

Lower theta inter-trial phase coherence during performance monitoring is related to higher reaction time variability: A lifespan study



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ABSTRACT

Trial-to-trial reaction time (RT) variability is consistently higher in children and older adults than in younger adults. Converging evidence also indicates that higher RT variability is (a) associated with lower behavioral performance on complex cognitive tasks, (b) distinguishes patients with neurological deficits from healthy individuals, and also (c) predicts longitudinal cognitive decline in older adults. However, so far the processes underlying increased RT variability are poorly understood. Previous evidence suggests that control signals in the medial frontal cortex (MFC) are reflected in theta band activity and may implicate the coordination of distinct brain areas during performance monitoring. We hypothesized that greater trial-to-trial variability in theta power during performance monitoring may be associated with greater behavioral variability in response latencies. We analyzed event-related theta oscillations assessed during a cued-Go/NoGo task in a lifespan sample covering the age range from middle childhood to old age. Our results show that theta inter-trial coherence during NoGo trials increases from childhood to early adulthood, and decreases from early adulthood to old age. Moreover, in all age groups, individuals with higher variability in medial frontal stimulus-locked theta oscillations showed higher trial-to-trial RT variability behaviorally. Importantly, this effect was strongest at high performance monitoring demands and independent of motor response execution as well as theta power. Taken together, our findings reveal that lower theta inter-trial coherence is related to greater behavioral variability within and across age groups. These results hint at the possibility that more variable MFC control may be associated with greater performance fluctuations.

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Introduction

Cross-sectional studies have repeatedly reported that within-person trial-to-trial reaction time (RT) variability decreases from childhood to adolescence and increases again from young adulthood to old age (e.g., Dykiert et al., 2012; Li et al., 2004, 2009; Williams et al., 2005, 2007). Intra-individual variability in reaction times is generally considered to be an index of central nervous system functioning (for a recent review, see Dykiert et al., 2012). Previous research has shown that elevated RT variability reflects the efficacy of higher level cognitive functioning above and beyond motor executive processes. For instance, RT variability in older adults has been attributed to the decision rather than the motor component of a task (e.g., Bunce et al., 2004). Moreover, higher trial-to-trial RT variability is associated with lower behavioral performance in a variety of complex cognitive tasks (e.g., Hultsch et al.,

2002) and has been shown to predict longitudinal cognitive decline in late adulthood, such as in executive functioning (Lövdén et al., 2007) and episodic memory (MacDonald et al., 2003).

RT variability as an indicator of age-related and individual differences in frontal lobe functions

In clinical research, deficiency in frontal lobe functioning has been related to higher processing fluctuations. Adult patients with lesions in the frontal lobes usually show more variable RTs in comparison to healthy controls (Murtha et al., 2002; Picton et al., 2007; Stuss et al., 2003; Walker et al., 2000). In healthy adult samples, age differences are particularly pronounced on tasks assessing frontal lobe functioning, such as inhibition (Strauss et al., 2007) and working memory (West et al., 2002; Dixon et al., 2007). Similarly, children with frontal-lobe mediated executive control deficits, such as patients with attention deficit hyperactivity disorder, show higher RT variability than healthy controls (for review, see Kuntsi and Klein, 2012). Indeed, structural, functional and neurochemical declines in the frontal lobes in old age (for reviews, see MacDonald et al., 2006, 2009) have been associated with higher within-person variability. However, the functional processes

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underlying the contribution of the frontal lobe to higher RT fluctuations remain poorly understood.

Theta band oscillations during performance monitoring as a neural correlate of behavioral RT variability

Three decades of cognitive neuroscience research have established the role of the medial frontal cortex (MFC) in performance monitoring and cognitive control (for review, see Ridderinkhof et al., 2004). More recent investigations on cognitive control suggest that the MFC exerts control by interacting with other task relevant brain regions through neural oscillations in the theta (4–7 Hz) band (e.g., Cavanagh et al., 2009; Cohen et al., 2011; Hanslmayr et al., 2008; Nigbur et al., 2012). Direct intracranial recordings confirm the MFC as a generator of theta band oscillations in humans (Cohen et al., 2008; Wang et al., 2005). Specifically, Cohen and colleagues found that performance during a modified Flanker task was associated with an enhancement of theta power following the response suggesting post-response performance monitoring. In addition, theta oscillations in the MFC and fronto-central scalp electrodes were coupled, indicating that scalp electrodes indeed reflect activity from intracranial sources. In line with the suggested role in cognitive control and monitoring, increases in medial frontal theta band power have been observed in more demanding performance monitoring conditions, such as during Go/NoGo tasks (e.g., Nigbur et al., 2011; Schmiedt-Fehr and Basar-Eroglu, 2011). Furthermore, medial frontal theta activity has been consistently observed to be higher during situations requiring more cognitive control, such as during errors or prior to performance adaptations (e.g., Cavanagh et al., 2012; Cohen et al., 2008, 2009; Luu and Tucker, 2002; Mazaheri et al., 2009).

Other than amplitude-related measures, the temporal synchronicity of theta oscillations has recently gained more attention in the research on cognitive control. It has been suggested that variability in the stimulus-locked theta phase across trials at single electrodes or between electrodes presumably reflects the temporal coordination of cortical processes (Klimesch et al., 2007; Sauseng and Klimesch, 2008). Given that the theta oscillation is a promising neural correlate for frontally coordinated cognitive control processes, the phase of the oscillation might provide a means for coordinating interactions between distant brain areas (e.g., Cavanagh et al., 2009; Cohen et al., 2011). Of specific relevance for the current study, increasing evidence shows that lower theta inter-trial phase locking at single electrodes is related to behavioral performance (e.g., Klimesch et al., 2004; Groom et al., 2010; Müller et al., 2009; Rutishauser et al., 2010). Specifically, higher RT variability in a Go/NoGo task has been found to be associated with lower inter-trial phase coherence in the theta band in adolescents (Groom et al., 2010), indicating that increased intraindividual variability may be related to more variable electroencephalographic signals in the theta range. However, participants in the Groom et al. (2010) study motorically responded during the condition of interest; therefore, lower coherence in this case may not necessarily reflect variability in higher-level control processes, as lower theta coherence could also have reflected neural variability associated with motor execution processes. To summarize, interindividual differences in RT variability may be due to deficient frontal cognitive control processing. Initial evidence suggests that temporal variability in performance monitoring in the MFC might be a suitable candidate process for studying lifespan developmental and individual differences in behavioral RT variability.

Study aims and key hypotheses

Given the involvement of the MFC in performance monitoring and motor control that is well-established in functional brain imaging studies (for review, see Ridderinkhof et al., 2004), we aimed at investigating whether more variable performance monitoring signals, which are not confounded with motor responses, would be associated with

greater variability in response latencies of behavior and brain electrophysiological responses. In addition, we aimed at investigating whether lifespan age differences in RT variability are also reflected in lifespan age differences in the temporal variability of performance monitoring processes.

We analyzed event-related theta oscillations assessed during a cued Go/NoGo task in a lifespan sample (children, adolescents, younger adults, older adults) with a specific focus on inter-trial phase coherence (ITPC). Based on initial evidence relating lower theta ITPC to higher RT variability (Groom et al., 2010) and the well-established lifespan patterns of RT variability (e.g., Li et al., 2004; Williams et al., 2005), we expected an increase in theta NoGo ITPC with maturation and a decrease in old age. Here, we focus particularly on the NoGo condition, as performance monitoring demands are highest in this condition and Go trials may be confounded with response-related activity. Further, we expected that within age groups variability of performance monitoring signals would predict individual differences in behavioral variability. Specifically, we expected that individuals with higher theta inter-trial phase synchrony during the NoGo condition show higher behavioral RT variability. In addition, it remains an open question whether theta power would also predict RT variability. Thus, we further tested whether the magnitude of the theta response would also be predictive of interindividual differences in RT variability or whether the link to behavioral variability is specific to the coherence measure.

Methods

Participants

The sample included 182 participants, with 35 children (aged 9 to 11 years; 21 girls), 43 adolescents (aged 12 to 16 years; 22 girls), 46 younger (aged 20 to 28 years; 22 women), and 47 older adults (aged 65 to 75 years; 24 women). Data from 10 children and 1 adolescent were excluded due to an insufficient number of available trials after artifact rejections for time–frequency analyses (i.e., fewer than 25 trials per condition). All participants were right-handed, as indexed by the Edinburgh Handedness Index (Oldfield, 1971). Written informed consent was obtained from all participant or parents and participants were paid for their participation. The study was approved by the ethics committee of the Max Planck Institute for Human Development.

Experimental task

A detailed description of the study design has been reported elsewhere (Hämmerer et al., 2010). In short, participants were assessed on a modified variant of the Continuous Performance Task (CPT; Beck et al., 1956), the AX-CPT task (Braver et al., 2001). During the task, participants were shown 12 squares of different colors sequentially on a white screen. Participants were required to respond to the presentation of a Target stimulus (a yellow square), whenever it was preceded by a Cue stimulus (a blue square). No response was required when the Cue stimulus was presented or any of the other 10 Non-Cue stimuli.

In the task, 270 Go pairs (Cue followed by Target) and 195 NoGo pairs were presented. For each possible type of NoGo pair, there were 65 trials: prime-based NoGo pair (Cue followed by Non-Target), response-based NoGo pair (Non-Cue followed by Target), and Non-Cue NoGo pair (Non-Cue followed by Non-Target). In total, 930 stimuli were presented in 5 blocks, with 186 stimuli per block. As Go pairs (Cue followed by Target; 58%) were more frequent than prime-based NoGo trials (Cue not followed by Target; 14%), response conflict was largest on prime-based NoGo trials. Therefore, we focused on Go and prime-based NoGo trials in our analyses. This allowed us to contrast two conditions with low and higher performance monitoring demands, in addition to the advantage that NoGo trials are not confounded by response-related activity.

In each trial, a colored square was presented for 200 ms, followed by a blank screen and a fixation cross, which was presented for 1500 ms and its appearance indicated the response time limit. Response time limits differed among age groups and were determined in pilot experiments. Different response time limits ensured that the four age groups would be motivated to the same extent to respond as quickly and accurately as possible, and that there would be age group differences in speed–accuracy trade-off (Hämmerer et al., 2010). Specifically, the fixation cross appeared 650 ms after the beginning of the trial for children and older adults and 500 ms after the beginning of the trial for adolescents and younger adults.

EEG recordings

The electroencephalogram (EEG) was recorded from 64 Ag/AgCl electrodes (BrainAmp DC amplifiers, Brain Products GmbH, Gilching, Germany) arranged according to the 10–10 system in an elastic cap (Braincap, BrainVision), using BrainVision Recorder. Electrode impedances were kept below 5 k Ω and all electrodes were referenced online to the right mastoid. The ground electrode was positioned above the forehead. Vertical and horizontal electrooculograms were recorded next to each eye and below the left eye. During recording, signals were bandpass-filtered from 0.01 to 250 Hz and the sampling rate was 1000 Hz.

Using BrainVision Analyzer, the recorded data were rereferenced to an averaged mastoid reference. Using the Fieldtrip software package (for more details see <http://www.ru.nl/fcdonders/fieldtrip>), the data were segmented into epochs of 1.5 s before and 2.5 s after the onset of the colored square.

Epochs or channels with severe muscular artifacts or saturated recordings were excluded manually. Using EEGLAB (Delorme and Makeig, 2004), ICA components of ocular and muscular artifacts were removed from the data. The recombined data were bandpass-filtered in the range of 0.5–70 Hz and epoched according to the time windows of interest (1.5 s before and 2.5 s after stimulus onset).

EEG analyses: Exclusion criteria and time–frequency decomposition

Given that the number of trials per condition (Go vs. NoGo) varied among individuals and ITPC is sensitive to the number of trials (Vinc et al., 2010), we selected 25 artifact-free epochs for each condition (Go and NoGo, respectively) and individual (cf. Schmiedt-Fehr and Basar-Eroglu, 2011). Trials were selected randomly, if more than 25 trials were available. Only correct trials were included in the analyses.

ITPC measures were computed using EEGLAB (Delorme and Makeig, 2004; `newtimef` function). 25 stimulus-locked epochs of –1500 to 2500 ms were decomposed using Morlet wavelets. The number of cycles for Morlet wavelets varied with the frequency being analyzed (1 cycle at 1 Hz to 6 cycles at 12 Hz, in 0.5 Hz steps). ITPC reflects the consistency of phase values across trials, at different frequencies, and at single electrodes. The ITPC is stimulus-locked and independent of amplitude changes. A value of 0 represents the absence of EEG phase synchronization across trials of the evoked response; a value of 1 indicates their perfect synchronization (for a detailed description of the method see Delorme and Makeig, 2004). For the purpose of control analyses, the event-related spectral power (ERSP), a measure of induced power, was computed using the same method. ERSP indicates the mean changes in log power at a given time–frequency point. In contrast to ITPC, ERSP is sensitive to the signal's amplitude and independent of the phase. In the following, we refer to theta ERSP as theta power. Given age differences in total power (e.g., Müller et al., 2009), which may be, at least in part due to age differences in brain size, brain geometry, or skull thickness (cf. Frodl et al., 2001 for effects of skull on event-related P300), an individual-based baseline correction was applied to the data. The power in the pre-stimulus

interval of –600 to –400 ms was subtracted from the post-stimulus theta power.

Behavioral indicators and exclusion criteria for behavioral data

RTs faster than 100 ms and slower than 2000 ms were excluded from the analyses. RT variability and processing speed were assessed in all available correct Go trials, since NoGo trials did not require a response. More specifically, RT variability was computed as the standard deviation of RTs across trials, whereas the median RT, which is less sensitive to outliers, was chosen as the indicator for the speed of responding. Deviations from normality within age group distributions were corrected by taking the square root of the RT variability (Tabachnick and Fidell, 2007). Further, outliers above and below 3.5 standard deviations were excluded from the data, separately for each age group.

Statistical analyses of behavioral and EEG data

Data were analyzed with SPSS for Windows 15.0 (SPSS, Chicago IL). In light of multivariate heterogeneity of variances and covariances in the behavioral data, as reflected in the Box's M tests for RT variability ($p < .05$), data were analyzed in SAS 9.1 (SAS Institute Inc., Cary, NC, USA) with mixed-effect models ("Proc Mixed" procedure), using maximum-likelihood estimation. In contrast to standard ANOVA, mixed-effect models do not assume equal variances and covariances between groups (Littell et al., 2002).

To examine whether lifespan differences in processing variability would be in line with previous studies (e.g., Williams et al., 2005), we conducted an omnibus test with trial-to-trial RT variability as dependent variable and age group (children, adolescence, younger adults, older adults) as between-subject factor. Given that sex differences in processing variability have been reported previously (e.g., Dykiert et al., 2012), with women being more variable than men, and the positive relationship between speed of responding and RT variability (e.g., Shammi et al., 1998), sex and median RT in the Go condition were included as covariates in the analysis.

For statistical comparisons of theta ITPC among age groups, we extracted the individual peak ITPC values at FCz, after averaging across the theta band. Given our interest in medial frontal theta oscillations, we focused on FCz, which has been associated with the MFC in source localization analyses (e.g., Nigbur et al., 2011) and intracranial recordings (Cohen et al., 2008; Wang et al., 2005). In the literature, early and late theta inter-trial phase synchronization have been described (Müller and Anokhin, 2012; Schmiedt-Fehr and Basar-Eroglu, 2011). However, cut-offs for the definition of early vs. late theta inter-trial phase coherence are varying across studies (e.g., 200 ms, 300 ms). Whereas late theta inter-trial phase synchrony has been associated with performance monitoring processes (Cavanagh et al., 2012; Müller and Anokhin, 2012; Schmiedt-Fehr and Basar-Eroglu, 2011), the role of early theta synchrony is still not well established, but may reflect rather response-related activity (Müller and Anokhin, 2012). Therefore, we focus on late theta phase oscillations, which peak after 200 ms at the individual and group level in our study (cf. Fig. 3). Specifically, we determined the maximal ITPC in the time window of 200 ms to 500 ms after stimulus presentation for each individual, separately for the Go and NoGo conditions. For further analyses, we extracted the mean theta ITPC in time windows of 50 ms around the individual maximum ITPC. The same approach was taken to assess theta ERSP at FCz and delta (1–3 Hz) ITPC at Cz within 200 to 500 ms for the control analyses reported below. To investigate lifespan differences in theta ITPC, we conducted a repeated measures analysis of variance (ANOVA) with condition (Go and NoGo at FCz) as within-subject factor and age group as between-subject factor (children, adolescence, younger adults, older adults).

Significant main effects of age group were followed by planned contrasts and pairwise comparisons to further describe lifespan patterns in RT variability and inter-trial phase synchrony. Specifically, we tested for a linear and a curvilinear pattern across age groups.

Effect sizes are reported by intraclass correlation coefficient (*ICC*) for main effects and interactions. The *ICC* has been recommended to be especially suitable for repeated measures designs (Fern and Monroe, 1996). *ICC* values were squared to ease interpretation in terms of the percentage of total variance associated with an effect. For planned contrasts and pairwise comparisons, effect sizes are indicated using Cohen's *d*, based on pooled standard deviations to account for differences in variances between age groups.

Finally, we were interested whether individual differences in theta ITPC during NoGo and Go would predict trial-to-trial RT variability. Therefore, we conducted regression analyses across the four age groups with RT variability as dependent variable. For this purpose, we created dummy variables to code for the main effects of age groups, which were entered first into the model. That way, there were no intercept differences across age groups, allowing us to perform the hierarchical regression analyses across all age groups (similar to correlational analyses that partials the effect of age group). Regression analyses were conducted for Go and NoGo conditions separately. In addition, median RTs of the Go condition were partialled out to test whether the relationship between processing variability and theta ITPC during NoGo trials was independent from speed of responding and response-related activity. Finally, Spearman correlations were computed separately for each age group.

Results

Lifespan differences in trial-to-trial RT variability

RT variability during the Go condition is presented in Fig. 1 for the four age groups. The omnibus test yielded a main effect of age group, $F(3,76.2) = 35.2$, $p < .05$, $ICC = 0.76$ (explaining 58% of the total variance in the data). Planned contrasts confirmed a linear, $t = 8.84$, $p < .05$, $d = 1.76$, and curvilinear pattern, $t = 8.31$, $p < .05$, $d = 1.35$, across the lifespan. In line with the curvilinear pattern, pairwise comparisons indicated that adolescents were less variable in their RTs than children, $t = 2.43$, $p < .05$, $d = 1.17$, younger adults were less variable in RTs than adolescents, $t = 3.40$, $p < .05$, $d = 0.68$, and older adults, $t = 3.32$, $p < .05$, $d = 0.65$.

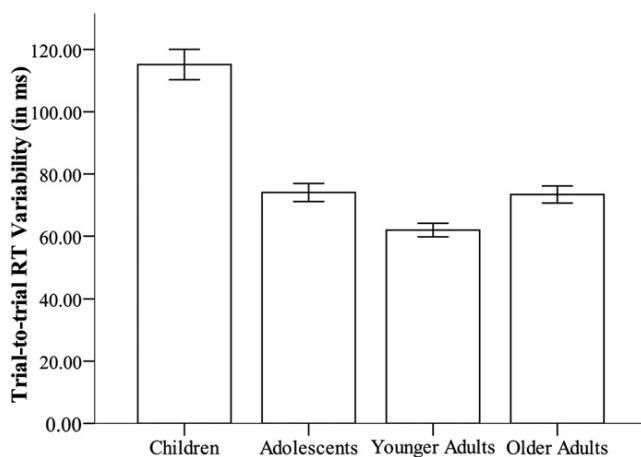


Fig. 1. Trial-to-trial RT variability during Go trials in the four age groups. Error bars represent one standard error around the mean.

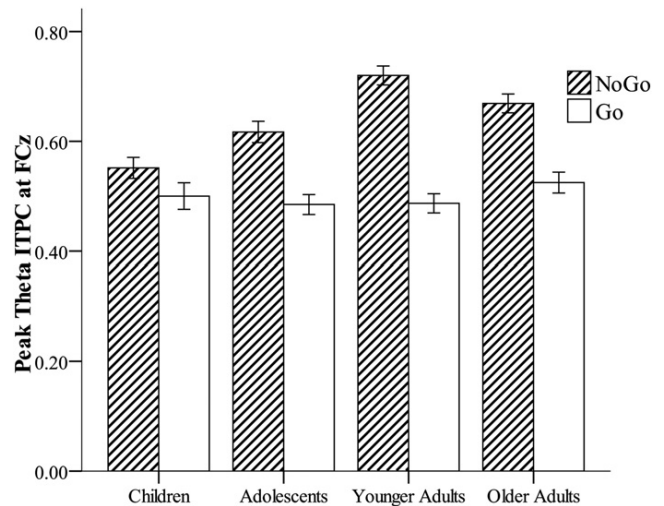


Fig. 2. Individual peak theta ITPC at FCz during Go and NoGo in the four age groups. Error bars represent one standard error around the mean.

Lifespan differences in theta ITPC at FCz

Bar graphs in Fig. 2 indicate individual peak theta ITPC during Go and NoGo at FCz for the four age groups. In Fig. 3, theta ITPC is depicted in topographical plots and the time–frequency plots indicate theta ITPC at FCz.

The analyses revealed a main effect of condition, $F(1,167) = 139.7$, $p < .05$, $ICC = .46$ (21%), indicating that theta ITPC was higher in the NoGo than the Go condition. Furthermore, the main effect of age group was significant, $F(3,167) = 6.1$, $p < .05$, $ICC = .10$ (1%), indicating lifespan differences in theta ITPC, which were more pronounced in the NoGo condition, as indicated by a significant age group \times condition interaction, $F(3,167) = 18.32$, $p < .05$, $ICC = .25$ (6.3%). In fact, neither the linear nor curvilinear contrast was significant ($ps > .1$) for the Go condition, suggesting no age group differences on the less demanding Go trials. In contrast, planned contrasts confirmed a linear, $t = 5.76$, $p < .05$, $d = 0.88$, and curvilinear pattern, $t = 3.22$, $p < .05$, $d = 0.49$, across the lifespan for theta ITPC during NoGo. Pairwise comparisons were again conducted to follow up on the contrast effects, confirming the results. In line with the behavioral data and with our predictions of a curvilinear relationship across the lifespan, theta ITPC was significantly higher in younger adults than in adolescents, $t = 4.17$, $p < .05$, $d = 0.89$, and older adults, $t = 2.06$, $p < .05$, $d = 0.43$. Children showed significantly lower theta ITPC than adolescents, $t = 2.48$, $p < .05$, $d = 0.57$ and older adults, $t = 4.45$, $p < .05$, $d = 1.00$.

Relationship between theta ITPC and RT variability

Regression analyses across the four age groups indicated that RT variability was significantly predicted by both theta ITPC during Go trials, $\beta = -.11$, $t(164) = 2.05$, $p < .05$, and NoGo ITPC, $\beta = -.34$, $t(164) = 6.02$, $p < .05$. However, hierarchical regression analyses showed that theta ITPC during the NoGo but not during the Go condition proved to be an independent predictor of RT variability. NoGo ITPC was a reliable predictor of RT variability after theta Go ITPC was adjusted for, as indicated by the change statistics, $R^2_{\text{change}} = .08$, $F_{\text{change}}(1, 164) = 32.14$, $p < .05$. In contrast, theta Go ITPC did not remain a significant predictor of RT variability beyond theta NoGo ITPC ($R^2_{\text{change}} = .00$, $F_{\text{change}}(1, 164) = 1.11$, $p > .05$). While the relationship between ITPC during Go trials and trial-to-trial RT variability was only reliable in younger adults (Spearman correlation: $r = -.41$, $p < .05$), lower theta ITPC during NoGo trials was related to higher trial-to-trial RT variability in all four age group: children, $r = -.35$, $p < .05$, adolescents, $r = -.44$, $p < .05$, younger, $r = -.62$,

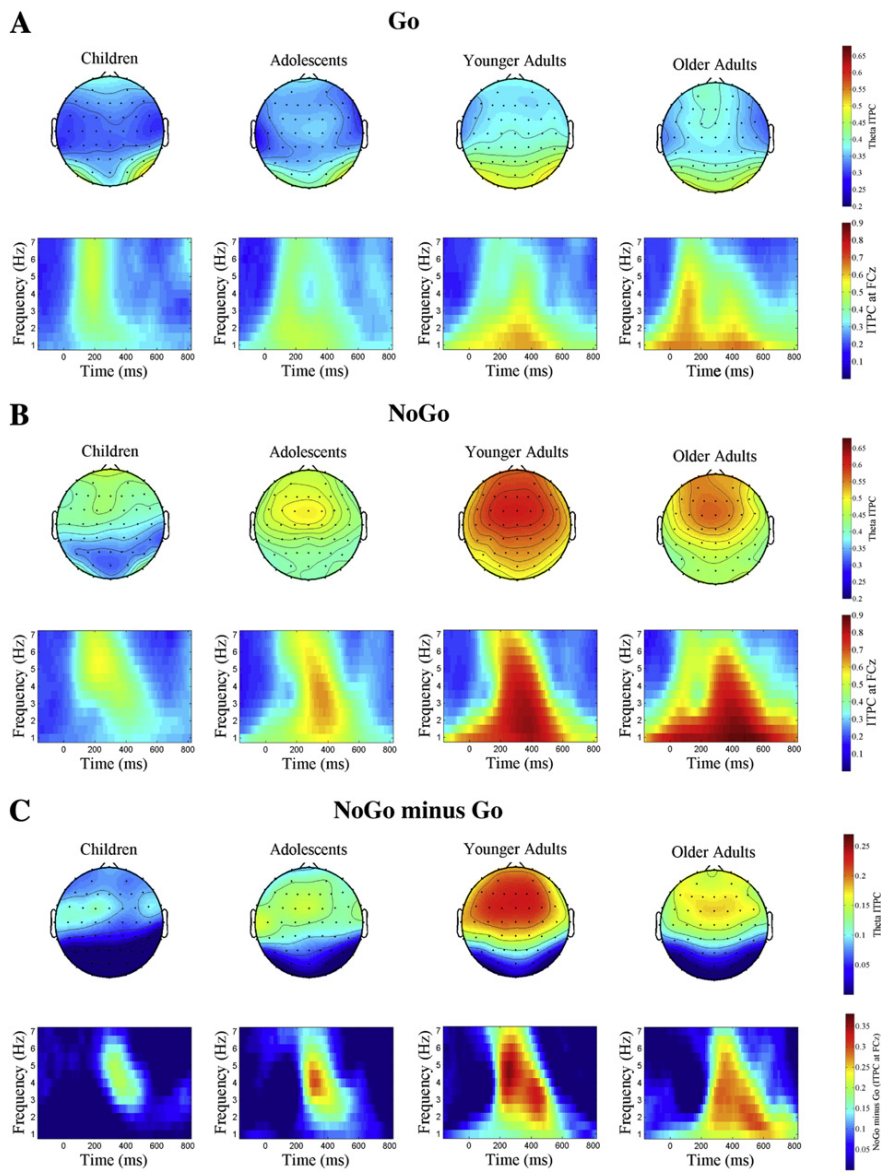


Fig. 3. Topographical maps reflect theta ITPC in the time window 200 to 500 ms and time–frequency plots indicate ITPC at FCz for the four age groups during Go (A), NoGo (B), and NoGo minus Go (C).

$p < .05$, and older adults, $r = -.42$, $p < .05$. Crucially, the relationship between NoGo theta ITPC and trial-to-trial RT variability remained significant in all four age groups, after controlling for theta ITPC during Go trials and speed of responding (see Fig. 4 for scatter plots). In contrast to RT

variability, regression analyses with speed of responding as dependent variable did not identify ITPC during Go and NoGo as reliable predictors ($ps > .1$). This pattern was confirmed in the four age groups, because none of the Spearman correlations was significant between median RT

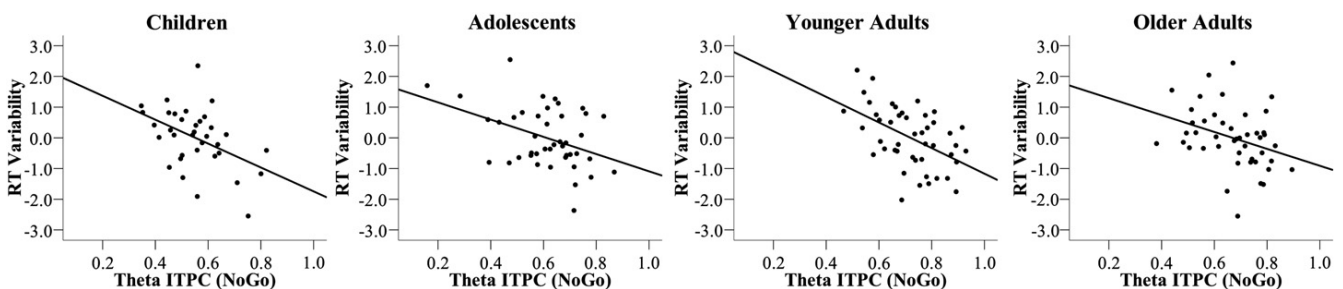


Fig. 4. Scatter plots of the correlation between peak theta ITPC during NoGo at FCz and trial-to-trial RT variability during Go (Spearman rank correlation coefficient: children, $r = -.50$, $p < .05$, adolescents, $r = -.31$, $p < .05$, younger, $r = -.48$, $p < .05$, and older adults, $r = -.35$, $p < .05$). RT variability scores refer to standardized residuals after statistically controlling for median RT and Go theta ITPC within age groups.

and theta ITPC during Go and NoGo, once potential relations to RT variability were adjusted for (all p s > .1 for Spearman correlations), indicating that variability in theta band oscillations is particularly related to RT variability and unrelated to speed of responding.

Control analyses

Two sets of additional control analyses were conducted, examining the relationship to trial-to-trial RT variability. First, the relationship between RT variability and theta power was investigated. Second, in light of higher inter-trial phase synchronization in the delta band during NoGo than Go, delta ITPC may contribute to successful performance monitoring as well and be potentially related to RT variability (see analyses below and time–frequency plots in Fig. 3).

Relationship of RT variability with event-related theta power

Similar to analyses focusing on theta ITPC, repeated measures ANOVA revealed a main effect of condition, $F(1,167) = 358.7, p < .05, ICC = .68$ (46.2%), indicating higher theta power in the NoGo condition (see Fig. A.1 for bar graph in the Appendix). The main effect of age group was significant, $F(3,167) = 13.5, p < .05, ICC = .20$ (4%), as well as the age group \times condition interaction, $F(3,167) = 14.3, p < .05, ICC = .20$ (4%). With respect to the Go condition, the linear contrast was significant, $t = 2.84, p < .05, d = 0.44$, indicating lower theta power in children and adolescents than in younger and older adults (children–adolescents: *n.s.*; adolescents–younger adults: $t = 2.21, p < .05, d = 0.47$; younger adults–older adults: *n.s.*). For NoGo theta power, both the linear, $t = 4.78, p < .05, d = 0.74$, and curvilinear contrast, $t = 6.27, p < .05, d = 0.97$, were reliable. Similar to the lifespan pattern of NoGo ITPC, theta power increased with maturation and decreased in older age again (children–adolescents: $t = -4.37, p < .05, d = 1.00$; adolescents–younger adults: $t = -3.53, p < .05, d = 0.71$; younger adults–older adults: $t = 4.52, p < .05, d = 0.94$).

Regarding the relationship between theta power and RT variability, the regression analyses across all four age groups (with dummy variables for age groups) revealed that theta power during Go, $\beta = -.13, t(164) = 2.31, p < .05$, and NoGo, $\beta = -.22, t(164) = 3.56, p < .05$, were significant predictors of RT variability. Within each of the four age groups, however, there was no reliable relationship between RT variability and NoGo theta power, after controlling for median RT and Go theta power (children, $r = -.06$; adolescents, $r = -.27$; younger adults, $r = -.23$; older adults, $r = .00$). To further examine whether RT variability would be more strongly related to theta phase dynamics or theta power, we conducted hierarchical regression analyses across the four age groups with RT variability as dependent variable. To test for the mutual contributions, theta power and theta ITPC were entered as last or second to last regressors. In all analyses, theta ITPC and power during Go were included as well, controlling for response-related activity. The hierarchical regressions showed that theta power was not an important predictor of RT variability beyond theta ITPC, which is indicated by the non-significant change statistics when theta power was entered in the last step, $R^2_{\text{change}} = .0, F_{\text{change}}(1, 162) = 0$. In comparison, theta ITPC during NoGo still accounted for variance in RT variability ($R^2_{\text{change}} = .05, F_{\text{change}}(1, 162) = 20.97, p < .05$), even after theta power and the other covariates were adjusted for. This pattern of results further supports that RT variability is strongly related to more variable theta oscillations assessed at the frontal electrode as reported above. In contrast, theta power is unrelated to performance variability, once other variables were adjusted for.

Relationship of RT variability with delta ITPC

The repeated measures ANOVA with delta ITPC as dependent variable revealed a higher delta ITPC in the NoGo condition, $F(1,167) = 9.86, p < .05, ICC = .06$ (0.3%), a main effect of age group, $F(3,167) = 52.0, p < .05, ICC = .48$ (23%), and a reliable age group \times condition interaction, $F(3,167) = 17.48, p < .05, ICC = .24$ (6%; see Fig. A.2 for bar

graph in the Appendix). In the Go condition, the linear contrast was significant, $t = 5.68, p < .05, d = 0.89$, indicating that delta ITPC is lowest in children (children–adolescents: $t = 4.92, p < .05, d = 1.11$). The three other age groups did not differ with respect to delta ITPC during Go. Further, the planned contrasts suggest a linear pattern for delta ITPC during NoGo as well, $t = 14.25, p < .05, d = 2.20$, indicating an increase in delta ITPC with maturation (children–adolescents: $t = -6.35, p < .05, d = 1.48$; adolescents–younger adults: $t = -6.30, p < .05, d = 1.34$; younger adults–older adults: *n.s.*).

To test for the influence of delta ITPC on the relationship of theta ITPC and RT variability, we conducted hierarchical regression analyses across the four age groups with RT variability as dependent variable, as described above. To control for response-related activity, delta and theta ITPC during Go trials were entered as well. In the last two steps, delta and theta ITPC during NoGo were entered sequentially. Delta ITPC was not an important predictor of RT variability beyond theta ITPC, $R^2_{\text{change}} = .01, F_{\text{change}}(1, 162) = 2.69, p = .10$. However, theta ITPC during NoGo still accounted for variance in RT variability ($R^2_{\text{change}} = .04, F_{\text{change}}(1, 162) = 14.92, p < .05$), once delta ITPC as well as the other variables were adjusted for. Spearman correlations between NoGo delta ITPC and processing variability, controlling for delta Go ITPC and speed of responding, were the following: children ($r = -.25, p = .20$), adolescents ($r = -.48, p < .05$), younger ($r = -.23, p = .13$) and older adults ($r = -.25, p = .10$). In sum, there appears to be a trend for a relationship of delta ITPC and RT variability. However, the hierarchical regression analyses further highlighted that the relation to RT variability is more prominent in the theta band.

Discussion

Here, we investigated whether EEG correlates of more variable performance monitoring signals in the MFC may be related to higher RT variability in a lifespan sample. We found that variability in stimulus-locked EEG signals during performance monitoring is higher at both ends of the lifespan, as indicated by theta ITPC during NoGo trials. This pattern was paralleled by lifespan differences in behavioral variability, with decreasing RT variability from childhood to young adulthood and increasing RT fluctuations in older age, which is a well established finding in the literature (e.g., Dykiert et al., 2012; Li et al., 2004, 2009; Tamnes et al., 2012; Williams et al., 2005). The pattern observed at the group level was further supported within all four age groups, suggesting that individuals with higher RT variability exhibit higher trial-to-trial variability in theta oscillations. Importantly, there was no relationship between theta ITPC and speed of responding in any of the four age groups, suggesting a unique relationship with intraindividual variability. Interestingly, the lifespan pattern of theta power during NoGo also followed an inverted u-shaped function. However, control analyses confirmed that event-related spectral power in the theta band did not predict processing variability beyond theta ITPC, suggesting a unique relationship between theta phase consistency and behavioral RT variability. Thus, our findings suggest that increased RT variability is probably not related to weaker but rather to more variable control processes.

Our findings are in line with the notion that medial frontal theta is associated with performance monitoring processes (e.g., Cavanagh et al., 2012; Cohen et al., 2008; Mazaheri et al., 2009; Nigbur et al., 2011; Wang et al., 2005). An earlier study already reported a negative relationship between RT variability during Go trials and error-related NoGo theta ITPC in adolescents (Groom et al., 2010). While in this study theta phase synchrony across trials was confounded with response-related activity during error trials, we extend this previous finding and show that higher RT variability is also related to lower theta ITPC on correct NoGo trials, consistently across the lifespan. In the younger age groups, we report for the first time that medial frontal theta synchronization in the Go/NoGo task is increasing with maturation. This finding is consistent with previous data

showing lower inter-trial phase coherence in young age (Müller et al., 2009), for instance during an auditory oddball task. With respect to the other end of the lifespan, we replicate findings from another EEG study that reported lower NoGo theta ITPC in older than younger adults during a cued Go/NoGo task (Schmiedt-Fehr and Basar-Eroglu, 2011). The link between RT variability and theta ITPC was independent of theta phase synchronization during Go trials. In fact, a negative relationship between theta ITPC during Go and RT variability was observed only in younger adults, which was weaker than the link to theta phase synchronization during NoGo. There may be two reasons for this. First, age groups did not differ with respect to Go and generally theta ITPC during Go was lower than during NoGo trials. Thus, lower individual differences may reduce the probability of observing reliable relationships to RT variability. Second, Go trials are confounded with response-related activity. This may suggest that not the process of response execution itself, but the controlling or monitoring of response execution is related to RT variability. This is in line with previous results suggesting that cognitive processes contribute to RT variability, rather than motor responding (e.g., Bunce et al., 2004; Hultsch et al., 2002; Lövdén et al., 2007).

As emphasized by a recent review, midfrontal theta band oscillations are not uniquely associated with performance monitoring (Cavanagh et al., 2012), but are also relevant for feedback learning (Cohen et al., 2011; van de Vijver et al., 2011), working memory (e.g., Onton et al., 2005; Sauseng et al., 2010), episodic memory (e.g., Staudigl et al., 2010), and may indicate interregional control (Cavanagh et al., 2009). More generally, midfrontal theta phase consistency has been suggested to be a reflection of the coordination of performance-relevant information between distant brain areas in different tasks and domains of functioning (Cavanagh et al., 2012). Indeed, Cavanagh and colleagues have reported that theta measures covary across different conditions of novelty, conflict, punishment and error, suggesting a more general function of theta band coordination. The proposed generic role for midfrontal theta phase coherence and its link to within-person variability may, to some extent, account for the relationship of RT variability with performance on a wide variety of tasks assessing frontal lobe functioning and neurological conditions associated with frontal lobe deficiency (for review see, Stuss et al., 2003; Picton et al., 2007; Hultsch et al., 2008).

A recent neuroimaging study also supports the notion that higher RT variability assessed in Go trials might reflect more variable control signals. By applying Bayesian modeling to account for behavioral responses in a Go/NoGo task, Ide et al. (2013) generated trial-specific estimates of an individual's subjective probability estimate of encountering NoGo trials. Within subjects, these probability estimates were positively correlated with RTs on Go trials, and they modulated activity in the dorsal ACC. Ide et al.'s findings suggest that response conflict expectations are associated with dorsal ACC activity and account for a significant amount of trial-to-trial variability in RTs during Go trials.

Future studies should investigate whether experimental manipulation affecting theta inter-phase coherence may consequently result in less variable RTs. To further substantiate this association and ascertain the potential causal link between more variable MFC control processes and performance fluctuations, future studies need to investigate whether experimental manipulation, such as non-invasive brain stimulations, that enhance theta inter-phase coherence may consequently result in less variable RTs. For instance, transcranial magnetic stimulation (TMS) has been shown to affect inter-trial phase synchrony (e.g., Thut and Pascual-Leone, 2010; Vernet et al., 2013). Furthermore, it has been suggested that TMS stimulations may lead to an entrainment of synchronous brain activity (e.g., Thut et al., 2011; Vernet et al., 2013), resulting in reinforced synchrony across trials and consequently lower behavioral variability. Future studies along these lines will help to further confirm the link between MFC's cognitive monitoring mechanisms and performance fluctuations. It should be noted, however, deficient neural processing in other brain

areas, such as the parietal cortex (e.g., MacDonald et al., 2008), may contribute to increased RT variability as well.

While increases in delta ITPC were apparent in the NoGo condition as compared to the Go condition (also see, Schmiedt-Fehr and Basar-Eroglu, 2011; Müller and Anokhin, 2012), delta ITPC was associated with trial-to-trial RT variability in adolescents only, suggesting a less important role for RT variability. Supporting our theory-guided findings, a recent study reported that theta band coherence was related to RT adaptations during a response-conflict task, whereas delta band phase coherence was unrelated to adaptations in RTs (Cohen and Cavanagh, 2011). Although the functions and generators of delta oscillations still remain to be understood, current evidence suggests that delta ITPC may reflect motor execution processes rather than motor control processes (Cavanagh et al., 2012).

In sum, we report a consistent negative relationship between theta inter-trial phase synchrony and trial-to-trial RT variability during performance monitoring in a life-span sample, that is independent of age, interindividual differences in response speed, and theta power. Together with findings using imaging methods that have better spatial resolutions (for review, see Ridderinkhof et al., 2004), our results might reflect that more variable control processes in the MFC's coordination of distinct brain areas represent one potential mechanism, among other processes, contributing to greater variability of response latencies within and across age groups.

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Conflict of interest

The authors declare that there is no conflict of interest.

Appendix A

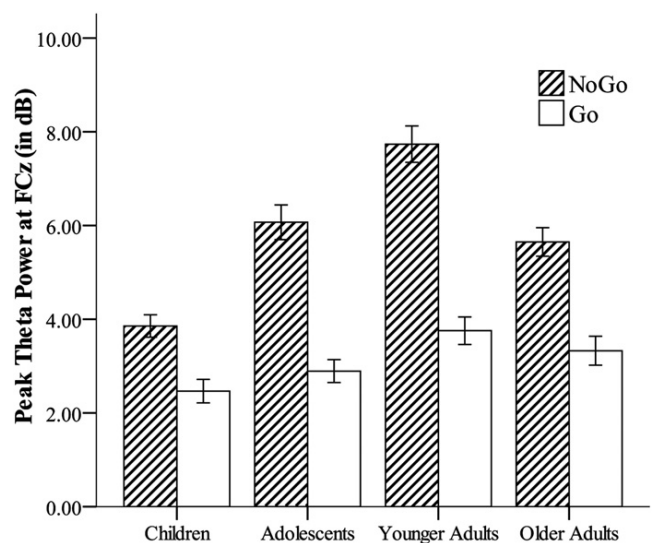


Fig. A.1. Individual peak theta power at FCz during Go and NoGo in the four age groups. Baseline corrected data is presented, with a pre-stimulus baseline interval of -600 to -400 ms. Error bars represent one standard error around the mean.

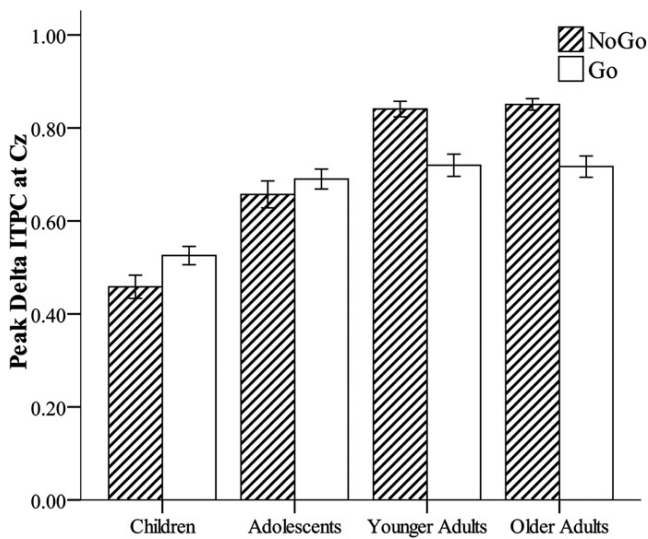


Fig. A2. Individual peak delta ITPC at Cz during Go and NoGo in the four age groups. Error bars represent one standard error around the mean.

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