Poorer white matter microstructure predicts slower and more variable reaction time performance: evidence for a neural noise hypothesis in a large lifespan cohort

Abbreviated Title: Poor WM predicts slow and variable RT performance

Ethan M. McCormick^{*1,2,3}, Cam-CAN⁴, & Rogier A. Kievit^{1,4}

¹ Cognitive Neuroscience Department, Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Center, Nijmegen, The Netherlands; ² Methodology and Statistics Department, Institute of Psychology, Leiden University, Leiden, Netherlands; ³ Department of Psychology and Neuroscience, University of North Carolina, Chapel Hill, United States; ⁴ MRC Cognition and Brain Sciences Unit, University of Cambridge, United Kingdom

*corresponding author
Ethan M. McCormick
Wassenaarseweg 52 2333 AK,
Leiden, The Netherlands
e.m.mccormick@fsw.leidenuniv.nl

Abstract

Most prior research has focused on characterizing averages in cognition, brain characteristics, or behavior, and attempting to predict differences in these averages among individuals. However, this overwhelming focus on mean levels may leave us with an incomplete picture of what drives individual differences in behavioral phenotypes by ignoring the variability of behavior around an individual's mean. Particularly, enhanced white matter (WM) structural microstructure has been hypothesized to support *consistent* behavioral performance by decreasing gaussian noise in signal transfer. Conversely, lower indices of white matter microstructure are associated with greater within-subject variance in deploying performance-related resources, especially in clinical populations. We tested a mechanistic account of a 'neural noise' hypothesis in a large adult lifespan cohort (Cam-CAN) with over 2500 adults (ages 18–102; 1508 female; 1173 male; 2681 behavioral sessions; 708 MRI scans) using WM fractional anisotropy (FA) to predict mean levels and variability in reaction time performance on a simple behavioral task using a dynamic structural equation model (DSEM). By modeling robust and reliable individual differences in within-person variability, we found support for a neural noise hypothesis (Kail, 1997), with lower FA predicted individual differences in separable components of behavioral performance estimated using DSEM, including slower mean responses and increased variability. These effects remained when including age, suggesting consistent effects of WM microstructure across the adult lifespan unique from concurrent effects of ageing. Crucially, we show that variability can be reliably separated from mean performance using advanced modeling tools, enabling tests of distinct hypotheses for each component of performance.

Significance Statement

Human cognitive performance is defined not just by the long-run average, but trial-to-trial variability around that average. However, investigations of cognitive abilities and changes during aging have largely ignored this variability component of behavior. We provide evidence that white matter microstructure predicts individual differences in mean performance *and* variability in a sample spanning the adult lifespan (18-102). Unlike prior studies of cognitive performance and variability, we modeled variability directly and distinct from mean performance using a dynamic structural equation model, which allows us to de-couple variability from mean performance and other complex features of performance (e.g., autoregression). The effects of WM were robust above the effect of age, highlighting the role of WM in promoting fast and *consistent* performance.

Introduction

Prominent theories of cognitive aging posit a central role for reductions in mental processing speed during later life (Salthouse, 1996). These theories focus primarily on decreases in mean performance (i.e. slowing-down) but mostly ignore variability in processing speed, despite a long acknowledgement that variability around the mean provides unique information (Fiske & Rice, 1955; Nesselroade, 1991; Woodrow, 1932). Prior work shows that average reaction time (RT) displays steep improvement early in life, followed by gradual slowing into aging (Li et al., 2004). Complementary work shows a similar pattern for behavioral variability (Williams et al., 2005). Crucially, despite these similar patterns, evidence strongly suggests that variability provides unique insight into cognitive aging above and beyond mean performance alone (Dykiert et al., 2012; Eizenman et al., 1997; Gamaldo et al., 2012). For instance, trial-to-trial variability might reflect different strategies, momentary lapses (Adam et al., 2015), or endogeneous differences in the signal-to-noise ratio of neural-evoked responses.

The neural noise hypothesis (Kail, 1997) posits that the signal-to-noise ratio of the central nervous system degrades during aging, leading to deficits in processing speed. Electrophysiological recordings have shown that increased neural noise (i.e., de-synchronized neural oscillations) led to slower behavioral performance in older adults (Dave et al., 2018; Voytek et al., 2015) due to disrupted long-range communication and synchronization between neural regions (Voytek & Knight, 2015). Reduced inter-region communication suggests a causal role for demyelination of neuronal axons carrying signals between cortical regions (Peters, 2009). While the mechanisms of progressive demyelination leading to slowing of RT is debated (Bartzokis et al., 2010; Peters, 2009), this relationship is robust in normative samples (Bennett & Madden, 2014; Fjell et al., 2011; Tamnes et al., 2012; Turken et al., 2008). Additionally, in clinical samples with

specific focal damage to white matter (e.g., multiple sclerosis), increased white matter damage is associated with increased behavioral variability (Britton et al., 1991; Bunce et al., 2007). While prior findings have focused primarily on mean processing speed (but see Li & Lindenberger, 1999), this logic extends naturally to variability (Halliday et al., 2019; MacDonald et al., 2006; Sorg et al., 2021). Impaired white matter is more prone to random leakage from axonal signals that lead to inconsistencies in behavioral performance. As such, we hypothesize that reduced white matter measures should predict slower overall performance *and* increased trial-to-trial variability.

A key limitation in prior work on variability is the widespread use of measures such as the standard deviation of response times (iSD) or coefficient of variation (iCV; equal to the iSD divided by the mean) across trials (e.g., Haynes et al., 2017). Unfortunately, these simple estimates of variability fail to account for complex features of behavioral performance (e.g., trends or autoregression), leading to systematic over- or under-estimates of variability (Wang & Grimm, 2012). To address these challenges, we employed dynamic structural equation modeling (DSEM; Asparouhov et al., 2018), which combines strengths of timeseries analysis with hierarchical random effects in a structural equation framework. This approach allows us to test trial-to-trial predictors of RT data at the within-person level, and explain person-to-person differences in mean RT and variability simultaneously (McNeish & Hamaker, 2020). Using this innovative framework for capturing variability de-confounds sources of variance that might otherwise bias individual differences performance features, and allows us to test different causal mechanisms associated with individual differences in mean and variability in RT.

We tested this neural noise hypothesis in a large cohort of adults (age 18–102; Shafto et al., 2014) who completed a set of reaction-time tasks (N=2681) and underwent a diffusion-weighted scan (N=708). We modeled individual differences in four aspects of behavioral

Poorer white matter microstructure predicts slower and more variable reaction time performance

performance: mean RT, variability, trends across the task, and the autoregressive effect between adjacent trials. We incorporated differences in white matter and age to examine how they predicted each component of processing speed performance. We hypothesized that reduced WM microstructure would predict increased mean RT and heightened variability (i.e., slower, less consistent performance), and that these effects would be robust to including age in the model. In doing so, we pursued dual goals: 1) to conduct a theoretical test of the neural noise hypothesis, and 2) to use that test to outline a generative DSEM framework for testing hypotheses related to variability for future work in this area.

Methods

For consistency and precision, portions of the text in this section are drawn from prior work describing the Cambridge Centre for Ageing and Neuroscience (Cam-CAN) dataset (Shafto et al., 2014; Taylor et al., 2017).

Participants

Data were provided by healthy adult participants in two phases of data collection. Stage I consisted of at-home interviews of individuals living in the Cambridge City, UK region. During Stage II, a subset of these participants was invited to complete a neuroimaging session, where structural and functional scans were obtained. Participants at Stage II were recruited in deciles between 18-87 years of age, with a goal of equal sample sizes (~100) at each decile. In the current analyses, we utilized behavioral data (SRT) from 2681 healthy adults (1508 female; 1173 male) from Stage I and additional behavioral data (VSTM) and measures of structural WM from 708 adults (359 female; 349 male) from Stage II. Note that a subset of these data have been analysed before in Kievit et al (2016) using more simplistic methods. Exclusion criteria included MR safety

contraindications (e.g., pacemakers), learning disability (living at home), cognitive impairment (Mini-Mental State Examination (MMSE; Folstein et al., 1975) score of 24 or less) and reduced response from individuals with limited longstanding illness or disability (for full information on exclusion criteria, see Table 1 in Shafto et al., 2014). Prior to the interview, individuals give written informed consent for the study and record linkage. Individuals who lack the capacity to give consent were not included. Written informed consent was also given by participants at each session for Stages 2 and 3 (Shafto et al., 2014).

Experimental Design

Behavioral Tasks

The description of the behavioral tasks is copied, in part, from Shafto and colleagues (2014). For additional information regarding the tasks and requests for data access, see the Cam-CAN dataset inventory (<https://camcan-archive.mrc-cbu.cam.ac.uk/dataaccess/>).

Simple Response Time Task. A “simple” response time task (SRT) was used to assess basic aspects of speeded responses. In the SRT, participants viewed an image of a hand with blank circles above each finger, while resting their right hand on a response box with four buttons, one for each finger. When a given circle turned black on the image, the participants were instructed to press with the relevant finger as quickly as possible. On pressing the button (or after a maximum of 3 seconds) the circle became blank again and the variable inter-trial interval (ITI) began. The ITI was varied pseudo-randomly with a positively skewed distribution (mean = 3.7 s, median = 3.9 s, range = 1.8 – 6.8 s). The SRT consisted of 50 trials, and the principal outcome measure was reaction time from stimulus onset to button press. For a visualization of the task, see Figure 2a in Kievit and colleagues (2016).

Visual Short Term Memory Task. This task assesses the processes underpinning visual

short-term memory (VSTM). In the VSTM, participants viewed a series of circular discs presented briefly on a computer screen. After a brief delay, participants reported the color of a cued disc, by selecting from a color wheel that displays a rainbow of hues. On each trial, participants saw a display for 250 milliseconds which contains a central fixation and one to four colored discs, with the colours chosen at random. The locations of the discs on the screen were randomly selected from eight points equidistant from a central fixation. Following the brief encoding display, there was a 900-millisecond blank screen, and then one of the disc locations was highlighted with a border and the response colour wheel appeared. On half of trials, any un-cued discs also reappeared, to provide the context within which the disc was encoded. Participants indicated their confidence in the selected colour by the length of time they held down their finger: as they held their finger down for longer, white confidence intervals spread out around the selected point indicating more uncertainty about their selection. The response interval did not have a time limit: after participants confirmed their response, there was an 830-millisecond fixation period before the next trial began. After a brief practice period, participants completed two blocks of 112 trials, with set-size and probe context being counterbalanced and randomly intermixed within each. Participants also completed a perceptual control block of 56 trials, where single discs were presented at fixation along with the colour wheel, until the participant matched their hue by selecting the appropriate point on the surrounding wheel. There were two possible responses to model with the VSTM data, a first response and a final response. In general, we discuss results related to the final response, but full results from both models are available (<https://osf.io/nkjdt/>). We note major differences if relevant.

White Matter Microstructure

White matter microstructure was assessed using the fractional anisotropy (FA) of WM tracts derived from diffusion weighted imaging – see prior work for full details on the relevant scan parameters (Taylor et al., 2017) and processing pipeline (Kievit et al., 2016). We utilized FA given its widespread use in investigations of aging and white matter, however, it should be noted that FA is a complex measure and its exact relation to white matter health is not fully understood (Jones et al., 2013). Furthermore, its relatively simple model structure may not capture especially complex features of white matter organization (e.g., crossing fiber bundles). Consistent with prior work, mean FA was computed for the ten tracts defined by the Johns Hopkins University white matter tractography atlas (Hua et al., 2008; see Kievit et al., 2016 for tract visualization): the anterior thalamic radiations (ATR), corticospinal tract (CST), dorsal cingulate gyrus (CING), ventral cingulate gyrus (CINGHipp), forceps major (FMaj), forceps minor (FMin), inferior fronto-occipital fasciculus (IFOF), inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), and uncinate fasciculus (UNC). As a sensitivity analysis, FA values more than 4 standard deviations from the mean in each tract (0.27% of values) were excluded for the core set of analyses. Model results were not substantively impacted and so all values were retained in the presented results.

We faced a challenge when using the different WM tracts as predictors in the DSEM (detailed below), due to the high correlations across measures (54% of the total variance explained by the first principal component). We considered several options, but each came with limitations: 1) PCA-derived scores did not allow for missing data, 2) WM tracts do not theoretically conform to a reflective latent variable structure, and 3) including all tracts as simultaneous predictors resulted in unstable results due to the high multi-collinearity (Lavery et al., 2019). Furthermore, prior work (de Mooij et al., 2018) showed that while white matter tracts are correlated, they do not

Poorer white matter microstructure predicts slower and more variable reaction time performance

show a unidimensional or simple factor structure (i.e., predominant loading onto a single factor, negative factor loadings, etc.). As such, we fit models for each tract separately and looked across models for consistent findings. We thereby present a single tract (the ATR) as a canonical example, while noting any deviation from the canonical pattern of effects if needed. We do not attempt to draw specific theoretical inferences for individual tracts, but rather take them as repeated instances of a WM-general effect. Consistent effects across tracts would indicate that the effects are generally related to WM fractional anisotropy, while inconsistent effects might suggest functional specificity – which we do not expect.

Statistical Analysis

Dynamic Structural Equation Model

All models were fit using the DSEM module in *Mplus* Version 8 for intensive longitudinal data (Asparouhov et al., 2018). DSEM is a flexible modeling framework which combines strengths of traditional time-series analyses, multilevel models, and structural equation models (for a primer on DSEM, see (McNeish & Hamaker, 2020). DSEM also allows for the simultaneous estimation of the random effects of behavioral performance and their association with covariates of interest, rather than a 2-step approach that does not propagate the uncertainty in estimates across levels of analysis (Wang & Grimm, 2012). At the within-person trial level, we modeled the natural log of reaction time (logRT) for both SRT and VSTM behavior on a given trial as a function of reaction time at the prior trial (φ) and the trial number (β_t). Phi (φ) represents the autoregressive effect, or inertia of performance between adjacent trials. Individuals with high autoregressive effects would show slower cycles of faster and slower performance around their mean, while smaller autoregressive effects would reflect larger differences in performance between adjacent trials (compare the grey and pink exemplar timeseries in Figure 1B). The trend (β_t) parameter reflects

overall gains or losses in performance across the task session (here the trend across trials but this could reflect other metrics of time; McCormick, 2021; compare the grey and blue exemplar timeseries in Figure 1B). At the person level, we modeled random effects for φ and the trend (β_t), as well as for the mean (μ) and variance (ψ) of RT across the task. By default the between-person ψ parameter was estimated with a log-linear model to aid in estimation (McNeish & Hamaker, 2020). For each task, we compared a fixed-effects model to one where each of these parameters was allowed to vary freely. To assess the robustness of the results and compare models, we took several steps to evaluate the results. Model convergence was achieved when the potential scale reduction (PSR) metric, which estimates the potential reduction in the width of the posterior parameter distribution with infinite subsequent draws, was less than 1.10 (Gelman & Rubin, 1992), reflecting less than a 10% potential narrowing compared the current distribution. Trace plots associated with the estimated parameter were examined visually to ensure that chains converged to a random scatter around a fixed mean (i.e., flat traces). To ensure model robustness, we compared a solution with 10,000 iterations to one with 20,000 iterations using the same random seed. Parameter changes between models were assessed with a measure of relative bias (i.e., the difference between the two parameter solutions divided by the original parameter). We then estimated the same model with 20,000 iterations twice more, with different random seeds to assess the impact of starting values on the final solution. If bias was low ($< 5\%$) across solutions, we retained the model; otherwise, we doubled the iterations for all solutions and assessed relative bias on the new models. All models presented here converged to acceptable values (for all model diagnostics and comparisons, see the analysis code; <https://osf.io/nkjdt/>). To correct for the multiple models, we applied false discovery rate correction to the significance tests. Because the

Poorer white matter microstructure predicts slower and more variable reaction time performance

standard *Mplus* output only gives floating point precision to the third decimal place, we calculated the adjusted p -values from the estimate and posterior standard error.

We then built a series of conditional models predicting the random effects by including the white matter tract FA (with the ATR as the canonical example) and age separately before including both in a final conditional model. The unconditional model can be expressed in the multilevel equation below, for person i at trial t (colors included to help keep track of the different components of behavior).

$$\begin{aligned} \text{Level 1:} \quad \log(RT_{t,i}) &= \mu_i + \varphi_i RT_{t-1,i} + \beta_{ti} Trial_{t,1} + \varepsilon_{t,i} \\ \varepsilon_{t,i} &\sim N(0, \psi_i) \end{aligned}$$

$$\begin{aligned} \text{Level 2:} \quad \mu_i &= \gamma_{00} + u_{0i} \\ \varphi_i &= \gamma_{10} + u_{1i} \\ \beta_{ti} &= \gamma_{20} + u_{2i} \\ \psi_i &= \exp(\omega_0 + u_{3i}) \end{aligned} \tag{1}$$

$$\mathbf{u}_i \sim MVN \left(\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{\mu} & & & \\ \tau_{21} & \tau_{\varphi} & & \\ \tau_{31} & \tau_{32} & \tau_{\beta_t} & \\ \tau_{41} & \tau_{42} & \tau_{43} & \tau_{\psi} \end{bmatrix} \right)$$

With covariates entering the model at Level 2 for the conditional model:

$$\begin{aligned} \text{Level 2:} \quad \mu_i &= \gamma_{00} + \gamma_{01} WM_i + \gamma_{02} Age_i + u_{0i} \\ \varphi_i &= \gamma_{10} + \gamma_{11} WM_i + \gamma_{12} Age_i + u_{1i} \\ \beta_{ti} &= \gamma_{20} + \gamma_{21} WM_i + \gamma_{22} Age_i + u_{2i} \\ \psi_i &= \exp(\omega_0 + \omega_1 WM_i + \omega_2 Age_i + u_{3i}) \end{aligned} \tag{2}$$

$$\mathbf{u}_i \sim MVN \left(\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \tau_{\mu} & & & \\ \tau_{21} & \tau_{\psi} & & \\ \tau_{31} & \tau_{32} & \tau_{\beta_t} & \\ \tau_{41} & \tau_{42} & \tau_{43} & \tau_{\psi} \end{bmatrix} \right)$$

Note that in the conditional model, the elements in $\mathbf{u}_i$ are residual (co)variances. We can also represent this model graphically (Figure 1A), where we can see that our 4 random effects reflect between-person differences in the within-person effects. For illustration purposes, we simulated exemplar timeseries highlighting how high levels of a given random effect would change performance output (Figure 1B).

Figure 1. A) Model Schematic. We estimated 4 random effects (μ , ψ , β_t , and φ) at the between-person level from the within-person model (dashed lines) of reaction time (RT_t) regressed on its prior value (RT_{t-1}) and the current trial number ($Trial_t$). Observed variables are depicted in boxes and latent variables in circles as is conventional. The random effects were regressed (solid single-headed arrows) on the covariates, Age and WM fractional anisotropy (tracts were modeled individually so the identity of this covariate varied over models). Finally, the covariance between Age and FA (solid double-headed arrow, left) and residual covariances between the random effects (solid double-headed arrows, right) were estimated. **B) Exemplar Timeseries.** We simulated exemplar timeseries to highlight the impact of higher values on each of the 4 random effects. The exemplars differed from the reference timeseries (grey) in mean (red; High μ), variance (green; High ψ), trend (blue; High β_t), and autoregressive (purple; High φ) parameters.

The inclusion of age served as an important covariate to ensure that our results were not driven solely by systematic differences across age in mean RT ($r = 0.242$) and co-occurring age and WM FA ($r = -0.470$) across the lifespan. Because only a subset of participants who contributed data at

Stage I (SRT) were invited to Stage II (VSTM and WM measures), we used a joint likelihood approach instead of the default conditional likelihood to allow missingness on exogenous variables without listwise deletion by estimating the mean and variance of each predictor (i.e., age and WM tract FA). The raw data are available upon signing a data sharing request form (see <http://www.mrc-cbu.cam.ac.uk.libproxy.lib.unc.edu/datasets/camcan/> for more detail). Analysis code and full model results are available on OSF (<https://doi.org/10.17605/OSF.IO/BN6YU>).

Results

Unconditional Model

We began by fitting two unconditional models to the SRT data, one with only fixed (i.e., zero variance) effects and the other with four random effects. The deviance information criteria ($DIC_{\text{fixed}} = 1793$, $DIC_{\text{random}} = -44107$, $\Delta DIC = -45900$) overwhelmingly favored the inclusion of the four random effects (Asparouhov et al., 2018; McNeish & Hamaker, 2020). Fixed effects-only models in the VSTM data also showed very poor fit bolstering the rationale for adopting a random effects approach to capture individual variability in the different components of the RT data. In a follow-up analyses, we compared the full random effect model to a set of models where we constrained each random effect to zero in turn. Model comparisons provided strong evidence in favor of including all random effects (ΔDIC s ranging from -193 to -20222). In other words, the model fit results suggested that the complexity of the behavioral data could not be appropriately captured by a single effect that held for all members of the sample and rather that allowing for individual differences in all four components of performance was necessary. For the SRT data, a model with 4 random effects showed that there is significant person-to-person variability in all 4 of the parameters modeled (Table 1). Examining the average within-person standardized effects (Schoorman et al., 2016), there was small positive inertia in participants' response time across

adjacent trials (RT_{t-1} ; $\beta = 0.036$, $SD_{\text{posterior}} = 0.003$, 95% C.I. = [0.030, 0.042]) and participants got faster on average across the task ($Trial_t$; $\beta = -0.062$, $SD_{\text{posterior}} = 0.003$, 95% C.I. = [-0.067, -0.056]). Results for the VSTM data confirmed this same general pattern.

When examining the pattern of correlations there was some heterogeneity between the tasks. In the SRT data, the mean (μ), variability (ψ), and autoregressive (φ) random effects were all positively correlated with one another, and all negatively correlated with the trend effect (β_t ; see Figure 2). Of particular note was the correlation between mean RT and response variability which was moderately positive ($r = 0.397$, 95% C.I. = [.359, .434]), suggesting that we could achieve separation of individuals' mean and variability in performance (compared with $r = 0.666$ between mean RT and a simple iSD measure). Interestingly, mean RT in the VSTM data showed a different pattern of relations (Final Response: $r = -0.398$, 95% C.I. = [-0.465, -0.328]), being negatively correlated with the other random effects. This perhaps indicates more of a ceiling effect, rather than the floor effect seen in simple speeded response tasks.

Figure 2. Distributions of Random Effects from the Simple RT task. Each of the four random effects showed significant between-person variability. Mean performance (μ), variability (ψ), and inertia (ϕ ; i.e., the autoregressive effect) were all positively correlated, and negatively correlated with the trend of performance across the task (β_t).

Model Based and Observed Measures of Variability

To further clarify the relationship between the DSEM-derived components of behavioral performance and traditional measures calculated directly from the data (iSD and iCV). We calculated these observed measures on the trial level RT values after taking the natural log and entered the factor score estimates of the random effects as predictors in a multiple regression analysis (Figure 3). The iSD measure was significantly predicted by all four random effects, while the iCV measure was significantly predicted by the mean, variability, and trend but not inertia factor scores. Interestingly, while variability strongly related to iSD ($\beta = 0.885$, $SE = 0.007$, $p <$

.001), it weakly and negatively related to iCV ($\beta = -0.167$, $SE = 0.021$, $p < .001$). Indeed, iCV was most strongly related to mean performance ($\beta = -0.293$, $SE = 0.027$, $p < .001$) and the variance explained in iCV was relatively low ($R^2 = 0.111$), especially compared with the high variance explained by the four random effects in iSD ($R^2 = 0.894$). However, both analyses suggest that these observed metrics of intraindividual variability are significantly contaminated by the more complex components of performance, highlighting the utility of the DSEM approach.

Figure 3. Explaining Observed Metrics of Interindividual Variability in SRT. While iSD was well described by the linear combination of the four random effects, the iCV showed surprising negative relationships with the metrics of mean and variability in performance derived from the dynamic structural equation model. However, both metrics showed significant contamination by more than one random effect, especially mean performance (μ) and the trend (β_t).

Conditional Model without Age

We next included the 10 white matter tracts as predictors in separate models at the between-person level predicting the random effects. As mentioned previously, we focus here on the model with the anterior thalamic radiation (ATR) but note any differences between models with other

Poorer white matter microstructure predicts slower and more variable reaction time performance

tracts (all models for the other tracts are available at <https://osf.io/nkjdt/>). As hypothesized, reduced white matter FA predicted both slower response times ($\beta = -0.322$, $SD_{\text{posterior}} = 0.042$, 95% C.I. = [-0.401, -0.237]) and increased response variability ($\beta = -0.344$, $SD_{\text{posterior}} = 0.042$, 95% C.I. = [-0.423, -0.260]). Furthermore, lower white matter FA predicted a higher autoregressive effect ($\beta = -0.123$, $SD_{\text{posterior}} = 0.053$, 95% C.I. = [-0.229, -0.021]) and a less positive trend ($\beta = 0.119$, $SD_{\text{posterior}} = 0.034$, 95% C.I. = [0.053, 0.186]). The addition of the ATR covariate reduced the residual correlation between mean RT and response variability ($r' = 0.263$, 95% C.I. = [.268, .371]). The other tracts had similar effects (although the effects for the ventral cingulate gyrus [CINGHipp] were not significant) in the SRT data. In the VSTM data, reduced ATR FA predicted only slower mean RT ($\beta = -0.919$, $SD_{\text{posterior}} = 0.344$, 95% C.I. = [-1.581, -0.239]) but not response variability ($\beta = -0.653$, $SD_{\text{posterior}} = 0.787$, 95% C.I. = [-2.198, 0.878]).

Figure 4. White Matter Microstructure and Variability. Across nine of the ten canonical tracts, reduced white matter fractional anisotropy predicted more variability in response times (in the CINGHipp tract, there was no significant relationship).

Conditional Model with Age

Finally, we included age as an additional covariate predicting the random effects to account for the likely confounding of systematic WM FA variation decreases across the adult lifespan (Figure 1). Results suggested that older individuals showed slower average RT ($\beta = 0.351$, $SD_{\text{posterior}} = 0.032$, 95% C.I. = 0.287, 0.413]) and greater response variability ($\beta = 0.272$, $SD_{\text{posterior}} = 0.034$, 95% C.I. = 0.204, 0.337]; Table 1; Figure 5). Although somewhat attenuated compared to the conditional model without age, lower white matter FA continued to uniquely predict slower mean performance ($\beta = -0.149$, $SD_{\text{posterior}} = 0.049$, 95% C.I. = [-0.244, -0.051]) and increased behavioral variability ($\beta = -0.197$, $SD_{\text{posterior}} = 0.051$, 95% C.I. = [-0.296, -0.095]). The inclusion of age and WM FA together explained 17-20% of the between-person variance in mean RT ($R^2 = 0.201$, $SD_{\text{posterior}} = 0.018$, 95% C.I. = [0.167, 0.238]) and RT variability ($R^2 = 0.169$, $SD_{\text{posterior}} = 0.020$, 95% C.I. = [0.133, 0.212]), but only 1% of the variance in the trend across trials ($R^2 = 0.012$, $SD_{\text{posterior}} = 0.013$, 95% C.I. = [0.003, 0.041]) and the variance in the autoregressive effect ($R^2 = 0.010$, $SD_{\text{posterior}} = 0.010$, 95% C.I. = [0.001, 0.038]). At the within-person level, the lag-1 (i.e., autoregression) and trial (i.e., trend) effects accounted for 16% of the variance in individual trial RT ($R^2 = 0.163$, $SD_{\text{posterior}} = 0.003$, 95% C.I. = [0.158, 0.168]).

Figure 5. Conditional Model of Simple RT task with Age and White Matter Microstructure. Age and white matter FA had opposite predictive effects, with older individuals showing slower and more variable responding while those with greater white matter FA showed the opposite pattern (i.e., faster, more consistent responding). Paths in red represent positive unique effects or correlations, while those in blue represent negative relationships. The dashed blue line represents a non-significant effect of ATR FA on the autoregressive random effect (ϕ). Explained variance (i.e., R^2) is represented by the proportion of the outcome variable shaded in grey. Dashed black lines link random effects at the between-person level with their corresponding effect at the within-person level.

Table 1. Model Results for Unconditional and Full Conditional Model.

	Unconditional Model				Full Conditional Model			
	Est	S.D. _{post}	Lower	Upper	Est	S.D. _{post}	Lower	Upper
<i>Within-Person Standardized Effects</i>								
γ_{10}	0.036	0.003	0.030	0.079	0.043	0.003	0.036	0.049
γ_{20}	-0.053	0.003	-0.059	-0.047	-0.055	0.005	-0.063	-0.044
<i>Between-Person Unstandardized Effects</i>								
γ_{00}	-0.908	0.006	-0.920	-0.896	-0.495	0.253	-0.996	-0.008

γ_{10}	0.036	0.004	0.029	0.043	0.196	0.128	-0.059	0.446
γ_{20}	-0.001	0.000	-0.002	-0.001	-0.007	0.016	-0.041	0.022
ω_0	-3.292	0.014	-3.309	-3.254	-1.689	0.594	-2.880	-0.536
τ_{μ}	0.083	0.003	0.078	0.089	0.066	0.002	0.062	0.071
τ_{φ}	0.008	0.001	0.006	0.010	0.013	0.001	0.011	0.015
τ_{β_i}	1.9e-5	5.1e-7	1.8e-5	2.0e-5	1.7e-5	6.4e-7	1.5e-5	1.8e-5
τ_{ψ}	0.424	0.014	0.398	0.452	0.356	0.013	0.330	0.382

Between-Person Standardized Covariate Effects

ATR FA

γ_{01}	-0.149	0.049	-0.244	-0.051
γ_{11}	-0.085	0.063	-0.209	0.040
γ_{21}	0.042	0.074	-0.096	0.194
ω_1	-0.197	0.051	-0.296	-0.095

Age

γ_{02}	0.351	0.032	0.287	0.413
γ_{12}	0.012	0.047	-0.082	0.105
γ_{22}	-0.072	0.045	-0.157	0.020
ω_2	0.272	0.034	0.204	0.337

Variance Explained (R^2)

$\log(RT_{t,i})$	0.096	0.001	0.094	0.099	0.163	0.003	0.158	0.168
μ_i					0.201	0.018	0.167	0.238
φ_i					0.010	0.010	0.001	0.038
β_{ii}					0.013	0.020	0.003	0.041
ψ_i					0.169	0.020	0.133	0.212

324 Note: Est. is the sample-recovered parameter. Std. Err. is the standard error of the estimate.
325 S.D._{post} is the posterior standard deviation. Lower and Upper are the boundaries of the credible
326 intervals.

Discussion

In the modeling of human behavior, analysis of mean performance has preoccupied the majority of research focus. Here, we offer compelling evidence that variability in performance holds unique additional value for a broader understanding of human behavior. Crucially, to accurately isolate the mechanisms and consequences of this parameter as distinct from the mean requires appropriate quantitative tools. Utilizing a dynamic structural equation model (DSEM; Asparouhov et al., 2018) approach, we fit a model that separates out four distinct components of human reaction time behavior: mean performance, variability in response times, linear trends across the task, and inertia (i.e., autoregression) in performance from trial-to-trial. In a large lifespan cohort (Cam-CAN; Shafto et al., 2014), we then used this model to examine the associations between these components of performance across aging and individual differences in white matter microstructure. Following from a ‘neural noise’ hypothesis (Kail, 1997; Peters, 2009; Voytek et al., 2015), we posited that reduced white matter microstructure would predict greater variability in behavioral performance, reflecting a less consistent signal-to-noise ratio in the propagation of speeded responses in the task (Dave et al., 2018; Kievit et al., 2016; Peters, 2009). We found evidence that poorer white matter microstructure – measured through fractional anisotropy – predicted increased variability, as well as decreased mean level performance (Figure 2) and these relationships held when controlling for age (Figure 5). Overall, these results highlight the promise of approaches that directly incorporate variability as a parameter in the model, with potentially unique etiological mechanisms and consequences.

Modeling Complex Human Behavior

One of the primary benefits of adopting a DSEM framework here is the ability to directly model within- and between-person features that are often treated as noise in simpler analyses (e.g., variability and trend), as well as complex temporal features of performance (e.g., autoregression) that would be invisible to those models. Doing so not only allows us to de-confound measures of mean performance and variability (de Haan-Rietdijk et al., 2016), but to model individual differences in all four components of performance that can show unique patterns of relationship with other individual differences measures. In each of the three tasks, model comparisons overwhelmingly favored models with random effects of the four components over a model with fixed effects, suggesting that human behavioral performance cannot be captured adequately by models that do not incorporate individual differences. Even in reaction time data, which often has a strong correlation between mean performance and variability due to floor effects on RT, DSEM was able to model individual differences in these components with reasonably low correlation ($r = 0.397$).

The DSEM approach to modeling variability also allowed us to explore the relationships between the random effects of the four behavioral components and observed measures of interindividual variability calculated directly from the trial-level data. We showed that the iSD measure was strongly related to variability (ψ) from the DSEM, but with significant contributions from the other random effects, while iCV was most strongly related to the mean performance factor (μ) and negatively related to both the mean and variability factors (Figure 3). Taken together, these results highlight the strength of the DSEM to separate out these confounded factors of performance into unique factors and cautions us against using simple observed measures of variability without taking steps to ensure that they are not confounded by other sources of individual differences (e.g., differential trends or autoregression).

The DSEM framework presented here has the potential for many additional expansions that can help to broaden our understanding of the role that variability plays in a wide range of phenomenon. Two such extensions include showing that individual differences in variability have unique consequences by including distal outcomes from longitudinal data into this model. Another exciting extension would be to incorporate the between-person level of the DSEM into a standard growth model (Hancock et al., 2001) to map trajectories of individual differences in mean performance and variability. This type of approach could help to disentangle within- from between-person differences in variability that we found across age in the current investigation. The flexibility of DSEM to incorporate these, and other, complex effects make it a powerful tool for understanding the interplay between individual differences in mean performance and variability across the lifespan.

Testing a Neural Noise Hypothesis

Neural noise has been hypothesized to play a role in age-related changes in motor (Sosnoff & Newell, 2011; Voytek et al., 2015), sensory (Tran et al., 2020), and cognitive (Pertermann et al., 2019; Voytek et al., 2015) abilities. Neural noise has also been proposed as a mechanism in various non-normative states like ADHD (Hearne et al., 2021) and dyslexia (Frey et al., 2019). Common between these different theories is the idea that noisy firing in neural networks impairs consistent and efficacious behavior. Kail (1997), proposed that white matter impairment offered a potential structural mechanism for increase in neural noise across aging, which we tested in the current study. White matter has also been shown to be important for predicting response time variability associated with attentional problems in adolescence, providing additional evidence that this is a theoretically plausible target for investigation (Wiker et al., 2022).

We utilized the dynamic structural equation model to test our hypothesis that reduced white matter microstructure would predict less consistent behavioral performance. To do so, we entered each of the 10 white matter tracts (Hua et al., 2008; Kievit et al., 2016) in separate models as a predictor of each of the four components of behavior. Prior work had shown consistent evidence that enhanced white matter measures related to faster overall performance (Fjell et al., 2011; Turken et al., 2008) and observed measures of variability (Tamnes et al., 2012). Here, we confirm these prior findings, showing that white matter FA predicts both slower mean RT performance and heightened variability in reaction time. These results held across the different white matter tracts, with the exception of the ventral cingulate gyrus (CINGHipp), which showed a non-significant effect. White matter FA did not predict individual differences in the trend or autoregressive effects, although we have much less power to detect effects in the autoregressive parameter as it depends on complex temporal information. While further work remains to incorporate direct measures of neural oscillations into this model, this provides consistent evidence with prior electrophysiological data where greater neural noise is related to poorer performance (Dave et al., 2018; Tran et al., 2020; Voytek et al., 2015), increases during aging (Nobukawa et al., 2019; Voytek & Knight, 2015), and is correlated with white matter morphology (Smit et al., 2012; van Straaten et al., 2015).

To establish the specificity of these relationships, we introduced age into the model as an additional predictor to control for the systematic differences in white matter FA and associated changes in speeded responses across the adult lifespan (Bartzokis et al., 2010). In this full conditional model, we show that the relationships between white matter and the mean and variability factors are preserved, although somewhat attenuated. Consistent with prior work, increased age and reduced white matter FA was associated with poorer (i.e., slower and more

variable) performance (Figure 5). In sum, these results provide additional support for the neural noise hypothesis (Kail, 1997), reflecting a role for white matter in the signal propagation needed for consistent performance and performance deficits when these fibers are compromised.

Directions for Future Research

While there are many strengths to the current approach taken here, there are several avenues for further testing of the neural noise hypothesis that should be addressed in future research. First, longitudinal measures of white matter tract and behavioral change over time would allow us assess within-person dynamic relationships across aging. Additionally, while we tested the relationship between structure and behavioral output variability, an important follow-up test of the neural noise hypothesis would be to link structural brain changes during aging to evoked neural responses during behavior. Combining functional recordings, either fMRI (Garrett et al., 2021) or electrophysiological (McIntosh et al., 2008; Woolnough et al., 2022), with structural measures (e.g., Hearne et al., 2021) would shed important light onto the consequences of white matter loss for function and behavior. One strength of the DSEM approach would be to combine timeseries models for both recordings and behavior and link them at the factor level to measurements of structural WM, or to important cognitive outcomes across aging.

When studying the broader construct of variability, it is important to note that the adaptive versus maladaptive nature of variability is context dependent. In the current work, variability of speeded responses on a relatively simple RT appears to reflect performance deficits. However, in other contexts, such as learning (McCormick & Telzer, 2017) or more complex tasks (Garrett et al., 2011; McIntosh et al., 2008), variability may allow for greater flexibility in representing the task space. Understanding when variability is related to improvements versus declines in cognitive

performance will offer greater insights into the mechanistic processes underlying lifespan brain development.

Conclusions

The study of variability as an important marker of individual differences in behavior and cognition is still in the early phases of development. We presented here a powerful framework for modeling variability in concert with other components of behavior, including mean performance, trends over time, and inertia in trial-level performance. We further show that these individual differences can be used to test a theory of neural noise by including person-level predictors and found that both reduced white matter microstructure and increased age uniquely predict poorer task performance, consistent with the importance of intact white matter tracts for appropriate signal propagation. The results here highlight the promise of leveraging advanced behavioral modeling to move beyond a sole focus on mean differences and recognize variability as an important individual difference marker for understanding human behavior. By combining these models with measures of brain structure and function, this framework can be used to test a wide array of hypotheses for how these individual differences variability emerge.

Acknowledgements

RAK is supported by a Hypatia Fellowship at the RadboudUMC.

The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) research was supported by the Biotechnology and Biological Sciences Research Council (BB/H008217/1). The Cam-CAN corporate author consists of the Project principal personnel: Lorraine K Tyler, Carol Brayne, Edward T Bullmore, Andrew C Calder, Rhodri Cusack, Tim Dalgleish, John Duncan, Richard N Henson, Fiona E Matthews, William D Marslen-Wilson, James B Rowe, Meredith A Shafto; Research Associates: Karen Campbell, Teresa Cheung, Simon Davis, Linda Geerligs, Rogier Kievit, Anna McCarrey, Abdur Mustafa, Darren Price, David Samu, Jason R Taylor, Matthias Treder, Kamen A Tsvetanov, Janna van Belle, Nitin Williams; Research Assistants: Lauren Bates, Tina Emery, Sharon Erzinçlioglu, Andrew Gadie, Sofia Gerbase, Stanimira Georgieva, Claire Hanley, Beth Parkin, David Troy; Affiliated Personnel: Tibor Auer, Marta Correia, Lu Gao, Emma Green, Rafael Henriques; Research Interviewers: Jodie Allen, Gillian Amery, Liana Amunts, Anne Barcroft, Amanda Castle, Cheryl Dias, Jonathan Dowrick, Melissa Fair, Hayley Fisher, Anna Goulding, Adarsh Grewal, Geoff Hale, Andrew Hilton, Frances Johnson, Patricia Johnston, Thea Kavanagh-Williamson, Magdalena Kwasniewska, Alison McMinn, Kim Norman, Jessica Penrose, Fiona Roby, Diane Rowland, John Sargeant, Maggie Squire, Beth Stevens, Aldabra Stoddart, Cheryl Stone, Tracy Thompson, Ozlem Yazlik; and administrative staff: Dan Barnes, Marie Dixon, Jaya Hillman, Joanne Mitchell, Laura Villis, Ethan Knights.

References

- Adam, K. C. S., Mance, I., Fukuda, K., & Vogel, E. K. (2015). The Contribution of Attentional Lapses to Individual Differences in Visual Working Memory Capacity. *Journal of Cognitive Neuroscience*, 27(8), 1601–1616. https://doi.org/10.1162/jocn_a_00811
- Asparouhov, T., Hamaker, E. L., & Muthén, B. (2018). Dynamic Structural Equation Models. *Structural Equation Modeling: A Multidisciplinary Journal*, 25(3), 359–388. <https://doi.org/10.1080/10705511.2017.1406803>
- Bartzokis, G., Lu, P. H., Tingus, K., Mendez, M. F., Richard, A., Peters, D. G., Oluwadara, B., Barrall, K. A., Finn, J. P., Villablanca, P., Thompson, P. M., & Mintz, J. (2010). Lifespan trajectory of myelin integrity and maximum motor speed. *Neurobiology of Aging*, 31(9), 1554–1562. <https://doi.org/10.1016/j.neurobiolaging.2008.08.015>
- Bennett, I. J., & Madden, D. J. (2014). Disconnected aging: Cerebral white matter integrity and age-related differences in cognition. *Neuroscience*, 276, 187–205. <https://doi.org/10.1016/j.neuroscience.2013.11.026>
- Britton, T. C., Meyer, B.-U., & Benecke, R. (1991). Variability of cortically evoked motor responses in multiple sclerosis. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section*, 81(3), 186–194. [https://doi.org/10.1016/0168-5597\(91\)90071-5](https://doi.org/10.1016/0168-5597(91)90071-5)
- Bunce, D., Anstey, K., Christensen, H., Dear, K., Wen, W., & Sachdev, P. (2007). White matter hyperintensities and within-person variability in community-dwelling adults aged 60–64

years. *Neuropsychologia*, 45(9), 2009–2015.

<https://doi.org/10.1016/j.neuropsychologia.2007.02.006>

Dave, S., Brothers, T. A., & Swaab, T. Y. (2018). 1/f neural noise and electrophysiological indices of contextual prediction in aging. *Brain Research*, 1691, 34–43.

<https://doi.org/10.1016/j.brainres.2018.04.007>

de Haan-Rietdijk, S., Kuppens, P., & Hamaker, E. L. (2016). What's in a Day? A Guide to Decomposing the Variance in Intensive Longitudinal Data. *Frontiers in Psychology*, 7, 891. <https://doi.org/10.3389/fpsyg.2016.00891>

de Mooij, S. M. M., Henson, R. N. A., Waldorp, L. J., & Kievit, R. A. (2018). Age Differentiation within Gray Matter, White Matter, and between Memory and White Matter in an Adult Life Span Cohort. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 38(25), 5826–5836. <https://doi.org/10.1523/JNEUROSCI.1627-17.2018>

Dykiert, D., Der, G., Starr, J. M., & Deary, I. J. (2012). Age Differences in Intra-Individual Variability in Simple and Choice Reaction Time: Systematic Review and Meta-Analysis. *PLOS ONE*, 7(10), e45759. <https://doi.org/10.1371/journal.pone.0045759>

Eizenman, D. R., Nesselroade, J. R., Featherman, D. L., & Rowe, J. W. (1997). Intraindividual variability in perceived control in a older sample: The MacArthur successful aging studies. *Psychology and Aging*, 12(3), 489–502. <https://doi.org/10.1037/0882-7974.12.3.489>

Fiske, D. W., & Rice, L. (1955). Intra-individual response variability. *Psychological Bulletin*, 52(3), 217–250. <https://doi.org/10.1037/h0045276>

- 520 Fjell, A. M., Westlye, L. T., Amlien, I. K., & Walhovd, K. B. (2011). Reduced White Matter
 521 Integrity Is Related to Cognitive Instability. *Journal of Neuroscience*, 31(49), 18060–
 522 18072. <https://doi.org/10.1523/JNEUROSCI.4735-11.2011>
- 523 Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). “Mini-mental state”. *Journal of*
 524 *Psychiatric Research*, 12(3), 189–198. [https://doi.org/10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)
- 525 Frey, A., François, C., Chobert, J., Besson, M., & Ziegler, J. C. (2019). Behavioral and
 526 electrophysiological investigation of speech perception deficits in silence, noise and
 527 envelope conditions in developmental dyslexia. *Neuropsychologia*, 130, 3–12.
 528 <https://doi.org/10.1016/j.neuropsychologia.2018.07.033>
- 529 Gamaldo, A. A., An, Y., Allaire, J. C., Kitner-Triolo, M. H., & Zonderman, A. B. (2012). Variability
 530 in performance: Identifying early signs of future cognitive impairment.
 531 *Neuropsychology*, 26(4), 534–540. <https://doi.org/10.1037/a0028686>
- 532 Garrett, D. D., Kovacevic, N., McIntosh, A. R., & Grady, C. L. (2011). The Importance of Being
 533 Variable. *Journal of Neuroscience*, 31(12), 4496–4503.
 534 <https://doi.org/10.1523/JNEUROSCI.5641-10.2011>
- 535 Garrett, D. D., Skowron, A., Wiegert, S., Adolf, J., Dahle, C. L., Lindenberger, U., & Raz, N. (2021).
 536 Lost Dynamics and the Dynamics of Loss: Longitudinal Compression of Brain Signal
 537 Variability is Coupled with Declines in Functional Integration and Cognitive Performance.
 538 *Cerebral Cortex*, 31(11), 5239–5252. <https://doi.org/10.1093/cercor/bhab154>
- 539 Gelman, A., & Rubin, D. B. (1992). Inference from Iterative Simulation Using Multiple
 540 Sequences. *Statistical Science*, 7(4). <https://doi.org/10.1214/ss/1177011136>

- 541 Halliday, D. W. R., Gawryluk, J. R., Garcia-Barrera, M. A., & MacDonald, S. W. S. (2019). White
542 Matter Integrity Is Associated With Intraindividual Variability in Neuropsychological Test
543 Performance in Healthy Older Adults. *Frontiers in Human Neuroscience*, 13, 352.
544 <https://doi.org/10.3389/fnhum.2019.00352>
- 545 Hancock, G. R., Kuo, W.-L., & Lawrence, F. R. (2001). An Illustration of Second-Order Latent
546 Growth Models. *Structural Equation Modeling: A Multidisciplinary Journal*, 8(3), 470–
547 489.
- 548 Haynes, B. I., Bauermeister, S., & Bunce, D. (2017). A Systematic Review of Longitudinal
549 Associations Between Reaction Time Intraindividual Variability and Age-Related
550 Cognitive Decline or Impairment, Dementia, and Mortality. *Journal of the International*
551 *Neuropsychological Society*, 23(5), 431–445.
552 <https://doi.org/10.1017/S1355617717000236>
- 553 Hearne, L. J., Lin, H.-Y., Sanz-Leon, P., Tseng, W.-Y. I., Gau, S. S.-F., Roberts, J. A., & Cocchi, L.
554 (2021). ADHD symptoms map onto noise-driven structure-function decoupling between
555 hub and peripheral brain regions. *Molecular Psychiatry*, 26(8), 4036–4045.
556 <https://doi.org/10.1038/s41380-019-0554-6>
- 557 Hua, K., Zhang, J., Wakana, S., Jiang, H., Li, X., Reich, D. S., Calabresi, P. A., Pekar, J. J., van Zijl, P.
558 C. M., & Mori, S. (2008). Tract probability maps in stereotaxic spaces: Analyses of white
559 matter anatomy and tract-specific quantification. *NeuroImage*, 39(1), 336–347.
560 <https://doi.org/10.1016/j.neuroimage.2007.07.053>

- 561 Jones, D. K., Knösche, T. R., & Turner, R. (2013). White matter integrity, fiber count, and other
 562 fallacies: The do's and don'ts of diffusion MRI. *NeuroImage*, 73, 239–254.
 563 <https://doi.org/10.1016/j.neuroimage.2012.06.081>
- 564 Kail, R. (1997). The neural noise hypothesis: Evidence from processing speed in adults with
 565 multiple sclerosis. *Aging, Neuropsychology, and Cognition*, 4(3), 157–165.
 566 <https://doi.org/10.1080/13825589708256644>
- 567 Kievit, R. A., Davis, S. W., Griffiths, J., Correia, M. M., Cam-CAN, & Henson, R. N. (2016). A
 568 watershed model of individual differences in fluid intelligence. *Neuropsychologia*, 91,
 569 186–198. <https://doi.org/10.1016/j.neuropsychologia.2016.08.008>
- 570 Lavery, M. R., Acharya, P., Sivo, S. A., & Xu, L. (2019). Number of predictors and
 571 multicollinearity: What are their effects on error and bias in regression?
 572 *Communications in Statistics - Simulation and Computation*, 48(1), 27–38.
 573 <https://doi.org/10.1080/03610918.2017.1371750>
- 574 Li, S.-C., & Lindenberger, U. (1999). Cross-level unification: A computational exploration of the
 575 link between deterioration of neurotransmitter systems and dedifferentiation of
 576 cognitive abilities in old age. In *Cognitive Neuroscience of Memory* (pp. 103–146).
 577 Hogrefe & Huber Publishers.
- 578 Li, S.-C., Lindenberger, U., Hommel, B., Aschersleben, G., Prinz, W., & Baltes, P. B. (2004).
 579 Transformations in the Couplings Among Intellectual Abilities and Constituent Cognitive
 580 Processes Across the Life Span. *Psychological Science*, 15(3), 155–163.
 581 <https://doi.org/10.1111/j.0956-7976.2004.01503003.x>

Poorer white matter microstructure predicts slower and more variable reaction time performance

- 582 MacDonald, S. W. S., Nyberg, L., & Bäckman, L. (2006). Intra-individual variability in behavior:
583 Links to brain structure, neurotransmission and neuronal activity. *Trends in*
584 *Neurosciences*, 29(8), 474–480. <https://doi.org/10.1016/j.tins.2006.06.011>
- 585 McCormick, E. M. (2021). Multi-Level Multi-Growth Models: New opportunities for addressing
586 developmental theory using advanced longitudinal designs with planned missingness.
587 *Developmental Cognitive Neuroscience*, 51, 101001.
588 <https://doi.org/10.1016/j.dcn.2021.101001>
- 589 McCormick, E. M., & Telzer, E. H. (2017). Adaptive Adolescent Flexibility: Neurodevelopment of
590 Decision-making and Learning in a Risky Context. *J. Cogn. Neurosci.*, 29(3), 413–423.
- 591 McIntosh, A. R., Kovacevic, N., & Itier, R. J. (2008). Increased Brain Signal Variability
592 Accompanies Lower Behavioral Variability in Development. *PLOS Computational Biology*,
593 4(7), e1000106. <https://doi.org/10.1371/journal.pcbi.1000106>
- 594 McNeish, D., & Hamaker, E. L. (2020). A primer on two-level dynamic structural equation
595 models for intensive longitudinal data in Mplus. *Psychological Methods*, 25(5), 610–635.
596 <https://doi.org/10.1037/met0000250>
- 597 Nesselroade, J. (1991). *The Warp and Woof of the Developmental Fabric*.
- 598 Nobukawa, S., Kikuchi, M., & Takahashi, T. (2019). Changes in functional connectivity dynamics
599 with aging: A dynamical phase synchronization approach. *NeuroImage*, 188, 357–368.
600 <https://doi.org/10.1016/j.neuroimage.2018.12.008>
- 601 Pertermann, M., Mückschel, M., Adelhöfer, N., Ziemssen, T., & Beste, C. (2019). On the
602 interrelation of $1/f$ neural noise and norepinephrine system activity during motor

response inhibition. *Journal of Neurophysiology*, 121(5), 1633–1643.

<https://doi.org/10.1152/jn.00701.2018>

Peters, A. (2009). The effects of normal aging on myelinated nerve fibers in monkey central nervous system. *Frontiers in Neuroanatomy*.

<http://dx.doi.org/10.3389/neuro.05.011.2009>

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition.

Psychological Review, 103(3), 403–428. <https://doi.org/10.1037/0033-295X.103.3.403>

Schuurman, N. K., Ferrer, E., de Boer-Sonnenschein, M., & Hamaker, E. L. (2016). How to

compare cross-lagged associations in a multilevel autoregressive model. *Psychological*

Methods, 21(2), 206–221. <https://doi.org/10.1037/met0000062>

Shafto, M. A., Tyler, L. K., Dixon, M., Taylor, J. R., Rowe, J. B., Cusack, R., Calder, A. J., Marslen-Wilson, W. D., Duncan, J., Dalgleish, T., Henson, R. N., Brayne, C., & Matthews, F. E.

(2014). The Cambridge Centre for Ageing and Neuroscience (Cam-CAN) study protocol:

A cross-sectional, lifespan, multidisciplinary examination of healthy cognitive ageing.

BMC Neurology, 14, 204. <https://doi.org/10.1186/s12883-014-0204-1>

Smit, D. J. A., Boersma, M., Schnack, H. G., Micheloyannis, S., Boomsma, D. I., Pol, H. E. H.,

Stam, C. J., & Geus, E. J. C. de. (2012). The Brain Matures with Stronger Functional

Connectivity and Decreased Randomness of Its Network. *PLOS ONE*, 7(5), e36896.

<https://doi.org/10.1371/journal.pone.0036896>

Sorg, S. F., Merritt, V. C., Clark, A. L., Werhane, M. L., Holiday, K. A., Schiehser, D. M., Bondi, M.,

& Delano-Wood, L. (2021). Elevated Intraindividual Variability in Executive Functions

and Associations with White Matter Microstructure in Veterans with Mild Traumatic

- 625 Brain Injury. *Journal of the International Neuropsychological Society*, 27(4), 305–314.
626 <https://doi.org/10.1017/S1355617720000879>
- 627 Sosnoff, J. J., & Newell, K. M. (2011). Aging and motor variability: A test of the neural noise
628 hypothesis. *Experimental Aging Research*, 37(4), 377–397.
629 <https://doi.org/10.1080/0361073X.2011.590754>
- 630 Tamnes, C. K., Fjell, A. M., Westlye, L. T., Ostby, Y., & Walhovd, K. B. (2012). Becoming
631 Consistent: Developmental Reductions in Intraindividual Variability in Reaction Time Are
632 Related to White Matter Integrity. *Journal of Neuroscience*, 32(3), 972–982.
633 <https://doi.org/10.1523/JNEUROSCI.4779-11.2012>
- 634 Taylor, J. R., Williams, N., Cusack, R., Auer, T., Shafto, M. A., Dixon, M., Tyler, L. K., Cam-CAN, &
635 Henson, R. N. (2017). The Cambridge Centre for Ageing and Neuroscience (Cam-CAN)
636 data repository: Structural and functional MRI, MEG, and cognitive data from a cross-
637 sectional adult lifespan sample. *NeuroImage*, 144, 262–269.
638 <https://doi.org/10.1016/j.neuroimage.2015.09.018>
- 639 Tran, T. T., Rolle, C. E., Gazzaley, A., & Voytek, B. (2020). Linked sources of neural noise
640 contribute to age-related cognitive decline. *Journal of Cognitive Neuroscience*, 32(9),
641 1813–1822. https://doi.org/10.1162/jocn_a_01584
- 642 Turken, U., Whitfield-Gabrieli, S., Bammer, R., Baldo, J. V., Dronkers, N. F., & Gabrieli, J. D. E.
643 (2008). Cognitive processing speed and the structure of white matter pathways:
644 Convergent evidence from normal variation and lesion studies. *NeuroImage*, 42(2),
645 1032–1044. <https://doi.org/10.1016/j.neuroimage.2008.03.057>

- 646 van Straaten, E. C. W., den Haan, J., de Waal, H., van der Flier, W. M., Barkhof, F., Prins, N. D., &
 647 Stam, C. J. (2015). Disturbed phase relations in white matter hyperintensity based
 648 vascular dementia: An EEG directed connectivity study. *Clinical Neurophysiology: Official*
 649 *Journal of the International Federation of Clinical Neurophysiology*, 126(3), 497–504.
 650 <https://doi.org/10.1016/j.clinph.2014.05.018>
- 651 Voytek, B., & Knight, R. T. (2015). Dynamic Network Communication as a Unifying Neural Basis
 652 for Cognition, Development, Aging, and Disease. *Biological Psychiatry*, 77(12), 1089–
 653 1097. <https://doi.org/10.1016/j.biopsych.2015.04.016>
- 654 Voytek, B., Kramer, M. A., Case, J., Lepage, K. Q., Tempesta, Z. R., Knight, R. T., & Gazzaley, A.
 655 (2015). Age-Related Changes in 1/f Neural Electrophysiological Noise. *Journal of*
 656 *Neuroscience*, 35(38), 13257–13265. <https://doi.org/10.1523/JNEUROSCI.2332-14.2015>
- 657 Wang, L. (Peggy), & Grimm, K. J. (2012). Investigating Reliabilities of Intraindividual Variability
 658 Indicators. *Multivariate Behavioral Research*, 47(5), 771–802.
 659 <https://doi.org/10.1080/00273171.2012.715842>
- 660 Williams, B. R., Hultsch, D. F., Strauss, E. H., Hunter, M. A., & Tannock, R. (2005). Inconsistency
 661 in Reaction Time Across the Life Span. *Neuropsychology*, 19(1), 88–96.
 662 <https://doi.org/10.1037/0894-4105.19.1.88>
- 663 Woodrow, H. (1932). Quotidian variability. *Psychological Review*, 39(3), 245–256.
 664 <https://doi.org/10.1037/h0073076>
- 665 Woolnough, O., Kadipasaoglu, C. M., Conner, C. R., Forseth, K. J., Rollo, P. S., Rollo, M. J.,
 666 Baboyan, V. G., & Tandon, N. (2022). Dataset of human intracranial recordings during

667 famous landmark identification. *Scientific Data*, 9(1), Article 1.

668 <https://doi.org/10.1038/s41597-022-01125-8>

669