

White matter volume predicts reaction time instability

Kristine B. Walhovd^{a,b,*}, Anders M. Fjell^{a,b,*}

^a University of Oslo, Institute of Psychology, POB 1094 Blindern, 0317 Oslo, Norway

^b Ullevaal University Hospital, Department of Neuropsychology, Oslo, Norway

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Abstract

Information processing speed is a central concept in cognitive psychology and neuropsychology. Previous studies have mostly focused on mean reaction time (RT), and largely ignored intra-individual differences (the standard deviation of the RT: sdRT). Still, intra-individual inconsistency across trials has been shown to correlate with age, neurological disorders, intelligence, and performance on cognitive tests. However, sdRT has not been correlated with neuroanatomical variables. Such knowledge is important to the understanding of the neurobiological foundation for intra-individual variability. In the present study, white matter (WM) and cortical gray matter (GM) volume obtained from the average of two MR scans of 71 healthy participants (aged 20–88 years) were correlated with sdRT and mean RT obtained from a 3-stimulus visual oddball task. Negative correlations were hypothesized between sdRT and WM and between mean RT and cortical GM volume. These hypotheses were confirmed. The correlation between sdRT and WM volume was significant also independently of effects of age, gender, and mean RT, while there was a trend towards a significant correlation ($p = .085$) between cortical GM volume and mean RT independently of age. A path model was constructed, showing that age and sdRT gave independent contributions to the variance in performance intelligence, and that WM volume predicted performance score through the influence of sdRT. Further, sdRT was a stronger predictor of performance intelligence than mean RT. It is concluded that sdRT and mean RT may have different neuroanatomical correlates, and that sdRT is related to WM characteristics of the brain.

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1. Introduction

Speed of information processing is related to general intelligence (Deary, 2001), brain volume (Walhovd, Fjell, Reinvang, Lundervold, Fischl, et al., 2005), and cognitive abilities in normal aging (Salthouse & Ferrer-Caja, 2003), and standardized neuropsychological batteries contain speeded tests. Often, speed of information processing is operationalized as reaction time (RT), usually measured as the mean or median across multiple trials. This rests on an assumption that inter-trial inconsistencies can be treated as “noise”, and that the mean constitutes the “signal”. However, an accumulating body of evidence indicates that the variability of the single trial RT, the intra-individual variability, is in itself a measure of cognitive and central nervous system

function. Jensen (1992) showed that mean RT and variations in single trial RT, even though correlated, have independent components, both related to the psychometric g . In a review, Hultsch and MacDonald (2004) argue that intra-individual inconsistency across trials, tasks, and times correlates with age, neurological disorders, intelligence and performance on cognitive tests. Still, much less attention has been devoted to variability across single trial RTs within the same task, than mean RTs across persons. While studies have reported correlations between speed of processing and measures of brain volume (e.g. Haier, Jung, Head, & Alkire, 2005; Walhovd, Fjell, Reinvang, Lundervold, Fischl, et al., 2005; Wickett, Vernon, & Lee, 2000), none has investigated relationships between volumetric measures and variability in single trial RT. The strategy of the present study is to correlate variability in single trial RT with volumes of cerebral gray (GM) and white matter (WM), and relate this to cognitive function.

Three main hypotheses were tested:

- (1) *Intra-individual variability in RT is negatively correlated with performance abilities, but not verbal abilities.* The

* Corresponding authors at: University of Oslo, Institute of Psychology, POB 1094 Blindern, 0317 Oslo, Norway. Tel.: +47 22 84 51 30; fax: +47 22 84 50 96.

E-mail addresses: k.b.walhovd@psykologi.uio.no (K.B. Walhovd), andersmf@psykologi.uio.no (A.M. Fjell).

rationale is that information processing speed is more important for time-limited cognitive tasks, i.e. performance abilities, than tasks where speed in itself is irrelevant. In the present study, the performance tests are speeded and time-limited, while the verbal tests do not have time limits. (This is, however, not true for all performance and verbal tests.)

(2) *Intra-individual variability in RT is negatively correlated with WM volume.*

Thickness of the myelin sheath is related to nerve conduction velocity, and correlations between WM characteristics and information processing speed have been reported (Cardenas et al., 2005; Haier et al., 2005; Tuch et al., 2005). The significance of WM for cognitive function is rooted in the spatial distribution of cognitive tasks in the brain, which typically involves a complex interplay between multiple areas, implying that the connections are important (Colom, Jung, & Haier, 2006; Schmithorst & Holland, 2006). Several previous studies, using different methods, e.g. diffusion tensor imaging (Schmithorst, Wilke, Dardzinski, & Holland, 2005) and measurements of *N*-acetylaspartate in WM (Jung et al., 1999, 2005), have reported relationships between WM characteristics and general intelligence. A relationship between intra-individual variability in RT and WM would fit well with the fact that WM volume mainly consists of myelinated neural connections, and that a high degree of myelination yields better isolation and hence more stable flow of electrical currents in dendrites and axons. Deficient myelination and neural noise can cause disruptions in the efficiency of the conduction of the action potential along the axon, and WM alterations may thus be a possible mechanism related to intraindividual variability in e.g. reaction time (Russell et al., 2006). Neural noise, caused by information loss (Myerson, Hale, Wagstaff, Poon, & Smith, 1990), or even random breaks in neural networks (Cerella, 1990), has also been implicated in age decline in cognitive performance. The connection between intraindividual variability and WM is further supported by evidence showing that WM volume increases until middle-age, before declining (Walhovd, Fjell, Reinvang, Lundervold, Dale, et al., 2005; Walhovd, Fjell, Reinvang, Lundervold, Eilertsen, et al., 2005), and that this quadratic, inverse U-form may fit with the nonlinear changes in intraindividual variability with increasing age (Li et al., 2004; MacDonald, Nyberg, & Bäckman, 2006; Williams, Hultsch, Strauss, & Hunter, 2005). The WM hypothesis is intriguing, because it relates the variability directly to flow of information in the CNS. This fits nicely also with models of neuromodulatory effects on variability. For instance, computational modeling has shown that reductions in dopamine levels will increase the intra-individual variability in RT (Li, Lindenberger, & Frensch, 2000). In sum, there is a possible correlation between WM volume and single trial variation in RT: less myelin may yield more neural noise and instability in the communication between areas. We expect correlations with single-trial variation in RT to be higher for WM than for cortical GM volume, since

myelination is especially important for stability of signal conduction.

- (3) *Mean RT is negatively correlated with cortical GM volume.* This is based on the reasoning that cortically distributed processing is needed to make decisions regarding stimulus classification, response selection and execution. Cautions must be noted, however. First, as argued by Haier et al. (2005), there is no clear empirical basis for predicting the directions of any correlations between RT and specific regional brain volumes. Haier et al. found that several Brodmann areas differed between a group of middle-aged and a group of elderly participants, such that less GM was related to slower RTs in a memory task in the middle-aged group, but to faster RTs in the group of elderly. However, Walhovd, Fjell, Reinvang, Lundervold, Fischl, et al. (2005), in a previous publication from the present study, found that the latency of the event-related component P3a correlated negatively with cortical GM volume, but only when age was not regressed out. Further, it was found that the P3a latency and cortical volume complementary predicted score on the performance scale of Wechsler's Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). Thus, this issue is not settled. Second, correlations also between mean RT and WM characteristics can be expected (Tuch et al., 2005). Haier et al. (2005) found that simple RT correlated negatively with WM in the right fusiform gyrus. The basis for this specific correlation is unclear, and no coherent set of findings exists to guide hypotheses regarding the exact nature of WM-RT correlations. However, a negative WM-RT correlation is expected.

If these hypotheses are confirmed, we will use structural equation modeling to construct and test a path model of relationships between mean RT and intra-individual variability in RT, WM and cortical GM volume, age, and performance ability.

2. Methods

2.1. Sample

Participants were recruited among employees from a local hospital, through charity organizations, activity centers for the elderly, and newspaper ads. All gave informed consent, and were screened by interview for conditions known to affect CNS-functioning (see Walhovd and Fjell, 2002). Further, Beck Depression Inventory (BDI; Beck & Steer, 1987), Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999), and the Mini Mental Status Exam (MMSE; Folstein, Folstein, & McHugh, 1975) were administered. The final sample consisted of 71 participants (40 females), aged 20–88 years (mean = 52.1). Participants were given a moderate sum of money to refund possible costs, and were required to have normal or corrected to normal vision, a MMSE score >25 (range 26–30, mean = 28.9), a BDI score <15 (range 0–14, mean = 4.3, administered to 63 of 71 participants), and an IQ score of ≥ 85 (range 85–134, mean = 114).

2.2. Reaction time task

RT was recorded during a three-stimuli visual oddball task with a total of 210 stimuli in an event-related potential (ERP) experiment. The ERP-data are reported elsewhere (Walhovd, Fjell, Reinvang, Lundervold, Fischl, et al., 2005). An overview of the task is presented in Fig. 1. Target and standard probability were both .10. Participants were instructed to press a button when seeing a

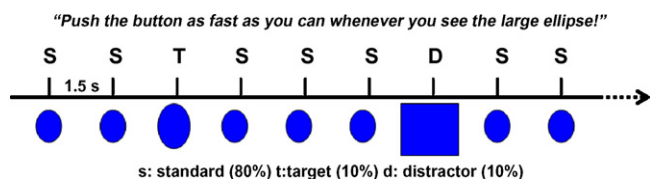


Fig. 1. Overview of the task. The reaction times were recorded in a 3-stimuli oddball task performed under an ERP-experiment. The task was to push a button as fast as possible whenever the larger of two elliptic shapes were presented. The large ellipse was the target, and a small ellipse was the standard. In addition, a distractor stimuli (a large square) was presented on some trials. The task included a total of 210 stimuli, with 80% standards and 10% targets and distractors. Inter-stimulus interval was 1.5 s, and each stimulus was presented for 0.5 s.

target stimulus, and ignore the standard and distractor stimuli. Standards were blue elliptic shapes (height 15 cm, width 12.5 cm), targets were blue elliptic shapes (height 17.5 cm, width 14.5 cm), and distractors were blue rectangles (21 cm × 17 cm). In the string of the 168 standards, 21 distractors and 21 targets were presented at random intervals. Stimuli were presented on a 21-in. computer screen with a black background, with a visual field of about $9^\circ \times 7^\circ$, $10^\circ \times 8^\circ$, and $12^\circ \times 10^\circ$ for standards, targets, and distractors, respectively. Viewing distance was 100 cm. Presentation time was 0.5 s and ISI was 1.5 s. Before recording, an example with eight standard and three target stimuli was presented to prime participants for the task and ascertain that all could discriminate targets from standards. The example was repeated if necessary. Participants were asked to press the button as fast as they could, but prioritize few errors over fast reaction times. Cut-off criteria for task performance were set to 20% target misses, 20% responses to standards, or 25% responses to distractors. All participants but one performed above these criteria, yielding the above described $n = 71$.

In multi-trial tasks, there is a risk that RT on some trials can deviate much from the rest, e.g. RT on the first trial. Inter-item reliability analysis of the 21 trials was performed to check whether any were deviant and should be excluded. In these analyses, missing values were replaced by values inferred from linear interpolations. Cronbach's alpha was .96 and mean inter-item correlation was .60, indicating high inter-item reliability. Inspections of the corrected item-total correlations revealed that trial 1 and 21 had lower correlations than the other 19 items, with r 's of .38 and .23, respectively. The third lowest correlation coefficient was .49. Thus, trials 1 and 21 were excluded from the rest of the analyses, yielding a new alpha of .97. Odd-even analyses were then computed, yielding correlations for mean RT of .99 ($p < .0001$) and for intra-individual variability in RT (sdRT, see below) of .90 ($p < .0001$). Together with the high Cronbach's alpha value, this indicates that both the mean RT and the sdRT have some degree of stability.

2.3. Intelligence testing

WASI measures verbal and performance abilities and consists of four subtests which were used to calculate an age-adjusted IQ-score. In addition, a performance and a verbal score not adjusted for age were computed. This was done by calculating a mean T -score using the sample mean and standard deviations, for

the two time-limited performance subtests; matrix reasoning and block design, and a mean T -score for the two verbal subtests; similarities and vocabulary, which are not time limited. The mean IQ in the total sample and on the female and male part is presented in Table 1.

2.4. 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. All scans were segmented as described by Fischl et al. (2002), yielding volumetric data for cortical GM volume and WM volume. The results of manual labeling using the validated techniques of the Center for Morphometric Analysis (Caviness, Filipek, & Kennedy, 1989; Goldstein et al., 1999; Kennedy, Filipek, & Caviness, 1989; Seidman et al., 1999) are used to automatically extract the information required for automating the segmentation procedure. This procedure automatically assigns a neuroanatomical label to each voxel in an MRI volume based on probabilistic information automatically estimated from a manually labeled training set. Briefly, the segmentation is carried out as follows. First, an optimal linear transform is computed that maximizes the likelihood of the input image, given an atlas constructed from manually labelled images. Next, a nonlinear transform is initialized with the linear one, and the image is allowed to further deform to better match the atlas. Finally, a Bayesian segmentation procedure is carried out, and the maximum a posteriori (MAP) estimate of the labeling is computed. The segmentation uses three pieces of information to disambiguate labels: (1) the prior probability of a given tissue class occurring at a specific atlas location, (2) the likelihood of the image given that tissue class, and (3) the probability of the local spatial configuration of labels given the tissue class. This latter term represents a large number of constraints on the space of allowable segmentations, and prohibits label configurations that never occur in the training set. The technique has previously been shown to be comparable in accuracy to manual labeling (Fischl et al., 2002). Intracranial volume (ICV) was calculated based on proton density- (PD) weighted low-flip angle FLASH scans obtained during the same scanning session as the scans used for automatic labeling. A deformable template procedure, similar to the "Shrink Wrapping" procedure described by Dale and Sereno (1993) and Dale, Fischl, and Sereno (1999), was used to obtain an estimate of the smooth surface surrounding the intracranial space (containing brain, CSF, and meninges).

Left and right hemisphere WM both correlated .999 with total WM volume, and left and right cortical GM volume correlated .997 and .996 with total cortical GM volume, respectively. Thus, all analyses were done with total WM and total cortical GM volume, not with volumes for each hemisphere separately. Mean and S.D. for cortical GM, WM, and intracranial volume are presented in Table 1.

2.5. Statistical analyses

WM and cortical GM volume values were summed across hemispheres and regressed on intracranial volume. The standardized residuals were used in all

Table 1
Sample characteristics

	Total sample ($n = 71$) mean (S.D.)	Females ($n = 40$)	Males ($n = 31$)
Age	51.9 (20.6)	48.4 (20.1)	56.5 (20.6)
IQ	114 (10)	112 (10)	115 (10)
Mean RT (ms)	505 (74)	509 (75)	500 (73)
sdRT (ms)	85 (31)	84 (32)	87 (29)
sdRT normalized (ms)	0 (0)	−0.09 (0.88)	.11 (1.13)
Cortical GM volume (mm ³)	463385 (61139)	453153 (57282)	476588 (64317)
WM volume (mm ³)	388289 (55967)	375574 (38894)	404695 (69632)
Intracranial volume (mm ³)	1582074 (103295)	1506811 (948375)	1679186 (126494)

RT: reaction time; WM: white matter; sdRT: the standard deviation of the RT; sdRT normalized: the residuals after the effect of mean RT is regressed out from the sdRT.

analyses. This approach is commonly used (Van Petten, 2004), and was chosen to remove variance associated with head size, which is related to variables such as general body size and gender (Peters et al., 1998). Two measures of intra-individual variability in RT were used. sdRT is the standard deviation of the RT's for each participant. Since sdRT and mean RT are expected to correlate, we also computed a normalized sdRT, where the effect of mean RT was regressed out, and the standardized residuals were used in the analyses.

Pearson correlations between RT (mean RT, sdRT, normalized sdRT) and cognition (performance and verbal score), age, and brain volumes (WM, cortical GM volume) were computed. The relationships were re-tested by partial correlations controlling for the effect of age, and for the effect of age and gender. To test whether gender interacted with any of the independent variables, all the significant relationships were re-tested by multiple regression analyses. In these analyses, each dependent variable was simultaneously predicted from the independent variable it correlated with, in addition to gender, and the interaction of gender and the independent variable. If the interaction term was significant, it was concluded that gender had an effect on the observed relationship between the dependent and the independent variables. The same question was also tested with regard to age, where the same procedure of testing age-interactions by multiple regression analyses was performed.

Outlier analyses were performed based on calculating the studentized deleted residuals and the standardized predicted values. First, these were correlated. Correlations close to zero indicate that the residuals are non-related to the predicted variables, and thus that there are not general tendencies for outliers to strongly influence the observed relationships in certain directions. Next, individual occurrences of large studentized deleted residuals were inspected, leading to re-calculation of the correlations with a sample where all observations with a value of the square root of the square of the studentized deleted residual exceeding 2.5 were excluded.

Finally, a path model was constructed, with age as the single exogenous variable, performance score as the dependent variable, and WM, cortical GM volume, sdRT, and mean RT as mediators. Paths were drawn between all variables and performance score, from WM and cortical GM volume to sdRT and mean RT, from WM to cortical GM volume, and from sdRT to mean RT. The strategy was to test both the goodness of fit of the model, and the significance of each individual path. In case of insignificant paths, these were removed with a criterion of $p \geq .10$ (as is usual in stepwise approaches), and the model was tested again.

Amos 5 software was used for the path analyses (maximum likelihood method for fitting the model function), and SPSS 12.0.1 was used for the rest of the statistical analyses.

3. Results

First, mean RT and sdRT, with and without gender, age, and ICV regressed out, were correlated with the thickness of the cerebral cortical GM continuously across the brain surface. The false discovery rate was set to 0.05, and no results survived this

Table 3

Partial correlations between RT measures and cognitive ability and brain volumetry, controlling for the effect of age

	Mean RT	sdRT	Normalized sdRT
Performance ability	-.05	-.31	-.34
Verbal ability	.04	-.01	-.03
WM volume	-.09	-.30	-.30
Cortical volume	-.21	-.14	-.03

RT: reaction time; sdRT: standard deviation of the reaction time; normalized sdRT: sdRT/mean RT. Bold characters indicate $p < .05$.

Table 4

Partial correlations between RT measures and cognitive ability and brain volumetry, controlling for the effects of age and gender

	Mean RT	sdRT	Normalized sdRT
Performance ability	-.03	-.32	-.36
Verbal ability	.05	-.01	-.04
WM volume	-.10	-.30	-.29
Cortical volume	-.22	-.14	-.03

RT: reaction time; sdRT: standard deviation of the reaction time; normalized sdRT: sdRT/mean RT. Bold characters indicate $p < .05$.

correction. Thus, total cortical GM volume was used in further analyses.

Mean RT correlated negatively with cortical GM volume, and sdRT and normalized sdRT both correlated negatively with performance ability and WM volume (Table 2). Scatterplots depicting individual data points for females and males separately are shown in Fig. 2. The significant relationships were confirmed by partial correlations controlling for the effect of age, rendering the correlation between mean RT and cortical GM volume only marginally significant ($r = -.21, p = .083$, Table 3). A final partial correlation analysis where both age and gender were controlled for were computed, yielding almost identical results (Table 4). To formally check whether gender interacted with any of the independent variables to predict the mean RT or sdRT, multiple regression analyses were performed. This was done in those cases where sdRT or mean RT correlated significantly with any other variable of interest. In these analyses, an interaction term of gender and the variable of interest

Table 2

Correlations between the different variables of interest

	2	3	4	5	6	7	8	9
(1) Mean RT	.56	.00	-.14	.01	-.15	-.25	.15	-.06
(2) sdRT		.83	-.36	-.03	-.35	-.24	.19	.05
(3) Normalized sdRT			-.34	-.05	-.32	-.12	.13	.10
(4) Performance ability				.46	.41	.60	-.67	-.03
(5) Verbal ability					-.08	.15	-.14	.07
(6) WM volume						.57	-.50	-.21
(7) Cortical GM volume							-.78	-.19
(8) Age								.20
(9) Gender (female = 1, male = 2)								

RT: reaction time; sdRT: the intra-individual standard deviation of the rt; normalized sdRT: the residuals of the sdRT when the influence of mean rt is regressed out; WM: white matter volume; GM: gray matter volume. Bold characters indicate $p < .05$.

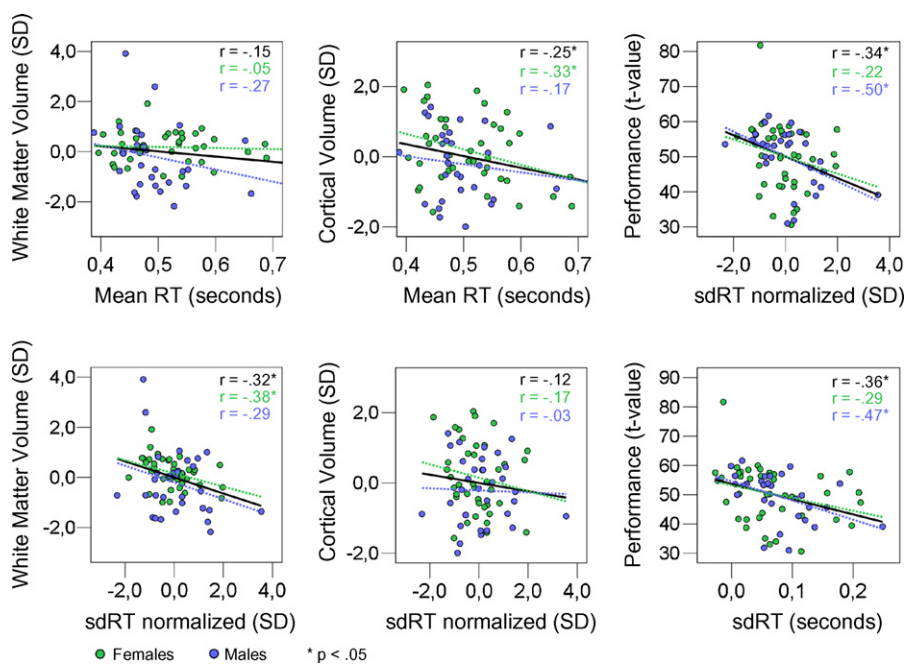


Fig. 2. Scatterplots showing the relationship between individual data points and white matter and cortical volume. The brain volumes are regressed on intracranial volume, and the standardized residuals (S.D.) are presented. Mean RT is mean reaction time in a 3-stimuli oddball task. The sdRT is the standard deviation of the reaction times for the single trials. The normalized sdRT is the sdRT where the influence of mean reaction time is regressed out, and the standardized residuals are presented (S.D.). Green circles and lines represent females, while blue circles and lines represent males. The Pearson correlation coefficients are presented in the top right corner of each square. * indicates that $p < .05$.

were added to the list of predictors. Thus, sdRT and normalized sdRT were predicted from age, performance abilities, gender, and the interaction of performance abilities and gender. Further, sdRT and normalized sdRT were predicted from age, WM volume, gender, and the interaction of WM volume and gender. Finally, mean RT was predicted from age, cortical GM volume, gender, and the interaction between gender and cortical GM volume. In all but one case was the interaction term not significant. However, performance abilities \times gender contributed independently in the prediction of sdRT (standardized $\beta = -1.57$, $t = -2.19$, $df = 4.66$, $p < .05$). A follow up analysis showed that the partial correlation (controlling for age) between performance scores and sdRT was $-.25$ ($df = 37$, $p = .12$) in the female and $-.45$ ($df = 28$, $p < .05$) in the male part of the sample.

The same strategy was then used to test whether the observed relationships were different at different ages. This was done for all the significant relationships from the correlation analyses. Cortical GM volume was first simultaneously predicted from mean RT, age and the interaction of mean RT and age, and then from rtSD, age, and the interaction of rtSD and age. White matter volume was first predicted from rtSD, age, and the interaction of rtSD and age, and then from the normalized sdRT, age, and the interaction of the normalized sdRT and age. Finally, performance ability was predicted first from mean RT, age and the interaction of mean RT and age, and then from rtSD, age, and the interaction of rtSD and age. In none of these analyses did the interaction term even approach significance (all p 's $> .40$). Thus, the relationships between the different

variables of interest do not seem to be different at different ages.

3.1. Outlier analysis

To check whether the observed relationships were dependent upon single extreme observations, outlier analyses were performed. First, for each of the four significant partial correlations where age was controlled for, a multiple regression analysis with age as one of the predictors were computed, and the studentized deleted residuals and the standardized predicted values were saved and correlated. Near-zero correlation would indicate that there are no systematic relationship between potential outliers and the criterion variable. The values obtained for the four correlations tested ranged between $-.003$ and $.01$, indicating that the relationships observed were not mainly caused by outliers. Next, we searched for large values of the studentized deleted residuals. Inspection of the data revealed that values of about ± 2.5 seemed to be a reasonable criterion for defining an observation as an outlier. Thus, the four analyses were repeated with observations exceeding this criterion deleted, reducing n to 70 for these analyses. This lowered the correlations somewhat, with correlations between sdRT and performance ability dropping from $-.31$ to $-.27$, between sdRT and WM from $-.30$ to $-.25$, and between the normalized sdRT and WM from $-.30$ to $-.26$, while the correlation between the normalized sdRT and performance ability remained $-.34$. However, all these correlations were still significant. Thus, the observed relationships are probably not dependent upon single extreme values.

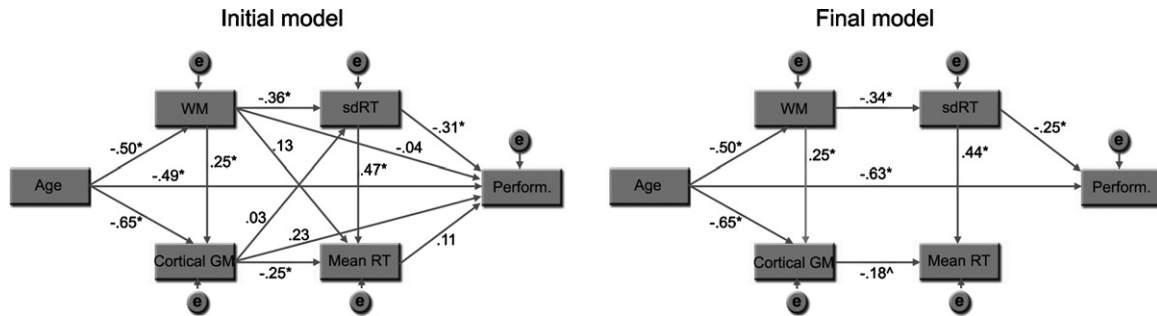


Fig. 3. Path models of age, morphometric variables, reaction time, and performance ability. Two models were constructed and tested. The first model is based on the hypotheses put forth in the study, as well as on the correlations between the variables included. The hypothetical causal relationships between variables are indicated by arrows, and the standardized partial regression weights are printed for each. The paths with p 's $> .05$ in the first model were removed, and the new model tested again. In the new model, all paths except the one from cortical gray matter to mean RT (reaction time) are significant, the latter being only marginally significant ($p = .085$). The relative Chi-square and rmsea indicated good fit to the data for both models, with relative Chi-squares of less than 1 and rmsea of .000 in both cases, indicating that both models were non-significantly different from a perfect fit.

3.2. Path analysis

A path model was constructed where age was treated as the only exogenous variable, and the criterion variable was performance score. Performance score, rather than verbal score, was chosen as the criterion variable for the path analysis based on the weak correlations between verbal score and the other variables. The model is shown in Fig. 3. Direct paths were drawn from all variables to performance score, from age to WM and cortical GM volume, from WM to cortical GM volume, from WM and cortical GM volume to sdRT and mean RT, and from sdRT to mean RT. This model yielded a very good fit to the data, satisfying the criterion of the relative Chi-square being less than 2 (cmin 0.578/2 df = 0.293, and rmsea = .000) and also being non-significantly different from a perfect fit ($p = .746$) (see Table 5). The insignificant paths between the volumetric variables and performance ability, between cortical GM volume and sdRT, between WM volume and mean RT, and between mean

Table 5
Estimates from the first path model

	Estimate	S.E.	C.R.	> p
WM volume \leftarrow age	-.024	.005	-4.831	.001
Cortical volume \leftarrow age	-.032	.004	-7.965	.001
Cortical volume \leftarrow WM volume	.247	.082	3.016	.01
sdRT \leftarrow WM volume	-.012	.005	-2.630	.01
sdRT \leftarrow cortical volume	.001	.005	.205	n.s.
Mean RT \leftarrow cortical volume	-.019	.009	-2.012	.05
Mean RT \leftarrow sdRT	1.017	.237	4.282	.001
Mean RT \leftarrow WM volume	.010	.010	1.018	n.s.
Performance ability \leftarrow sdRT	-81.079	26.036	-3.114	.01
Performance ability \leftarrow cortical volume	2.025	1.267	1.598	n.s.
Performance ability \leftarrow age	-.211	.057	-3.705	.001
Performance ability \leftarrow WM volume	-.399	.959	-.416	n.s.
Performance ability \leftarrow mean RT	13.837	11.666	1.186	n.s.

Estimate: unstandardized partial coefficients; S.E.: standard error; C.R.: critical ratio; n.s.: not significant ($p > .05$).

Table 6
Estimates from the second path model

	Estimate	S.E.	C.R.	> p
WM volume \leftarrow age	-.024	.005	-4.831	.001
Cortical volume \leftarrow age	-.032	.004	-7.965	.001
sdRT \leftarrow WM volume	-.012	.004	-3.066	.01
Cortical volume \leftarrow WM volume	.247	.082	3.016	.01
Mean RT \leftarrow cortical volume	-.013	.008	-1.720	.085
Performance ability \leftarrow sdRT	-66.851	22.590	-2.959	.01
Mean RT \leftarrow sdRT	.944	.229	4.123	.001
Performance ability \leftarrow age	-.273	.037	-7.364	.001

Estimate: unstandardized partial coefficients; S.E.: standard error; C.R.: critical ratio; n.s.: not significant ($p > .05$).

RT and performance were removed, and the model tested again. The relative Chi-square was now 0.689 (cmin 4.824/7 df, and rmsea = .000), and the model was still non-significantly different from a perfect fit ($p = .681$) (see Table 6). All paths were now significant, except a marginally significant path from cortical GM volume to mean RT ($p = .085$).

4. Discussion

As hypothesized, intra-individual variability in RT correlated negatively with performance abilities, but not verbal abilities. This is in accordance with previous research (Hultsch & MacDonald, 2004). The reasoning is that increased variability is a sign of cognitive instability, which is detrimental for performance in tasks requiring speeded and efficient processing of information, and which poses high loads on the attentional system. In the present study, the performance tests were time-limited and required fast processing and responses. In contrast, the verbal ability tests used were not time-limited, depend more on memory and previous learning, and were thus probably less vulnerable to small inconsistencies or instabilities in the information processing stream. The new contribution from the present study is identification of negative relationships between intra-individual variability and brain morphometry. We hypothesized that intra-individual variability would correlate negatively with WM volume, even when the effect of mean RT

was regressed out. The data confirmed this hypothesis, showing moderate correlations. Thus, WM characteristics were related to the stability of information processing and response execution in a relatively simple reaction time task. This fits well with the fact that WM volume mainly consists of myelinated neural connections, and that a high degree of myelination yields better isolation and hence more stable flow of electrical currents in dendrites and axons. As argued in the introduction, reductions in thickness of myelin sheaths may have a similar effect on the stability of signal transduction as reduced levels of neurotransmitters. Further, myelin thinning may cause the age decline in cognitive performance by leading to stepwise information loss due to neural noise (Myerson et al., 1990), or even random breaks in neural networks (Cerella, 1990).

Mean RT correlated negatively with cortical GM volume, as hypothesized, and no significant age-interaction was found. However, the relationship was mainly age-dependent, since the p -value dropped to .085 when age was regressed out. This result stands in contrast to Haier et al. (2005), who found negative correlations in middle-aged, but positive correlations in elderly. Even though this result was obtained in a memory task, and no significant results were obtained with simple reaction time, it is evident that more research is required before conclusions regarding the relationship between RT and GM can be drawn. Still, since a weak negative correlation was found in the present study, it is interesting that mean RT was non-correlated with WM volume. This indicates that WM may be more related to the stability of information processing, than the speed of the processes themselves. An implication is that even though response variability and mean RT is moderately correlated, the two variables are predicted by different neuroanatomical traits. The path model with paths from WM to sdRT and from cortical GM to mean RT yielded an excellent fit to the data. This supports Jensen's (1992) view that variability and mean RT are two fundamentally different properties of the human cognitive system. As Jensen (1982, p. 10) suggested: "Variability of RTs would seem to have priority over the average speed of RTs. Assuming an inherent periodicity in the nervous system, the average speed of RT can be seen as a consequence of variability of RT more easily than the reverse relationship". The present results indicate that the intra-individual variability of RT, here operationalized as sdRT, deserves more attention in neuroscience and neuropsychology than what has previously been the case.

In the present paper, we have drawn a distinction between speeded performance tests and non-speeded verbal tests. However, it is not possible from the present data to distinguish between effects of speed and effects of the fact that the performance tests are spatial, while the verbal tests are not. Thus, it is possible that WM volume affects spatial, right hemisphere processes, but not verbal left hemisphere processes, and that the speeded versus non-speeded distinction is less important in this regard. Thus, correlations between performance ability and sdRT or neuroanatomical volume cannot with certainty be explained as related to speed-of-processing per se. Rourke (1987) has suggested that nonverbal learning disabilities is related to damage to the right hemisphere white matter function.

Further studies are needed to disentangle the effects of verbal versus nonverbal and speeded versus non-speeded tests and their interactions with neuroanatomical volume and cognitive abilities.

4.1. Limitations and future research

The RTs in this study were taken from a task designed as an ERP-paradigm, and will therefore differ somewhat from other tasks often used in cognitive experiments. Even though participants were instructed to respond as fast as possible, accuracy was stressed as the most important. We expected, but did not find correlations between age and mean RT or sdRT. This may be related to motivational factors differing between older and younger participants, or the generally high level of functioning in the present sample. Further, possibly related to this, we did not find correlations between RT and performance intelligence. A more suitable instruction would be to stress the importance of fast RT over accuracy. Still, RT and especially normalized sdRT correlated significantly with neuroanatomical variables in expected directions, indicating that the task probably yielded valid results. Further research should replicate the present finding with different types of RT tasks and different instructions. Also, it will be interesting to relate RT variability to DTI measures, a WM measure that may be more related to cognitive factors. Finally, a research protocol that allows a distinction between decision time and movement time would make it possible to pinpoint central versus peripheral nervous system contributions to RT and sdRT, and their relationship with brain anatomy and cognitive function.

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The two authors have contributed equally to the present paper, and their names are presented in random order.

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