Cerebral Cortex February 2011;21:345-356
doi:10.1093/cercor/bhq101
Advance Access publication June 4, 2010

Associations between Regional Cortical Thickness and Attentional Networks as Measured by the Attention Network Test

Lars T. Westlye, Håkon Grydeland, Kristine B. Walhovd and Anders M. Fjell

Center for the Study of Human Cognition, Department of Psychology, University of Oslo, Blindern, 0317 OSLO, Norway

Address correspondence to Lars T. Westlye, Center for the Study of Human Cognition, Department of Psychology, University of Oslo, PO Box 1094 Blindern, 0317 OSLO, Norway. Email: l.t.westlye@psykologi.uio.no.

Efficient attention is pivotal for cognitive functioning, and individual differences in attentional functions are likely related to variations in structural properties of the brain. Attention is supported by separate processes, and models of the relationship between attention and brain structure must take this into account. The Attention Network Test (ANT) yields behavioral measures of 3 independent attentional components: executive control (EC), alerting, and orienting. EC relates to resolving cognitive interference, alerting refers to continuous maintenance of a vigilant state, and orienting to selection of and orienting toward sensory information. Evidence from functional neuroimaging studies suggests that the ANT components recruit different cortical networks. However, the structural correlates are not established. Therefore, ANT scores were correlated with cortical thickness across the brain surface in 268 healthy adults spanning 20–84 years of age. Specific correlations were found between cortical thickness and EC and alerting in regions implicated by functional neuroimaging and lesion studies, including anterior cingulate, lateral prefrontal, and right inferior frontal gyri for EC and parietal areas for alerting. The brain–behavior correlations were relatively stable across adulthood, indicating that factors influencing cortical maturation rather than aging-related atrophy specifically were instrumental in shaping the structural foundation for visuospatial attention in adults.

Keywords: alerting, attention network test, cortical thickness, executive control, orienting

Introduction

The ability to efficiently utilize available information in the environment in order to control behavior and cognition is a core function of attention. An efficient attentional system is thus pivotal for most other types of cognitive functioning, and ultimately, through evolution, for survival. The neuronal basis of attentional processing has been defined in terms of large-scale neuronal networks in areas shown by neuroimaging studies to be recruited during attention-demanding tasks and regions producing specific attentional deficits, including neglect, when damaged (Mesulam 1981, 1999; Posner and Petersen 1990). While previous studies have shown associations between general neuropsychological functions and regional cortical thickness (Fjell et al. 2006; Walhovd et al. 2006; Narr et al. 2007; Chee et al. 2009), it is not known to which degree similar relationships exist for specific experimentally assessed attentional functions. As we have knowledge about the anatomical location of the brain areas supporting different attentional subprocesses, it is also possible to use attention as a model for exploring the specificity of brain structure–cognition relationships. The aim of the present study was to test the structural correlates of different attentional subprocesses, by correlating cortical thickness with scores on specific parts of a widely used test of visual attention, the Attention Network Test (ANT) (Fan et al. 2002).

The ANT is a widely used experimental cognitive task that differentiates independent attentional components. The ANT combines the cued reaction time (RT) task (Posner 1980) and the Eriksen flanker task (Eriksen BA and Eriksen CW 1974) into one experimental paradigm calling on 3 largely independent attentional components: executive control (EC), alerting, and orienting (Fan et al. 2009). Briefly, the EC component pertains to the process of resolving cognitively incongruent stimuli, the alerting component to the achievement and maintenance of a vigilant state, and orienting to the selection of and orienting toward sensory information (Posner and Petersen 1990; Posner 2008). Although still a matter of investigation (Callejas, Lupianez, and Tudela 2004; Callejas, Lupianez, Funes, and Tudela 2005), evidence from both genetic (Fan, Fossella, et al. 2003; Fossella et al. 2002, 2008), pharmacological (Brunye et al. 2010), electrophysiological (Fan et al. 2007; Neuhaus et al. 2010), functional neuroimaging (Thiel et al. 2004; Fan et al. 2005), and behavioral (Fan et al. 2002) studies support the relative independence of the different ANT components.

Functional neuroimaging studies have shown that the different attentional components are subserved by anatomically separate cortical networks (Fan et al. 2005). The EC component has been shown to invoke cortical areas typically associated with cognitive control tasks, including the anterior cingulate, lateral prefrontal cortices, and the right inferior frontal gyrus (Bush et al. 2000; MacDonald et al. 2000; Aron et al. 2004; Fan et al. 2005), and is probably largely influenced by the ventral tegmental dopamine system (Egan et al. 2001; Brocki et al. 2009). The alerting system has been associated with frontoparietal cortical networks, especially in the right hemisphere, and the thalamus and is assumed to be modulated by the cerebral distribution and availability of noradrenaline (Coull et al. 1996; Davidson and Marrocco 2000; Beane and Marrocco 2004). Finally, the orienting network, which is manipulated by the presentation of a cue indicating the spatial localization of attention, has been related to both superior parietal (Corbetta et al. 2000) and superior frontal (Fan et al. 2005) areas and has been linked to the acetylcholine system (Davidson and Marrocco 2000; Parasuraman et al. 2005).

The ANT has been used to uncover attentional deficits in various clinical disorders, including attention deficit hyperactivity disorder (Konrad et al. 2006; Adolfsdottir et al. 2008; Johnson et al. 2008), schizophrenia (Wang et al. 2005; Nestor et al. 2007), and Alzheimer's disease (AD) (Fernandez-Duque and Black 2006). Furthermore, the task has revealed beneficial

effects of bilingualism on the EC and alerting systems (Costa et al. 2008). A modified children's version of the ANT revealed specific EC network deficits and also less behavioral differentiation between attentional networks in 6-year-old children born prematurely (Pizzo et al. 2009). The task has also been used to delineate normal cognitive development (Rueda et al. 2004) and aging (Fernandez-Duque and Black 2006; Jennings et al. 2007). However, it is not known whether ANT subcomponents correlate with macrostructural brain measures, that is, cortical thickness in relevant regions, in healthy populations. This is an important question pertaining to the neurocognitive sensitivity of a widely applied magnetic resonance imaging (MRI) derived morphometric measure.

Another important question is related to the dynamics of brain–behavior relationships through the life span, that is, to which degree such correlations in adult samples are caused by early developmental or later atrophy-related variability. For instance, Shaw, Greenstein, et al. (2006) reported that the neurodevelopmental trajectories of cortical thickness differed between groups of highly and moderately intellectual children but that the differences leveled off in late adolescence (~18 years of age). Narr et al. (2007) reported positive correlations between general intellectual abilities and cortical thickness in healthy young adults (17–44 years of age). Taken together, these results indicate that early maturation of cortical thickness modulate the development of general cognitive skills. According to this view, one would expect that the brain–behavior correlations should be relatively constant through the healthy adult life span.

An alternative hypothesis is that variability due to cortical atrophy in higher age drives the brain–behavior relationships in adults. This view may be referred to as a neuropsychological perspective (Van Petten 2004). According to this view, "we might expect to find positive correlations between hippocampal volume and memory performance in older [. . .], but perhaps not in younger participants [. . .] correlations between hippocampal volume and memory should become increasingly positive as the age of the sample increases" (Van Petten 2004, p. 1396). In the metaanalysis of studies relating hippocampus volume to memory function, Van Petten (2004) found support for both the developmental and neuropsychological hypothesis in that the volume–memory correlation tended to grow more positive as the age of the sample increased. However, increased variability in the volume–memory correlations with age was also reported, which suggests a complex interplay between brain and cognition through the life span.

We believe that the general mechanisms for brain–cognition relationships during different phases of life suggested by Van Petten may be applicable to other cognitive domains and other brain structures than hippocampus. Based on this assumption, the developmental and neuropsychological perspectives provide testable hypotheses regarding the dynamic relationships between regional cortical thickness and attention through the life span.

Although the hypotheses are not mutually exclusive, an indirect test of the validity of the atrophy hypothesis would be to explore the stability of the correlations between thickness and cognitive function throughout the adult life span. According to the neuropsychological view, the relationships between cortical thickness and cognition will be strongest in old age where the accumulation of atrophy is largest and weaker in middle age where less aging-related structural alterations are seen (Van Petten 2004; Fjell et al. 2006). If the relationships between attentional functions and cortical thickness increase in strength with increasing age, this would yield support to the neuropsychological perspective. However, if the correlations are present in the youngest part of the sample and not increasing significantly, it follows that they are caused by factors influencing cortical thickness at an early stage, that is, developmental processes.

The main aim of the present study was to establish the structural neuroanatomical correlates of the 3 ANT networks using detailed automated measures of cortical thickness across the entire brain surface in a large (n = 268) healthy sample spanning from 20 to 84 years of age. Based on previous functional neuroimaging and lesion studies, we expected the 3 networks to show differential regional correlations with cortical thickness. Specifically, we hypothesized bilateral caudal anterior cingulate, dorsolateral prefrontal cortex, and right-lateralized inferior frontal gyrus effects for the EC network (Bush et al. 2000; Fan, Flombaum, et al. 2003; Aron et al. 2004; Fan et al. 2005), bilateral frontoparietal effects for the alerting system (Fan et al. 2005; Posner 2008), and right-lateralized superior parietal and superior temporal effects for the orienting component (Kastner et al. 1999; Corbetta and Shulman 2002; Fan et al. 2005). Furthermore, we wanted to explore whether the brain–behavior relationships are caused by early developmental or later atrophy-related variability. Thus, we tested if the associations between cortical thickness and the ANT scores interacted with age in predicting cortical thickness. If the relationships between age and ANT components are stronger in elderly than in young groups of participants, this would indicate that aging-related variability (atrophy) drives the brain–behavior correlations. On the other side, a lack of interaction would suggest that the brain–behavior relationships are well established in the young participants and thus that developmental processes are likely more instrumental in shaping the associations between cortical thickness and visuospatial attention. Various accumulative life events may have a negative or positive impact on brain structure and cognitive functions. Aging may thus be related to increased between-subject variability and since such heteroscedasticity could reduce brain-behavior correlations with increasing age, we directly tested whether the behavioral and morphometric measures showed evidence of increased variability in an old compared with a young subsample.

Materials and Methods

Sample

The sample was drawn from the first wave of the longitudinal research project *Cognition and Plasticity through the Life-Span* administered at the Center for the Study of Human Cognition at the University of Oslo. The study was approved by the Regional Ethical Committee of Southern Norway. Participants were recruited through newspaper ads and among students and employees of the University of Oslo. Further details regarding recruitment and enrolment are given elsewhere (Fjell et al. 2008; Westlye, Walhovd, Bjørnerud, et al. 2009). Written and oral informed consent was obtained from all participants prior to assessments. In total, 268 subjects (150 females) ranging 20–84 years of age were included in the present analysis. Mean (standard deviation [SD]) age was 48.5 (17.1) years. Independent samples' t-test revealed no significant difference (t = –0.23, P = 0.82) in age between females (48.26, SD = 16.3 years) and males (mean 48.75, SD = 18.0) years).

Subject characteristics per decade and in the total sample are summarized in Table 1.

All subjects were right-handed Norwegian speakers and were screened using a standardized health interview prior to inclusion in the study. Subjects with a history of self-reported neurological or psychiatric conditions including clinically significant stroke, serious head injury, untreated hypertension, diabetes, and use of psychoactive drugs within the last 2 years were excluded. Furthermore, participants reporting worries concerning their cognitive status, including memory function, were excluded. All included participants scored <16 on Beck Depression Inventory (BDI) (Beck and Steer 1987) and subjects above 40 years of age ⩾26 on mini mental state examination (MMS) (Folstein et al. 1975; Bravo and Hebert 1997). General cognitive abilities were assessed by Wechsler Abbreviated Scale of Intelligence (Wechsler 1999). All participants scored within normal IQ range (mean: 114.5, SD = 8.6). All subjects' MR scans were examined by a neuroradiologist and all included scans were deemed free of significant anomalies.

ANT and MRI data were obtained from 2 different visits no more than 3 months apart.

ANT data were available from 282 subjects. None of the participants had been given the ANT task previously. Nine participants were excluded due to missing MRI data, and one was excluded after neuroradiological evaluation. Additionally, 4 subjects were excluded due to poor ANT performance (<50% accuracy on incongruent trials, see below), yielding a final sample of 268 subjects.

MRI Acquisition

Imaging was performed using a 12 channel head coil on a 1.5 T Siemens Avanto (Siemens Medical Solutions) at Oslo University Hospital, Rikshospitalet, Oslo.

The sequence used for morphometric analyses were 2 repeated T_1-weighted magnetization prepared rapid gradient echo, with the following parameters: repetition time/echo time/time to inversion/flip angle = 2400 ms/3.61 ms/1000 ms/8°, matrix 192 × 192, field of view = 240, voxel size = 1.25 × 1.25 × 1.20 mm, 160 sagittal slices. Scanning time was 7 min 42 s. The 2 runs were averaged during postprocessing to increase SNR. All data sets were processed and analyzed at the Neuroimaging Analysis Laboratory, Center for the Study of Human Cognition, University of Oslo, with additional use of computing resources from the Titan High Performance Computing facilities (http://hpc.uio.no/index.php/Titan) at the University of Oslo.

Morphometric Analysis

We estimated vertex-wise cortical thickness across the brain surface using FreeSurfer (http://surfer.nmr.mgh.harvard.edu/) by means of an automated surface reconstruction scheme described in detail elsewhere (Dale et al. 1999; Fischl, Sereno, and Dale 1999; Fischl, Sereno, Tootell, and Dale 1999; Fischl and Dale 2000; Fischl et al. 2001; Segonne et al. 2004). Briefly, a representation of the gray matter (GM)/white matter (WM) boundary was reconstructed using intensity and continuity information from the entire MR volume in segmentation and deformation procedures (Dale et al. 1999). Thickness measurements were obtained by reconstructing representations of the GM/WM boundary and the pial surface (Dale and Sereno 1993; Dale et al. 1999) and then calculating the distance between the surfaces at each vertex across the cortical mantle. The surfaces are created using spatial intensity gradients across tissue classes and are therefore not simply reliant on absolute signal intensity. The surfaces produced are not restricted to the voxel resolution of the original data, and the procedure is thus capable of detecting submillimeter differences between groups (Fischl and Dale 2000). The surface reconstructions and segmentations are run automatically but require supervision of the accuracy of the spatial registration and tissue segmentations. All reconstructed data sets were visually checked for accuracy, and segmentation errors were manually corrected by trained operators. Minor manual edits were performed on most subjects (>80%), usually restricted to removal of nonbrain tissue included within the cortical boundary. The individual thickness maps were resampled, mapped to a common surface, smoothed with a Gaussian kernel with a full width of half maximum of 30 mm and submitted to statistical analyses. The morphometric hypotheses were largely based on previous functional imaging studies, and due to the complex relationship between functional and structural imaging, we performed full brain surface analyses to minimize the risk of failing to detect relevant effects outside the hypothesized regions.

The Attention Network Test

We administered a version of the ANT (Fan et al. 2002) downloaded from Dr Jin Fan's website (http://www.sacklerinstitute.org/users/jin.fan/). The version used in the present study consisted of 2 runs of 96 trials preceded by one practice run with 20 trials. During assessment, participants were seated in a comfortable chair at approximately 60 cm distance from a 19-inch computer monitor. For each trial, the participants pressed a key indicating whether a target arrow was pointing to the left or right. The arrow was presented either above or below a centrally located fixation cross. The target arrow was flankered by 1 of 3 different types of stimuli; 1) pairs of congruent arrows, 2) pairs of incongruent arrows, or 3) pairs of neutral lines. Each type of flanker stimuli was presented 32 times per run. Furthermore, each trial was preceded by 1 of 4 cue conditions, with each variant occurring 24 times in each run: 1) no cue, 2) center cue, 3) double cue, and 4) spatial cue. The cues, when presented, were single (center and spatial cue condition) or double asterisks replacing (center cue) or accompanying the fixation cross. The size of the fixation cross was approximately 0.5 × 0.5 cm (~0.5°), and the diameter of the asterisks used for cuing was about 0.3 cm (~0.3°). Target arrows (or dashes in the neutral condition) were centered 1.3 cm (~1.2°) below or above the fixation cross. Each trial was initiated by the fixation cross of 400, 800, 1200, or 1600 ms duration, equally distributed across cuing and flanker conditions. The fixation cross was followed by the cue condition of 100 ms duration and then the target stimuli, which remained visible on the screen until response or until 1700 ms after target presentation. The participants were instructed to focus on both speed and accuracy throughout the session, and the length of the break between runs were controlled by the participants. Responses were obtained on a Psychology Software Tools Serial Response Box, and the experimental procedures and responses were collected using E-prime software (Psychology Software Tools, Pittsburgh, PA).

Table 1
Sample descriptives by age and total

Age group (yrs)	*n*	Females *N* (%)	FSIQ[a] mean (SD)	MMS[b] mean (SD)	Years education[c] mean (SD)	Age mean (SD)
20.0–30.0	53	27 (51)	112.6 (7.2)	na	15.1 (1.9)	23.8 (2.5)
30.1–40.0	37	22 (60)	115.0 (8.5)	na	17.2 (2.4)	34.5 (2.9)
40.1–50.0	33	21 (64)	115.4 (7.4)	29.4 (0.6)	15.3 (2.2)	45.2 (3.1)
50.1–60.0	68	38 (56)	113.2 (7.2)	29.2 (0.8)	15.2 (2.2)	54.2 (2.7)
60.1–70.0	45	27 (60)	114.6 (9.9)	29.2 (0.7)	16.3 (3.5)	64.1 (2.7)
70.1–80.0	24	12 (50)	118.3 (11.8)	28.8 (1.2)	16.0 (3.2)	72.6 (2.6)
80.1–85.0	8	3 (38)	119.0 (10.3)	28.5 (0.5)	15.3 (2.8)	81.9 (1.5)
Total	268	150 (56)	114.5 (8.6)	29.2 (0.82)	15.7 (2.6)	48.5 (17.1)

[a]Full scale IQ (FSIQ) was estimated from the Wechsler Abbreviated Scale of Intelligence (Wechsler 1999) subtests matrices, block design, vocabulary, and similarities.
[b]MMS (Folstein et al. 1975) scores not available for subjects below 40 years of age.
[c]Most subjects between 20 and 30 years of age were recruited among university students, and years of education were calculated as number of years completed at time of assessment.

Behavioral Analysis

The main strength of the ANT is the feasibility to extract information regarding specific attentional components based on RT in the various conditions; EC, alerting, and orienting (Fan et al. 2002). The EC network may be defined as the difference in RT between the incongruent and the congruent condition, alerting as the difference in RT between the no cue and the center cue condition, and orienting as the difference between the center cue and the spatial cue condition. The following processing steps were performed prior to computing the network scores: To remove outliers, all RTs >1500 ms and <200 ms were removed (less than 1/1000 of all correct responses were removed). Next, since error responses are assumed to originate from a different RT distribution than correct responses, we only analyzed correct responses. Also, because responses following erroneous responses typically are slower than responses following correct responses (posterror slowing), we also removed responses following erroneous responses. Since RTs are not normally distributed, we used median RT per condition as raw scores for each subject. Since overall RT is known to increase significantly with advancing age, we adjusted the component scores with the relevant baseline RT in order to isolate the attentional system from the anticipated increase in overall RT. Thus, after pruning of the behavioral data as described above, we computed the following scores, based on median RT.

$$\text{Executive control} = \left[RT_{\text{incongruent}} - RT_{\text{congruent}}\right] / RT_{\text{congruent}}$$

$$\text{Alerting} = \left[RT_{\text{no cue}} - RT_{\text{center cue}}\right] / RT_{\text{center cue}}$$

$$\text{Orienting} = \left[RT_{\text{center cue}} - RT_{\text{spatial cue}}\right] / RT_{\text{spatial cue}}$$

The ratio effect scores were scaled to percent relative to baseline condition as shown above. We also calculated mean accuracy in all conditions.

Statistical Analysis

Median RT for each subject in the various ANT cue and target conditions were correlated (Pearson's r) with age to explore the age dependency on the absolute RT measures. We tested for main effects of sex on RT using independent samples t-test. Next, we correlated the relative ANT component scores with age within and across genders (partialling out sex in the latter). Effects of sex on the age correlations were tested using Fischer's Z tests. To explore the relationships between the different ANT components, we correlated each of the RT composite scores before and after partialling out sex and age.

In order to test for relations between the experimental indices of attentional function to more general intellectual abilities, we correlated each of the ANT scores with full scale IQ while partialling out age and sex.

Brain–behavior relationships were tested vertex wise across the brain surface by fitting general linear models (GLMs) of the effect of ANT scores on thickness in every vertex across the surface. Since age is negatively associated with cortical thickness (Fjell, Westlye, et al. 2009; Salat et al. 2004; Westlye, Walhovd, Dale, et al. 2009), we included age and sex as covariates in the statistical models. All variables were mean centered prior to analyses. Since age is strongly correlated with RT across conditions (see Supplementary Table 3), we performed the analyses for the ANT scores adjusted for RT in the relevant baseline conditions. We performed separate analyses for EC, alerting, and orienting to explore common and unique relations to cortical thickness across attentional functions. Possible modulating effects of general intellectual functions on the brain–attention correlations were tested by including full scale intelligence quotient (FSIQ) as an additional covariate in multiple linear regressions together with age, sex, and the relevant ANT score as independent variable and cortical thickness as dependent variable. Specifically, we tested whether including FSIQ in the model removed the statistical relationship between thickness and ANT score.

To explore the stability of the brain–behavior correlations through the adult life span, we also tested for possible age × ANT score interactions on cortical thickness by including the interaction term as an additional covariate in multiple linear regression analyses with cortical thickness in the significant effect sites from the main effect analysis as dependent variables. To validate and further explore the stability of the brain–behavior relationships, we divided the full sample into 2 different age groups by splitting the full sample at median age and then calculated the brain–behavior correlations in the significant effect sites from the full-sample analysis within each age group. Since one could argue that age-related heteroscedasticity (i.e., increasing variability with age) may influence the brain–behavior correlations, we compared the variability in each of the measures between the 2 age groups. Specifically, we computed the relative coefficient of variation (rCoV) in cortical thickness in the relevant effect sites and compared between groups. rCoV was defined as (100 × SD/mean) and was computed for each group separately. Since rCoV may be misleading for variables that are not always positive, we computed the SD for each of the attention indices (EC, alerting, and orienting) and compared between groups.

To reduce the probability of Type I errors, all cortical thickness analyses were corrected for multiple comparisons using cluster size inference by means of Z Monte Carlo simulations as implemented in FreeSurfer (Hayasaka and Nichols 2003; Hagler et al. 2006). Here, clusters were tested against an empirical null distribution of maximum cluster size built using synthesized Z distributed data across 10 000 permutations, yielding clusters fully corrected for multiple comparisons across the surface. The initial cluster-forming threshold employed in the present study was $P < 0.05$. Although interpretations will be inferred from the corrected data, both corrected and uncorrected ($P < 0.05$) results will be presented to aid comparison with previous studies. We also present surface-based t-statistics for each ANT network, representing raw effect-sizes across the brain.

Results

ANT Components

Mean of all subjects' median RT in the various cue and flanker conditions, within and across genders, are shown in Table 2. Males had shorter mean RT in all conditions, but there were no main effects of sex. Table 3 summarizes the ANT component scores within and across genders relative to baseline RT. One sample t-tests of the component scores revealed significant EC ($t = 55.07$, $P < 0.00001$), alerting ($t = 14.46$, $P < 0.00001$), and orienting ($t = 32.66$, $P < 0.00001$) effects. There were no main effects of gender on the ANT scores. We found moderate but significant negative correlations between alerting and orienting ($r = -0.30$, $P < 0.01$) and between the EC and orienting network ($r = -0.17$, $P < 0.01$) when partialling out age and sex. Thus,

Table 2

Mean (standard deviation) RT (ms) in each cue and flanker condition for females, males, and across genders

Target	Cue	Females	Males	t_{diff}	Total
Congruent	No	584.6 (104.6)	572.1 (98.9)	1.00	579.1 (102.1)
	Center	550.2 (99.6)	541.7 (104.1)	0.68	546.4 (101.5)
	Double	542.0 (99.9)	532.8 (102.1)	0.74	538.0 (100.8)
	Spatial	502.7 (104.4)	490.5 (99.5)	0.80	497.3 (102.2)
Incongruent	No	679.7 (120.2)	675.2 (113.2)	0.31	677.7 (117.0)
	Center	687.9 (129.9)	672.7 (116.9)	1.01	681.2 (124.3)
	Double	667.9 (123.4)	659.4 (116.7)	0.58	664.2 (120.4)
	Spatial	595.9 (129.4)	585.2 (116.7)	0.71	591.2 (123.9)
Neutral	No	579.2 (99.5)	564.7 (94.8)	1.21	572.8 (97.5)
	Center	557.5 (106.9)	542.2 (101.9)	1.20	550.7 (104.8)
	Double	541.1 (99.6)	534.7 (101.1)	0.52	538.3 (100.1)
	Spatial	504.4 (99.7)	490.6 (96.7)	0.89	498.3 (98.3)

Note: The RTs are averaged median scores across participants. t_{diff} scores were obtained from independent samples t-tests comparing females and males. No significant differences between genders were found.

Table 3
Mean (SD) attention network effects for females, males, and across genders (total)

	Females	Males	t_{diff}	Total
EC	21.1 (6.0)	21.8 (6.8)	−0.78	21.4 (6.4)
Alerting	3.9 (4.6)	4.2 (4.7)	−0.55	4.1 (4.6)
Orienting	11.8 (5.9)	12.0 (6.1)	−0.15	11.9 (6.0)

Note: The effects are expressed in percent relative to the baseline condition. t_{diff} denotes the *t*-statistics obtained from independent samples *t*-tests comparing females and males. No significant differences between genders were found.

Table 4
Pearsons's correlations between the ANT networks (corrected for baseline median RT) and age for females, males, and across genders (sex partialled out)

	Females	Males	Fischer's *Z*	P_{diff}	Total (sex partialled out)
EC	−0.08	**−0.28**	1.74	ns	**−0.18**
Alerting	**−0.30**	**−0.46**	1.45	ns	**−0.37**
Orienting	−0.12	−0.04	0.66	ns	−0.08

Note: Fischer's *Z* is the *Z* score obtained from Fischer's *Z* tests comparing the coefficients betweens genders. P_{diff} marks the significance of the difference test. Critical *Z* value for a 2-tailed *t*-test is 1.96 at $P < 0.05$ level. There were no significant differences between females and males. The last column shows the partial correlations between RTs and age across genders when partialling out sex. Bold: $P < 0.01$; italic: $P < 0.05$; ns, not significant.

high orienting scores were associated with both relatively low alerting and EC scores. Alerting and EC were not correlated when partialling out age and sex ($r = 0.12$, $P > 0.05$).

Supplementary Table 1 shows mean percent accuracy in each of the flanker and cue conditions within and across genders. Mean accuracy was >94% in all conditions. Accuracy across subjects was lowest in the no-cue/incongruent condition (mean accuracy: 94.9%, SD = 7.6%) and highest in the double cue/congruent condition (99.5%, SD = 1.7%). Paired samples *t*-tests between the different conditions revealed significant EC ($t = 11.60$, $P < 0.00001$), alerting ($t = -3.55$, $P < 0.0005$), and orienting ($t = 3.71$, $P < 0.0003$) effects on accuracy across subjects. Female participants committed fewer errors than males in the center, double, and spatial cue conditions on incongruent trials ($P < 0.05$), and there was also a trend effect in the no-cue condition ($P = 0.063$). There were no other significant differences between genders on accuracy. Supplementary Table 2 shows accuracy for each of the components within and across genders. As suggested by the within-conditions analyses, significant ANT component effects were found across participants. Furthermore, female participants showed a significantly smaller congruency effect on accuracy than male participants. Summarized, the analyses yielded expected behavioral effects of cue and warning conditions. Relative to baseline, the EC component was largest in magnitude (114.5 ms or 21% increased RT in incongruent compared with congruent trials), followed by orienting (60.2 ms or 12% increased RT in the no cue vs. center cue condition) and alerting (21.5 ms or 4% increased RT in the no-cue vs. central cue condition).

ANT and Age

Supplementary Table 3 summarizes the Pearson's correlations between median RT in the various cue and flanker conditions and age within and across genders. Not surprisingly, there were strong positive correlations between age and RT across conditions and genders (all *P*s < 0.01). Age correlations across subjects (sex partialled out) ranged from $r = 0.73$ in the spatial cue/incongruent condition to $r = 0.80$ in the center cue/congruent condition. Fischer's *Z* tests revealed no significant differences in the age correlations between female and male participants.

Table 4 shows results from partial correlations between age and the ANT components adjusted for median RTs in the baseline conditions within and across genders (sex partialled out). We found a small negative correlation between EC and age ($r = -0.18$, $P < 0.01$), indicating relatively decreased RTs on incongruent compared with congruent trials with higher age. We also found a negative correlation between alerting and age ($r = -0.37$, $P < 0.01$), indicating that the beneficial effects of the alerting cues diminished with advancing age. There was no significant correlation between orienting and age ($r = -0.08$, $P > 0.05$). Fischer's *Z* tests revealed no significant differences in the correlations with age between female and male participants.

Supplementary Table 4 summarizes the correlations between mean accuracy in the different cue and flanker conditions and age within and across genders. Across subjects, we found a significant negative correlation (fewer errors with increasing age) in the double cue/congruent condition ($r = -0.18$, $P < 0.01$) and positive correlations (more errors with increasing age) in the no cue ($r = 0.17$, $P < 0.01$), center cue ($r = 0.23$, $P < 0.01$), double cue ($r = 0.25$, $P < 0.01$), and the spatial cue ($r = 0.12$, $P < 0.05$) in incongruent trials. Fischer's *Z* tests revealed no significant differences between male and female participants in the age correlations.

ANT and Intellectual Abilities

Correlation analysis (partialling out age and sex) revealed a significant negative correlation between FSIQ and EC ($r = -0.18$, $P < 0.01$), indicating that subjects scoring high on intellectual abilities performed better on the EC component. We also found a positive correlation between the orienting component and FSIQ ($r = 0.20$, $P < 0.01$), indicating that general intellectual abilities were positively related to spatial orienting. We found no significant correlation between alerting and FSIQ ($r = 0.10$, $P > 0.05$).

ANT and Cortical Thickness

Figure 1 shows spatial *t*- and *p*-maps from GLMs testing linear effects of each ANT score on cortical thickness in a vertex-wise manner. Sex and age were included as covariates in all analyses. The *t*-maps were thresholded at $t > 1$, and the uncorrected raw *p*-maps were thresholded at $P < 0.05$. The corrected maps show the significant clusters corrected for multiple comparisons across the surface thresholded at $P < 0.05$ (see Materials and Methods). Table 5 shows statistics for each significant cluster in the various conditions and results from linear regressions with each ANT component as dependent, sex as fixed factor and age and thickness in the maximum vertex in each cluster as covariates. The analyses were rerun with the age × ANT interaction terms included as covariates, and the resulting *t*-scores for the interaction terms are also shown in Table 5. Note that the clusters and the peak values represent the unique effects of ANT components on cortical thickness with age and sex as covariates, and not the full model fit, which is given as R^2.

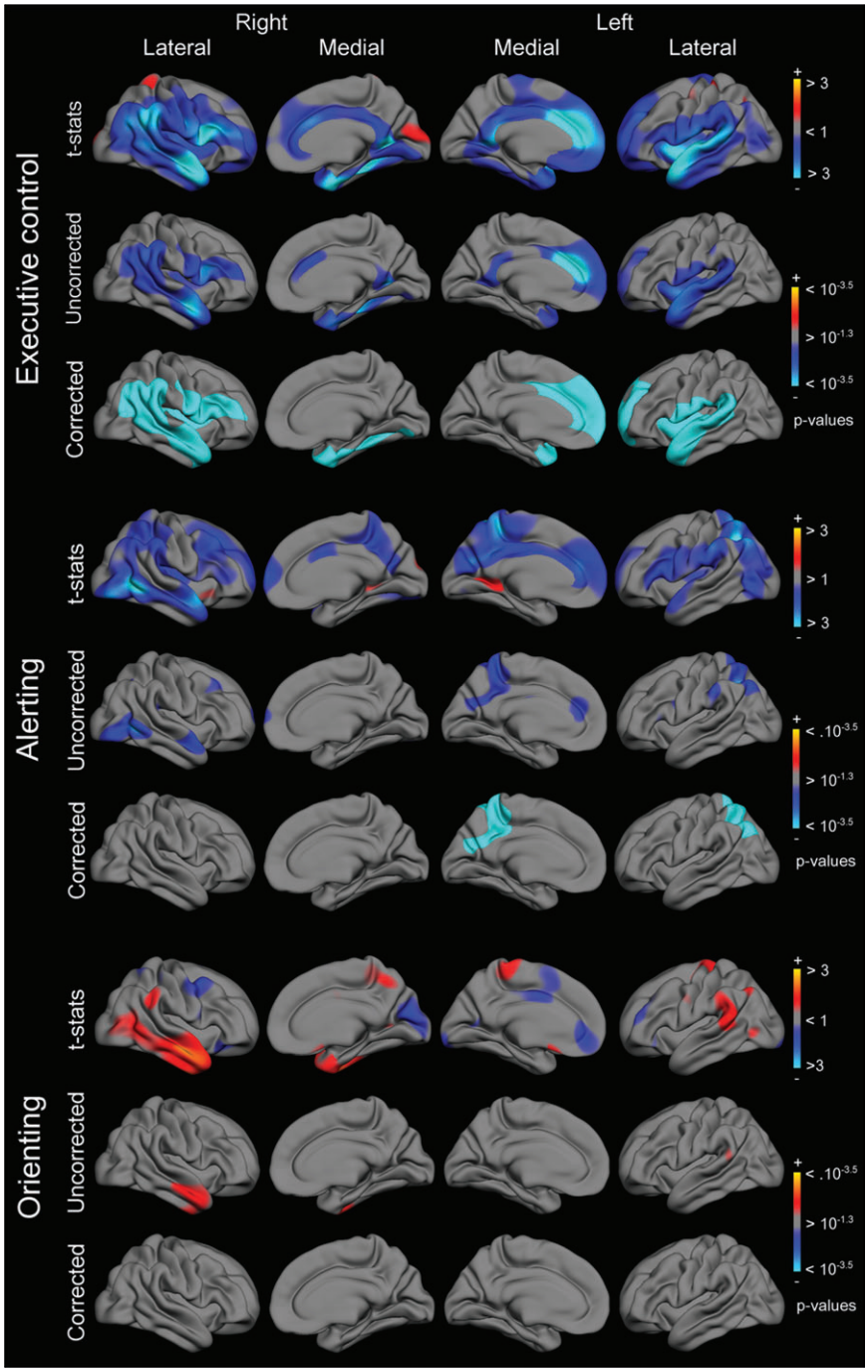

Figure 1. Spatial *t*- and *p*-maps from surface-based GLMs testing the effects of EC (top rows), alerting (middle rows), and orienting (bottom rows) scores on cortical thickness. Blue and red/yellow areas denote negative and positive relations between ANT score and thickness, respectively. Age and sex were included as covariates in all analyses. *t*-maps were thresholded at $t > 1$. Uncorrected ($P < 0.05$) and corrected ($P < 0.05$, corrected for multiple comparisons across the surface) statistical *p*-maps are shown.

Table 5

Results from multiple linear regressions with thickness at peak vertex as dependent variable, sex as fixed factor and ANT sub component (EC, alerting) and age as covariates

ANT network	Anatomical localization	Cluster size (mm^2)	Peak vertex (Talairach XYZ)	R^2	t_{age}	B_{age}	t_{ANT}	B_{ANT}	t_{sex}	B_{sex}	Age × ANT (t)
EC	L caudal acc	**6596**	[−9.9, 31.8, 16.2]	**0.22**	**−7.94**	**−0.44**	**−4.97**	**−0.29**	1.11	0.07	−1.28
	L superior temporal	**9975**	[−48.4, −15.0, −2.7]	**0.24**	**−9.29**	**−0.50**	**−2.82**	**−0.17**	−0.12	−0.01	−0.61
	R middle temporal	**20560**	[50.0, −6.2, −19.8]	**0.34**	**−11.68**	**−0.58**	**−3.26**	**−0.20**	*−2.26*	*−0.14*	−0.29
	R caudal acc	1082	[5.8, 20.1, 22.8]	0.07	**−4.18**	*−0.25*	*−2.68*	*−0.16*	1.45	0.08	−0.45
Alerting	L superior parietal	**7056**	[−28.8, −57.6, 40.9]	**0.33**	**−11.34**	**−0.57**	**−3.38**	**−0.20**	*2.09*	*0.13*	0.32

Note: Cluster size is the total size of the cluster. The anatomical description is corresponding to the peak vertex. R^2, adjusted R^2 for the full model; t, t-score for the different independent variables; B, standardized betas for the different independent variables, age × ANT (t) is the t value for the interaction term. None of the included interactions terms were significant. Bold: $P < 0.01$, italic: $P < 0.05$.

For EC, 2 significant clusters were found in the left and one in the right hemisphere. The largest cluster in the left hemisphere was located in the anterior cingulate cortex extending into the frontal pole and parts of the dorsolateral prefrontal cortex (cluster size: 6595.6 mm^2, Talairach coordinates of the maximum vertex: [–9.9, 31.8, 16.2], standardized beta = –0.29 after regressing out age and sex). The second cluster in the left hemisphere was located in the lateral superior temporal gyrus extending into the insular cortex, inferior frontal gyrus, and the temporoparietal junction (cluster size: 9974.9 mm^2, Talairach coordinates of the maximum vertex: [–48.4, –15.0, –2.7], standardized beta = –0.17). A significant cluster in the right hemisphere included the lateral and medial aspects of the temporal lobe extending into the temporoparietal junction, inferior parietal cortex, and lateral inferiofrontal areas (cluster size: 20560.6 mm^2, Talairach coordinates of the maximum vertex: [50.0, –6.2, –19.8], standardized beta = –0.20). This cluster was larger than the corresponding cluster in the left hemisphere, but mainly analogous regarding anatomical location. Bilateral effects in the caudal anterior cingulate were anticipated, but only the cluster in the left hemisphere survived the cluster size corrections. We still identified a cluster of significant (P < 0.05, uncorrected) vertices also in the right caudal anterior cingulate cortex, but this did not reach significance in the Z Monte Carlo simulation (cluster size: 1082. 6 mm^2, Talairach coordinates of the maximum vertex: [5.8, 20.1, 22.8], standardized beta = –0.16). The raw t-statistics map also supported the involvement of the cingulate cortices, with t > 1 across the full extent of the cingulate in both hemispheres. All significant clusters showed a negative association with the EC component, indicating decreasing conflict effect with increasing cortical thickness.

For alerting, we found one significant cluster encompassing the left medial and lateral superior parietal lobe (cluster size: 7056.4 mm^2, Talairach coordinates of the max vertex: [–28.8, –57.6, 40.9]). The association between the cortical thickness and alerting component was negative (standardized beta = –0.20), indicating increasing alerting effect with decreasing cortical thickness. As seen in Figure 1, the cluster also extended into the posterior cingulate and the precuneus. No significant clusters were found in the right hemisphere. The raw t-statistics map suggested subthreshold effects in large portions of the cingulate cortices, the left medial prefrontal cortex, and the right dorsolateral prefrontal cortex, but these areas did not reach significance.

For the orienting component, we found no significant effects after controlling for multiple comparisons. The raw t-statistics map suggested subthreshold positive effects in anterior temporal areas in the right hemisphere, and also in the temporoparietal junctions, bilaterally.

Including FSIQ in the linear regressions yielded no unique significant statistical contribution of general intellectual abilities on regional cortical thickness, and all thickness–attention correlations remained significant and generally unchanged. Thus, although FSIQ showed moderate correlations with the EC and orienting network, the relations between regional cortical thickness and ANT scores were not influenced by general intellectual functioning.

There were no significant age × ANT score interaction effects on thickness in any of the significant clusters (all Ps < 0.05). To validate and explore the lack of an age × ANT interaction on thickness, we split the full sample into 2 groups at the median age (51 years) and correlated cortical thickness in each cluster's peak vertex with its relevant ANT score in the youngest (n = 132) and the oldest (n = 128) group independently while partialling out age and sex. For the EC network, we found the following coefficients for the young/old groups in the left anterior cingulate cluster: r = –0.21/–0.39, the left superior temporal cluster: r = –0.15/–0.20, the right middle temporal cluster: r = –0.13/–0.28, and the right anterior cingulate cluster: –0.19/–0.15. For alerting, we found the following correlation coefficients in the left superior parietal cluster for the young/old group, respectively: r = –0.26/–0.14. Fischer's Z tests of the difference in the correlations revealed no differences between the young and the old group in any of the areas. Thus, although the brain–behavior relations were not entirely uniform across subgroups, no evidence of a systematically increasing or decreasing relationship with age was found in any of the clusters. This was also suggested by the lack of age × ANT interaction effects. For significance of the correlations and Fischer's Z scores of the difference between groups, please see Supplementary Table 5.

The mean and variability of the different measures is given in Supplementary Table 6. The 2 groups showed highly comparable variability in all measures. Briefly, the SD for the executive component was 6.64 and 6.03 for the young and old group, respectively. The rCoV for thickness in the peak areas showing significant correlations with the executive component were (young/old group) 6.9/7.8% and 9.4/10.0% for the 2 clusters in the left hemisphere and 8.8/9.4% and 7.9/7.7% for the 2 clusters in the right hemisphere. For alerting, SD in the young and old groups was 4.47 and 4.37, respectively. The rCoV for thickness in the peak vertex for the alerting effect was 7.6% in both groups. Lastly, SD for the orienting component was 6.00 and 5.89 in the young and old group, respectively. Summarized, we did not find evidence suggesting systematic differences in variability between the young and the old group in any of the measures. Thus, we do not think that the results can be explained by heteroscedasticity in any of the relevant variables.

Discussion

The current analyses demonstrated regionally specific correlations between cortical thickness and the EC and alerting attention components in a large healthy sample. The significant clusters comprised regions anticipated from previous functional neuroimaging and lesion studies, including the anterior cingulate cortex for EC and frontoparietal areas for alerting. The thickness–attention correlations were found independently of general intellectual abilities. Importantly, these findings pertain to the regional neurocognitive specificity of cortical thickness measures. Furthermore, the relatively stable brain–behavior relationships across age suggest that they at least in part likely originated in neurodevelopmental processes rather than aging-related cortical atrophy. The implications of the findings are discussed in detail below.

EC and Cortical Thickness

In line with our anatomical hypotheses based on previous functional neuroimaging and lesion studies, we found significant associations between EC and cortical thickness in the

caudal parts of the anterior cingulate gyri bilaterally, even though only the left anterior cingulate cluster survived the stringent correction for multiple comparisons. The right cluster was restricted to the cingulate and did thus not survive the cluster size thresholding applied. The anterior cingulate gyri, and in particular the caudal aspects, are implicated in a vast array of cognitive conflict processing (Bush et al. 2000; Cabeza and Nyberg 2000) and have also been shown to be activated in the ANT EC condition (Fan et al. 2005) as well as in other cognitive control tasks (Fan, Fossella, et al. 2003; Wager et al. 2005). The anterior cingulate cortex has a critical role in general cognitive conflict monitoring, while dorsolateral prefrontal cortex may be particularly implicated in the resolution of the perceived conflict (Carter et al. 1999; MacDonald et al. 2000; Botvinick et al. 2001; van Veen et al. 2001; Wager et al. 2005). Hence, the involvement of both areas in the EC network in the present study was anticipated. In line with this hypothesis, while the right cluster was spatially limited to the caudal anterior cingulate cortex, the left cluster also included other medial frontal areas extending into the frontal pole and parts of the dorsolateral prefrontal cortex. The raw *t*-maps suggested subthreshold effects across the full extent of the cingulate cortices, and the left posterior cingulate cortex showed uncorrected significant effects. Interestingly, we have previously demonstrated a correlation between the microstructural integrity of the subjacent white matter in the same area and the magnitude of the error-related negativity, which is an electrophysiological marker of error processing and conflict monitoring (Westlye, Walhovd, Bjørnerud, et al. 2009). In that study, we employed a modified version of the Eriksen flanker task (Eriksen BA and Eriksen CW 1974), which is very similar to the conflict condition in the ANT. Thus, evidence from 2 different modalities converges on the importance of structural properties of the posterior cingulate for efficient conflict monitoring and resolution as well as error processing.

The significant clusters also encompassed inferior frontal regions and insular cortices. The inferior frontal effects were especially pronounced in the right hemisphere, including the pars opercularis and triangularis as well as parts of the rostral middle frontal gyrus. Evidence from functional and structural neuroimaging and lesion studies suggests that the right inferior frontal gyrus is heavily involved in cognitive control processes related to inhibiting or delaying responses (Aron et al. 2003, 2004, 2007), processes facilitating performance on incongruent trials in the ANT. The right inferior frontal gyrus is also recruited when relevant cues are detected, regardless of whether that detection is followed by an inhibition of a motor response, the generation of a motor response, or no external process at all (Hampshire et al., 2010), which demonstrates the relevance to attentional processing.

We also found 2 bilateral clusters in the lateral aspects of the superior and middle temporal gyri extending into the occipitotemporal and temporoparietal junction. This is in line with previous studies having implicated the right superior and inferior temporal gyri in the EC network (Fan, Fossella, et al. 2003). Interestingly, in a developmental functional neuroimaging study, the right superior temporal gyrus was significantly more activated in children compared with adults in the conflict condition (Konrad et al. 2005), which either suggests a shift in the functional relevance of this area in a life span perspective or that children relies on different cognitive processes to solve the task. However, none of the effect sites showed an age by thickness interaction on the EC network in the present adult sample, suggesting stability of the brain–behavior correlations through the adult life span. This was also supported by the relatively constant correlations between ANT score and thickness across the age groups. Although the lack of an age × thickness interaction on ANT scores may be explained by insufficient statistical power, it could also suggest that the brain–behavior correlations are accounted for by neurodevelopmental processes rather than by aging-related atrophy. Further studies including children are needed to explore possible age by thickness interactions on the brain–behavior relations throughout maturation and aging.

Collectively, for the EC component, the analyses revealed a frontally distributed cortical network including the anterior cingulate cortices, which are involved in conflict and performance monitoring (Carter et al. 1999), and the right inferior frontal cortex, known to be important for response inhibition (Aron et al. 2004). All areas of effects showed a negative correlation with EC, indicating that thinner cortices in these areas are associated with relatively increased RT on incongruent compared with congruent trials independent of age and sex. This constitutes evidence that relationships between specific cognitive processes and brain structure in anatomically relevant areas can be identified, and further suggests that, at least for EC, this relationship results from neurodevelopmental processes.

Alerting and Cortical Thickness

We found a significant cluster in the lateral and medial aspects of the superior parietal lobe in the left hemisphere that correlated negatively with the alerting network. Thicker cortices in this cluster were associated with smaller alerting effects, independently of age and sex. The cluster also encompassed the posterior cingulate–retrosplenial cortices and parts of the precuneus. Early lesion studies suggested a specific involvement of frontoparietal areas in the alerting network, but in the right hemisphere (Posner and Petersen 1990; Robertson et al. 1995; Sturm and Willmes 2001). In line with our findings, a functional neuroimaging study reported increased alerting-related activation in left inferior and superior parietal lobes, as well as frontal areas (Fan et al. 2005). It has been speculated that strong left-hemisphere activation in the alerting condition (no cue–center cue) of the ANT could be explained by the fact that the warning cue is used by the participants to predict not only the location but also the timing of the target and thus serves both as a temporal and spatial cue (Coull et al. 2000; Fan et al. 2005). In the present version of the ANT, the interval between the warning cue and the target was kept constant, and it is thus reasonable to argue that the temporal aspect of the warning cue is important.

Two effect sites were found in the right temporal lobe, one in the anterior superior temporal gyrus and one in more posterior temporooccipital areas. The latter site is partly overlapping an area reported to be activated by Fan et al. (2005) as well as Thiel et al. (2004). However, since these effects did not survive corrections for multiple comparisons, further interpretations should be made with caution.

The associations between thickness and ANT component score were negative for both EC and alerting. Although the regional effects were nonoverlapping, this indicates that thinner cortices were associated with a relative decrease in attentional efficiency in incongruent compared with congruent

trials and increased beneficial effects of a warning cue. If assuming a simple bigger-is-better perspective and that increased alerting is positively related to cognitive function, the alerting results may seem counterintuitive. Several studies have revealed decreased cortical thickness in clinical disorders like AD (Singh et al. 2006; Lerch et al. 2008; Dickerson et al. 2009; Westlye, Walhovd, Dale, et al. 2009), schizophrenia (Kuperberg et al. 2003; Douaud et al. 2007; Nesvag et al. 2008), and ADHD (Shaw, Lerch, et al. 2006; Makris et al. 2007), and also in nonpathological aging (Salat et al. 2004; Fjell, Walhovd, et al. 2009; Fjell, Westlye, et al. 2009; Westlye et al., forthcoming a). A typical interpretation of adult cortical thinning is that degenerative processes including shrinkage of large neurons (Terry et al. 1987), loss of myelinated axonal fibers (Nairn et al. 1989), deafferentation (Bertoni-Freddari et al. 2002), and reduction in synaptic density (Morrison and Hof 1997) causes a shrinkage of the cortical ribbon. Thus, a relative thinning of the cerebral cortex in aging is usually associated with decreased cognitive function (Fjell et al. 2006; Dickerson et al. 2008; Chee et al. 2009).

A possible explanation for the negative correlations between alerting and thickness is that high alerting effects may be negatively related to cognitive function and brain integrity. However, we found no evidence of an intrinsic relationship between alerting and general intellectual abilities. Increased alerting effects have been reported in healthy old compared with young participants (Fernandez-Duque and Black 2006). The findings were interpreted to indicate that older subjects had difficulty sustaining attention in the absence of an external cue and that they therefore were disproportionally slow in the no-cue condition. Thus, although we found a negative correlation between alerting and age, increased alerting may be indicative of a relative slowing on the no-cue trials, which may be related to task motivation or reduced tonic vigilance in the absence of external cues, and not necessarily an increased alertness effect of the warning cues per se. Future studies should explore this hypothesis by exploring the age-related alterations in alertness while experimentally manipulating task-related motivation.

The finding of an age-related shift in efficiency of the alerting cues is in line with evidence showing that when external sources of information (cues) are present, older adults are much more likely than younger adults to use them (Spieler et al. 2006). This supports age-related differences in the use of environmental information and context processing, which is proposed as a core feature underlying age-related changes in cognitive control mechanisms (Braver and Barch 2002).

Estimated cortical thickness is modulated by various imaging-related factors, and an apparent cortical thinning may in fact result from increased myelination of the subjacent neuropil, causing a relative shift of the WM/GM boundary (Sowell et al. 2001). We have recently demonstrated a relative independence of cortical thickness to the T_1-weighted signal intensity (which is partly modulated by the myeloarchitecture of the brain tissue) of the subjacent white matter (Westlye, Walhovd, Dale, et al. 2009) but recognize the possibility of an imaging-related interaction producing an artifactual shift in the tissue boundaries. Cortical thickness could be inversely related to the integrity of the subjacent white matter. Increased myelination may stretch the cortical surface tangentially, increasing the cortical columnar spacing and subsequently decreasing the thickness of the cortex (Seldon 2005). Regional increase in columnar spacing may increase the capacity for differentiating afferent signals (Harasty et al. 2003) and thus produce a negative association between cortical thickness and function.

The brain–behavior correlations for alerting were not significantly different between the subsamples but the somewhat increased negative correlation in the young ($r = -0.26$, $P < 0.05$) versus the old group ($r = -0.14$, $P > 0.05$) could be taken to indicate that ongoing WM myelination in the young group (Westlye et al., forthcoming a, forthcoming b) may have modulated the negative correlations between alerting and cortical thickness. Although speculative, this model provides a possible mechanistic explanation for regionally specific negative associations between cortical thickness and cognitive function. Further studies utilizing multimodal imaging methodologies are needed in order to disentangle the neurocognitive correlates of cortical GM and white matter integrity, and the dynamic associations between cortical thickness and behavior throughout the life span.

Orienting and Cortical Thickness

We found no significant correlations between the orienting component and cortical thickness when correcting for multiple comparisons. Although left frontoparietal cortical areas have been shown to be implicated in this attentional system (Coull et al. 2000; Nobre 2001), a large body of evidence is pointing to the recruitment of a right-lateralized cortical network including prefrontal (the frontal eye fields) and parietal areas including the superior parietal cortex and the temporoparietal junction in orienting toward the spatial location of visual cues (Kastner et al. 1999; Corbetta and Shulman 2002; Fan et al. 2005). The raw *t*-maps yielded subthreshold positive relations between orienting and thickness in the temporoparietal junctions, bilaterally. These areas did not reach significance and should therefore be interpreted with great caution. The temporoparietal junction is, however, strongly activated when shifting or reorienting attention after an invalid cue (Corbetta and Shulman 2002; Thiel et al. 2004), which are not included in the version of ANT used in the present study. The present definition of the orienting network may recruit more distributed cortical areas and may therefore be less sensitive to systematic individual differences in regional cortical thickness. Although speculative, it is possible that including an invalid cue condition, and thereby invoking a reorienting component, could yield specific significant correlations with cortical thickness. Further studies should explore this hypothesis further.

Our hypotheses of neuroanatomical specificity in the present study were mainly based on previous functional imaging and lesion studies. However, the associations between functional and structural imaging indices of age-related decline and cognition are far from simple (Persson et al. 2006). For instance, cortical thickness alterations in response to cognitive training in one specific cortical area are not necessarily associated with regionally overlapping functional changes as indicated by functional MRI (Haier et al. 2009). Furthermore, functional imaging studies alone cannot establish that a brain area is necessary for a particular cognitive process (Fellows and Farah 2005) and converging evidence from lesion and structural and functional imaging studies are therefore highly valuable. To the degree that our results showed converging

evidence of regional correlations between cortical thickness and attentional functions, the present study strengthens the notion of specific involvement of functional cortical networks in the executive and alerting component of attention. However, interpretation of the present results must be done with caution, as the relationship between structural and functional brain measures are complex, especially in a life span perspective.

It is well known that various volumetric and other brain structural measures change in a nonlinear fashion through the life span (Jernigan et al. 2001; Raz et al. 2005; Walhovd et al. 2005; Raz and Rodrigue 2006; Walhovd et al., forthcoming; Westlye et al., forthcoming b). However, cortical thickness shows remarkably linear patterns of life span changes (Fjell, Westlye, et al. 2009; Westlye et al., forthcoming a). For instance, we did not find significant quadratic effects of age on cortical thickness in 883 adults aged 18–93 years of age (Fjell, Westlye, et al. 2009). Thus, we believe it is less likely that nonlinear age-related changes in thickness influenced the brain–behavior correlations in the present study.

Cognitive and brain functional and structural effects of aging may be interpreted within the framework of the hemispheric asymmetry reduction in older adults (Cabeza 2002). This model proposes that task-related changes in functional activity in aging may reflect different mechanisms, including functional compensation, dedifferentiation, and neural noise. While the compensation view proposes that age-related asymmetry reductions counteract age-related cognitive decline, the differentiation perspective posits that increased functional symmetry may be interpreted as difficulties in recruiting specialized neuronal circuits (Cabeza 2002). In the present study, we found a relative stability in the relations between regional cortical thickness and the executive and alerting components of attention in aging. However, we cannot rule out the possibility of age-related changes in processing mechanisms related to compensation or dedifferentiation of cognitive and neuronal recruitment. Thus, further studies combining functional and structural imaging in the same sample are warranted.

Conclusion

In conclusion, this is the first study to demonstrate specific correlations between the executive and alerting components of attention and cortical thickness in anatomically relevant regions. The results thus provide evidence for specific attention-related cortical networks based on structural neuroimaging. Although further studies are needed, our results suggest that the neuroanatomical basis for the individual differences in attention functions in healthy adults results from neurodevelopmental processes rather than cortical atrophy in aging. Future studies may utilize a longitudinal design in order to delineate behavioral and brain–behavior interactions on an individual level.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

Funding

Norwegian Research Council (177404/W50 to K.B.W. and 175066/D15 to A.M.F.); University of Oslo to K.B.W. and A.M.F.

Notes

Conflict of Interest: None declared.

References

Adolfsdottir S, Sorensen L, Lundervold AJ. 2008. The attention network test: a characteristic pattern of deficits in children with ADHD. Behav Brain Funct. 4:9.

Aron AR, Behrens TE, Smith S, Frank MJ, Poldrack RA. 2007. Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. J Neurosci. 27:3743–3752.

Aron AR, Fletcher PC, Bullmore ET, Sahakian BJ, Robbins TW. 2003. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat Neurosci. 6:115–116.

Aron AR, Robbins TW, Poldrack RA. 2004. Inhibition and the right inferior frontal cortex. Trends Cogn Sci. 8:170–177.

Beane M, Marrocco RT. 2004. Norepinephrine and acetylcholine mediation of the components of reflexive attention: implications for attention deficit disorders. Prog Neurobiol. 74:167–181.

Beck AT, Steer R. 1987. Beck depression inventory scoring manual. New York: The Psychological Corporation.

Bertoni-Freddari C, Fattoretti P, Delfino A, Solazzi M, Giorgetti B, Ulrich J, Meier-Ruge W. 2002. Deafferentative synaptopathology in physiological aging and Alzheimer's disease. Ann N Y Acad Sci. 977:322–326.

Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. 2001. Conflict monitoring and cognitive control. Psychol Rev. 108:624–652.

Braver TS, Barch DM. 2002. A theory of cognitive control, aging cognition, and neuromodulation. Neurosci Biobehav Rev. 26:809–817.

Bravo G, Hebert R. 1997. Age- and education-specific reference values for the Mini-Mental and modified Mini-Mental State Examinations derived from a non-demented elderly population. Int J Geriatr Psychiatry. 12:1008–1018.

Brocki K, Clerkin SM, Guise KG, Fan J, Fossella JA. 2009. Assessing the molecular genetics of the development of executive attention in children: focus on genetic pathways related to the anterior cingulate cortex and dopamine. Neuroscience. 164:241–246.

Brunye TT, Mahoney CR, Lieberman HR, Taylor HA. 2010. Caffeine modulates attention network function. Brain Cogn. 72:181–188.

Bush G, Luu P, Posner MI. 2000. Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci. 4:215–222.

Cabeza R. 2002. Hemispheric asymmetry reduction in older adults: the HAROLD model. Psychol Aging. 17:85–100.

Cabeza R, Nyberg L. 2000. Imaging cognition II: an empirical review of 275 PET and fMRI studies. J Cogn Neurosci. 12:1–47.

Callejas A, Lupianez J, Funes MJ, Tudela P. 2005. Modulations among the alerting, orienting and executive control networks. Exp Brain Res. 167:27–37.

Callejas A, Lupianez J, Tudela P. 2004. The three attentional networks: on their independence and interactions. Brain Cogn. 54:225–227.

Carter CS, Botvinick MM, Cohen JD. 1999. The contribution of the anterior cingulate cortex to executive processes in cognition. Rev Neurosci. 10:49–57.

Chee MW, Chen KH, Zheng H, Chan KP, Isaac V, Sim SK, Chuah LY, Schuchinsky M, Fischl B, Ng TP. 2009. Cognitive function and brain structure correlations in healthy elderly East Asians. Neuroimage. 46:257–269.

Corbetta M, Kincade JM, Ollinger JM, McAvoy MP, Shulman GL. 2000. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat Neurosci. 3:292–297.

Corbetta M, Shulman GL. 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci. 3:201–215.

Costa A, Hernandez M, Sebastian-Galles N. 2008. Bilingualism aids conflict resolution: evidence from the ANT task. Cognition. 106:59–86.

Coull JT, Frith CD, Buchel C, Nobre AC. 2000. Orienting attention in time: behavioural and neuroanatomical distinction between exogenous and endogenous shifts. Neuropsychologia. 38:808–819.

Coull JT, Frith CD, Frackowiak RS, Grasby PM. 1996. A fronto-parietal network for rapid visual information processing: a PET study of sustained attention and working memory. Neuropsychologia. 34:1085–1095.
Dale AM, Fischl B, Sereno MI. 1999. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage. 9:179–194.
Dale AM, Sereno MI. 1993. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. J Cogn Neurosci. 5:162–176.
Davidson MC, Marrocco RT. 2000. Local infusion of scopolamine into intraparietal cortex slows covert orienting in rhesus monkeys. J Neurophysiol. 83:1536–1549.
Dickerson BC, Feczko E, Augustinack JC, Pacheco J, Morris JC, Fischl B, Buckner RL. 2009. Differential effects of aging and Alzheimer's disease on medial temporal lobe cortical thickness and surface area. Neurobiol Aging. 30:432–440.
Dickerson BC, Fenstermacher E, Salat DH, Wolk DA, Maguire RP, Desikan R, Pacheco J, Quinn BT, Van der Kouwe A, Greve DN, et al. 2008. Detection of cortical thickness correlates of cognitive performance: reliability across MRI scan sessions, scanners, and field strengths. Neuroimage. 39:10–18.
Douaud G, Smith S, Jenkinson M, Behrens T, Johansen-Berg H, Vickers J, James S, Voets N, Watkins K, Matthews PM, et al. 2007. Anatomically related grey and white matter abnormalities in adolescent-onset schizophrenia. Brain. 130:2375–2386.
Egan MF, Goldberg TE, Kolachana BS, Callicott JH, Mazzanti CM, Straub RE, Goldman D, Weinberger DR. 2001. Effect of COMT Val108/158 Met genotype on frontal lobe function and risk for schizophrenia. Proc Natl Acad Sci U S A. 98:6917–6922.
Eriksen BA, Eriksen CW. 1974. Effects of noise letters upon the identification of a target letter in a nonsearch task. Percept Psychophys. 16:143–149.
Fan J, Byrne J, Worden MS, Guise KG, McCandliss BD, Fossella J, Posner MI. 2007. The relation of brain oscillations to attentional networks. J Neurosci. 27:6197–6206.
Fan J, Flombaum JI, McCandliss BD, Thomas KM, Posner MI. 2003. Cognitive and brain consequences of conflict. Neuroimage. 18:42–57.
Fan J, Fossella J, Sommer T, Wu Y, Posner MI. 2003. Mapping the genetic variation of executive attention onto brain activity. Proc Natl Acad Sci U S A. 100:7406–7411.
Fan J, Gu X, Guise KG, Liu X, Fossella J, Wang H, Posner MI. 2009. Testing the behavioral interaction and integration of attentional networks. Brain Cogn. 70:209–220.
Fan J, McCandliss BD, Fossella J, Flombaum JI, Posner MI. 2005. The activation of attentional networks. Neuroimage. 26:471–479.
Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. 2002. Testing the efficiency and independence of attentional networks. J Cogn Neurosci. 14:340–347.
Fellows LK, Farah MJ. 2005. Is anterior cingulate cortex necessary for cognitive control? Brain. 128:788–796.
Fernandez-Duque D, Black SE. 2006. Attentional networks in normal aging and Alzheimer's disease. Neuropsychology. 20:133–143.
Fischl B, Dale AM. 2000. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci U S A. 97:11050–11055.
Fischl B, Liu A, Dale AM. 2001. Automated manifold surgery: constructing geometrically accurate and topologically correct models of the human cerebral cortex. IEEE Trans Med Imaging. 20:70–80.
Fischl B, Sereno MI, Dale AM. 1999. Cortical surface-based analysis. II: inflation, flattening, and a surface-based coordinate system. Neuroimage. 9:195–207.
Fischl B, Sereno MI, Tootell RB, Dale AM. 1999. High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum Brain Mapp. 8:272–284.
Fjell AM, Walhovd KB, Fennema-Notestine C, McEvoy LK, Hagler DJ, Holland D, Brewer JB, Dale AM. 2009. One-year brain atrophy evident in healthy aging. J Neurosci. 29:15223–15231.
Fjell AM, Walhovd KB, Reinvang I, Lundervold A, Salat D, Quinn BT, Fischl B, Dale AM. 2006. Selective increase of cortical thickness in high-performing elderly-structural indices of optimal cognitive aging. Neuroimage. 29:984–994.
Fjell AM, Westlye LT, Amlien I, Espeseth T, Reinvang I, Raz N, Agartz I, Salat DH, Greve DN, Fischl B, et al. 2009. High consistency of regional cortical thinning in aging across multiple samples. Cereb Cortex. 19:2001–2012.
Fjell AM, Westlye LT, Greve DN, Fischl B, Benner T, van der Kouwe AJ, Salat D, Bjørnerud A, Due-Tønnessen P, Walhovd KB. 2008. The relationship between diffusion tensor imaging and volumetry as measures of white matter properties. Neuroimage. 42:1654–1668.
Folstein MF, Folstein SE, McHugh PR. 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 12:189–198.
Fossella J, Fan J, Liu X, Guise K, Brocki K, Hof PR, Kittappa R, McKay R, Posner M. 2008. Provisional hypotheses for the molecular genetics of cognitive development: imaging genetic pathways in the anterior cingulate cortex. Biol Psychol. 79:23–29.
Fossella J, Sommer T, Fan J, Wu Y, Swanson JM, Pfaff DW, Posner MI. 2002. Assessing the molecular genetics of attention networks. BMC Neurosci. 3:14.
Hagler DJ, Jr, Saygin AP, Sereno MI. 2006. Smoothing and cluster thresholding for cortical surface-based group analysis of fMRI data. Neuroimage. 33:1093–1103.
Haier RJ, Karama S, Leyba L, Jung RE. 2009. MRI assessment of cortical thickness and functional activity changes in adolescent girls following three months of practice on a visual-spatial task. BMC Res Notes. 2:174.
Hampshire A, Chamberlain SR, Monti MM, Duncan J, Owen AM. 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage. 50:1313–1319.
Harasty J, Seldon HL, Chan P, Halliday G, Harding A. 2003. The left human speech-processing cortex is thinner but longer than the right. Laterality. 8:247–260.
Hayasaka S, Nichols TE. 2003. Validating cluster size inference: random field and permutation methods. Neuroimage. 20:2343–2356.
Jennings JM, Dagenbach D, Engle CM, Funke LJ. 2007. Age-related changes and the attention network task: an examination of alerting, orienting, and executive function. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 14:353–369.
Jernigan TL, Archibald SL, Fennema-Notestine C, Gamst AC, Stout JC, Bonner J, Hesselink JR. 2001. Effects of age on tissues and regions of the cerebrum and cerebellum. Neurobiol Aging. 22:581–594.
Johnson KA, Robertson IH, Barry E, Mulligan A, Daibhis A, Daly M, Watchorn A, Gill M, Bellgrove MA. 2008. Impaired conflict resolution and alerting in children with ADHD: evidence from the Attention Network Task (ANT). J Child Psychol Psychiatry. 49:1339–1347.
Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG. 1999. Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron. 22:751–761.
Konrad K, Neufang S, Hanisch C, Fink GR, Herpertz-Dahlmann B. 2006. Dysfunctional attentional networks in children with attention deficit/hyperactivity disorder: evidence from an event-related functional magnetic resonance imaging study. Biol Psychiatry. 59:643–651.
Konrad K, Neufang S, Thiel CM, Specht K, Hanisch C, Fan J, Herpertz-Dahlmann B, Fink GR. 2005. Development of attentional networks: an fMRI study with children and adults. Neuroimage. 28:429–439.
Kuperberg GR, Broome MR, McGuire PK, David AS, Eddy M, Ozawa F, Goff D, West WC, Williams SC, van der Kouwe AJ, et al. 2003. Regionally localized thinning of the cerebral cortex in schizophrenia. Arch Gen Psychiatry. 60:878–888.
Lerch JP, Pruessner J, Zijdenbos AP, Collins DL, Teipel SJ, Hampel H, Evans AC. 2008. Automated cortical thickness measurements from MRI can accurately separate Alzheimer's patients from normal elderly controls. Neurobiol Aging. 29:23–30.
MacDonald AW, 3rd, Cohen JD, Stenger VA, Carter CS. 2000. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science. 288:1835–1838.
Makris N, Biederman J, Valera EM, Bush G, Kaiser J, Kennedy DN, Caviness VS, Faraone SV, Seidman LJ. 2007. Cortical thinning of the

attention and executive function networks in adults with attention-deficit/hyperactivity disorder. Cereb Cortex. 17:1364–1375.
Mesulam MM. 1981. A cortical network for directed attention and unilateral neglect. Ann Neurol. 10:309–325.
Mesulam MM. 1999. Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. Philos Trans R Soc Lond B Biol Sci. 354:1325–1346.
Morrison JH, Hof PR. 1997. Life and death of neurons in the aging brain. Science. 278:412–419.
Nairn JG, Bedi KS, Mayhew TM, Campbell LF. 1989. On the number of Purkinje cells in the human cerebellum: unbiased estimates obtained by using the "fractionator". J Comp Neurol. 290:527–532.
Narr KL, Woods RP, Thompson PM, Philip Szeszko P, Robinson D, Dimtcheva T, Gurbani M, Toga AW, Bilder RM. 2007. Relationships between IQ and regional cortical gray matter thickness in healthy adults. Cereb Cortex. 17:2163–2171.
Nestor PG, Kubicki M, Spencer KM, Niznikiewicz M, McCarley RW, Shenton ME. 2007. Attentional networks and cingulum bundle in chronic schizophrenia. Schizophr Res. 90:308–315.
Nesvag R, Lawyer G, Varnas K, Fjell AM, Walhovd KB, Frigessi A, Jonsson EG, Agartz I. 2008. Regional thinning of the cerebral cortex in schizophrenia: effects of diagnosis, age and antipsychotic medication. Schizophr Res. 98:16–28.
Neuhaus AH, Urbanek C, Opgen-Rhein C, Hahn E, Ta TM, Koehler S, Gross M, Dettling M. 2010. Event-related potentials associated with Attention Network Test. Int J Psychophysiol. 76:72–79.
Nobre AC. 2001. Orienting attention to instants in time. Neuropsychologia. 39:1317–1328.
Parasuraman R, Greenwood PM, Kumar R, Fossella J. 2005. Beyond heritability: neurotransmitter genes differentially modulate visuospatial attention and working memory. Psychol Sci. 16:200–207.
Persson J, Nyberg L, Lind J, Larsson A, Nilsson L-G, Ingvar M, Buckner RL. 2006. Structure-function correlates of cognitive decline in aging. Cereb Cortex. 16:907–915.
Pizzo R, Urben S, Van der Linden M, Borradori-Tolsa C, Freschi M, Forcada-Guex M, Huppi P, Barisnikov K. 2009. Attentional networks efficiency in preterm children. J Int Neuropsychol Soc. 16:130–137.
Posner MI. 1980. Orienting of attention. Q J Exp Psychol. 32:3–25.
Posner MI. 2008. Measuring alertness. Ann N Y Acad Sci. 1129:193–199.
Posner MI, Petersen SE. 1990. The attention system of the human brain. Annu Rev Neurosci. 13:25–42.
Raz N, Lindenberger U, Rodrigue KM, Kennedy KM, Head D, Williamson A, Dahle C, Gerstorf D, Acker JD. 2005. Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. Cereb Cortex. 15:1676–1689.
Raz N, Rodrigue KM. 2006. Differential aging of the brain: patterns, cognitive correlates and modifiers. Neurosci Biobehav Rev. 30:730–748.
Robertson IH, Tegner R, Tham K, Lo A, Nimmo-Smith I. 1995. Sustained attention training for unilateral neglect: theoretical and rehabilitation implications. J Clin Exp Neuropsychol. 17:416–430.
Rueda MR, Fan J, McCandliss BD, Halparin JD, Gruber DB, Lercari LP, Posner MI. 2004. Development of attentional networks in childhood. Neuropsychologia. 42:1029–1040.
Salat DH, Buckner RL, Snyder AZ, Greve DN, Desikan RS, Busa E, Morris JC, Dale AM, Fischl B. 2004. Thinning of the cerebral cortex in aging. Cereb Cortex. 14:721–730.
Segonne F, Dale AM, Busa E, Glessner M, Salat D, Hahn HK, Fischl B. 2004. A hybrid approach to the skull stripping problem in MRI. Neuroimage. 22:1060–1075.
Seldon HL. 2005. Does brain white matter growth expand the cortex like a balloon? Hypothesis and consequences. Laterality. 10:81–95.
Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, Evans A, Rapoport J, Giedd J. 2006. Intellectual ability and cortical development in children and adolescents. Nature. 440:676–679.
Shaw P, Lerch J, Greenstein D, Sharp W, Clasen L, Evans A, Giedd J, Castellanos FX, Rapoport J. 2006. Longitudinal mapping of cortical thickness and clinical outcome in children and adolescents with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry. 63:540–549.
Singh V, Chertkow H, Lerch JP, Evans AC, Dorr AE, Kabani NJ. 2006. Spatial patterns of cortical thinning in mild cognitive impairment and Alzheimer's disease. Brain. 129:2885–2893.
Sowell ER, Thompson PM, Tessner KD, Toga AW. 2001. Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: inverse relationships during postadolescent brain maturation. J Neurosci. 21:8819–8829.
Spieler DH, Mayr U, LaGrone S. 2006. Outsourcing cognitive control to the environment: adult age differences in the use of task cues. Psychol Bull Rev. 13:787–793.
Sturm W, Willmes K. 2001. On the functional neuroanatomy of intrinsic and phasic alertness. Neuroimage. 14:S76–S84.
Terry RD, DeTeresa R, Hansen LA. 1987. Neocortical cell counts in normal human adult aging. Ann Neurol. 21:530–539.
Thiel CM, Zilles K, Fink GR. 2004. Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: an event-related fMRI study. Neuroimage. 21:318–328.
Van Petten C. 2004. Relationship between hippocampal volume and memory ability in healthy individuals across the lifespan: review and meta-analysis. Neuropsychologia. 42:1394–1413.
van Veen V, Cohen JD, Botvinick MM, Stenger VA, Carter CS. 2001. Anterior cingulate cortex, conflict monitoring, and levels of processing. Neuroimage. 14:1302–1308.
Wager TD, Sylvester CY, Lacey SC, Nee DE, Franklin M, Jonides J. 2005. Common and unique components of response inhibition revealed by fMRI. Neuroimage. 27:323–340.
Walhovd KB, Fjell AM, Dale AM, Fischl B, Quinn BT, Makris N, Salat D, Reinvang I. 2006. Regional cortical thickness matters in recall after months more than minutes. Neuroimage. 31:1343–1351.
Walhovd KB, Fjell AM, Reinvang I, Lundervold A, Dale AM, Eilertsen DE, Quinn BT, Salat D, Makris N, Fischl B. 2005. Effects of age on volumes of cortex, white matter and subcortical structures. Neurobiol Aging. 26:1261–1270: discussion 1275–1278.
Walhovd KB, Westlye LT, Amlien I, Espeseth T, Reinvang I, Raz N, Agartz I, Salat D, Greve DN, Fischl B, et al. Forthcoming. Consistent neuroanatomical age-related volume differences across multiple samples. Neurobiol Aging. doi: 10.1016/j.neurobiolaging.2009.05.013.
Wang K, Fan J, Dong Y, Wang CQ, Lee TM, Posner MI. 2005. Selective impairment of attentional networks of orienting and executive control in schizophrenia. Schizophr Res. 78:235–241.
Wechsler D. 1999. Wechsler abbreviated scale of intelligence. San Antonio (TX): The Psychological Corporation.
Westlye LT, Walhovd KB, Bjørnerud A, Due-Tønnessen P, Fjell AM. 2009. Error-related negativity is mediated by fractional anisotropy in the posterior cingulate gyrus—a study combining diffusion tensor imaging and electrophysiology in healthy adults. Cereb Cortex. 19:293–304.
Westlye LT, Walhovd KB, Dale AM, Bjørnerud A, Due-Tønnessen P, Engvig A, Grydeland H, Tamnes CK, Østby Y, Fjell AM. Forthcoming a. Differentiating maturational and aging-related changes of the cerebral cortex by use of thickness and signal intensity. Neuroimage. doi: 10.1016/j.neuroimage.2010.03.056.
Westlye LT, Walhovd KB, Dale AM, Bjornerud A, Due-Tonnessen P, Engvig A, Grydeland H, Tamnes CK, Ostby Y, Fjell AM. Forthcoming b. Life-span changes of the human brain white matter: Diffusion Tensor Imaging (DTI) and volumetry. Cereb Cortex. doi: 10.1093/cercor/bhp280.
Westlye LT, Walhovd KB, Dale AM, Espeseth T, Reinvang I, Raz N, Agartz I, Greve DN, Fischl B, Fjell AM. 2009. Increased sensitivity to effects of normal aging and Alzheimer's disease on cortical thickness by adjustment for local variability in gray/white contrast: a multi-sample MRI study. Neuroimage. 47:1545–1557.