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The Modulation of Neural Noise Underlies the Effectiveness of Methylphenidate Treatment in Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

BACKGROUND: Various lines of research suggest that the stability of neural processes is low in attention-deficit/hyperactivity disorder (ADHD). Considering overarching neural principles, this lack of stability relates to increased levels of neural noise. However, no study has directly examined neural noise in ADHD. Likewise, it is unknown whether the modulation of neural noise reflects a mechanistic link as to why methylphenidate (MPH) is effective in treating impulsivity in ADHD.

METHODS: We compared neural noise between 29 juvenile patients with ADHD and 32 healthy control subjects and examined the effects of MPH. We examined 1/*f* neural noise of electroencephalogram data collected while participants performed a response inhibition (Go/NoGo) task.

RESULTS: Specific during NoGo trials, children with ADHD showed more neural noise than healthy control subjects. This was especially the case with regard to the theta frequency band, which is very closely related to cognitive control. MPH treatment reduced neural noise in ADHD to the level of healthy control subjects. Correlational analyses showed a direct relationship between decreases in neural noise and increases in behavioral performance. Mechanistically, this can be explained by the MPH-induced increase in dopaminergic neurotransmission that enhances the signal-to-noise ratio in neural networks and thus reduces neural noise.

CONCLUSIONS: This study is the first to demonstrate increased (pink) neural noise in patients with ADHD and its reduction through MPH treatment. The study reveals an important mechanistic link as to why MPH is effective in treating impulsivity in ADHD.

Keywords: ADHD, EEG, Inhibitory control, Methylphenidate, Neural noise

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Attention-deficit/hyperactivity disorder (ADHD) is a prevalent disorder during childhood and adolescence (1). A common theme that runs through various lines of research is that ADHD is associated with a strong intraindividual variability of behavioral control (2–6) and neurophysiological processes associated with dysfunctions in various cognitive domains (2,3,6,7). Because these aspects are associated with symptom severity (8,9), they are of high clinical relevance. However, these aspects have not been considered from the perspective of overarching neural principles. Several lines of evidence (e.g., in aging) suggest that increased levels of intraindividual variability indicate noisier neural processes (10,11). If this aspect is transferred to ADHD, which is also characterized by high intraindividual variability, this means that neural noise should play an important role in ADHD. Neural noise emerges from random fluctuations in background electrical activity (11,12) and compromises the robustness of neural processes, leading to reduced stability of performance across time. Increased neural noise has previously been directly related to symptomatology in children with reading disorder (13), but no study has directly examined neural noise in ADHD despite the fact that modulation of neural noise may represent a key aspect. It is highly relevant to examine whether neural noise is influenced by first-line pharmacological treatment for ADHD (see below).

We use electroencephalogram (EEG) recordings in which neural noise can be directly examined by calculating 1/*f* noise (14–16). There are many definitions of neural noise and many ways to measure it (17). 1/*f* noise (or pink noise) is ubiquitous in nature and, importantly, is also generated in the cerebral cortex (17,18). It is hence reasonable to analyze 1/*f* noise in EEG data. This 1/*f* activity represents arrhythmic activity that does not contain a predominant temporal scale (i.e., is scale free) and does coexist with rhythmic (periodic) activity known as brain oscillations (e.g., evident in the power spectrum) (19). Yet, the power spectrum forms the basis to calculate 1/*f* neural noise in EEG data. It is assumed that the distribution of neural activation (i.e., the power spectral density [PSD]) across the entire (EEG) frequency spectrum reflects neural noise (14). The distribution of EEG data in the frequency domain is inversely proportional (20); thus, the linear relationship described by the power law ($P \sim 1/f^{\beta}$) can be approximated by calculating the logarithm of the PSD (14,19). The slope of this relationship

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provides a measure of 1/*f* neural noise (15), and brain activity that contributes to this 1/*f* slope in the power spectrum is devoid of periodicity (19). A flatter slope indicates more neural noise (15). The reason behind this relates to alterations in the underlying population spiking statistics aggregating local field potentials (15), which also contribute to EEG signals (21,22). It has been shown that when a large number of spikes occur relatively simultaneously, the aggregate local field potential 1/*f* slope will be more negative. When spiking is relatively asynchronous, the local field potential 1/*f* slope will be flatter (16,23). In line with other recent studies examining EEG data from tasks taxing cognitive control functions (14,15), we examined 1/*f* neural noise on EEG data collected while participants performed a response inhibition task (Go/NoGo task). The reason for choosing this specific task is that deficits in inhibitory control are of high clinical relevance in ADHD (24–26). Moreover, the amelioration of inhibitory control deficits has been closely associated with the dopaminergic actions of methylphenidate (MPH) (27–34), which is currently the recommended first-line pharmacological intervention in ADHD (35,36). MPH is a mixed dopamine/norepinephrine transporter blocker, increasing dopamine and norepinephrine levels in the synaptic cleft (37). These effects are highly relevant because increasing dopaminergic and norepinephrine activity enhances the signal-to-noise ratio in neural networks and thus reduces neural noise (11,38–41). We hypothesized that neural noise is more pronounced in patients with ADHD compared with healthy control subjects; that is, the 1/*f* neural noise slope parameter is smaller in patients with ADHD than in the control group. We further hypothesized that this parameter becomes larger (steeper) in patients with ADHD after initiation of MPH treatment, rendering it no longer different from that measured in healthy control subjects. Because especially inhibitory control deficits are central in ADHD and have been shown to be modulated by MPH, we hypothesized that MPH reduces neural noise specifically in NoGo trials but not in Go trials. Similarly, we hypothesized that differences between healthy control subjects and patients with ADHD prior to MPH treatment are mainly evident in NoGo trials but not in Go trials.

Yet, an important aspect to consider regarding the neural dynamics is that inhibitory control processes are peculiarities of different frequency bands. Although theta frequency activity is commonly assumed to reflect drowsiness in resting EEG data, there is mounting evidence that inhibitory control strongly depends on oscillations in the theta frequency band (42–48), which is in line with findings suggesting that theta frequency oscillations are particularly important for cognitive control and executive functions (49–53). While beta band activity has also been associated with inhibitory control (54), recent evidence suggests that theta band activity mainly predicts response inhibition performance (48). Moreover, theta frequency band variability appears to be particularly and strongly related to ADHD symptoms and to the underlying neurobiology (55). Therefore, it is possible that the effects hypothesized above predominantly occur in the theta frequency band and not in the beta band; that is, only the theta band reveals differences in 1/*f* neural noise between healthy control subjects and patients with ADHD prior to MPH treatment in NoGo trials. This difference is supposed to vanish after MPH treatment.

METHODS AND MATERIALS

Participants

In total, 29 patients with ADHD were included in the study (mean age = 9.9 ± 2.1 years; mean IQ = 100 ± 14). The diagnosis in each child had been determined in a multidisciplinary outpatient setting according to standard clinical guidelines (including family and school interviews, symptom questionnaires, neuropsychological testing [IQ and attention], and the exclusion of possible somatic differential diagnoses via blood analyses, EEG, and audiometry and vision testing). The patients were not affected by any additional severe or acute psychiatric comorbidities (e.g., autism, tics, depressive episodes). The healthy control sample consisted of 32 participants (mean age = 11.6 ± 2.1 years; mean IQ = 108 ± 12). Groups differed with regard to age ($p = .001$) and IQ ($p = .029$). Therefore, these factors were included as covariates in all subsequent analyses. Using the ADHD Symptom Checklist (56), all parents rated their children on a scale of 0 (no problems) to 3 (severe problems) with regard to ADHD core symptoms (inattention: control subjects, 0.5 ± 0.5; patients with ADHD, 2.1 ± 0.7; hyperactivity: control subjects, 0.1 ± 0.3; patients with ADHD, 1.2 ± 0.8; impulsivity: control subjects, 0.3 ± 0.5; patients with ADHD, 1.7 ± 0.8). Healthy control subjects had significantly lower scores than the patients on all three subscales (all Fs > 47.2, all ps $< .001$).

Children with ADHD and healthy control subjects were examined twice. Patients were medication naive at time point 1 (T1). First-line pharmacological treatment for ADHD using MPH was then initiated, with titration taking place over a period of 8 weeks. All patients received a low dose of immediate-release MPH initially and switched to extended-release MPH during the course of treatment. According to clinical guidelines, this dose was increased until 1) a significant and satisfactory symptom reduction was reported by parents or 2) the target dose of 1 mg/kg body weight had been reached. Final doses ranged from 10 to 40 mg extended-release MPH per day. The healthy control subjects also took part in two EEG tests 8 weeks apart. No treatment took place in the control group. Written informed consent and assent were obtained from all legal guardians and participants, respectively, in accordance with the Declaration of Helsinki. The ethics committee of the Dresden University of Technology approved the study.

Task

We used a Go/NoGo task in which either the word DRÜCK (German for PRESS; Go stimulus) or the word STOP (NoGo stimulus) was presented for 300 ms in white font on a black background. The participants were asked to respond as quickly and accurately as possible whenever the DRÜCK stimulus was presented. Responses needed to be carried out within 500 ms. Participants needed to refrain from responding when seeing the STOP stimulus. The intertrial interval was jittered between 1600 and 1800 ms. The experiment consisted of 248 Go trials and 112 NoGo trials presented in a pseudorandomized order. Thus, the ratio of Go and NoGo trials was 70%:30%. The task lasted approximately 20 minutes. For the EEG data analysis, only correct trials were included, that is,

trials with in-time responses on Go trials and with no responses on NoGo trials.

EEG Recording, Processing, and Neural Noise Estimation

As done in other studies (26), the EEG was recorded using 60 equidistant Ag/AgCl electrodes mounted in an elastic cap. The sampling rate was 500 Hz (reference at Fpz, ground electrode at $\theta = 58$, $\phi = 78$). All electrode impedances were kept below 5 kΩ. During offline data processing, a bandpass filter (0.5–20 Hz, slope = 48 dB/octave) was applied. This is comparable to other studies (14,15), but the analysis contains only lower beta frequencies (13–20 Hz) (often called beta-1). The reason is that higher-frequency activity (25–100 Hz) in scalp recordings likely overlaps with face and eye muscle activity (14,57). Henceforth, we use the term beta for the sake of simplicity. Technical artifacts were removed during the manual inspection of the raw data before an independent component analysis (infomax algorithm) was used to detect and discard periodically occurring artifacts (pulse artifacts and horizontal and vertical eye movements). Then, the EEG data were segmented (locked) to the onset of Go and NoGo stimuli. The segments had a length of 1700 ms, starting 200 ms before the target stimulus. Only trials with correct responses on Go trials and without responses on NoGo trials were analyzed further. In the segmented data, epochs were discarded from further data analyses during the artifact rejection procedures if at least one of the following criteria were met: amplitudes within this epoch higher than 200 μV and lower than −200 μV, voltage increases of 200 μV in a 200-ms interval, and activity below 0.5 μV in a 100-ms period. On average, 2.9% (±2.5) of trials were discarded during the artifact rejection step with no differences between conditions, groups, and testing time points ($p > .60$). To remove the reference potential from the data, a current source density transformation was applied (58). Afterward, the data were baseline corrected to a time interval from −200 to 0 ms.

To calculate 1/*f* neural noise in the segmented EEG data, a time window of interest from 0 ms (i.e., target stimulus onset) to 1000 ms after the stimulus presentation was selected. According to previous work (59), the PSD for each frequency was computed using Welch's method (15). Welch's method reduces leakages that can be induced because of the finite dataset during the estimation of the power of a time-limited signal. In doing so, each time signal (x) is split into two segments (L), each of 500 ms with 50% overlap and windowed with a Hamming window (w). Subsequently, the discrete Fourier transform is computed, obtaining the modified periodograms [$X_l = F(x\,w)$]. The squared magnitude is calculated, and finally the periodograms are averaged to gain the PSD estimate (60):

$$\textit{estimated PSD} = \frac{1}{L}\sum_{l=1}^{L}\left(|X_l|^2\right)$$

For every single trial, this procedure was run in MATLAB (The MathWorks, Inc., Natick, MA) applying the pwelch function. To obtain the estimated PSD, the data were averaged separately over subjects, channels, and conditions. To estimate 1/*f* neural noise represented by the slope (β) of the logarithm of the power spectral density, a linear regression with respect to the frequency (f) was calculated according to

$$\log_{10}(\text{PSD}) = \beta f + \varepsilon,$$

where ε represents the error variable. In addition, for the linear regression, the power spectral density values within the frequency range from 4 to 8 Hz were considered for the theta frequency band, and those from 13 to 20 Hz were considered for the beta frequency band. As done in previous studies (14,15), the alpha band from 8 to 13 Hz was excluded because this frequency band is assumed to represent activity deviating from principles governing pink noise (17,61,62). Moreover, previous data show that especially theta band activity is most important for response inhibition (48), as examined in the current study.

Statistics

The 1/*f* neural noise data were analyzed using mixed-effects analyses of variance. This was done for the theta and beta frequency bands separately. The factor group (healthy control subjects vs. patients with MPH treatment) was used as a between-subject factor. The factors condition (Go vs. NoGo) and time point (T1 vs. T2) were used as within-subject factors. Greenhouse–Geisser correction was applied for tests. Post hoc tests were Bonferroni corrected. The variables included in the analysis were normally distributed as indicated by Kolmogorov–Smirnov tests (all $zs < 0.90$, $ps > .21$). For the descriptive statistics, the mean and standard error of the mean are given. Age and IQ were used as covariates in all subsequent analyses.

RESULTS

Behavioral Data

For the behavioral data, the number of correct rejections in NoGo trials was analyzed, that is, the number of trials in which

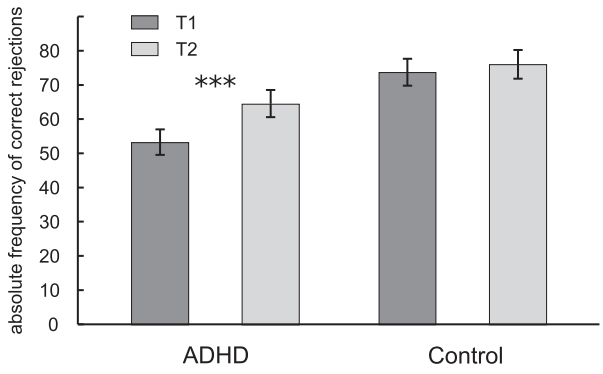

Figure 1. The absolute frequency of correct rejections (i.e., no responses on NoGo trials) for attention-deficit/hyperactivity disorder (ADHD) and control group at time point 1 (T1) (i.e., prior to initiation of methylphenidate treatment; dark bars) and time point 2 (T2) (i.e., after methylphenidate treatment; light bars). Error bars show standard error of means. The significant difference is marked with *** ($p < .001$).

no prepotent response was carried out in NoGo trials. The results are shown in Figure 1.

There was a main effect of time point ($F_{1,53}$ = 10.85, p = .002, η_p^2 = .170), showing that the number of correct rejections was higher at T2 (70.29 ± 2.89) than at T1 (63.50 ± 2.71). The main effect of group showed that the number of correct rejections was generally higher in the control group (74.88 ± 3.78) than in the patients with ADHD (58.91 ± 3.58) ($F_{1,53}$ = 9.39, p = .003, η_p^2 = .151). Crucially, there was a time point × group interaction ($F_{1,53}$ = 4.73, p = .034, η_p^2 = .082). Post hoc dependent-samples t tests revealed that the number of correct rejections was higher at T2 (64.55 ± 3.82) than at T1 (53.27 ± 3.38) in the ADHD group (t_{28} = 4.35, p < .001). In the control group, no differences occurred (t_{25} = −1.03, p > .21). Analysis of performance in Go trials (i.e., accuracy and response times) revealed no significant main effects or interactions (all Fs < 1.36, ps > .247), showing that performance on Go trials was not differentially modulated by group and time point. The effects of the covariates IQ and age were not significant (all Fs < 0.12, ps > .60).

Neurophysiological Data

The data from the theta and beta frequency bands are shown in Figure 2A, B.

As can be seen in Figure 2, maximal slope values in the theta frequency band were clustered around electrodes FC1, FC2, FCz, and Cz. Importantly, these electrode sites are also known to reveal maximal activity when analyzing standard event-related potentials (45) and therefore are taken as sites for the data analysis. For the data analysis, the mean slope across these electrodes was used (Figure 2A, right). There was a main effect of Go/NoGo ($F_{1,53}$ = 5.43, p = .024, η_p^2 = .093), showing that the slope was steeper in NoGo trials (−0.1176 ± 0.004) than in Go trials (−0.1002 ± 0.004). The main effect of time point ($F_{1,53}$ = 8.30, p = .006, η_p^2 = .135) revealed that the slope was steeper at T1 (−0.1236 ± 0.004) than at T2 (−0.0941 ± 0.004). There was no main effect of group ($F_{1,53}$ = 0.20, p > .80), but the condition × time point × group interaction was significant ($F_{1,53}$ = 6.74, p = .012, η_p^2 = .113). This interaction is shown in Figure 3A.

For the Go trials, there were no differences between patients with ADHD and healthy control subjects at T1 (t_{53} = −0.25, p > .80) or at T2 (t_{53} = −1.13, p > .20). However, for the NoGo trials, the slope was flatter in the ADHD group compared with the control group (t_{53} = 3.31, p < .002) at T1 (i.e., prior to initiation of MPH treatment). Importantly, dependent-samples t tests that were calculated to compare the slope in NoGo trials between T1 and T2 within each group revealed that there was a difference in the ADHD group (t_{28} = 4.32, p < .001) but not in the control group (t_{25} = −0.87, p > .39). As can be seen in Figure 3A, the slope became steeper in the ADHD group after MPH administration. It is further shown that there was no difference between the ADHD group and the control group at T2 (t_{53} = −1.23, p = .223). The data suggest that the increase in the slope of the 1/f neural noise parameter in NoGo trials occurring after the initiation of MPH treatment is associated with a performance increase at the behavioral level in the ADHD group; that is, that the number of correct rejections in NoGo trials increased significantly between the two testing time points. Notably, correlation analysis showed that the degree of change in the slope of the 1/f neural noise parameter was linearly correlated with the degree to which the number of correct rejections increased between testing time points (r = −.710, R^2 = .504, p < .001) (see Figure 3B). This correlation shows that the higher the increase in the steepness of the slope of the 1/f neural noise parameter, the stronger the increase in behavioral performance. The effects of the covariates IQ and age were not significant (all Fs < 0.23, ps > .60). An analysis of the theta power can be found in Supplemental Figure S1 and the first Supplemental Analyses section. A plot showing the scalp distribution of alpha band power can be shown in Supplemental Figure S2 and the second Supplemental Analyses section. The obtained results do not simply reflect modulations of the power spectra or event-related activity as reflected in event-related potentials (see third and fourth Supplemental Analyses sections, respectively).

The data from the beta frequency band at central electrode sites are shown in Figure 2B. The analysis of variance revealed no main or interaction effects or an effect of the covariates (all Fs < 0.65, ps > .560). However, as seen in the scalp topography plots (Figure 2B), the 1/f neural noise parameter in the beta band was accentuated at posterior (parietal) electrode sites. Examining the cluster of electrodes Pz, P1, and P2 did not, however, reveal significant main or interaction effects or an effect of the covariates (all Fs < 0.59, ps > .510). To validate these lacks of effect, additional Bayesian analyses were conducted. We used the method of Masson (63) to calculate the probability of the null hypothesis being true given the data $p(H_0/D)$. For the beta frequency band data, this analysis revealed a probability of $p(H_0/D)$ = .90. According to Raftery (64), this provides strong evidence for the null hypothesis, that is, that there is no modulation in the beta frequency band.

DISCUSSION

Several lines of evidence suggest that the modulation of neural noise is a central aspect when aiming to understand the nature of ADHD in more detail, but no study has yet directly examined neural noise in ADHD, and it is unknown whether first-line pharmacological treatment may be effective because it ameliorates neural noise. In the current study, we directly examined neural noise in ADHD and its modulation by a first-line pharmacological treatment (i.e., MPH). Participants performed a Go/NoGo task, and 1/f neural noise was calculated in two different EEG frequency bands.

The data show that children with ADHD were characterized by more neural noise while being engaged in response inhibition processes than was the case for healthy control children. This is indicated by the flatter slope of the 1/f neural noise parameter in the ADHD group than in the control group at T1 (prior to initiation of MPH treatment). No group differences in the 1/f neural noise parameter were observed in the Go trials. The ratio of Go and NoGo trials used (i.e., 70% Go and 30% NoGo trials) has been shown to induce a strongly automated mode of responding (44,47,65–67). This task, therefore, entails particularly high processing demands when the prepotent response tendency needs to be inhibited in NoGo trials (44,68–70). Therefore, the results show that neural noise is not generally elevated in ADHD. Rather, neural noise seems to

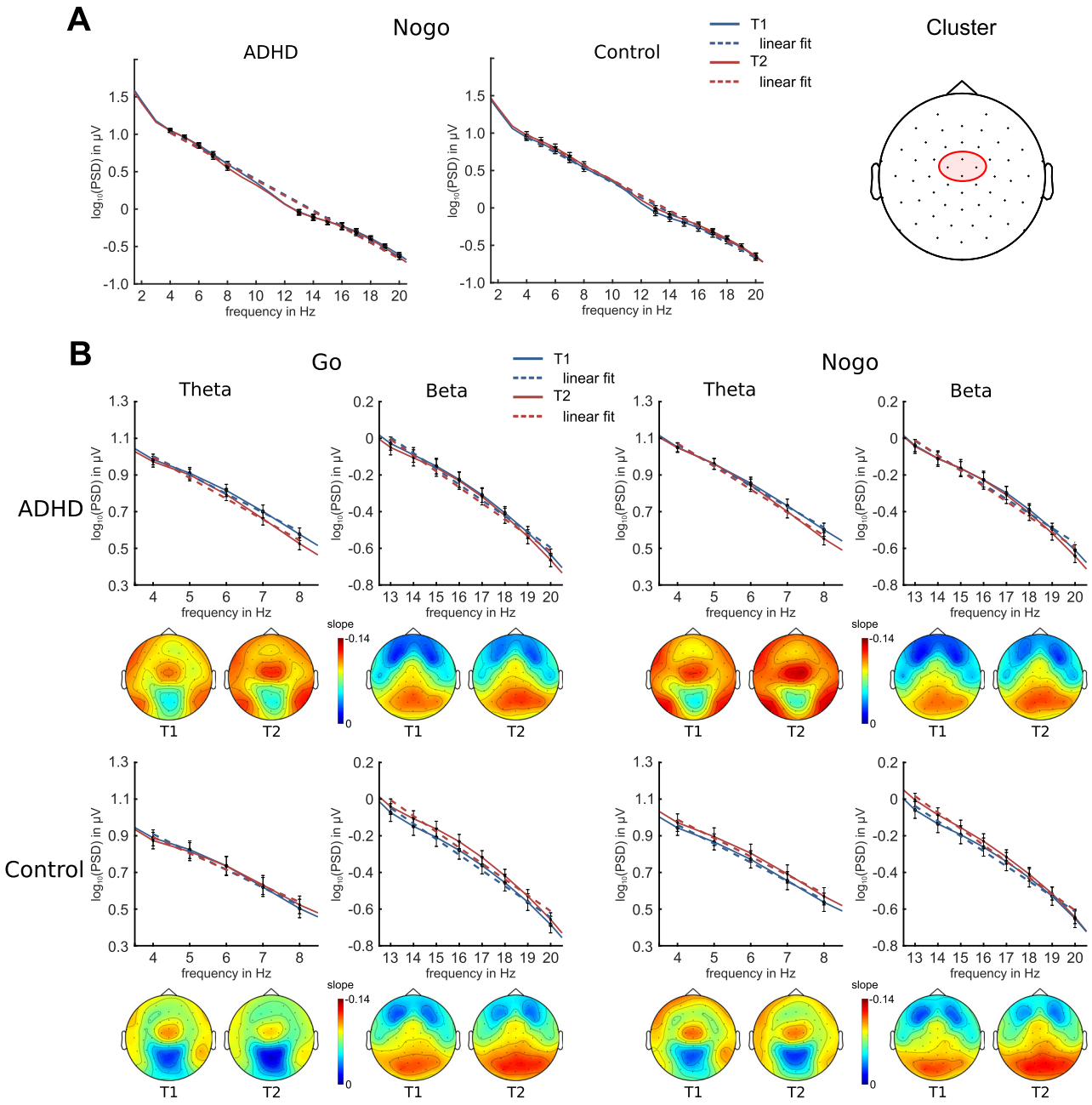

Figure 2. **(A)** 1/*f* neural noise as indicated as the slope of the linear regression (linear fit) of the power spectral density [$\log_{10}$(PSD)] across frequency. Correct NoGo trials for the attention-deficit/hyperactivity disorder (ADHD) group (left) and control group (middle) are shown as a linear regression for the frequency intervals 4 to 8 Hz (theta band) and 13 to 20 Hz (beta band), excluding the alpha band. This is shown for a cluster of electrodes FC1, FC2, FCz, and Cz (see rightmost plot) for the ADHD group and control group at time point 1 (T1) (i.e., prior to initiation of methylphenidate treatment; dark blue) and time point 2 (T2) (i.e., after methylphenidate treatment; dark red). Error bars show standard error of means. **(B)** A linear fit of the $\log_{10}$(PSD) of the clustered electrodes for correct Go trials (left) and correct NoGo trials (right) of ADHD group (upper row) and control group (lower row) for the theta and beta frequencies separately. The scalp topography plots show the noise parameter (slope) for each frequency band.

become a problem in ADHD whenever inhibitory control processes are highly demanding. It seems that neural noise scales with requirements for cognitive control in ADHD.

Importantly, MPH treatment also had very specific effects on neural noise. In the ADHD group, the slope of the 1/*f* neural noise parameter during NoGo trials became steeper after initiation of MPH treatment. Crucially, there were no differences between children with ADHD and healthy control children at T2 (i.e., after MPH treatment had been initiated in the patients with ADHD). This shows that MPH decreases neural

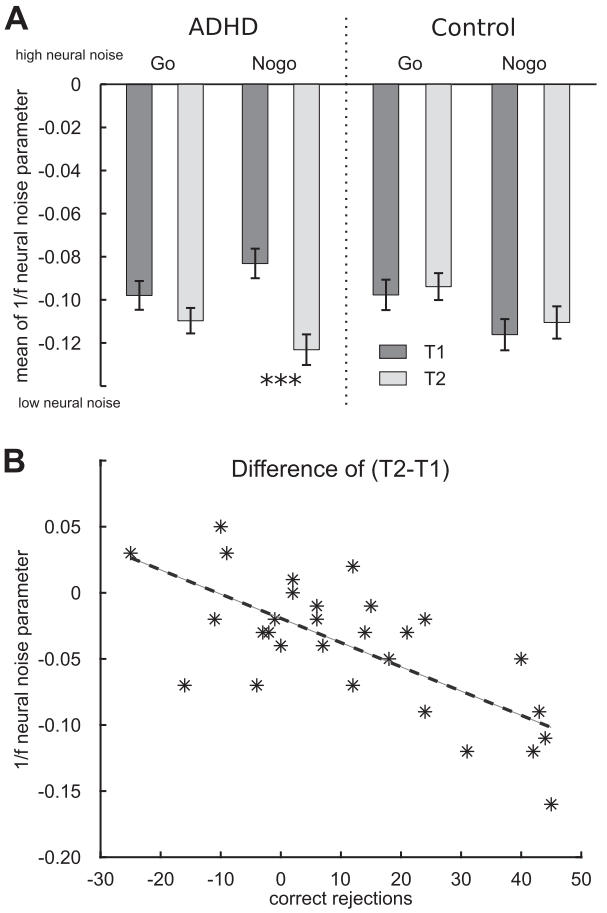

Figure 3. **(A)** Descriptive data showing the condition × time point × group interaction. The mean of the 1/*f* neural noise parameter in the theta frequency band at time point 1 (T1) (i.e., prior to initiation of methylphenidate treatment; dark bars) and time point 2 (T2) (i.e., after methylphenidate treatment; light bars) for the attention-deficit/hyperactivity disorder (ADHD) group (left) and control group (right) for Go and NoGo conditions is shown. Error bars show standard error of means. The significant difference is marked with *** ($p < .001$). **(B)** Correlation of the difference of the 1/*f* neural noise parameter between T2 and T1 and the difference of the correct rejections (NoGo) between T2 and T1 within the ADHD group.

noise in ADHD and that MPH is able to adjust neural noise to a level comparable to that of healthy children. Notably, the correlation analyses show that decreases in neural noise in the ADHD patients induced by MPH treatment are directly related to increases in behavioral performance. The more MPH could reduce neural noise, the stronger was the behavioral improvements in the examined task. This shows that neural noise is an essential mechanism to be targeted when aiming to ameliorate cognitive deficits and impulsivity in ADHD. The data show that the main mechanism underlying the effectivity of MPH to reduce cognitive deficits in ADHD is the fact that it likely affects neural noise. This interpretation fits very well with what is known about the mechanisms underlying MPH effects. Importantly, MPH increases dopamine and norepinephrine levels (37). This is well known to enhance the signal-to-noise ratio in neural networks and thus to reduce neural noise (11,38–41). Thus, the observed treatment effect in ADHD is well in line with known biophysical mechanisms of dopamine/norepinephrine system activity and noise in neural networks. Interestingly, atomoxetine, which is currently used as a second-line pharmacological approach to ADHD, has been shown to decrease noise in neural signaling by indirectly increasing dopamine stimulation of D_1 and norepinephrine receptors (71,72). Atomoxetine seems to be equally as potent as MPH to treat ADHD (73,74). To gain further insights into the differential underlying mechanisms and effects, future studies should aim to directly compare these lines of treatment with regard to their ability to reduce neural noise in ADHD. It seems to be important to lower neural noise to optimal levels rather than to aim to abolish it completely because too little neural noise has equally been suggested to have detrimental effects on cognitive processing (75).

Crucially, the discussed effects were confined to neural noise in the theta frequency band. No modulations or group differences in the 1/*f* neural noise parameter were observed for beta frequency oscillations, which was supported by Bayesian analysis. Inhibitory control processes strongly depend on oscillations in the theta frequency band (42–48), and recent evidence suggests that oscillations in the beta frequency band are less important than theta band activity during response inhibition (48). Notably, the variability of theta band activity especially strongly relates to ADHD symptoms and their neurobiological underpinnings (55). Thus, the results show that neural noise, especially in frequency ranges that are generally important for cognitive control (50), is strongly modulated by the pathophysiology of ADHD and is affected by the first-line pharmacological treatment.

A limitation of this study is that no randomized, double-blind study design was used. This needs to be done in future studies also evaluating modulating changes in the examined neural noise parameter in response to other treatments. Because a major intervention depends on the modulation of theta/beta frequencies in ADHD (76,77), the effects of this treatment on neural noise properties should also be investigated.

In summary, the study shows that (pink) neural noise (i.e., scale-free activity) (19) is increased in ADHD and that MPH reduces neural noise in ADHD to the level found in healthy subjects. The reduction in neural noise is directly related to increases in the ability to inhibit prepotent responses. The data reveal a missing mechanistic link as to why MPH is effective in treating cognitive dysfunctions and impulsivity in ADHD.

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ARTICLE INFORMATION

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