25, 24), which has been shown to be involved in both higher order cognition and regulation of emotion (for a review, see Bush et al., 2000). Recently, posterior cingulate cortex as a part of larger neural networks has gained more interest (Buckner, 2004). Since the neuroanatomy and cytoarchitecture of the cingulate cortex is very complex (Elston et al., 2005), different parts of the structure are obviously involved in different aspects of human cognition. Studies of monkeys have shown that the posterior cingulate is close to or encompass major cortical connections to medial temporal structures important for memory function and that it may be highly associated with visuospatial functions (Kobayashi and Amaral, 2003). In a recent review, Buckner (2004) suggested that dysfunction of a neural network including the medial temporal lobe and the precuneus, extending into the posterior cingulate

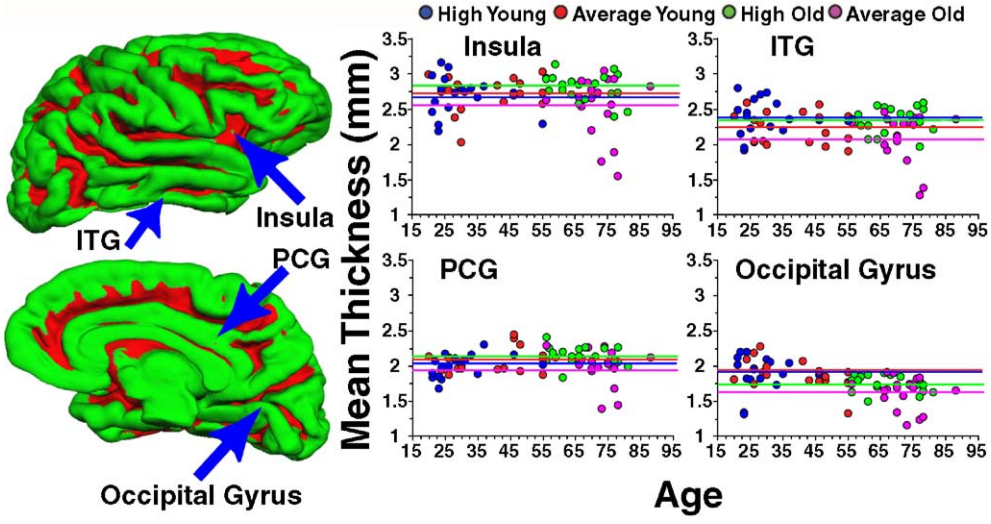

Fig. 8. Scatterplots for selected vertexes on the cortical surface. Scatterplots showing the cortical thickness for each participant at four different points (PCG: posterior cingulate gyrus; insula; ITG: inferior temporal gyrus; the occipital gyrus) on the cortex. The participants are grouped based on age (old versus young) and fluid performance (high versus average). The colored lines indicate the mean cortical thickness for each group at each point on the brain surface.

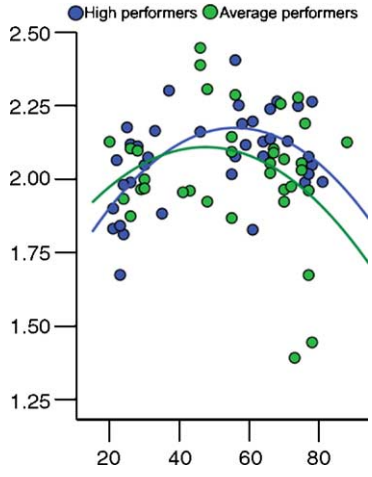

Fig. 9. Non-linear regression lines for high and average performers in PCG. Scatterplots showing the non-linear relationships between age and cortical thickness in a point in posterior cingulated gyrus (see Fig. 8) for the high and the average fluid performers (old and young polled together).

and retrosplenial cortex, may be central in explaining the memory deficits associated with Alzheimer's disease. The cortical thickness in posterior cingulate differed between the function groups in the present study. As seen in the non-linear analyses, these differences are results of complex interactions between the groups and the rate of early thickening and later thinning of the cerebral cortex in this area.

Fluid ability fundamentally depends on visuospatial orienting. One may reason that a ceiling effect exists for these capabilities in young age, but more variance may be found in aging. Preservation, as well as prolonged thickening of relevant areas may help uphold such basal and essential capacities. The latter may, as evident from Fig. 9, account for a relationship between increased thickness of the posterior cingulate cortex and fluid ability in old age. Based on the present cross-sectional data, it appears that, even though the cortical thickness of the posterior cingulate eventually starts decreasing also in elderly with high fluid function, this decrease may not result in a thinning relative to young adulthood since this area appears to become thicker throughout middle adulthood in persons with high fluid ability.

Finally, some distinct but scattered frontal lobe areas were identified as significantly different between the high and average old groups. Parts of the superior and middle frontal gyrus (BA 6, 8, 9, 10, 11) and gyrus rectus (part of BA 11), which may be considered an extension of cingulate gyrus onto the frontal lobes, were related to superior fluid function in high age. As parts of the frontal and prefrontal cortex, these structures are close to areas involved in working memory and executive and control functions necessary in performance on fluid neuropsychological tests. Even though no previous studies have pointed to a role for the morphometric characteristics of this cluster of gyri in successful aging, brain imaging studies have indicated that some cortical regions are more critical than others in fluid intelligence tasks, e.g. the frontal lobes (Duncan et al., 2000; Gray et al., 2003). Thus, the present finding may be understood in relation to previous research on the general function of the frontal lobe in human higher-order cognition.

Interhemispheric comparison is not the topic of this paper, but it is noted that medial structures, including posterior sections of the cingulate gyrus, the isthmus of the cingulate gyrus and gyrus rectus, differed between high and average scorers in both hemispheres. Furthermore, frontal and prefrontal areas differed between the groups in both hemispheres, but not invariably the same areas across hemispheres.

Evidently, the present results point to a possible role of cortical thickness of specific brain areas in achieving or maintaining superior fluid cognitive performance in high age. This result stands in contrast to the findings related to executive abilities. Thickness measures could only to a very modest extent explain the difference between elderly of high and average performance on neuropsychological tests related to executive functions. The small effects indicate that cortical thickness does not distinguish well between superior vs. average executive function in high age. It must be noted, however, that since analyses were performed on the residuals when the effects of performance on simpler test conditions were regressed out, this is a very strict procedure. In the fluid domain, no such correction was performed, and, as such, the results are not directly comparable.

Still, one reason for the lack of differences between the executive groups may be that neuropsychological tests of executive function traditionally are validated by use of patient populations or functional brain imaging studies. However, the necessity of a cortical area for maintenance of function does not entail that normal variation in morphometric characteristics of these areas is related to cognitive abilities. Based on the present data, it seems that established neuropsychological tests of frontal pathology are not related to differences in cortical thickness in an average to superior functioning population. This result is in accordance with the study by Van Petten et al. (2004), where volumes of neither superior, middle, nor inferior frontal gyrus correlated significantly with executive tests. The authors noted that the lack of significant relationships could reflect limitations in the regions measured, which did not cover the orbital gyrus, gyrus rectus, or cingulate gyrus. In the present study, the whole cortical surface is measured on a point-by-point basis, thus making the latter explanation less probable. At least two additional explanations for the lack of correspondence between the test scores and cortical thickness exist. First, structural changes in the frontal lobe do not necessarily entail changes in the thickness of cortex. Second, other parts of circuits involving frontal cortex, e.g. within the striatum (Rubin, 1999), may be more powerful predictors of age decline in the functions referred to as executive.

High and average fluid functioning old versus young

As expected, both the superior and the average functioning old had thinner cortex than the young, and the thinning was much more profound in the average than in the high function group. This confirms the effect of age on cortical thickness. Of more interest here, however, was that the high functioning group displayed thicker cortex than the young group in mainly two distinct areas: a small area of the subcallosal gyrus and posterior parts of cingulate cortex. The differences were not found between high and average functioning young participants, indicating that older high performers actually have thicker cortex than young high performers as a result of aging. Especially interesting is the thickening of posterior parts of cingulate gyrus since this area may support evaluative functions such as monitoring sensory events and the organism's own behavior in the service of spatial

orientation and memory (Vogt et al., 1992). As argued, this structure may also serve as an important link between neocortex and several brain areas, including hippocampus. Evident from the non-linear analyses, high performers will decline in thickness in posterior cingulated after a certain age, but the thinning follows decades of thickening and is not as profound as the thinning seen in average performers.

Decline in the efficiency of more specialized cognitive subprocesses may be compensated by increase of monitoring and control. It can be argued that cognitive activity itself can alter the brain morphometry in relevant structures (e.g. Draganski et al., 2004) and may lead to actual increase of cortical thickness in certain critical areas. As a consequence, one may speculate that thicker cortex in specific areas in the high-functioning group may be a structural effect of successful compensatory processing. However, this result needs to be replicated and further investigated, ideally with a longitudinal design, before it can be readily accepted. Furthermore, it is important to reconcile this compensation view with findings of increased heritability estimates for cognitive function with age (McClearn et al., 1997). The latter could be interpreted as evidence against an environmentalist view of brain and cognitive aging. However, a link between these finding may be established within a framework of cognitive reserve, where genetic factors may influence the thickness of certain cortical areas and this may either directly or indirectly be related to changes in cognitive subprocesses.

Limitations and conclusion

The conclusions from the present study should be drawn with caution, and limitations should be noted: first, the subject groups studied here are not large. Second, while predictions can be made regarding cortical thickness based on ability group status, the cortical thickness measures indeed also show scatter. For instance, as seen from Fig. 8, there are a few persons with very thin cortex in the average fluid ability older group. Furthermore, it should be noted that predictions cannot easily be made from cortical thickness in young adulthood since there are several with thin cortices especially in the posterior cingulate in the young high fluid ability group. It seems that mechanisms acting to enhance cortical thickness of the posterior cingulate along with fluid ability work throughout the adult life span, and the group effects are not observable until late adulthood.

In conclusion, the present data imply a relationship between cortical thickness and cognitive function in higher age. While previous reports have been inconsistent, the point-by-point strategy employed here may be an appropriate and sensitive approach to study the relationship between cortical structure and cognitive function. Furthermore, while a close relationship between fluid cognitive function and cortical thickness was found, only very small effects were observed for executive functions. Finally, the present results indicate that both cortical preservation and, to some extent, thickening may be necessary to ensure optimal cognitive aging. Both processes are detectable by morphometric methods. Of course, longitudinal studies are necessary to ensure that the effects observed really are functions of age. Still, the differences between the old performance groups versus the differences between the young performance groups give some indications that the observed effects are due to age, and not only a reflection of characteristics that are also observed at an earlier age.

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