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## From noise to insight: the functional role of BOLD signal variability and aperiodic neural activity in metacontrol

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# **Chapter 5**

## **Summary and Discussion**

This thesis aims to explore the role of what has traditionally been considered as neural “noise”, specifically BOLD signal variability and aperiodic neural activity, in cognitive functions. It comprises three empirical studies (Chapters 2 to 4), which investigate the relationship between resting-state BOLD signal variability, the aperiodic component of the EEG power spectrum, and metacontrol biases.

Chapter 2 investigates the association between temporal variability of rs-fMRI signals and individual differences in metacontrol biases toward persistence or flexibility. The temporal variability of resting-state fMRI data was estimated using both standard deviation (SD) and mean square successive differences (MSSD) of the time series. Metacontrol biases were assessed through three tasks sensitive to metacontrol: the Stroop task, the Remote Associates Task (RAT), and the Alternate Uses Task (AUT). The results revealed that higher resting-state BOLD signal variability in specific brain networks associates with increased flexibility bias (or reduced persistence bias). These findings underscore the importance of resting-state BOLD signal variability in understanding the neural foundations of cognitive control.

Chapter 3 explores the relationship between the aperiodic component of the EEG power spectrum and different states of metacontrol or the dynamic of metacontrol adjustments. The aperiodic component, characterized by exponent and offset parameters, was estimated using the FOOOF algorithm. Metacontrol states toward persistence or flexibility were induced by using a Simon Go/NoGo task. The results indicated an increase in aperiodic exponent and offset values during NoGo trials relative to Go trials, and in incongruent (Go) trials when compared to congruent (Go) trials. This pattern suggests that aperiodic activity reflects metacontrol states, with a higher exponent and offset during persistence-heavy processing, and a lower exponent and offset during flexibility-heavy processing. The insights gained in this chapter highlight the importance of aperiodic neural activity in reflecting metacontrol states, enhancing our understanding of its functional significance in cognitive functions.

Chapter 4 extends the investigation by examining the role of aperiodic activity in different types of creative thinking, specifically divergent thinking (DT) and convergent thinking (CT). It is posited that DT benefits from a metacontrol bias toward flexibility, while CT benefits from a metacontrol bias toward persistence. Participants performed DT and CT

tasks while their EEG activity was recorded. Aperiodic activity was estimated using the FOOOF algorithm, which is consistent with the approach employed in Chapter 3. The results demonstrated that engaging in DT is associated with a significant drop in the aperiodic exponent. Moreover, individuals with a greater decrease in the aperiodic exponent generated more innovative ideas during DT. This chapter emphasizes the significant role of aperiodic EEG activity in advancing our understanding of human higher-level cognitive functions, including creative processing and metacontrol processing.

In sum, this thesis systematically investigates the functional relevance of neural elements traditionally considered as “noise” – specifically, BOLD signal variability and aperiodic neural activity in human cognitive functions. Chapter 2 emphasizes the importance of resting-state BOLD signal variability in understanding individualized cognitive control styles. Chapter 3 highlights the importance of the aperiodic component of the EEG power spectrum in reflecting demand-specific metacontrol states. Notably, Chapter 4 illuminates the functional significance of aperiodic activity in creative thinking. Collectively, the research presented in this thesis highlights the importance of resting-state BOLD signal variability and aperiodic activity in the EEG power spectrum for understanding the neural underpinnings of cognitive functions. Future research in cognitive neuroscience would benefit from a specific focus on these metrics to comprehensively understand the neural foundations of human cognition and behavior.

This thesis concludes by discussing the broader implications of these findings for the field of cognitive neuroscience, as well as potential limitations and future research directions.

## **Theoretical implications**

### **Rethinking neural “noise” and cognitive neuroscience methodologies**

In the field of neuroscience, distinguishing signals from noise can be challenging, as universally accepted classifications are still evolving. Non-neuronal physiological fluctuations, variability of neuronal responses, and  $1/f$ -like activity have all been referred to as ‘noise’ in the literature (Faisal et al., 2008; Groppe et al., 2013; Uddin, 2020). This thesis

challenges this traditional view, suggesting that what was previously considered ‘noise’ might actually be significant ‘signals’ essential to brain function.

The thesis emphasizes the importance of temporal variability of fMRI signals and the aperiodic component of the EEG power spectrum in brain function and cognitive processes. A wealth of recent research aligns with this perspective. For example, BOLD signal variability has been identified as a marker for neural flexibility and efficiency, and has been linked to various aspects of human behavior and cognitive functioning (Armbruster-Genç et al., 2016; Garrett et al., 2011; Waschke, Kloosterman, et al., 2021). There is now a burgeoning literature linking aperiodic exponent ( $1/f$  slope) to aging (Merkin et al., 2023; Voytek et al., 2015), neurological and psychiatric conditions (Münchau et al., 2021; Ostlund et al., 2021; Peterson et al., 2023; Shuffrey et al., 2022), and cognitive processes (Pertermann, Mückschel, et al., 2019; Virtue-Griffiths et al., 2022). Therefore, both this thesis and existing research suggest that elements previously deemed as ‘noise’ can transition to being recognized as significant ‘signals’. This paradigm shift holds the potential to significantly enhance our understanding of brain function and the relationship between the brain and behavior.

Given these insights, the field might benefit from adopting a framework that views the brain as a nonlinear dynamical system (Breakspear, 2017; Uddin, 2020), which may provide a more accurate representation of its complex and self-organizing nature. In terms of methodological approaches, the thesis advocates for a reevaluation of data analysis techniques. Rather than aiming to minimize or eliminate neural variability, components traditionally considered as ‘noise’ should be intentionally examined and integrated into analyses. Advanced data analytical methods such as machine learning algorithms and nonlinear dynamics could be systematically employed to unravel the complexities inherent in neural activity.

### **Neural variability and its role in cognitive control**

Chapter 2 of this thesis suggests that the intrinsic variability of neural signals in our brain, as captured through rs-fMRI signals, can offer valuable insights into individualized cognitive control styles. In other words, the naturally occurring temporal fluctuations in specific regions of our brain may be indicative of our default strategies when facing different

conditions in goal-directed behaviors. This thesis highlights the importance of resting-state BOLD variability in understanding human cognition and behavior, in alignment with recent evidence. Moment-to-moment variability in the rs-fMRI signal has been associated with both traits emotional intelligence and variations in emotion regulation strategies (Zanella et al., 2022). Incorporating machine learning techniques, recent work showed that resting-state neural signal variability in women might serve as a significant marker for depression (Pessin et al., 2022).

A growing body of studies has shown that increased levels of neural variability facilitate flexible behavior and are linked to faster and better task performance. However, this thesis suggests a different perspective: while increased neural variability can be advantageous for tasks that demand cognitive flexibility and switching, it could be counterproductive for tasks that require maintaining current task goal(s) and inhibiting distractions. This finding aligns with previous task-fMRI research, where higher levels of neural variability are beneficial for cognitive flexibility but detrimental for cognitive stability (Armbruster-Genç et al., 2016). Thus, this work underscores the idea that the advantages of higher neural variability are not universally beneficial for all cognitive processes but are context-dependent.

### **Aperiodic neural activity and higher-level cognitive functions**

Chapters 3 and 4 suggest that aperiodic neural activity, in addition to the frequently analyzed oscillatory patterns, plays a crucial and functional role in human higher-level cognitive functions.

Chapter 3 reveals the link between aperiodic EEG features and the dynamics of metacontrol states. The findings suggest that our brain adjusts its neural activity to meet the demand for either flexibility or persistence in tasks. Moreover, such adjustments are reflected by the level of aperiodic activity in EEG signals. This chapter highlights the functional importance of the aperiodic component of the EEG power spectrum in understanding cognitive functions.

Chapter 4 provides further support for the functional significance of aperiodic activity by underscoring the association between aperiodic exponent and creativity. In this chapter, a smaller aperiodic exponent was observed during the divergent thinking task which

demands flexibility of metacontrol, compared to the convergent thinking task which requires persistence of metacontrol. This is consistent with findings from Chapter 3 regarding the relationship between aperiodic exponent and metacontrol. Both chapters consistently reveal decreased exponent during flexibility-heavy processing and increased aperiodic exponent during persistence-heavy processing. These findings suggest that aperiodic exponent may serve as a direct measure of metacontrol biases toward persistence or flexibility.

Chapter 4 further illustrates that aperiodic exponent is correlated with performance in the divergent thinking task. A smaller exponent (indicative of more aperiodic activity) is correlated with the generation of more innovative ideas. Additionally, this chapter highlights a task-specific modulation of the aperiodic activity level (in the IT period) and a process-specific modulation (restricted to the AUT task period). This suggests that people can increase their general aperiodic activity levels throughout a task and increase this level even further when engaged in a particular problem-solving process. Importantly, individuals might be able to voluntarily increase their aperiodic activity levels to generate more novel ideas. These findings imply that the brain may dynamically adjust its aperiodic activity levels to accommodate the cognitive requirements of a given task. Furthermore, aperiodic activity could potentially underlie the neural mechanisms that drive human creativity.

It should be noted that in this context, a lower aperiodic exponent is indicative of more aperiodic activity. A decreased exponent suggests that there is increased power across the higher frequency bands of the EEG signal, which has been associated with more ‘noise-like’ activity (Bak et al., 1987; Voytek et al., 2015). However, terminology varies in the literature; elsewhere (as in Chapter 3), an “increase in aperiodic activity” refers to a higher aperiodic exponent and offset, reflecting stronger low-frequency power and a general elevation in the overall power spectrum.

While the neurophysiological and cognitive mechanisms underlying aperiodic activity are not yet fully elucidated, recent work suggests that a smaller aperiodic exponent, indicative of more aperiodic (‘noise-like’) activity, is associated with greater variability in the brain’s electrical signaling (Waschke, Kloosterman, et al., 2021). During tasks that require flexible processing, such as generating new ideas or adapting to new circumstances, a brain with more aperiodic activity might better support the rapid reconfiguration of neural networks, enabling the brain to remain responsive and adaptable to new information or

stimuli. Such a brain may be better at breaking from established cognitive patterns and considering a broader range of possibilities or solutions, thereby fostering innovative problem-solving and divergent thinking. Conversely, during persistence-heavy processing, the brain may optimize for efficiency and stability, thus exhibiting reduced aperiodic activity. This may lead to more stable and less dynamically changing brain activity, which benefits tasks that require concentration and restrictive processing.

Together, Chapters 3 and 4 provide compelling evidence that aperiodic activity holds significant functional importance in high-level cognitive functions. It may be a potential neural mechanism underlying metacontrol biases and creativity. We believe that only by incorporating a specific focus on aperiodic neural activity will the neural foundation of cognitive functions be comprehensively understood.

### **Practical implications**

While the thesis mainly focuses on the cognitive processes of the general population, it holds potential clinical implications. The link between neural parameters and metacontrol implies the possibility that alterations in these neural metrics serve as early markers for certain neuropsychiatric conditions, such as obsessive-compulsive disorder (OCD) and attention-deficit hyperactivity disorder (ADHD). Prior research suggests that OCD can be characterized by a chronic bias toward exaggerated cognitive persistence, while ADHD can be characterized by a chronic bias toward excessive cognitive flexibility (Colzato et al., 2022). Abnormally high levels of BOLD signal variability and small aperiodic exponent might be early markers for ADHD, whereas abnormally low levels of BOLD signal variability and large aperiodic exponent might be indicative of OCD. Furthermore, this thesis sheds light on the development of novel treatments for these disorders using non-invasive brain stimulation techniques.

Additionally, this thesis provides insights into the domain of neural modeling. Emphasizing the importance of neural variability in human cognition, the research implies that incorporating, rather than minimizing, this variability might lead to more accurate models of human cognition.



### **Limitations and future directions**

This thesis revealed associations between BOLD signal variability, aperiodic neural activity, and metacontrol biases. However, the causal relationship between high or low BOLD variability/aperiodic neural activity and metacontrol biases toward persistence or flexibility remains elusive. It has yet to be clarified whether these neurological activities cause particular metacontrol biases or merely serve as functional markers indicating the presence of specific biases.

The neurochemical mechanisms underlying the association between neural “noise” parameters and cognitive processes are not yet fully understood. While several neurotransmitters, such as dopamine, glutamate/GABA, and norepinephrine (NE), have been implicated in modulating neural variability and aperiodic activity, it remains unknown how the manipulation of these neurotransmitters specifically impacts cognitive functions. Further work may uncover the neurochemical mechanisms via manipulating drug agonism/antagonism of candidate neurochemical systems (e.g., DA, glutamate/GABA, NE) and observing changes in cognitive performance.

From a methodological standpoint, we adopted Welch’s method to estimate the power spectral density, aligning with prior research (Adelhöfer, Paulus, et al., 2021; Donoghue et al., 2020; Ostlund et al., 2021). However, Welch’s method might produce biased estimations of power spectral density on shorter data fragments. Future investigations could consider alternative methodologies like wavelet transform to estimate EEG power spectral density. In addition, recent work introduces spectral parameterization resolved in time (SPRiNT) (Wilson et al., 2022) for a time-resolved decomposition of neural dynamics into their periodic and aperiodic components. Future work may test whether the association between aperiodic activity and different cognitive processes can be replicated using SPRiNT.