

FROM BRAIN DYNAMICS TO COGNITION - TIMESCALES ARE KEY

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Thesis submitted to the University of Ottawa
in partial Fulfillment of the requirements for the
PhD in Psychology

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Abstract

Our environment is continuously changing with both gradual and rapid shifts. How does the brain adapt to and process such continuous change? And how does that shape cognition? Addressing these questions is the goal of my thesis. In the first project, I focus on neural dynamics and their relationship to behavior. I show how the brain's intrinsic neural timescales mediate our sense of self and how that impacts our subsequent decision making. The second main project of my thesis extends the view beyond the relationship of neural dynamics and cognition by including the impact of the environmental dynamics (the temporal structure of stimuli) on the brain's neural dynamics, the body's physiological dynamics and cognitive functions. Using EEG and fMRI in three published papers, I demonstrate that the environmental dynamics modulate the brain's power spectrum in corresponding frequency ranges, which in turn modulates performance in a Go-NoGo task and working memory. Taken together, these findings suggest that the brain's neural dynamics, in their interplay with the environmental dynamics, strongly shape different forms of cognition like the self, decision making, sustained attention and working memory. This research offers a broader, direct connection between brain dynamics and cognitive function, aligning well with the recently established model of "Spatiotemporal Neuroscience".

Co-Authorship

Xu, J., Wainio-Theberge, S., Wolff, A., Qin, P., Zhang, Y., She, X., Wang, Y., **Wolman, A.**, Smith, D., Ignaszewski, J., Choueiry, J., Knott, V., Scalabrini, A., & Northoff, G. (2023). Culture shapes spontaneous brain dynamics – Shared versus idiosyncratic neural features among Chinese versus Canadian subjects. *Social Neuroscience*, 18(5), 312–330.

<https://doi.org/10.1080/17470919.2023.2278199>

- Providing data

Smith, D., Wolff, A., **Wolman, A.**, Ignaszewski, J., & Northoff, G. (2022). Temporal continuity of self: Long autocorrelation windows mediate self-specificity. *NeuroImage*, 119305.

<https://doi.org/10.1016/j.neuroimage.2022.119305>

- Revision

Arantes-Gonçalves, F., **Wolman, A.**, Bastos-Leite, A. J., & Northoff, G. (2021). Scale for Space and Time Experience in Psychosis: Converging Phenomenological and Psychopathological Perspectives. *Psychopathology*, 1–11. <https://doi.org/10.1159/000519500>

- Statistics/analysis, visualization.

Scalabrini, A*., **Wolman, A.***, & Northoff, G. (2021). The Self and Its Right Insula—Differential Topography and Dynamic of Right vs. Left Insula. *Brain Sciences*, 11(10), 1312.

<https://doi.org/10.3390/brainsci11101312>

- Equal contribution. Recording data, analyzing data, visualization, writing.

Ventura, B., Çatal, Y., Wolman, A., Buccellato, A., Cooper, A. C., & Northoff, G. (2024). Intrinsic neural timescales exhibit different lengths in distinct meditation techniques. *NeuroImage*, 297, 120745.

<https://doi.org/10.1016/j.neuroimage.2024.120745>

- Methods, revision

Arantes-Gonçalves, F., Wolman, A., Bastos-Leite, A. J., & Northoff, G. (2021). Scale for Space and Time Experience in Psychosis: Converging Phenomenological and Psychopathological Perspectives. *Psychopathology*, 1–11. <https://doi.org/10.1159/000519500>

- Statistical analyses

Lu, C.-J., Goheen, J., Wolman, A., Lucherini Angeletti, L., Arantes-Gonçalves, F., Hirjak, D., Wolff, A., & Northoff, G. (2024). Scale for time and space experience in anxiety (STEA): Phenomenology and its clinical relevance. *Journal of Affective Disorders*, 358, 192–204. <https://doi.org/10.1016/j.jad.2024.04.099>

- Statistical supervision

Acknowledgements

Completing this PhD thesis has been a challenging but incredibly rewarding journey, and I am grateful to many individuals for their support and guidance along the way.

First and foremost, I would like to express my deepest gratitude to my supervisor, Georg Northoff. Your unwavering support, insightful advice, and patience have been invaluable. Your expertise and dedication have inspired me throughout this research, and I am profoundly grateful for the opportunity to learn from you about the miracles of the brain and mind.

I would like to extend a special thanks to Mr. El Ahmadi for his exceptional assistance with the statistical analysis. His expertise and unwavering willingness to help have been crucial to the successful completion of this project.

I extend my heartfelt appreciation to my lab members and collaborators. Your camaraderie, intellectual discussions, and collaborative spirit have made this journey enjoyable and intellectually stimulating.

Working alongside such a dedicated and talented group has been an honor.

To my family, your love, support, and encouragement have been my anchor throughout this process. To my parents, for their endless support and belief in me and to my siblings, for their understanding and cheerleading: your presence in my life has been a source of strength and motivation.

Finally, to my friends, thank you for your constant encouragement, understanding, and for providing much-needed breaks and laughter. Your support has been essential in maintaining a balance between work and life, making this journey manageable and enjoyable.

Thank you all for being a part of this journey with me. This accomplishment would not have been possible without each and every one of you.

Preface

Authorship contributions are included in each published paper and in section “VI. 1 List of papers and contribution”. For Ethical details (REB and informed consent), please see each paper.

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Introduction

1.1 Goal of thesis

Our environment is in a state of perpetual flux, characterized by both regular and irregular transformations. Understanding how the brain adapts to and processes these ongoing changes is a fundamental focus of my research. Specifically, my thesis aims to explore the mechanisms through which the brain perceives and integrates continuous environmental dynamics, and how these processes influence cognitive functions. By investigating these questions, I aim to shed light on the intricate relationship between environmental dynamics and cognitive adaptation.

1.2 Different cognitive functions of the brain – are they modulated by the brain's neural dynamics?

The self is a core feature of our mental life and plays an important role in perception, action, and cognition. The mediation of our personal preferences and the cognitive strategies adopted under uncertainty are key mechanisms through which the self exerts a bias on our cognitive processes (Amodeo et al., 2021; Barton et al., 2021; Nijhof et al., 2020; Sparks et al., 2016; Sui & Humphreys, 2015). Humans are subjected to such cognitive bias, as self-specific stimuli are processed differently compared to non-self-specific information (Christoff et al., 2011; Northoff, 2011; Northoff et al., 2006; Sui & Humphreys, 2015). In particular, self-specific stimuli induce a benefit in response time and precision in diverse tasks (Jiang et al., 2019; Sui et al., 2012) and are more easily remembered (for an overview, see (Cunningham & Turk, 2017)). On the neural side, several studies have linked self-referential processing to the higher-order regions like cortical midline structures (CMS, (Frewen et al., 2020; Kelley et al., 2002; R. J. Murray et al., 2012; Northoff & Bermpohl, 2004; Qin et al., 2020)), the dorsolateral prefrontal cortex (dlPFC), and the default mode network (DMN, (Frewen et al., 2020; Kolvoort et al., 2020; Qin & Northoff, 2011)).

In our daily activities, we perform many different cognitive operations on various inputs, for instance manipulating, monitoring and storing specific stimuli in working memory. Working memory (WM) refers to the dynamic process of maintaining and manipulating information over short time delays despite the presence of newly incoming, interfering information (Li et al., 2022; Sreenivasan & D’Esposito, 2019). A key feature of WM is its capacity or WM span which has been conceptualized as a containment ability referring to the amount of information a system (e.g. short-term memory buffer) can possibly process and store (Atkinson & Shiffrin, 1968). While in a more dynamic conceptualization, capacity is compared to a system’s robustness, that is, how much the system can be loaded before it breaks down; or bandwidth, e.g., how much information can be processed or transmitted in a given unit of time (Wenger & Townsend, 2000).

Accordingly, a person with higher WM capacity can easily manipulate both higher and lower cognitive loads in working memory compared to a low-capacity person.

Working memory operates through a neuronally distributed network of brain regions (Berger et al., 2019; Christophel et al., 2017; de Mooij-van Malsen et al., 2023; Li et al., 2022; Owen et al., 2005; Rose, 2020). Higher-order regions like the parietal or dorsolateral prefrontal cortex (DLPFC) as well as lower-order regions like visual cortex (Borders et al., 2022; Christophel et al., 2017; Gayet et al., 2018; Yonelinas, 2013; Zhao et al., 2022) are associated with WM performance. The role of the hippocampus in WM has been the subject of extensive research and debate, with multiple studies providing evidence both supporting and challenging its involvement in WM processes (Borders et al., 2022; Leszczynski, 2011; Shavitt et al., 2020; Tambini et al., 2023; Yonelinas, 2013).

Specific temporal patterns of neural activity have been identified as characteristic of WM (Bhattacharya et al., 2022; Liu et al., 2023; Wasmuht et al., 2018). One key process mediating WM performance is delay activity. *Delay activity* is a sustained neural activity over the retention delay (Christophel et al., 2017; Curtis & D’Esposito, 2003; D’Esposito & Postle, 2015; Li et al.,

2022; Sreenivasan & D’Esposito, 2019). This delay activity is mainly observed in parietal and frontal cortices (Li et al., 2022). Another dynamic process reported in WM literature is *cortical short-term plasticity* wherein information is temporarily maintained through changes in synaptic weights. This dynamic neural functioning is referred to as ‘activity-silent WM’ (Beukers et al., 2021; Courtney, 2022) as it does not appear as blood-oxygenation-level-dependent (BOLD) signal increase as commonly measured via general linear modeling (GLM) of hemodynamic signal.

To specify the activity-silent neural dynamics in more detail, we suggest a variety of neural dynamics contribute to WM. These neural dynamics operate across various timescales, ranging from milliseconds to seconds (Cavanagh et al., 2020; Golesorkhi, Gomez-Pilar, Zilio, et al., 2021; Huang et al., 2018a; J. D. Murray et al., 2014; Wengler et al., 2020). Different mental processes have been associated with the recruitment of varying timescales (Wolff et al., 2022; Zilio et al., 2021). For instance, a shift toward slower timescales has been related to loss of consciousness (Wolff et al., 2022; Zilio et al., 2021, 2023) while the recruitment of multiple timescales has been shown in cognitive processes like attention (Zeraati et al., 2023). How these multiple timescales of neural activity mediate working memory capacity remains to be explored.

Decision making is a complex process. When we make a decision, we rely on both objectively accurate external criteria and more subjective internal factors, such as personal preferences for a specific response style or stimulus type, response style or specific biases (Nakao et al., 2013, 2019; Wolff et al., 2019). Signal detection theory (SDT) distinguishes between objective and more subjective criteria influencing the decision in forced choice tasks (Macmillan & Creelman, 2005). The general assumption of SDT is that decisions are made against a background of uncertainty, e.g., noise (Anderson, 2015). The goal of the decision-maker is to extract the decision-relevant signal from such background noise, a process that may introduce a bias into decisions. This bias is operationalized in SDT by the Criterion C. In contrast, the sensitivity

measure d' in SDT is an indicator of the external, objective criteria, thus reflecting a measure of accuracy.

1.3 Dynamic investigation of cognitive functions – Timescales are key

The standard procedure in cognitive neuroscience is to search for specific regions and frequencies in the brain's neural activity that are related to particular functions. This is typically achieved through block or event related task-designs. We refer to such neural activity as task-specific activity. Associating neural activity with specific functions in a task-specific way is the focus of the various branches of neuroscience including cognitive (Poeppel et al., 2020), affective (Panksepp, 1998) or social neuroscience (Lieberman, 2010). This neglects important dynamics that characterize both the brain and the environment, such as their respective timescales. For instance, the brain is constantly active, regardless of any particular cognitive task. This so-called intrinsic activity exhibits its own dynamics and timescales, which we suppose may influence the cognitive or task-related neural activity.

Timescales refer to the segmentation of time, often used to understand and organize events, processes, or phenomena in various systems (Buzsáki, 2006). They can range from microseconds to millions of years, depending on the context. In science and engineering, timescales are crucial for studying dynamic processes, from subatomic particle interactions to geological epochs (Cohen, 2014). In everyday life, timescales help us plan, schedule, and make sense of past, present, and future events, enabling effective communication and decision-making. Timescales are essential tools for comprehending the temporal aspects of our world and the universe, providing a framework for understanding the sequencing and duration of events across a wide spectrum of domains.

In neuroscience, timescales play a critical role in understanding the functioning of the nervous system at various levels, from milliseconds to years (Buzsáki, 2006; Cohen, 2014; J. D. Murray et al., 2014). At the shorter end of the spectrum, firing of individual neurons and synaptic

transmission occur in the millisecond or microseconds range. Moving to slightly longer timescales, neural oscillations and their role in cognitive processes occur in the range of milliseconds to seconds (Cohen, 2014). Processes such as short-term memory and sensory integration occur on timescales of seconds to minutes while timescales in the realm of hours to days are relevant for processes like learning and memory consolidation. Finally, timescales of weeks to years are crucial for developmental changes like aging and long-term plasticity in the brain. Social transmission can span over several generations.

Timescales at the neuronal level can be measured in various ways. In the time domain, a common method is autocorrelation, often referred to as a measure of intrinsic neural timescales or temporal receptive windows (TRW)(Honey et al., 2012; Wolff et al., 2022). In the frequency domain, brain fluctuations can be assessed through the power spectrum, which indicates activity across different frequencies. Many studies have investigated the role of specific frequency bands and their interaction in cognition and various disorders (Maturana-Candelas et al., 2020). In this thesis, however, I will employ a frequency measure that is gaining increasing interest in the scientific community – the median frequency (MF) (Golesorkhi et al., 2022a; Huang et al., 2018b; Klar et al., 2023b, 2023a).

Some first studies suggest that neural timescales are implicated various in mental processes.

Timescales appear to play a role in the sense of self in healthy (Scalabrini et al., 2021; Smith et al., 2022) and schizophrenic subjects (Lechner & Northoff, 2023; Northoff et al., 2021).

Clinically, altered timescales have been reported in autism (Uscătescu et al., 2023; Watanabe et al., 2019), schizophrenia (Northoff et al., 2021; Uscătescu et al., 2021, 2023) and disorders of consciousness (Zilio et al., 2021). Cognitively, timescales on a cellular level have been shown to be implicated in working memory (Wasmuht et al., 2018) and attention (Zeraati et al., 2023). The concept of self includes an intrinsic temporal component that operates across different timescales (Ersner-Hershfield, Garton, et al., 2009; Ersner-Hershfield, Wimmer, et al., 2009; Huang et al.,

2016; Kolvoort et al., 2020; Wolff et al., 2019). In the brain, these timescales have been operationalized as intrinsic neural timescales (INTs) which refers to the temporal autocorrelation properties of neuronal populations (Demirtaş et al., 2019; Gao et al., 2020; Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Golesorkhi, Gomez-Pilar, Zilio, et al., 2021; Ito et al., 2020; Raut, Mitra, et al., 2020; Stephens et al., 2013; Watanabe et al., 2019).

For instance, primary sensory neurons exhibit rapid firing rates, resulting in shorter temporal windows in response to external stimuli (Runyan et al., 2017) whereas activity in transmodal regions can persist over extended periods, during longer temporal windows (Zylberberg & Strowbridge, 2017). Recently, three studies have demonstrated a relationship between INTs in the resting state and facets of the self. Wolff et al. (2019) found that longer INTs in resting-state EEG signals correlate with higher levels of private self-consciousness. Similarly, a positive association between longer INTs and private self-consciousness was observed in fMRI (Huang et al., 2016). An EEG study by Kolvoort et al. (2020) found a positive correlation between resting-state INTs and the degree of self-prioritization effect (SPE) during a perceptual matching task with temporal delays. While these studies clearly link resting-state INTs to self-related processing, it remains unclear whether--and by what mechanism --INTs differentiate between self- and non-self-specificity during task-evoked activity.

INTs are measured by the autocorrelation window (ACW), which reflects the degree to which the brain's activity correlates with itself over time (Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Golesorkhi, Gomez-Pilar, Zilio, et al., 2021; Hasson et al., 2015; Honey et al., 2012; Wolff et al., 2022; Yeshurun et al., 2021). As temporal windows, the INT play an important role in input processing and cognition driven through temporal integration and segregation (Himberger et al., 2018a; Wolff et al., 2022; Yeshurun et al., 2021). Temporal integration involves smoothing information from distinct time points into a coherent stream, such as combining separate words into a sentence through long INTs(Himberger et al., 2018a; Wolff et al., 2022). On the other

hand, temporal segregation of features in external stimuli is primarily mediated by shorter ACWs in unimodal sensory regions, such as primary visual cortex, etc. (Golesorkhi, Gomez-Pilar, Tumati, et al., 2021). Hence, the length of the ACW can be conceived as a proxy of the balance of temporal segregation and integration (Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Golesorkhi, Gomez-Pilar, Zilio, et al., 2021; Himberger et al., 2018a; Wolff et al., 2022).

In the frequency domain, timescales as indexed by MF have been related to consciousness (Bergamasco et al., 2021; Chen et al., 2021; Kumar et al., 2022; McDonald et al., 1999; Jacob et al., 2022), epilepsy (Elsherif & Esmael, 2022; Vlachou et al., 2022), motricity (Balbinot et al., 2023; Cavalcante et al., 2022; Ettema et al., 2022; Gaspar-Junior et al., 2022; Gizzi et al., 2021; Ortega-Becerra et al., 2021; Silva et al., 2022; Sozzi & Schieppati, 2022) and fatigue (De la Fuente et al., 2021; Ebenbichler et al., 2023; Ettema et al., 2022; Florencio et al., 2021; Habets et al., 2021; Hou et al., 2021; Jurasz et al., 2022; Lowery et al., 2002; Moll et al., 2022; Puce et al., 2021; Tang et al., 2022). In the cognitive domain, MF has been linked to cognitive decline (Benz et al., 2014; Choi et al., 2019; Hoshi et al., 2022; Ruiz-Gómez et al., 2018; Verrusio et al., 2015). For instance, MF in resting-state EEG and MEG has been proposed as predictor of Mini-Mental State Examination (MMSE)(Choi et al., 2019; Hoshi et al., 2022) and Frontal Assessment battery (FAB) scores (Hoshi et al., 2022). A slowing in neural activity has been associated with a higher cognitive decline.

The wide array of topics covered here highlights the crucial role of timescales across numerous processes spanning various domains. This underscores the notion that neural timescales can serve as a unifying organizational principle for neural processing throughout the brain (Manea et al., 2022; Raut, Snyder, et al., 2020).

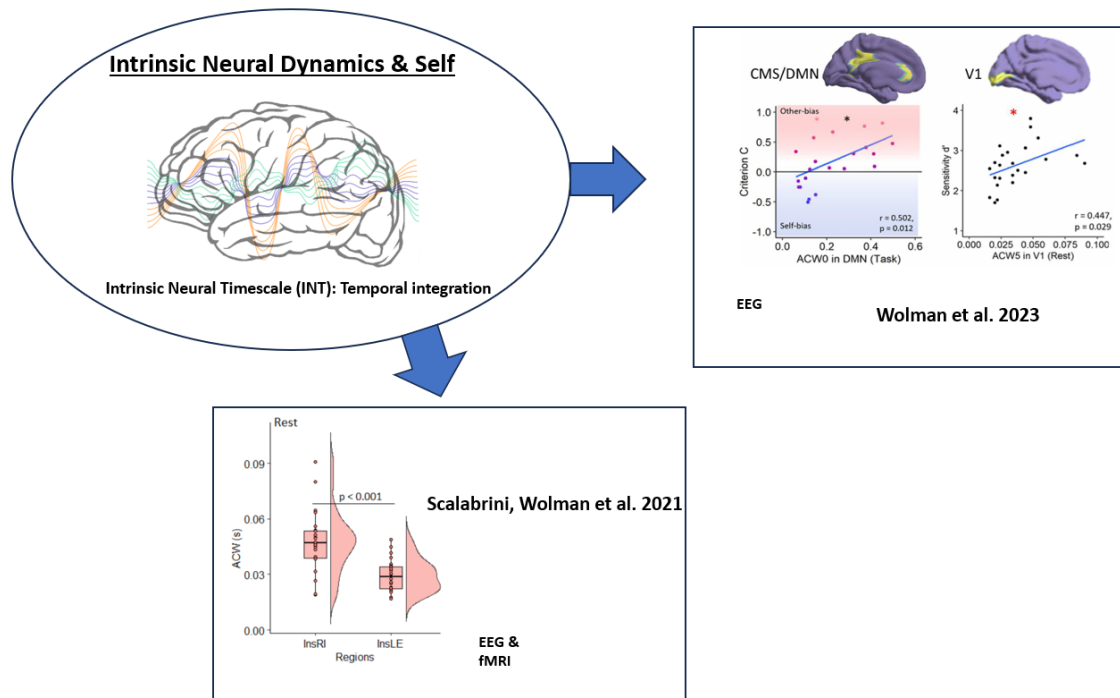
Chapter 2

Research Projects – Timescales and different cognitive functions

2.1 Timescales of self-cognition

One psychological feature emerging of the intrinsic neural activity is the self-a deeply personal and defining element of a person. The self encompasses distinctive features that differentiate one person from another, not only in terms of physical appearance, behavior and cognition, but also in terms of perception. The spatio-temporal approach posits that interindividual differences in perception, cognition or affect are biologically reflected through topographical and temporal variability in neural processes. Although some studies highlight a wide range of neural differences in topography and processing, these are often not explored further. The spatiotemporal approach suggests that such interindividual differences relate to unique perceptual and behavioral characteristics (as seen in correlational studies) and ultimately constitute the self. For more information about the self, please refer to (Northoff, 2011; Northoff et al., 2006). In summary, the analyses of interindividual differences refer to a very basic notion of the self. The first part of my thesis focuses on the relation between intrinsic dynamics and self-related behavior. This part comprises two EEG papers, one first author paper (Wolman et al., 2023) and one co-authored paper with equal contribution (Scalabrini et al., 2021).

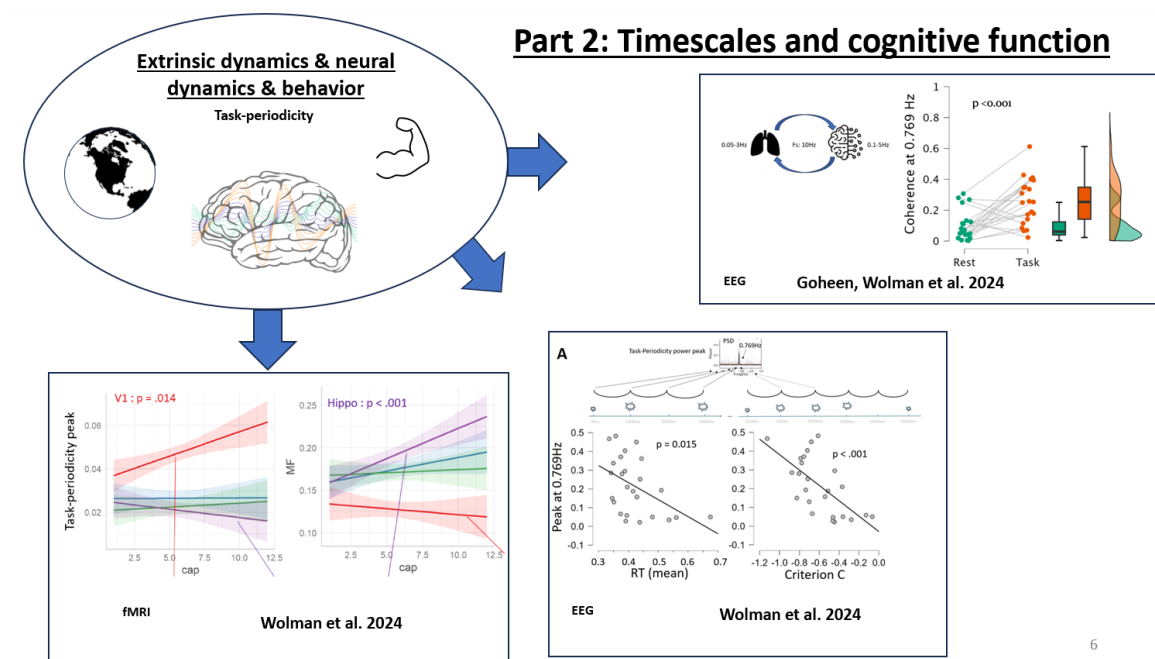
Part 1: Timescales of self-cognition



2.2 From the timescales of the environment to cognition

Research in neuroscience suggests the implication of timescales in information and input processing. Shorter timescales enable quick responses to dynamic environments, while longer time windows facilitate the gradual accumulation of information over time (Chaudhuri et al., 2015; Cusinato et al., 2023; Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Hasson et al., 2008; Honey et al., 2012; Wolman et al., 2023). This is supported by human neuroimaging studies and comprehensive artificial network models which attributed distinct processing time scales to various cortical regions (Fallon et al., 2020; Golesorkhi et al., 2022b; Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Hasson et al., 2008; Himberger et al., 2018b; Kiebel et al., 2008; R. J. Murray et al., 2012). This variability of neural timescales within and across regions and their implication in input processing of timescales suggests that they may play a role in a variety of sensory as well as behavioral and cognitive functions.

Therefore, the second part of my thesis focuses on the relationship of the inputs' or stimuli external timescales on the internal timescales of the brain and the resulting behavior. This part comprises three papers, two first author papers (Wolman et al 2024, Wolman et al. 2024) and one second author paper with equal contribution (Goheen et al 2024). Wolman et al. 2024 and Wolman et al (2024) shows that the brain's encoding of the external inputs' dynamics affect the brain's neural dynamics and also the subjects' behavior. While my paper with Goheen et al. (2024) illustrates how the brain aligns to environmental and bodily rhythms.



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2.3 Spatiotemporal Neuroscience

This thesis adheres to the spatio-temporal theory of cognitive functions (Northoff, 2024; Northoff et al., 2020a, 2020b). The spatio-temporal approach, as the name suggests, takes a particular perspective on neuroscientific and psychological questions. It complements traditional cognitive analyses by focusing on temporal and spatial relationships among environment, brain and

behavior. This may be operationalized via the analyses of temporal variability over time instead of the comparisons of the mean and standard deviation of a measure.

A second characteristic of this approach is a special interest in the temporal dynamics of the input stimuli, how these influence neural dynamics and ultimately reverberates to behavioral output dynamics. In other words, it investigates the hypothesis that the temporal dynamics of the brain's individual environment – such as heart or breathing activity – or the dynamics of the task design create corresponding dynamics in neural and, ultimately, in behavior.

One crucial mechanism by which this may be possible is timescales. Each system has its own internal temporal characteristics or rhythm, which comes with its own range of possible patterns in variability. An example to illustrate this is human gait: five people walk down the street. Each has two legs, two arms, one head, and an upper body. By this description, one might expect them all to walk in exactly the same manner. Instead, we see that each individual has their own characteristic way of walking, perhaps with longer or shorter steps, more or less left-right movement, etc. These slight differences in gait result from minor variability in body composition, such as differing upper-to-lower-body ratios, narrower or wider shoulders or hips, and more. These slight physical variances provide each person with a specific repertoire of movements. This example illustrates the importance of spatial and ultimately temporal characteristics in describing the observed phenomenon, in this case, gait. The spatio-temporal approach sheds special light on the relationship between spatial and temporal aspects in relation to our mental life, cognitive processes, and experiences.

The third important aspect of the spatio-temporal approach is its focus on intrinsic neural activity, which serves as the baseline for any task-specific activity. Intrinsic activity refers to neural activity independent of task-specific cognitive functions. It includes neural dynamics related to the processing of physiological rhythms as well as dynamics emerging from neural activity, such

as topographical connectivity dynamics. This type of activity is well-suited for studying the basic functions of different brain regions and their temporal features.

The best way nowadays to measure the most basic neural functioning in awake humans using EEG and fMRI is through the so-called resting state. When recording a resting state, participants are instructed either to close their eyes or keep them fixed on a cross in front of them, remaining relaxed without focusing on anything in particular. This includes avoiding personal thoughts, counting, planning, or daydreaming.

It is not a simple task for participants to limit mind wandering over a longer period while focusing on a simple cross. Additionally, many processes beyond basic physiological ones will be recorded, such as thoughts, spatial positioning of the body, or postural control. Nevertheless, this remains the best option for researchers working with healthy human participants. In this sense, resting state recordings remain an important element in human system neuroscience.

In contrast to intrinsic activity, task states refer to periods of controlled activity. Depending on the research question, a variety of tasks may be performed. These states are the most frequently studied in behavioral neuroscience and psychology. Often, event-related designs are used, where the subject is repeatedly exposed to a stimulus. This results in a series of similar neural activities, which are typically averaged over trials (e.g., ERP).

Chapter 3

First Part: Intrinsic neural timescales and the Self

3.1 Paper: Intrinsic neural timescales mediate the cognitive bias of self – Temporal integration in default-mode network

Wolman, A., Çatal, Y., Wolff, A., Wainio-Theberge, S., Scalabrini, A., El Ahmadi, A., &

Northoff, G. (2023). Intrinsic neural timescales mediate the cognitive bias of self – Temporal integration in default-mode network. *NeuroImage*, 268, 119896.

18 Citations

Abstract:

Our perceptions and decisions are not always objectively correct as they are featured by a bias related to our self. What are the behavioral, neural, and computational mechanisms of such cognitive bias? Addressing this yet unresolved question, we here investigate whether the cognitive bias is related to temporal integration and segregation as mediated by the brain's Intrinsic neural timescales (INT). Using Signal Detection Theory (SDT), we operationalize the cognitive bias by the Criterion C as distinguished from the sensitivity index d' . This was probed in a self-task based on morphed self- and other faces. Behavioral data demonstrate clear cognitive bias, i.e., Criterion C. That was related to the EEG-based INT as measured by the autocorrelation window (ACW) in especially the transmodal regions dorsolateral prefrontal cortex (dlPFC) and default-mode network (DMN) as distinct from unimodal visual cortex. Finally, simulation of the same paradigm in a large-scale network model shows high degrees of temporal integration of temporally distinct inputs in CMS/DMN and dlPFC while temporal segregation predominates in visual cortex. Together, we demonstrate a key role of INT-based temporal integration in CMS/DMN and dlPFC including its relation to the brain's uni-transmodal topographical organization in mediating the cognitive bias of our self.

3.2 Paper: The Self and Its Right Insula—Differential Topography and Dynamic of Right vs. Left Insula

Scalabrini, A., **Wolman, A.**, & Northoff, G. (2021). The Self and Its Right Insula—Differential Topography and Dynamic of Right vs. Left Insula. *Brain Sciences*, 11(10), 1312. <https://doi.org/10.3390/brainsci11101312>

34 Citations

Abstract: Various studies demonstrate a special role of the right compared to the left anterior insula in mediating our self. However, the neural features of the right insula that allow for its special role remain unclear. Presupposing a spatiotemporal model of self—“Basis model of self-specificity” (BMSS)—we here address the following question: what spatial-topographic and temporal-dynamic features render neural activity in the right insula to be more suitable in mediating self-specificity than the left insula? First, applying fMRI, we demonstrate that the right insula (i) exhibits higher degrees of centrality in rest, and (ii) higher context-dependent functional connectivity in a self-specific task among regions of distinct layers of self (intero-, extero-proprioceptive, and mental). Second, using EEG in rest and task, we show that the right insula shows longer autocorrelation window (ACW) in its neural activity than both left insula and other regions of the different layers of self. Together, we demonstrate special topographic, i.e., high functional connectivity, and dynamic, i.e., long ACW, neural features of the right insula compared to both left insula and other regions of the distinct layers of self. This suits neural activity in the right insula ideally for high functional integration and temporal continuity as key features of the self including its intero-, extero-proprioceptive, and mental layers.

Chapter 4

Second Part: Extrinsic dynamics in relation to neural dynamics and behavior

4.1 Paper: Repertoire of timescales in uni – and transmodal regions mediate working memory capacity.

Wolman, A., Çatal, Y., Klar, P., Steffener, J., & Northoff, G. (2024). Repertoire of timescales in uni – and transmodal regions mediate working memory capacity. *NeuroImage*, 291, 120602. <https://doi.org/10.1016/j.neuroimage.2024.120602>

Abstract:

Working memory (WM) describes the dynamic process of maintenance and manipulation of information over a certain time delay. Neuronally, WM recruits a distributed network of cortical regions like the visual and dorsolateral prefrontal cortex as well as the subcortical hippocampus. How the input dynamics and subsequent neural dynamics impact WM remains unclear though. To answer this question, we combined the analysis of behavioral WM capacity with measuring neural dynamics through task-related power spectrum changes, e.g., median frequency (MF) in functional magnetic resonance imaging (fMRI). We show that the processing of the input dynamics, e.g., the task structure's specific timescale, leads to changes in the unimodal visual cortex's corresponding timescale which also relates to working memory capacity. While the more transmodal hippocampus relates to working memory capacity through its balance across multiple timescales or frequencies. In conclusion, we here show the relevance of both input dynamics and different neural timescales for WM capacity in uni – and transmodal regions like visual cortex and hippocampus for the subject's WM performance.

4.2 Paper: From input dynamics to behavior: Neural dynamics shape bias in decision making

Wolman, A., Lechner, S., Angeletti, L. L., Goheen, J., & Northoff, G. (2024). From the brain's encoding of input dynamics to its behavior: Neural dynamics shape bias in decision making. *Communications Biology*, 7(1), 1–9. <https://doi.org/10.1038/s42003-024-07235-w>

Abstract:

The human brain is tightly connected to the individual's environment and its input dynamics. How the dynamics of periodic environmental stimuli influence neural activity and subsequent behavior via neural entrainment or alignment is not fully clear yet. In this study, we investigate the neural mechanism of how periodic stimulation shapes subsequent neural processing and associated behavior. Participants' electrical brain activity (EEG) was recorded during resting state and an auditory Go-NoGo task. The task was presented with a periodic intertrial interval (ITI) of 1.3sec (0.768Hz). Results revealed that the temporal structure of the task induced an increase in the power spectrum at exactly the frequency of the stimuli' ITI, that is, 0.768Hz, which showed high intersubject variability. A higher task-periodicity effect in the power spectrum was related to stronger phase based intertrial coherence (ITC) and lower Lempel-Ziv-Complexity (LZC), the latter reflecting a higher degree of signal compression as index of reduced neural complexity. Additionally, a higher task periodicity effect in the power spectrum co-occurred with a faster RT and a stronger response bias (Criterion C in signal detection theory). We conclude that the encoding of the inputs' dynamics into the brains power spectrum shapes subsequent behavior, e.g., RT and response bias, through reducing neural complexity. More generally, we show a direct neural relation of the brain's input encoding with its behavioral output through their shared dynamics.

4.3 Paper: Dynamic Mechanisms That Couple the Brain and Breathing to the External Environment

Goheen, J., Wolman, A., Angeletti, L. L., Wolff, A., Anderson, J. A. E., & Northoff, G. (2024). Dynamic mechanisms that couple the brain and breathing to the external environment. *Communications Biology*, 7(1), 938. <https://doi.org/10.1038/s42003-024-06642-3>

*equal contribution

Abstract:

Brain and breathing activities are closely related. However, the exact neurophysiological mechanisms that couple the brain and breathing to stimuli in the external environment are not yet agreed upon. Our data support that synchronization and dynamic attunement are two key mechanisms that couple local brain activity and breathing to external periodic stimuli. First, we review the existing literature, which provides strong evidence for the synchronization of brain and breathing in terms of coherence, cross-frequency coupling and phase-based entrainment. Second, using EEG and breathing data, we show that both the lungs and localized brain activity at the Cz channel attune the temporal structure of their power spectra to the periodic structure of external auditory inputs. We highlight the role of dynamic attunement in playing a key role in coordinating the tripartite temporal alignment of localized brain activity, breathing and input dynamics across longer timescales like minutes. Overall, this perspective sheds light on potential mechanisms of brain-breathing coupling and its alignment to stimuli in the external environment.

Discussion

The central goal of this thesis was to investigate how neural and environmental dynamics interact and relate to behavior. This was accomplished through a set of studies examining i) intrinsic neural dynamics and ii) the impact of external dynamics (task dynamic) on neural dynamics and behavior. We found i) a strong relevance of intrinsic neural timescales for the self and ii) a significant impact of task periodicity on neural activity and subsequently on WM and attentional performance. These findings align with other neuroscientific discoveries.

Research in neuroscience suggests that timescales play a crucial role in information and input processing. Shorter timescales enable rapid responses to dynamic environments, while longer time windows facilitate the gradual accumulation of information over time (Chaudhuri et al., 2015; Cusinato et al., 2023; Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Hasson et al., 2008; Honey et al., 2012; Wolman et al., 2023). This concept is further supported by human neuroimaging studies and comprehensive artificial network models, which attribute distinct processing timescales to various cortical regions (Fallon et al., 2020; Golesorkhi et al., 2022b; Golesorkhi, Gomez-Pilar, Tumati, et al., 2021; Hasson et al., 2008; Himberger et al., 2018b; Kiebel et al., 2008; R. J. Murray et al., 2012). This variability of neural timescales within and across regions, along with their impact on input processing of timescales, suggests that they may play a key role in a variety of sensory, behavioral and cognitive functions.

The variety of cognitive functions related to timescales suggest that temporal dynamics operate in a task – and modality-unspecific manner. Future studies should focus on fine-tuning the temporal features of tasks: Are there optimal time windows for specific cognitive functions? To what extend does the brain adapt to temporal dynamics based on characteristics such as cognitive or psychiatric disorders? could these adaptations even serve as neural marker?

Engelen et al. (2023) note that neural functions are temporally shaped by diverse bodily rhythms such as heartbeat, respiration and digestion. Their focus is more on the temporal *rhythms*

generated by these physiological processes (e.g., respiration) than on the actual strength or depth of the rhythm. In the case of olfaction, for instance, there is a clear temporal continuity during inhalation, which is interrupted during exhalation. Even the much shorter timescales of heartbeats may provide a temporal framework for neural activity and ultimately cognitive functioning, as illustrated by the modulation of the latter by the former. These various findings on body-brain interaction may, therefore, paradigmatically illustrate the importance of the temporal, task-unspecific shaping or scaffolding of cognitive function (Engelen et al., 2023).

In addition, there may also be extrinsic or external temporal features related to the tasks or environmental inputs. Various examples demonstrate that the temporal structure of tasks, such as longer or shorter intertrial intervals, exert strong impact on neural activity, as seen in entrainment (see this thesis and Lakatos et al., 2019) and alignment (Klar et al., 2023b, 2023a, p. 202; Northoff et al., 2023). In this context, external or extrinsic temporal features related to the task or environmental inputs modulate the intrinsic temporal features of the brain's neural dynamics.

Accordingly, we propose that the brain's neural dynamics allow for the convergence and connection of both the body's intrinsic dynamics and the environment's extrinsic dynamics. Hence, these dynamics may be shared across the physical boundaries of brain, body and environment serving as their "common currency" (Northoff et al., 2020a, 2023). This shared brain-body-environment dynamics, in turn, provides the temporal shaping and scaffolding for the brain's various cognitive functions.

Conclusion

This thesis focused on the relationship between neural dynamics and cognition. For this, we investigated EEG and fMRI recordings during rest and task states to capture intrinsic and task-related dynamics, respectively. The results from the various studies conducted as part of this thesis align with and extend the current literature, demonstrating a strong relationship between input dynamics, neural dynamics and behavior. This suggests a dynamic shaping of the brain's various cognitive functions, which, from a theoretical perspective, suggests the need to complement current Cognitive Neuroscience with what has recently been introduced as "Spatiotemporal Neuroscience" (Northoff, 2024; Northoff et al., 2020a, 2020b).

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Appendix A

Articles



Intrinsic neural timescales mediate the cognitive bias of self – temporal integration as key mechanism

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ARTICLE INFO

Keywords:

Decision making
Temporal integration and segregation
Intrinsic neural timescales
Self
Signal detection theory

ABSTRACT

Our perceptions and decisions are not always objectively correct as they are featured by a bias related to our self. What are the behavioral, neural, and computational mechanisms of such cognitive bias? Addressing this yet unresolved question, we here investigate whether the cognitive bias is related to temporal integration and segregation as mediated by the brain's Intrinsic neural timescales (INT). Using Signal Detection Theory (SDT), we operationalize the cognitive bias by the Criterion C as distinguished from the sensitivity index d' . This was probed in a self-task based on morphed self- and other faces. Behavioral data demonstrate clear cognitive bias, i.e., Criterion C. That was related to the EEG-based INT as measured by the autocorrelation window (ACW) in especially the transmodal regions dorsolateral prefrontal cortex (dlPFC) and default-mode network (DMN) as distinct from unimodal visual cortex. Finally, simulation of the same paradigm in a large-scale network model shows high degrees of temporal integration of temporally distinct inputs in CMS/DMN and dlPFC while temporal segregation predominates in visual cortex. Together, we demonstrate a key role of INT-based temporal integration in CMS/DMN and dlPFC including its relation to the brain's uni-transmodal topographical organization in mediating the cognitive bias of our self.

1. Introduction

The self is a core feature of our mental life and plays an important role in perception, action, and cognition. The mediation of our personal preferences and the cognitive strategies adopted under uncertainty are key sources by which the self exerts a bias on our cognitive processes (Amodeo et al., 2021; Barton et al., 2021; Nijhof et al., 2020; Sparks et al., 2016; Sui and Humphreys, 2015). Humans are subjected to such cognitive bias in the sense that self-specific stimuli are differently treated compared to non-self-specific information (Sui and Humphreys, 2015; Christoff et al., 2011; Northoff, 2011; Northoff et al., 2006). In particular, self-specific stimuli induce a benefit in response time and precision in diverse tasks (Jiang et al., 2019; Sui et al., 2012) and are more easily remembered (for an overview, see

(Cunningham and Turk 2017)). On the neural side, several studies have linked self-referential processing to the higher-order regions like cortical midline structures (CMS, (Frewen et al., 2020; Kelley et al., 2002; Murray et al., 2012; Northoff and Bermpohl, 2004; Qin et al., 2020)), the dorsolateral prefrontal cortex (dlPFC), and the default mode network (DMN, (Frewen et al., 2020; Kolvoort et al., 2020; Qin and Northoff, 2011)). What are the behavioral, neural and computational mechanisms by which the CMS/DMN mediate the cognitive bias? Addressing this yet unresolved question is the goal of our study.

Decision making is a complex process. When we have to make a decision, we base our judgment on objectively accurate external criteria but also on more subjective internal criteria like intrasubject processes or personal preferences for a specific response style or stimulus type etc. (Nakao et al., 2013, 2019; Wolff et al., 2019). Signal detec-

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<https://doi.org/10.1016/j.neuroimage.2023.119896>.

Received 16 August 2022; Received in revised form 10 January 2023; Accepted 20 January 2023

Available online 21 January 2023.

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tion theory (SDT) distinguishes between objective and more subjective criteria influencing the decision in forced choice tasks (Macmillan and Creelman, 2005). The general assumption of SDT is that decisions are made against a background of uncertainty, e.g., noise (Anderson, 2015); the goal of the decision-maker is to extract the decision signal from such background noise which may lead the participants to introduce a bias in their decisions. This bias is operationalized in SDT by the Criterion C. In contrast, the sensitivity measure d' in SDT is an indicator of the external, objective criteria that indicate the discriminability between the two stimuli by the participant, thus reflecting a measure of accuracy.

While the dorsolateral prefrontal cortex (dlPFC) is known to be implicated in decision making (Reckless et al., 2013; Krain et al., 2006) as it mediates executive function (Dubreuil-Vall et al., 2019), working memory (Balderston et al., 2020) and the self (Frewen et al., 2020), little is known about the neuro-temporal mechanisms underlying Criterion C and Sensitivity d' . Recent studies suggest a link between the Criterion C and spontaneous or ongoing activity like in the pre-stimulus neural activity of monkeys (van Vugt et al., 2018) and humans (Iemi et al., 2017; Iemi and Busch, 2018; Limbach and Corballis, 2016; Samaha et al., 2020). The apparent role of the spontaneous activity in mediating Criterion C suggests that the former's Intrinsic Neural Timescales (INT) (Wolff et al., 2022) may be involved in mediating the cognitive bias. The INT are particularly long in the spontaneous activity of the cortical midline regions of the default-mode network (DMN) which, interestingly, are key regions in mediating self-specificity (Kolvoort et al., 2020; Wolff et al., 2019; Smith et al., 2022). Together, these observations suggest a relationship of INT in CMS/DMN and the dlPFC with the cognitive bias, that is, the Criterion C.

The INT are measured by the autocorrelation window (ACW) through determining the degree to which the brain's activity correlates with itself over time (Wolff et al., 2022; Golesorkhi et al., 2021b; 2021a; Hasson et al., 2015; Honey et al., 2012; Yeshurun et al., 2021). Constituting temporal windows, the INT play an important role in input processing and cognition driven through temporal integration and segregation (Wolff et al., 2022; Yeshurun et al., 2021; Himberger et al., 2018). Temporal integration occurs by temporally smoothing different inputs at different timepoints into one coherent source of information, e.g., summing different words to one sentence through a long INT (Wolff et al., 2022; Himberger et al., 2018). On the other hand, temporal segregation of the external stimuli features is mediated primarily by short ACW in unimodal sensory regions (i.e. primary visual cortex, etc. (Golesorkhi et al., 2021b)). Hence, the length of the ACW can be conceived as a proxy of the balance of temporal segregation and integration (Wolff et al., 2022; Golesorkhi et al., 2021b; 2021a; Himberger et al., 2018). How such balance of temporal integration-segregation through long-short INT/ACW is related to the cognitive bias as measured by the SDT indices (and specifically Criterion C) remains yet unclear, though.

To clarify this relationship, we conducted a combined behavioral, neural, and computational study. Probing the cognitive bias, we used a modified version of a well-established task (Tsakiris, 2008) on visual perception of faces presented in a self-other continuum of different morphed pictures. Given the key importance of timescales with their supposed role in temporal integration-segregation, we presented the task in two temporally distinct ways (Huk et al., 2018). Once we presented it in a discontinuous or discrete way as typical event-related paradigm (separate single faces with different degrees of morphing in order to calculate Criterion C and Sensitivity d' based on the SDT). Additionally, we presented the same task also in a continuous way with an ongoing sequence of morphed faces where the participant had to indicate the transition between the two faces; this allowed us to specifically test for temporal integration-segregation within the paradigm itself, that is on the psychological level. EEG was recorded during both resting state and task-related activity and analysed on both channel and source space regional level. Finally, applying a data-driven network model (Chaudhuri et al., 2015), we included computational modeling to further support the as-

sumption of different processes in CMS/DMN and sensory regions like temporal integration and segregation respectively.

First, we will analyze the behavioral data by extracting the SDT indices and the transitions between self-other faces in both the discontinuous and continuous version of our task. We hypothesize a relation between the discontinuous and the continuous paradigm, that is a correlation between participants' bias (Criterion C) in the discontinuous paradigm with the participants' behavior in the continuous one. Given that the continuous version explicitly probes temporal integration versus segregation, it provides behavioral evidence for the involvement of temporal integration and segregation in the cognitive bias, i.e., Criterion C, and accuracy, i.e., sensitivity d' .

Next, we extract the ACW of EEG resting and task state activity in order to establish its link to the SDT indices. We expect the longer ACW (ACW0) to be implicated in the cognitive bias (Criterion C) while the shorter ACW (ACW5) supposedly mediates discrimination (sensitivity d'). We then also conducted source space reconstruction in EEG. This served to probe whether the cognitive bias, namely Criterion C, is related to the long ACW (ACW0) in the CMS/DMN (as being closely related to the self; (Northoff et al., 2006; Frewen et al., 2020; Qin et al., 2020)) and the dlPFC (as being implicated in decision making; (24, 25)), while the sensitivity d' supposedly is more associated with shorter timescales (ACW5) in sensory regions like primary visual cortex. Does this uni-transmodal hierarchy of ACW play a role in the temporal integration-segregation of inputs? We probed this question by applying the temporal input structure of the empirical-behavioral study in a computational realistic neural network model relying on Chaudhuri et al. (Chaudhuri et al., 2015). This model reinforces the idea that the CMS/DMN's neural activity shows high degrees of temporal integration of distinct inputs across time, while primary visual cortex favors temporal segregation of temporally distinct inputs. Moreover, elimination of the uni-transmodal hierarchy in the computational model abolishes any differences in input processing with regard to different degrees of temporal integration and segregation. That supports the assumption that the long ACW in CMS/DMN with its relation to the cognitive bias (Criterion C) is indeed related to temporal integration, that is, the temporal smoothing of temporally parsed inputs or stimuli across time, along a uni-transmodal hierarchy. Finally, we confirm the specific relationship between ACW and the cognitive bias as a stimulus-unspecific basic decision-making process by investigating the ACW – cognitive bias relationship in the dorsolateral prefrontal cortex (dlPFC), as well as in the fusiform face area specialized for the perception of faces (Kanwisher and Yovel, 2006).

2. Methods

2.2. Participants

Twenty-seven participants (15 women, 12 men, age: 22.18, SD: 4.28, range: 19 to 36) were recruited. All of them had a current or history of psychiatric or neurological disorders and normal or corrected-to-normal vision. We excluded one participant due to technical problems with EEG recordings in rest and task state and another participant was excluded only for the task state. Participants performed two morphed face recognition tasks adapted from (Tsakiris, 2008): In the discontinuous task, one participant was excluded. In the continuous task, one participant had no behavioural data due to a technical problem. Written informed consent for each participant was obtained prior to study participation. The study was approved by the local Research Ethics Board (REB # 2018054).

2.3. Materials

Prior to the experiment, pictures were taken from each of the participants with a Samsung A50 phone. Participants were asked to show

a neutral facial expression, mouth closed. The pictures were then prepared in the free and open-source graphics editor GIMP (2.10.12). All faces were turned to black and white (grayscale) and cut in an oval circle, with only the eyes, nose, and mouth areas remaining on a black background. Then, each face was morphed with a same-sex and same-race face from the NimStim facial pictures set (Tottenham et al., 2009). Morphings were realized with the Abrosoft Fantamorph 5 Software in 1% steps (from 0% self to 100% self-face).

2.4. Continuous morphing task (Fig. 1A left)

A hundred and one morphed pictures in 1% morphing steps were extracted from the continuum between the own and the other's face. A control continuum between a famous and an unknown face has also been created, leaving us with four morphing conditions based on the order and the identity depicted on the pictures. The 'self' conditions have the morphing order (Amodeo et al., 2021) from the 'self' face to other face (SO), or from (Barton et al., 2021) other face to 'self' face (OS). The control conditions have a morphing order from a (Nijhof et al., 2020) famous face to an unknown face (FU), or from the (Sparks et al., 2016) unknown face to the famous face (UF). The order of the conditions was randomised.

Pictures were presented in a continuous manner to create the experience of a morphed movie between the two faces. Movie duration was between 10 and 15 s and the interstimulus interval varied between 4 and 6 s. A total of 200 trials, 50 trials per condition in 8 blocks was presented. Participants were instructed to press a key when they stop to see the first face and to give another key when they started to see the second face. Two keypresses are of particular interest as they are the most self-related: In the morphing order from self to other (SO), the first keypress indicates the loss of the own face, while the second keypress in the order from other to self (OS) indicates the emergence or extraction of the own face. In order to record neuronal activity without motor activity noise due to a keypress (Tsuchiya et al., 2015), five trials in each condition were visualized and recorded while no keypress was given (no-report paradigms). The no-report trials took place before the report-trials for the half of participants, and afterwards for the other ones. To ensure that the moment of the keypress was time-independent, we randomly varied the movie length between 10 and 15 s. In addition, the intertrial interval was jittered between 4 and 6 s (jittered by 1 s). This task has been recorded in EEG.

Such a continuous paradigm structure serves the purpose of probing for participants' capacity to integrate or segregate temporally disjointed but sequential inputs, i.e., the morphed self-other faces. Temporally adjacent stimuli like two morphed faces may be temporally integrated/separated entailing separate judgement as self or other; alternatively, they may be integrated entailing subsumption of both under either self or other.

2.5. Discontinuous signal detection task (Fig. 1A right)

This task purely served to extract the SDT indices. From the morphed pictures, 13 pictures were selected at a morphing degree from 0% to 100% self in 10% steps. The middle morphing values (40 to 60%) are selected in 5% morphing steps to gather a more fine-grained behavior in the ambiguous range. Each picture was presented 12 times in a random order for 200 ms, with a total 156 trials per participant (Fig. 1A right). Participants were instructed to classify each of the pictures in 'self' pictures (more self than the other) or in 'other' pictures (more other than self). No correct response was possible for the 50% morphing, while morphings above 50% are self-pictures and below 50% are other-pictures. We analysed the data with Signal Detection Theory (SDT) which offers cognitive bias (Criterion C) and sensitivity (d') measures based on the relation of hits and false alarms.

2.6. Resting-state

Eyes open resting-state was recorded in EEG for 7 min. The participants were fixating a white cross on a gray background.

3. Data analysis

3.1. Signal detection theory (SDT)

The discontinuous task was analysed with SDT (Macmillan and Creelman, 2005) because it yields separate indicators for the accuracy in form of the cognitive bias Criterion C and sensitivity d' (Fig. 1B). **3.1.1. Criterion C:** The criterion C of the signal detection theory (Macmillan and Creelman, 2005) indicates the preference of the participant to report rather one than the other of the two faces when committing an error (false alarms or misses). It is calculated based on the Hit and False alarm rate as follows (Anderson, 2015):

$$\text{Criterion } C = -0.5 * (z_{Hit} + z_{FA})$$

Some participants tend to indicate perceiving their own face more often than the other's face (liberal response style with a Criterion C > 0), whereas other participants rather see the 'other' face than themselves (conservative response style with a Criterion C < 0). Some participants show no bias (C = 0).

3.1.2. Sensitivity d'

d' is a measure of discriminability and indicates the ability of a participant to distinguish between two stimuli. In our case, it indicates how well the participant distinguished between their own and someone else's face. It is calculated based on the hit and false alarm rate (Anderson, 2015).

$$\text{Sensitivity } d' = z_{Hit} - z_{FA}$$

If the hit rate equals the false alarm rate, $d' = 0$ where the participant is unable to discriminate between the two stimuli. A higher d' corresponds to less errors and therefore indicates a higher sensitivity towards the differences between two faces.

3.2. EEG data acquisition and preprocessing

EEG data was recorded using Ag/AgCl electrodes through a 64-channel Brain Vision Easycap (according to the International 10–20 System) referenced to the right mastoid. The data was sampled at 1,000 Hz with DC recording. The EEG data preprocessing was performed using the EEGLAB toolbox for MATLAB (R2017b; (Delorme and Makeig, 2004), RRID: SCR_007292). The data was downsampled to 500 Hz and filtered with a FIR zero-phase low-pass filter at 50 Hz and a high-pass filter at 1 Hz. With a custom script, noisy channels (defined as 5 interquartile above or below each channels mean) have been spherically interpolated before re-referencing to the average. Further, artifacts were identified using independent component analysis (ICA) via the EEGLAB software (infomax) creating 63 independent components. Next, we used MARA implementation to automatically reject noisy components (Winkler et al., 2011).

3.3. Autocorrelation window (ACW)

The autocorrelation function measures the similarity of a time series with a time-lagged version of itself. We distinguished, following Goleosorkhi et al. (2021b) and Smith et al. (2022), ACW5 and ACW0. We defined ACW5 and ACW0 as the first lag where the autocorrelation function (ACF) reaches half of its maximum value (AC = 0.5) or zero (AC = 0.0), respectively (Honey et al., 2012; Murray et al., 2014). We calculated both ACW0 and ACW5 to see the impact of longer (ACW0) and shorter (ACW5) windows on the different behavioral indices, i.e., d' and C. Similarly, we further defined ACW4 (AC = 0.4), ACW3 (AC = 0.3),

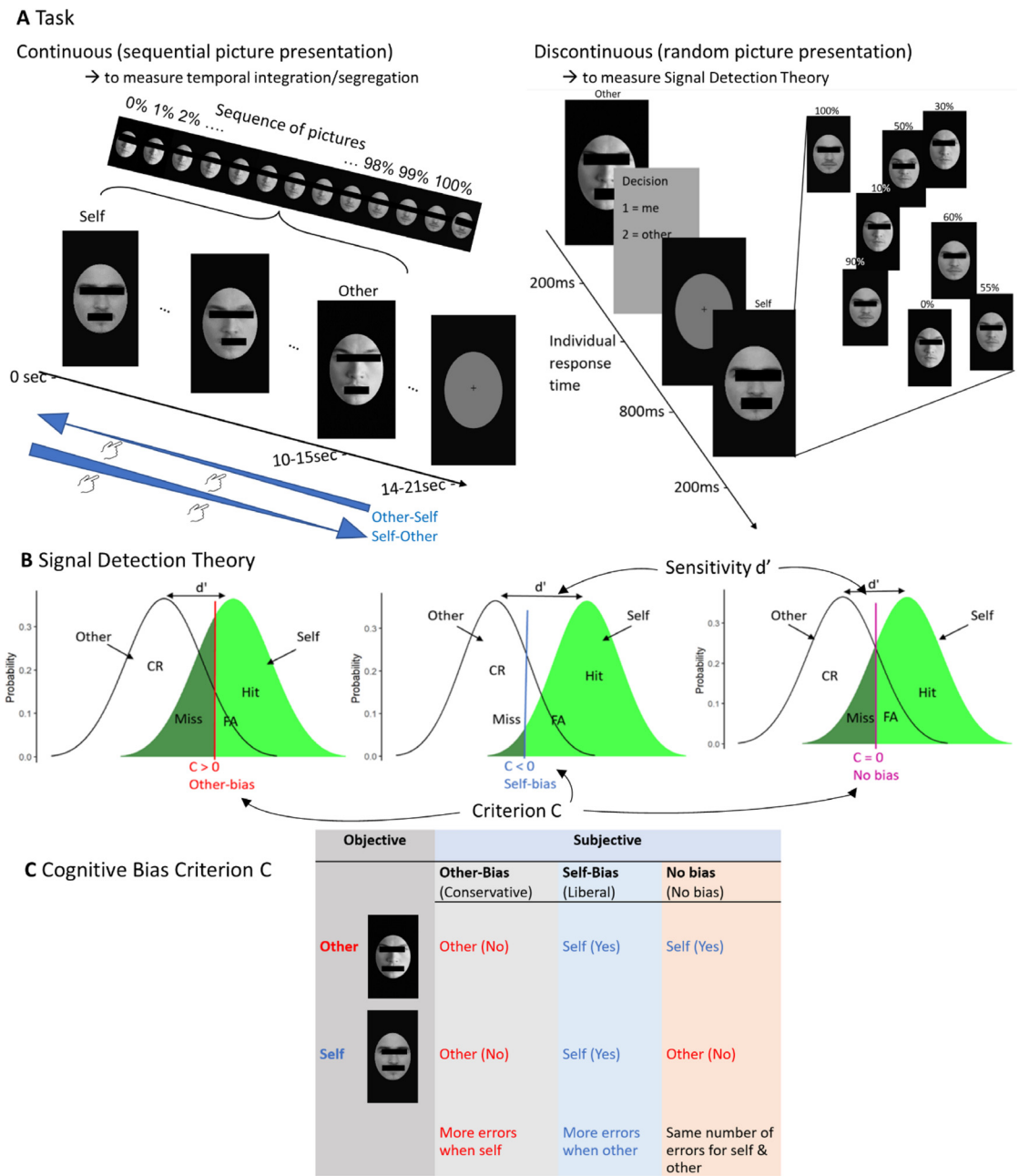


Fig. 1. **A** Procedure of the morphing tasks. In the continuous task (left) morphings of faces were shown in form of a smooth video (ordered sequence of faces). Participants were asked to indicate when they stop to see the first face and when they started to see the second face. Of particular interest are the two self-related keypresses which indicate the loss and the emergence of the own face. On the right is the discontinuous design (right) elaborated to extract Signal detection theory (SDT) indexes. Participants were asked to classify randomly presented morphed faces into ‘self’ (>50% morphing) or ‘other’ (<50% morphing) faces. Identities have been made unrecognizable for publication purposes. **B** Schematic description of the SDT. The Sensitivity d' indicates how well a participant discriminates between the two stimulus types ‘other’ and ‘self’ faces by indicating the distance between the white (other) and the green (self) curve. The Criterion C indicates a favoritism to one of the two error types miss or false alarm. This indicator will be used to assess the self – and the other bias. **C** Simplified representation of the cognitive bias.

ACW2 (AC = 0.2) and ACW1 (AC = 0.1) to investigate an eventual gradient that links the timescales to the behavioral indices.

All autocorrelations were calculated on 7 min rest and task state EEG data, for each channel (or region of interest (ROI) for eLORETA before being averaged across all electrodes/ROIs to extract one ACW value per participant.

3.4. Source localization with eLORETA

Regions were defined according to the Glasser parcellations (Glasser et al., 2016). Exact Low Resolution Electromagnetic Tomog-

raphy (eLORETA (Pascual-Marqui et al., 1994)) was performed by estimating the virtual-channel source for each region of the Glasser atlas in FieldTrip (Oostenveld et al., 2011). The output is a timeseries of estimated source level activity for each region. We investigated the core DMN (Andrews-Hanna et al., 2014) consisting of the posterior cingulate cortex (PCC) and the pregenual anterior cingulate cortex (pACC) because of its known implication in self-related functioning. As a control region not specifically implicated in self-related processing, we choose the visual primary cortex (V1). We investigated the dorsolateral pre-frontal cortex (dlPFC) because of its implication in decision making and the FFA due to its implication in face processing. The precise Glasser-

parcels used were the following: V1: LV1, RV1. CMS/DMN: LRSC, RRSC, L23d, R23d, Ld23ab, Rd23ab, L23c, R23c, Rp24, Lp24, Ra24, La24, L31a, R31a, L31pv, R31pv. dlPFC: L8C, R8C, L8Av, R8Av, Li68, Ri68, LSFL, RSFL, L8BL, R8BL, L9p, R9p, L9a, R9a, L8Ad, R8Ad, Lp946v, Rp946v, La946v, Ra946v, L46, R46, L946d, R946d. Fusiform face complex: LFFC, RFFC.

3.5. Statistical analyses

Comparisons of the ACW based on the thresholds were performed via a repeated measures ANOVA with a Greenhouse-Geisser correction for sphericity violations. The link between the behavioral and neuronal measures was obtained via simple Pearson's correlations. For the mathematical models describing the gradient between ACW and the behavioral variables, the ACW0 was replaced by 0.01 for logarithmic transformation. The remaining ACW values are their AC value (e.g., 0.1 for ACW1, 0.2 for ACW2 etc.). Inferential analyses were run in JASP or R. ACW was extracted in Python (3.8). SDT indices were calculated in Excel following the instructions in (Macmillan and Creelman, 2005).

3.6. Computational model

To further probe the effect of different regions on temporal segregation and integration, we used a computational model based on (Chaudhuri et al., 2015). In essence, this model comprises two differential equations:

$$\tau_E \frac{d}{dt} v_E^i = -v_E^i + \beta_E \left[(1 + \eta h_i) \left(w_{EE} v_E^i + \mu_{EE} \sum_{j=1}^N FLN_{ij} v_E^j \right) - w_{EI} v_I^i + I_{ext,E}^i \right]_+$$

$$\tau_I \frac{d}{dt} v_I^i = -v_I^i + \beta_I \left[(1 + \eta h_i) \left(w_{IE} v_E^i + \mu_{IE} \sum_{j=1}^N FLN_{ij} v_E^j \right) - w_{II} v_I^i + I_{ext,I}^i \right]_+$$

v is the firing rate, τ is the intrinsic time constant, I_{Ext} is the external input to the system governed by the slope b of the f - I curve. w values are coupling parameters. m is a fixed parameter that controls the strength of long-range excitatory input. FLN (Fraction of Labeled Neurons) is the structural connectivity matrix based on a macaque study (Markov et al., 2014). E and I correspond to excitatory and inhibitory, respectively; i and j denote different regions. Solving these differential equations gives us 29 time series, one per region in the model. We used the exact same parameters as (Chaudhuri et al., 2015). The hierarchy index h is a sigmoid function scaled between 0 and 1, increasing from periphery to core. First, we used a continuous input of 1 s and plotted activity the same way. We also simulated the input as close as the real discontinuous paradigm in this study. We gave 200 ms inputs with amplitude 1 to the outermost region (V1) and randomized the inter-stimulus interval (ISI) between the mean of the ISI in the study (0.528 s) $\pm$ 1SD (0.253 s) and plotted the resulting neural activity changes in both periphery (V1) and core (24c) regions. In a second step, to probe the effect of the hierarchical uni-transmodal topography on temporal segregation and integration, we eliminated the hierarchy by setting the hierarchical index h to 0.5 for all regions.

4. Results

4.1. Behavioral results

In the discontinuous self-task (Fig. 1A right, see Methods), participants indicated the predominant facial identity (self or other) of single randomly presented morphed faces reflecting an event-related paradigm structure. The psychometric function (Fig. 2B) indicating the proportion

of correct classifications for each morphing degree shows more variability in the middle morphings (where the subjective uncertainty is higher) than in the extreme ones (where the subjective uncertainty is lower). The Sensitivity index d' had a mean (SD) of 2.65(0.52) (range: 1.6 to 3.79). The cognitive bias Criterion C had a mean (SD) of 0.25 (0.5) (range: -0.51 to 1.34).

Next, for each participant, we calculated the average of the morphing degree at the moment a keypress was given. The descriptive results are as follows: Loss of self: $m = 50.77$, $SD = 7.88$, range = 30.27, max = 60.33, min = 30.06; Emergence of other: $m = 75.789$, $SD = 7.001$, range = 28.31, max = 88.74, min = 60.43; Loss of other: $m = 46.59$, $SD = 7.19$, range = 24.38, max = 60.49, min = 36.11; Emergence of self: $m = 71.8$, $SD = 8.33$, range = 31.75, min = 54.86, max = 86.61; Fig. S1). The simultaneous effect revealed by a repeated ANOVA is significant ($F(3,75) = 104.467$, $p < .001$, $h^2_{\text{partial}} = 0.807$; $e_{GG} = 0.697$), post hoc differences are reported in Fig. S1. We observe no effect specific to the order of morphing presentation (SO or OS).

Due to our particular interest in the self, we will specifically focus on its loss and its emergence (as obtained by the continuous task). Hence, we correlated these two keypresses with C and d' (as obtained in the discontinuous task). We see that only the keypress related to the emergence of the self correlated with the Criterion C ($r = 0.486$, $p = 0.014$, Loss: $r = -.275$; $p = .215$; Fig. 2C) but not with the sensitivity d' (Emergence: $r = 0.150$, $p = .474$; Loss: $r = -.299$, $p = .147$). This indicates that an early detection of the own face is linked to a liberal self-bias. A later self-emergence is linked to a conservative 'other'-bias.

4.2. Intrinsic neural time scales in rest and task states

We assessed the intrinsic neural timescales (INT) by the autocorrelation window (ACW; Fig. 3A). We investigated the topographic maps of ACW (Fig. 3B) which show the expected rostro-caudal gradient (Golesorkhi et al., 2021b, 2021a; Kiebel et al., 2008) and observe an overall significantly longer ACW during task compared to rest (Fig. 3C), indicating a sensitivity of the ACW to external stimuli.

4.3. Relationship of intrinsic neural timescales with behavioral measures

First, we identify the correlational strength between the different behavioral measures (Emergence of Self, Criterion C, Sensitivity d') with the ACW via Pearson's correlations (Table S2a to Table S3b). Next, we investigated the relationship between these different correlations via different mathematical functions (Fig. 4, for more details see Table S4). In resting state, the correlation between the moment of the Emergence of Self is strongest for ACW0 and decays following a logarithmic function ($p = 0.003$). We observe the same evolution for the Criterion C ($p = 0.014$). Inversely, an increasing logarithmic function links the d' to the ACW ($p = 0.0003$), with the strongest correlation observed for ACW5. In task state, the relationship of ACW with the Emergence of Self and Criterion C can be described via a quadratic function ($p = 0.007$ and $p = 0.009$, respectively). This link is lost (due to one data point) for sensitivity d' ($p = 0.1$). By taking the difference between rest and task state, we confirm the differential correlation gradient between Criterion C and d' and confirm the similarity between the Emergence of Self and Criterion C: The rest-task difference of Emergence of Self and Criterion C follows a quadratic function ($p = 0.023$ and $p = 0.011$, respectively), while the rest-task difference of Sensitivity d' shows a simple linear relationship ($p = 0.0003$). No coherent relationship links the ACW to the Loss of self (Fig. S2).

4.4. Source space reconstruction eLORETA in CMS/DMN and V1

We extracted regional activity via eLORETA for the DMN focusing on CMS/DMN (PCC and pACC) and the primary visual area (V1; see Methods). ACW was calculated on the extracted DMN regions and correlated with d' and Criterion C (Table 1). The Criterion C is only associated

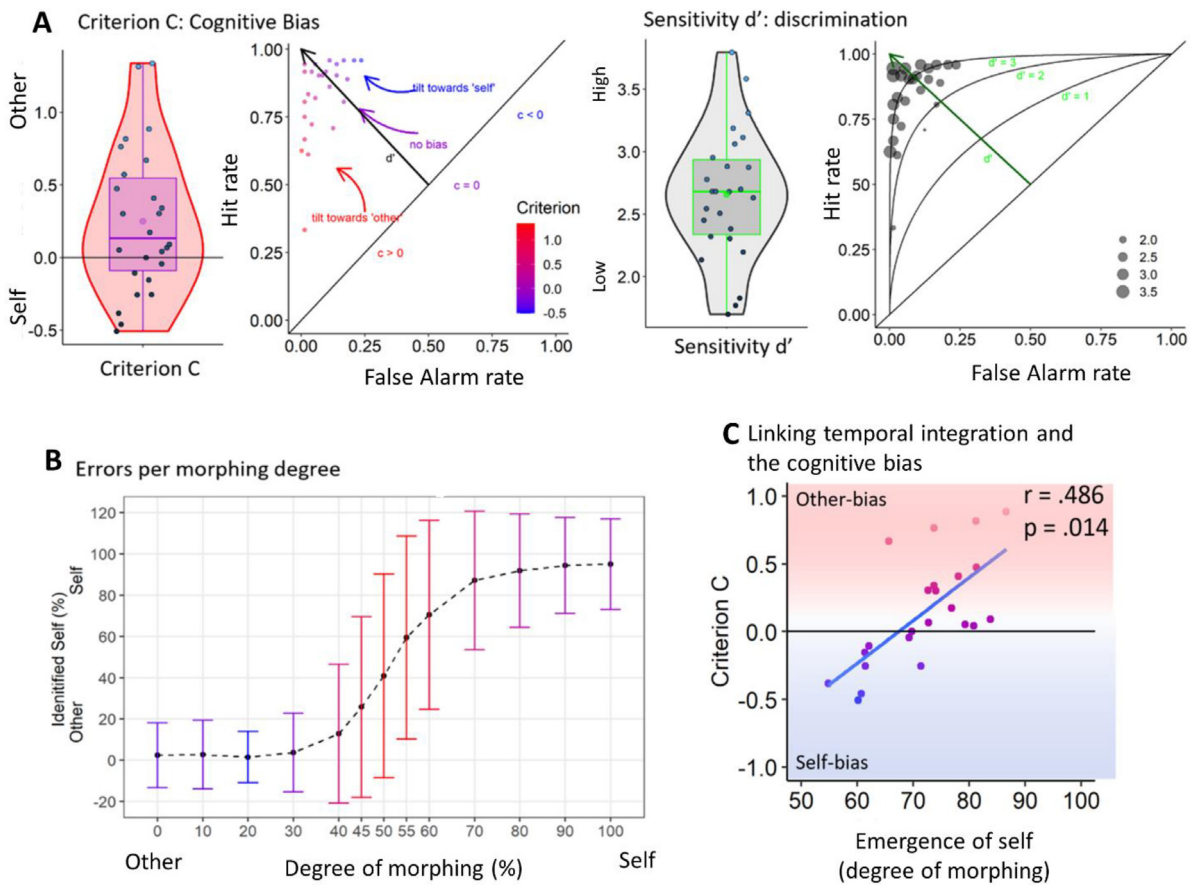


Fig. 2. A Sensitivity d' and Criterion C extracted based on the discontinuous task. Descriptive data of the d' (left) and Criterion C (right) in a violin plot and a ROC space. B Psychometric function of the participant's responses to the different morphing degrees in terms of identified self (error bars indicate SD) C The strong correlation of the Criterion C and the Emergence of self keypress indicates that an early detection of the own face is linked to a self-bias. A later self-emergence is linked to an 'other'-bias.

Table 1

Correlations between Criterion C (Crit C) and Sensitivity d' (Sens d') in the DMN and the primary visual area V1 via the ACW0 (0) and ACW5 (5).

State		Crit C		Sens d'	
		r	p	r	p
DMN_0	rest	0.342	0.094	0.207	0.321
	task	0.502*	0.012	0.188	0.38
DMN_5	rest	0.308	0.143	0.339	0.106
	task	0.251	0.238	0.242	0.254
V1_0	rest	-0.043	0.838	0.007	0.973
	task	0.387	0.062	0.11	0.608
V1_5	rest	0.071	0.735	0.469*	0.018
	task	0.283	0.191	0.306	0.155

with the ACW0 in the DMN, measured during task-state (DMN-ACW0: $r = 0.502$, $p = 0.012$, Fig. 5A). Neither the V1 nor the ACW5 elicited a significant correlation with the Criterion C ($p > .05$). The Sensitivity index d' is only correlated with the ACW5 in the resting state V1 activity (V1-ACW5: $r = 0.469$, $p = .018$, Fig. 5A). Neither the DMN nor the ACW0 showed significant correlation with the d' ($p > .05$).

4.5. Computational modeling – temporal integration and segregation in CMS and sensory cortex

The hierarchy of different regions in the model was defined by a sigmoid function scaled between 0 and 1 (see methods). First, we applied the continuous task paradigm on the model to probe temporal segregation in hierarchically low regions (periphery / V1) and integration in

hierarchically high regions (core / 24c; Fig. 6, left column). In a second step, in order to investigate the effect of the differential hierarchical positions of visual cortex and CMS/DMN in their short and long timescales, we eliminated the hierarchy in our computational model by assigning the same hierarchical index to all regions. We now observed similar activity in both V1 and midline 24c (Fig. 6, right column).

4.6. ACW mediates the bias in decision making in a stimulus-unspecific rather than -specific way

In a next step, we wish to investigate if the link between the cognitive bias and the ACW is mediated by the process of decision making itself operating across different types of stimuli, e.g. stimulus-unspecific, rather than by the content of the facial stimuli (self vs. other vs. famous vs. unknown), e.g., stimulus-specific. For this, we will first confirm the link between the long ACW and the cognitive bias in the dlPFC. Hence, we extracted the ACW of the dlPFC and found a correlation between the ACW0 in the dlPFC only with the Criterion C in rest ($r = 0.485$, $p = 0.014$) and task ($r = 0.530$, $p = 0.008$, Fig. 7). This confirms the intimate link between the long ACW and the cognitive bias in our decisions and supports the association of ACW with the decision-making process itself. The short ACW5 of the dlPFC is exclusively linked to the Sensitivity d' in rest ($r = 0.420$, $p = 0.036$, Fig. 7; Table S5), confirming the link between the short ACW and sensitivity d' in the accuracy of decision making.

In a second step, we extracted the ACW during the visualization of each face identity (self, other famous, unknown). A repeated measures ANOVA shows no significant differences in the ACW between the facial

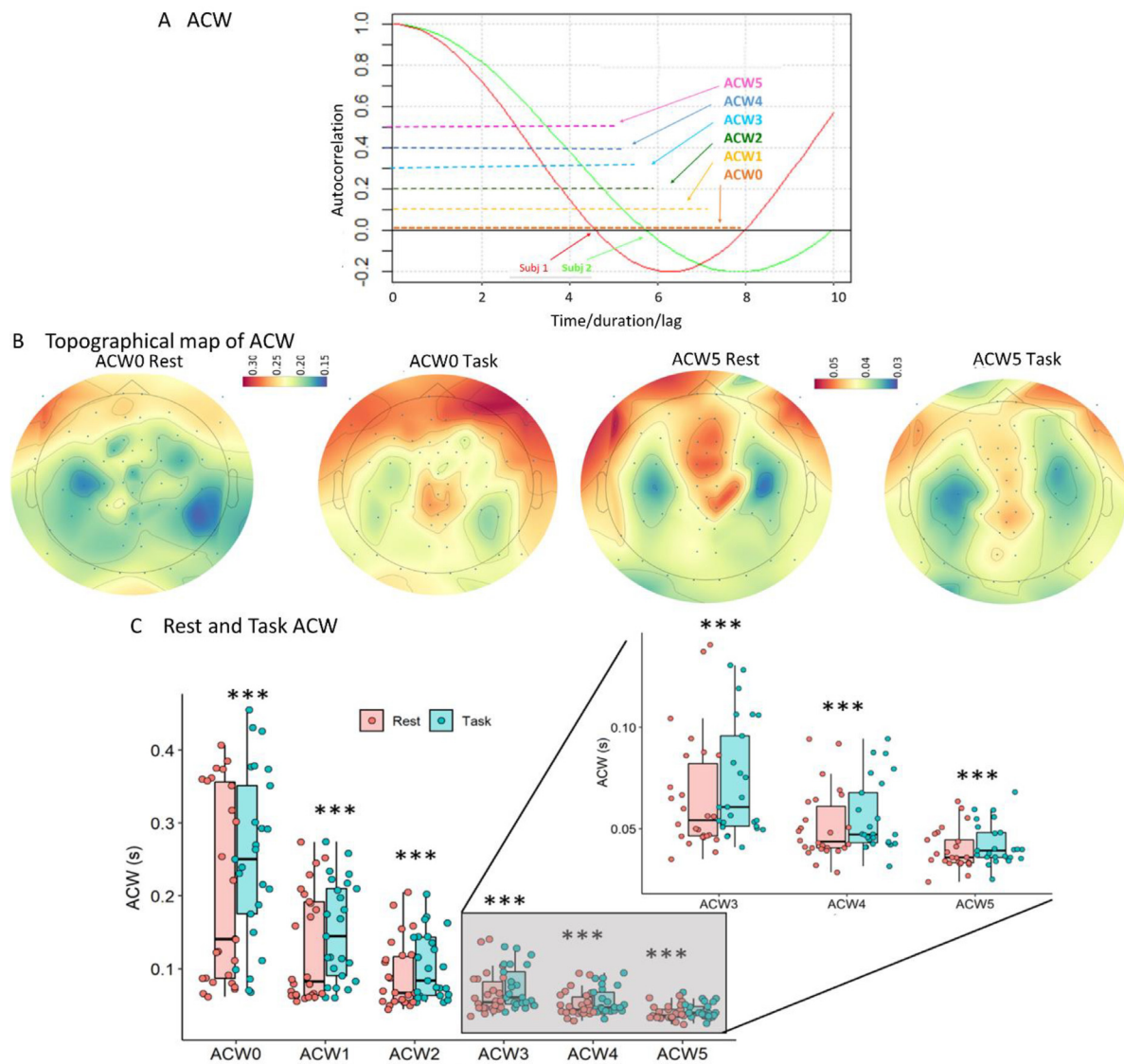


Fig. 3. **A** Autocorrelation Window (ACW) of two schematic participants (green and red). Indicated are the six degrees of AC (in color from pink to orange) on the y-axis, and the duration on the x-axis. The ACW is the lag until a certain correlation value within the overall autocorrelation function is reached. We observe the expected rostro-caudal gradient of ACWs. **B** Topographical maps of the ACW0 and ACW5 in rest and task state averaged across participants. **C** Boxplots of all six ACWs averaged across participants and EEG-channels show a clear rest-task differences.

identity (ACW0: $F(3,72) = 1.207$, $p = 0.313$; ACW5: $F(3,72) = 0.282$, $p = 0.838$; see Fig. S3), indicating a certain insensitivity of the ACW towards the stimuli content.

We then correlated the ACW of the different facial stimuli with the Criterion C and Sensitivity d'. The ACW0 extracted from each face correlated with the Criterion C ($p < .05$; Table S6), confirming an insensitivity of the ACW towards the facial identity or the stimulus content in relation to the cognitive bias.

Finally, we calculated the ACW on activity extracted from the fusiform face area (FFA) and correlated it with the SDT measures. No significant correlations were found ($p > .05$; Table S7), indicating that the FFA is not mediating the link between cognitive bias and ACW. Together, these findings strongly indicate the stimulus-unspecific effects of ACW on the bias in decision making.

5. Discussion

In the present study, we investigated whether temporal integration mediates the cognitive bias of self in perception and decision making.

For this, we combined behavioral, neural and computational levels of analyses. Using Signal Detection Theory (SDT), we observed the cognitive bias on the behavioral level (Criterion C) with different participants showing bias towards either the own or other face. Given the nature of our paradigm, this implies high temporal integration on the psychological level. This was further extended to the neural level by showing that the cognitive bias is specifically associated with longer INT (ACW0) in CMS/DMN and dlPFC, thus suggesting high temporal integration on the neural level. This is complemented by computational neural network modeling showing high degrees of temporal integration of temporally distinct inputs in specifically CMS/DMN as distinct from visual cortex, suggesting a strong implication of the uni-transmodal hierarchical topography in the cognitive bias.

5.1. Behavioral analyses

First, we observed a strong correlation between the cognitive bias and the keypress indicating the emergence of the own face. This indicates that an early detection of the own face is linked to a liberal self-

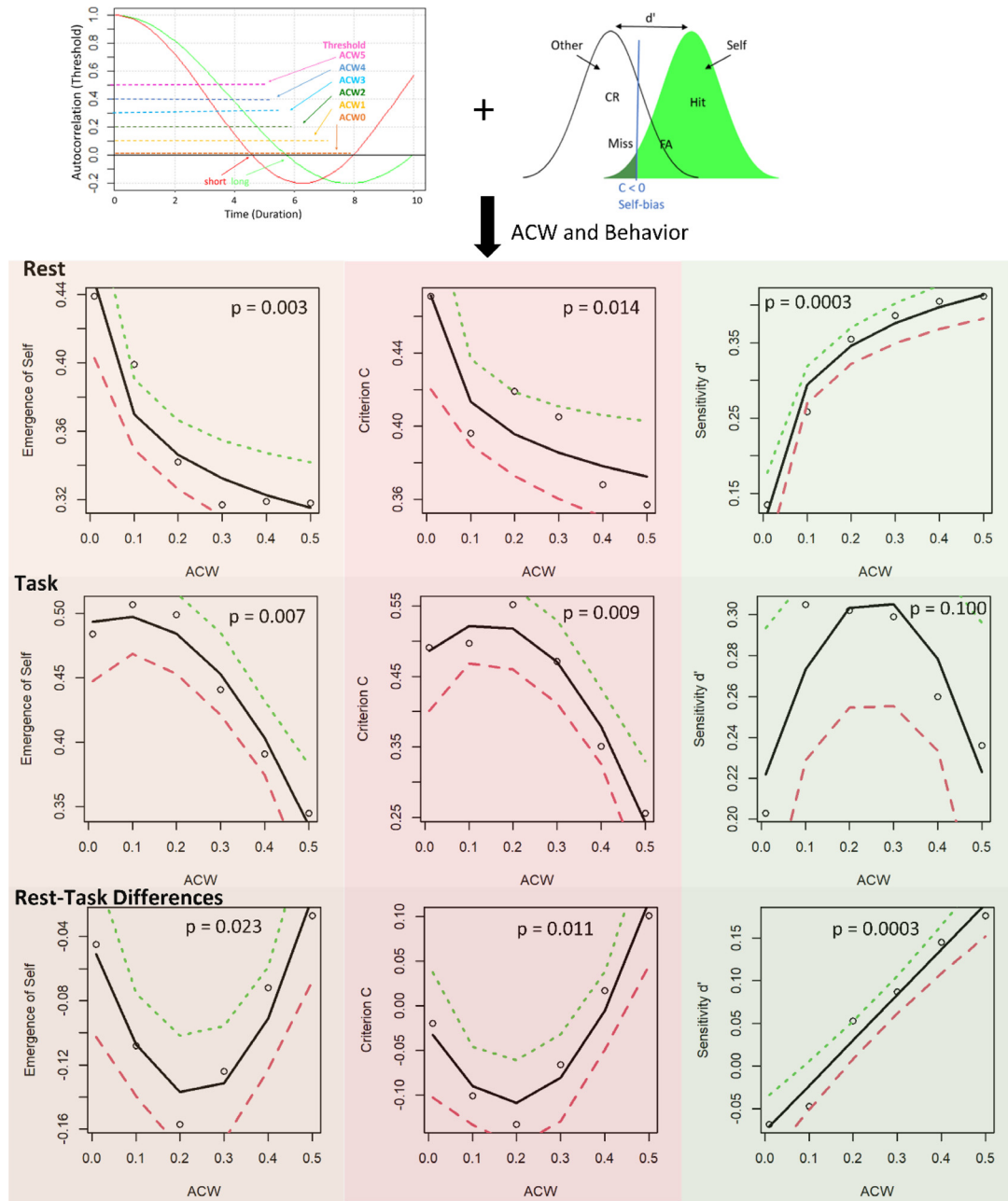


Fig. 4. Relationship between the neuronal and behavioral measures. Each column represents one behavioral measure (left: Emergence of self; middle: Criterion C; right: Sensitivity d'). In resting state (upper), task state (middle) and the rest-task difference (lower). The ACW thresholds (e.g., 0.5 for ACW5) are on the x-axis. The y-axis shows the Pearson's correlation coefficient between the behavioral variable and the different ACWs. In resting state, the curves show a decreasing logarithmic evolution for the Emergence of Self and Criterion C but an increasing logarithmic evolution for d' . Similarly in task state, Criterion C and the Emergence of Self show a quadratic function, which is non-significant in the d' . Finally, rest-task differences confirm the differential relationship between the ACW with Criterion C and Emergence vs. ACW with d' : For Criterion C or the Emergence, we find stronger correlation with the longer ACW0, while the d' is strongly linked to the shorter ACW5.

bias. A later emergence is linked to a conservative 'other'-bias. Together, these findings strongly support that temporal integration is a key factor in mediating the bias Criterion C. We will next demonstrate the key role of temporal integration in the cognitive bias by investigating the ACW.

5.2. Intrinsic neural timescales

Employing the different ACWs enabled us to investigate a more fine-grained temporal resolution. A shorter ACW can be observed in primary sensory areas like the temporal and occipital channels while a longer ACW is mostly observed in parietal and frontal channels. We expect

shorter temporal windows (i.e., ACW5) to represent stronger degrees of temporal segregation while the long temporal windows of ACW (i.e. ACW0) are more related to high degrees of temporal integration. We observe an overall significantly longer ACW during task compared to rest (Fig. 3C), indicating a sensitivity of the ACW to external stimuli. This is well in accordance with its supposed role in input processing (Smith et al., 2022; Golesorkhi et al., 2021b, 2021a; Zilio et al., 2021). A longer ACW in task than in rest seems to be related to continuous paradigms which demand stronger temporal integration, while shorter ACW in task than in rest are found in event related paradigms which are demanding in temporal segregation (Wolff et al., 2022; Smith et al.,

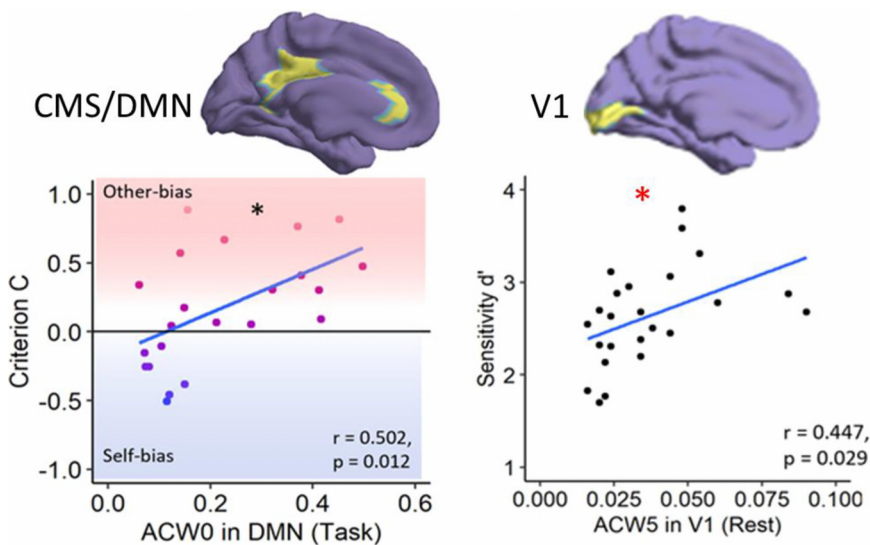


Fig. 5. A Linking the Sensitivity d' and Criterion C to the cerebral regions via the ACW. The Criterion C is correlated with the eLORETA CMS/DMN activity while the Sensitivity d' correlated with the V1 activity. A long ACW0 is linked to an other-bias, while a shorter one is associated to a self-bias. A longer ACW5 is linked to a better performance (d').

2022). Further, rest and task correlate highly ($r > 0.85$) with each other (Table S1), indicating a strongly shared or common neural basis between rest and task confirming previous data (see (Smith et al., 2022; Golesorkhi et al., 2021b)).

5.3. Relationship of intrinsic neural timescales with behavioral measures

To demonstrate the implication of temporal integration and segregation on a psychological level, we investigate the link between the behavioral measures (self-related keypresses, d' and Criterion C) and ACW (which is an indicator of temporal integration and segregation on the neural level (Wolff et al., 2022)). Given that both, perception-based Criterion C (van Vugt et al., 2018; Iemi et al., 2017; Iemi and Busch, 2018; Limbach and Corballis, 2016; Samaha et al., 2020) and self-consciousness (Qin and Northoff, 2011; Wolff et al., 2019; Davey et al., 2016; Huang et al., 2016), have been associated with the brain's spontaneous activity, we associated the behavioral variables with both, rest – and task-related ACW.

Firstly, the Emergence of Self is strongly correlated with the longer ACW (ACW0), indicative of a higher degree of temporal integration. This confirms the integrative nature of the continuous task and shows that it is the emergence, not the loss of the self, that is specifically linked to temporal integration and long ACW (Kolvoort et al., 2020; Wolff et al., 2019; Smith et al., 2022). It is to notice that an antagonistic logarithmic function describes the association between Criterion C and Sensitivity d' to the ACW in resting state. While in task state, behavioral and neural variables are linked via a quadratic function. The rest-task difference confirms the differential role of short and long INT in Criterion C and Sensitivity d' , respectively.

Together, these findings support the assumption that the Criterion C is related to higher degrees of temporal integration due to its link to longer ACW. The longer ACW increases the tendency of temporal smoothing and thus lumping together temporally disjointed inputs like the morphed faces. In result of its link to shorter ACW, sensitivity d' is more linked to temporal segregation and the increased capacity to discriminate between sequential faces in a temporally precise way.

5.4. Neuroanatomical grounds

The differentiated implications of the ACW in the cognitive indices is further supported and extended on neuroanatomical grounds. The self is known to be closely associated with the cortical midline structures (CMS) like anterior and posterior cingulate cortex of the default-mode network (DMN) (Northoff et al., 2006; Frewen et al., 2020; Qin et al.,

2020; Northoff, 2016) while the dlPFC is known for its role in decision making. Moreover, the core regions CMS/DMN and dlPFC in general are known to exhibit the longest ACW compared to primary sensory regions (Qin and Northoff, 2011; Wolff et al., 2022; Golesorkhi et al., 2021b, 2021a; Ito et al., 2020; Raut et al., 2020). Spontaneous activity (Buzsáki, 2006) as for instance pre-stimulus activity in these regions predict the subsequent judgement of stimuli as self-related (Qin et al., 2016). Our data extend these results by showing that the spontaneous and task-related activity in these regions mediate the cognitive bias through long INT (ACW0) and temporal integration.

How is our main finding (longer ACW (ACW0) linked to Criterion C and shorter ACW (ACW5) linked to Sensitivity d') represented in the DMN/dlPFC and the primary sensory regions? In other words, are the Criterion C and the d' modulated by the long and short ACW in DMN/dlPFC and primary visual area? Using eLORETA source space reconstruction, we observed a similar link of the cognitive bias (Criterion C) with the ACW0 and of the ACW5 with the d' . The topographical specifications through eLORETA show that the cognitive bias Criterion C is linked to the DMN and the dlPFC, while the discriminability d' is more related to the dlPFC and the primary visual area.

Together, these results confirm the specific link of the longer ACW0 in the DMN/dlPFC and Criterion C while the shorter ACW5 in dlPFC and V1 relates to Sensitivity d' (Golesorkhi et al., 2021b, 2021a; Chaudhuri et al., 2015). This supports a special role of CMS/DMN and dlPFC in mediating specifically higher degrees of temporal integration (Golesorkhi et al., 2021b, 2021a; Chaudhuri et al., 2015) underlying the cognitive bias in visual perception and subsequent decision making. The Sensitivity d' instead is linked to the shorter timescales (ACW5) of the dlPFC and the primary visual area favouring temporal segregation over integration. Importantly, the Criterion C is an indicator of a continuum between the self- and the other bias.

We observed that a self-bias is linked to short ACW0, while long ACW0 are associated with an other-bias. This is in line with the findings by Smith et al. (2022) who, in a different paradigm, demonstrate that ACW0 is associated with self-related processing. Moreover, Northoff et al. (2021) demonstrate that an abnormally long ACW is related to the basic self-disturbance in schizophrenia. Together, these findings support the key role of especially the longer ACW (ACW0) for mediating the bias, e.g., Criterion C, including self-bias or self-specificity as distinguished from the shorter ACW (ACW5) which mediates accuracy (d').

Is the ACW a stimulus-specific indicator of the facial identity presented in the stimuli (self vs. other vs. famous vs. unknown) rather than being part of the decision processes itself operating in a stimulus-

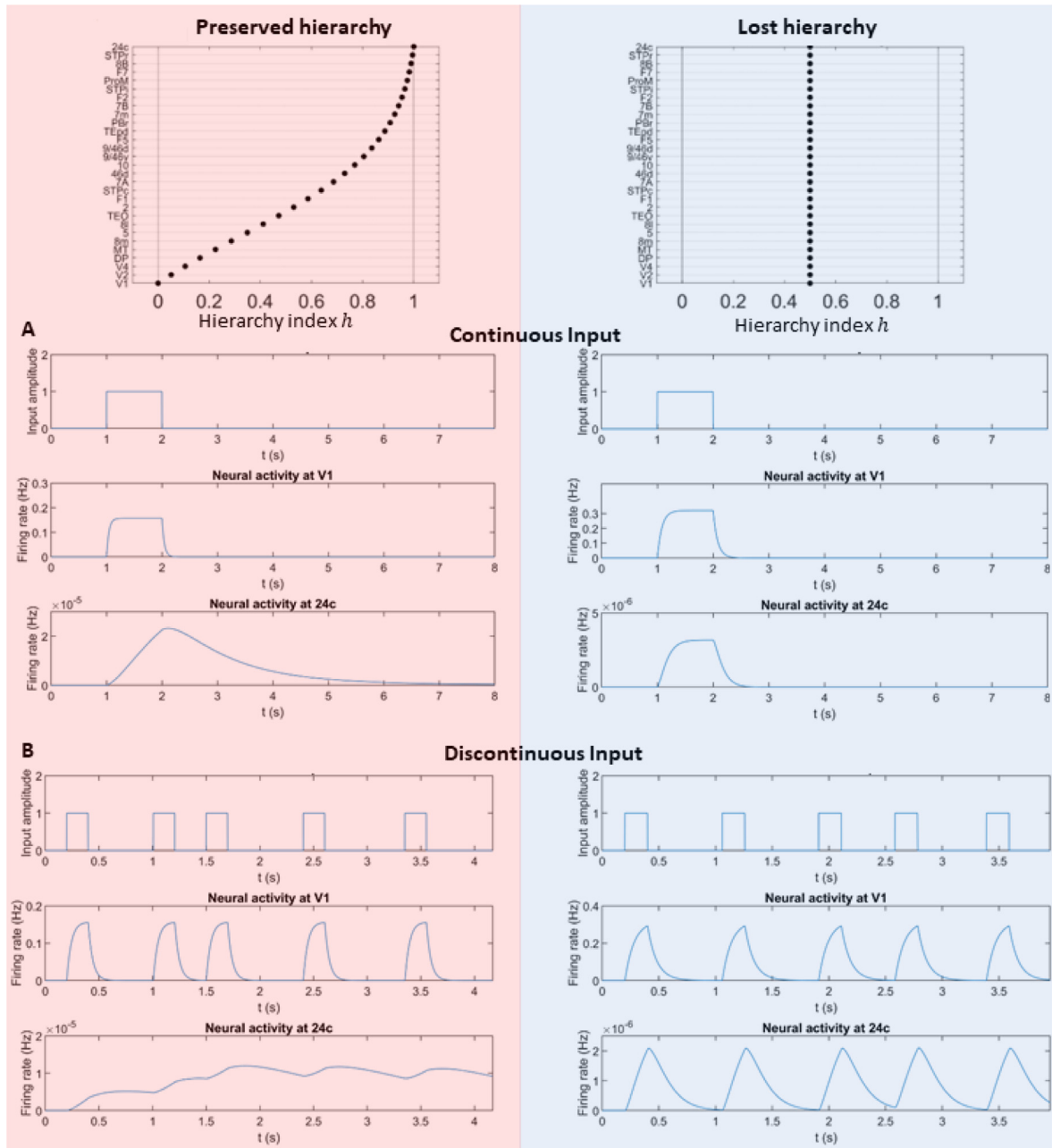


Fig. 6. Computational modeling of input processing. Top row depicts the hierarchical structure which scales the effect of local and long-range activity (left) vs. the absence of this hierarchy (right). **A** Continuous task paradigm: When a hierarchy of intrinsic neural timescales apply, the input leads to an extended and expanded neural activity in 24c, whereas it is more or less of the same duration in V1 (left). The elimination of hierarchy renders both regions the same (right). **B** Discontinuous task paradigm: Similarly to the continuous task, the neural activity of the peripheral region V1 shows temporal segregation whereas the core region 24c predominantly integrates different inputs (left). The elimination of hierarchy gives us very similar input processing in both V1 and 24c (right).

unspecific way? To answer this question we correlated the ACW of the fusiform face area (FFA), known by its role in facial processing (Kanwisher and Yovel, 2006) with Criterion C and Sensitivity d' . No link between the SDT measures and the ACW in the FFA was found. Further, we extracted the ACW during the visualization of each face identity (self, other famous, unknown) and no significant difference between them has been shown.

Together, these results show that the ACW mediates the cognitive bias on a basic stimulus-unspecific neuronal level of the decision making itself operating across the different facial stimuli. This supports our assumption that the ACW mediates the stimulus-unspecific temporal processing of all stimuli by providing a temporal envelop for them which,

as per our results, shapes our decision-making process featured by cognitive bias and sensitivity d' .

5.5. Computational mechanisms

The large-scale computational model of the dynamical hierarchy of timescales (Chaudhuri et al., 2015) gave us the possibility to probe the effect of different timescales on input processing in our specific task structure (continuous and discontinuous paradigms). Based on our eLORETA results, we were particularly interested to probe temporal segregation in hierarchically low regions (periphery / V1) and integration in hierarchically high regions (core / 24c). Our findings emphasize

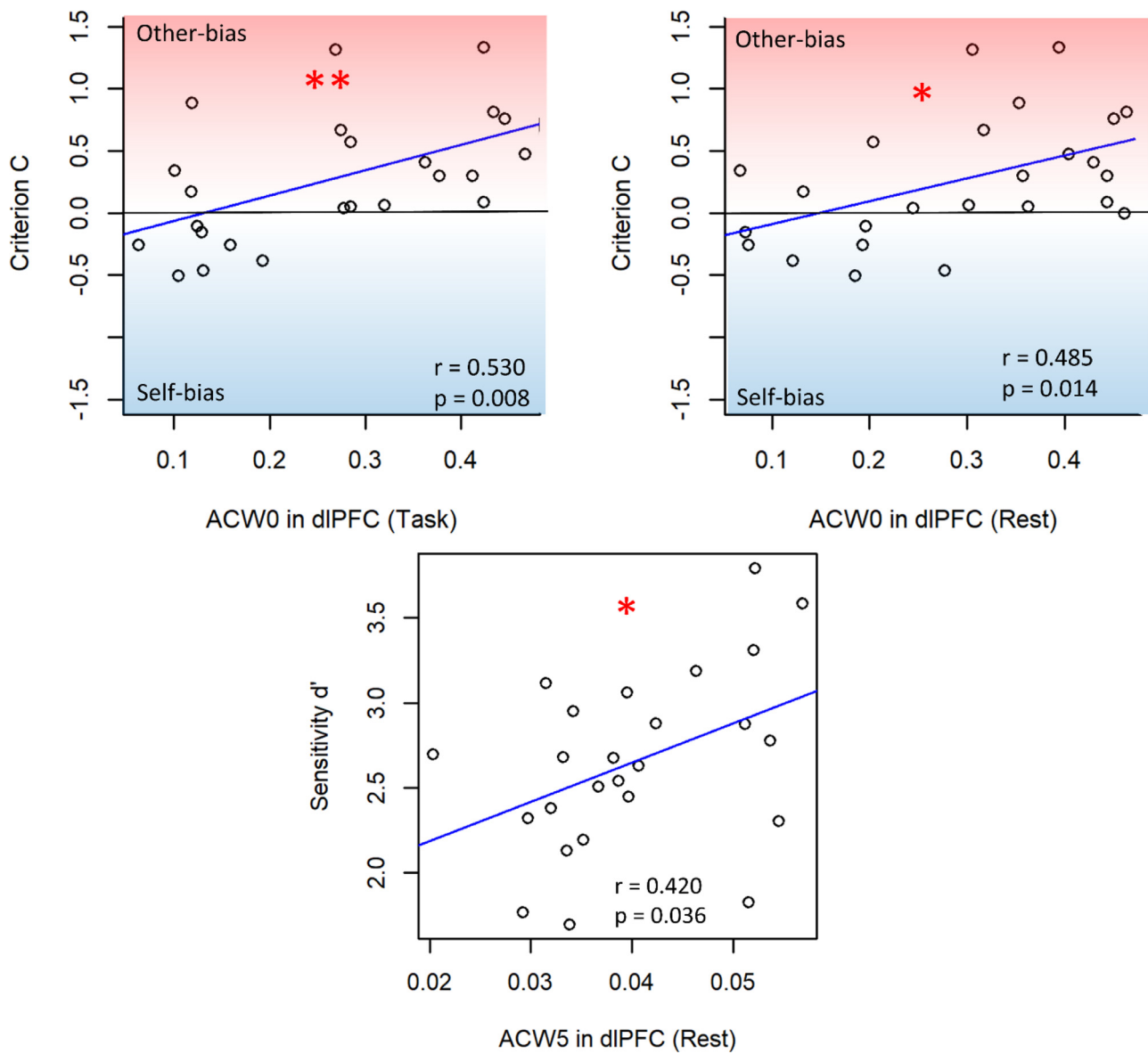


Fig. 7. Correlation between the ACW in the dIPFC with the cognitive bias (upper) and sensitivity d' (lower). A long ACW0 is linked to an other-bias, while a shorter one is associated to a self-bias. A longer ACW5 is linked to a better performance (d').

that the temporal hierarchy proposed by Chaudhuri pertains in our task structure. This confirms the implication of temporal segregation in sensory regions like V1 in the processing of disjoint external inputs in a temporally (and objectively) accurate way, related to the sensitivity. On the other hand, the cortical midline region 24c integrates different temporally disjoint inputs along with baseline activity which was shown to be related to self, thus showing a high degree of temporal integration and self bias.

Once we eliminated the hierarchy in our computational model by assigning the same hierarchical index to all regions, we now observed similar activity in both V1 and midline 24c. This suggests that the different degrees of temporal integration and segregation as well as extension during input processing in unimodal regions like V1 and transmodal midline regions like 24c are, at least in part, related to their differential hierarchical positions in the brain's overall uni-transmodal topography. Temporal integration-segregation may thus be an intrinsic feature of the brain's uni-transmodal topography rather than being primarily related to the extrinsic or external input of the paradigm; for that reason, it may remain independent of the specific task, e.g., task-unspecific. Given

that these differential phenomena of temporal integration and segregation in uni- and transmodal regions disappear when abolishing the hierarchy in our model, we suppose, albeit tentatively, a key role of the brain's uni-transmodal topographic organization in mediating the cognitive bias (Criterion C) through the INT.

5.7. Limitations

One potential limitation of our study is the novel use of ACW0 as distinct from ACW5 including their association with distinct cognitive features, namely sensitivity d' and Criterion C. However, two previous studies (Smith et al., 2022; Golesorkhi et al., 2021b) also demonstrated differential association of ACW5 and ACW0 with neural, e.g., topographic distinction of transmodal DMN vs unimodal sensory regions, and psychological, e.g., self-continuity, features. This is well in line with our observation of especially the longer variant (ACW0) in trans-modal CMS/DMN being associated with Criterion C.

Yet another potential issue in our study concerns temporal integration. While especially the longer variant, ACW0, strongly suggests high

degrees of temporal integration (Wolff et al., 2022), we did not show it in a more direct way in our empirical EEG data. However, various indirect lines strongly suggest temporal integration to be the main mechanism. First, especially the continuous version of our paradigm with the sequential self-other face morphing required temporal integration and segregation: if two sequential faces are associated with one and the same person, e.g., self or other, the two temporally distinct inputs (or stimuli/faces) must be integrated across their distinct time points. If, in contrast, they are attributed to distinct persons, e.g., self and other, they must be segregated. Temporal integration is thus required on the psychological level of the paradigm itself. Second, we demonstrate temporal integration on the computational level in our simulation where CMS/DMN, unlike visual cortex, do indeed integrate temporally parsed inputs into one activity change.

Additionally, we would like to mention that the CMS/DMN is known to be recruited in self-processing but that the association with this region does not necessarily engender self-specific processing (Frewen et al., 2020). Further studies would be necessary to confirm this link and to extend the knowledge to probe for self-relatedness in our own study.

One may wonder why a majority of participants present an other-bias instead of a self-bias, as per self-prioritization effect. We have to consider that our task is primarily a task about bias in decision making with subjects being forced (due to the morphed nature of the faces) to make mistakes as measured by the Criterion C. This has been described as self-related processing (Northoff et al., 2006; Northoff, 2016). Within that given framework, the bias or error can occur either with respect to other or self which is described as self-referential processing or self-prioritization (Sui and Humphreys, 2015). Our study and its paradigm operate primarily on the first level, the level of self-related processing as operationalized by the Criterion C, the bias, rather than on the second level of self-referential processing (as the typical trait adjective tasks). Therefore, we do not see our results in contradiction to the self-reference effects as that operates on the level of self-referential processing rather than self-related processing as target in our study.

Finally, we demonstrate the importance of topographic hierarchy for temporal integration. That, however, was shown only in an indirect way, that is, by abolishing the uni-transmodal hierarchy in our computational model. Future studies in for instance patients with CMS/DMN lesions are warranted that relate different degrees of uni-transmodal topographic hierarchy with different degrees of both temporal integration and cognitive bias.

6. Conclusion

In conclusion, we demonstrate the key role of temporal integration for our cognitive bias in perception and decision making. We demonstrate temporal integration on the behavioral level using signal detection theory that allows distinguishing Criterion C (bias) and sensitivity d' (accuracy). This is complemented on the neural level by showing that the cognitive bias is related to longer INT (ACW0) of especially the CMS/DMN and dlPFC. The involvement of temporal integration and the uni-transmodal topography is substantiated by computational modeling showing high degrees of temporal integration of temporally parsed inputs in the neural response of specifically transmodal CMS/DMN and dlPFC (as distinct from unimodal primary visual cortex). Together, we demonstrate that the cognitive bias in perception and decision making is intimately linked to the intrinsic neural timescales as based on the brain's uni-transmodal topographical organization.

Significance statement

Every day humans take decisions which are frequently characterized by a cognitive bias. We demonstrate the key role of temporal integration in this bias in perception and decision making on a behavioral level using signal detection theory. Neurally, the cognitive self-bias is related to longer Intrinsic Neural Timescales of especially the cortical midline

structures (CMS) of the default mode network (DMN). The involvement of temporal integration in CMS/DMN is further substantiated by computational modeling showing high degrees of temporal integration of temporally parsed inputs in the neural response of specifically CMS/DMN (as distinct from primary visual cortex). Together, we demonstrate that the cognitive bias in perception and decision making is intimately linked to the longer intrinsic neural timescales in core regions.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Credit authorship contribution statement

Angelika Wolman: Methodology, Software, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing, Visualization. **Yasir Çatal:** Software, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Annemarie Wolff:** Resources, Software, Validation, Writing – review & editing. **Soren Wainio-Theberge:** Software, Writing – review & editing. **Andrea Scalabrini:** Methodology, Validation, Writing – review & editing. **Abdessadek El Ahmadi:** Software, Formal analysis, Validation, Writing – review & editing. **Georg Northoff:** Methodology, Validation, Conceptualization, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration, Funding acquisition.

Data Availability

Data will be made available on request.

Acknowledgment

This research has received funding from the European Union's Horizon 2020 Framework Program for Research and Innovation under the Specific Grant Agreement No. 785907 (Human Brain Project SGA2). G.N. is grateful for funding provided by UMRP, uOBMRI, CIHR and PSI. We are also grateful to CIHR, NSERC, and SSHRC for supporting our tri-council grant from the Canada-UK Artificial Intelligence (AI) Initiative The self as agent-environment nexus: crossing disciplinary boundaries to help human selves and anticipate artificial selves' (ES/T01279X/1) (together with Karl J. Friston from the UK).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.neuroimage.2023.119896](https://doi.org/10.1016/j.neuroimage.2023.119896).

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Article

The Self and Its Right Insula—Differential Topography and Dynamic of Right vs. Left Insula

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Abstract: Various studies demonstrate a special role of the right compared to the left anterior insula in mediating our self. However, the neural features of the right insula that allow for its special role remain unclear. Presupposing a spatiotemporal model of self—"Basis model of self-specificity" (BMSS)—we here address the following question: what spatial-topographic and temporal-dynamic features render neural activity in the right insula to be more suitable in mediating self-specificity than the left insula? First, applying fMRI, we demonstrate that the right insula (i) exhibits higher degrees of centrality in rest, and (ii) higher context-dependent functional connectivity in a self-specific task among regions of distinct layers of self (intero-, extero-proprioceptive, and mental). Second, using EEG in rest and task, we show that the right insula shows longer autocorrelation window (ACW) in its neural activity than both left insula and other regions of the different layers of self. Together, we demonstrate special topographic, i.e., high functional connectivity, and dynamic, i.e., long ACW, neural features of the right insula compared to both left insula and other regions of the distinct layers of self. This suits neural activity in the right insula ideally for high functional integration and temporal continuity as key features of the self including its intero-, extero-proprioceptive, and mental layers.

Keywords: self; basis model of self-specificity (BMSS); right anterior insula; topography; dynamic; fMRI; EEG; resting state; autocorrelation window; degree of centrality



Citation: Scalabrini, A.; Wolman, A.; Northoff, G. The Self and Its Right Insula—Differential Topography and Dynamic of Right vs. Left Insula. *Brain Sci.* **2021**, *11*, 1312. <https://doi.org/10.3390/brainsci11101312>

Academic Editor: Dang Khoa Nguyen

Received: 31 August 2021

Accepted: 28 September 2021

Published: 2 October 2021

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1. Introduction

The self is a key feature of our mental life that allows integrating various inputs including intero-, extero-, and proprioceptive [1,2]. Besides cortical midline structures [3–6], one key region is the insula. Several studies observed the predominant involvement of the right rather than left insula during self-referential tasks or stimuli [7–14]. The key role of the right insula for self-reference has been hypothesized early on by Craig who, based on anatomical differences, suggested the right insula to preferentially mediate the self [15,16]. What are the neural features that render the right insula more suitable than the left insula to process self-specificity? Addressing this yet open question is the main goal of our study.

A recent large-scale imaging/fMRI meta-analysis by Qin et al. [17] confirmed the key role of the right insula for the self. They observed especially the right insula, together with left insula, dorsal anterior cingulate cortex, thalamus, and parahippocampus, to be involved in mediating the interoceptive self, that is, the self that is recruited during tasks

requiring interoceptive awareness like the awareness of one's own heartbeat. The role of the insula was not limited to the interoceptive self though. They also observed the right insula, together with left insula, interior frontal gyrus, premotor cortex, temporo-parietal junction (TPJ), and medial prefrontal cortex (MPFC), to be recruited in other studies of self like extero- proprio-ceptive self about the outer boundaries of the own body (see also [18]). Finally, the right insula was also observed in the typical studies on mental or cognitive self-reference using trait adjectives (and related paradigms) that strongly recruit the DMN, i.e., cortical midline structure.

Together, these observations suggest that especially the right insula provides the “glue” or connection between different layers of self, interoceptive, proprioceptive, and mental by means of which it can be distinguished from familiarity. Together, these findings describe hierarchical model of self [17] showing how regions of the interoceptive self were also included in the other layers like extero-proprioceptive and mental self where they were complemented by additional regions extending the topography of the self.

The goal of our study is to address the following question: what renders neural activity in the right insula special compared to the left insula such that the former can provide the “glue” or connection between the different layers of self? For that purpose, we investigate spatial topography and temporal dynamic of right vs. left insula with respect to those regions mediating the different layers of self. Our first specific aim was to analyse spatial topography of right vs. left insula in fMRI rest and task states by a network model approach and task context dependent functional connectivity of all those regions implicated in the Qin et al. [17] meta-analysis on self. Given that the self is suggested to serve an integrative role on neural [17] and cognitive [1] grounds, we hypothesized higher degrees of centrality and context-dependent functional connectivity (as measure of functional integration during a self-related vs. non self-related task) of the right insula to the rest of the brain's self-specific regions compared to the left insula.

Our second specific aim was to analyse the temporal features of the right vs. left insula with respect to the self. That was investigated in an EEG data set applying resting state and a morphed self-face task. We focused specifically on the Intrinsic Neural Timescales (INT; also called temporal receptive window; TRW [19]) defined as the duration of the brain to integrate information [20] and is known to mediate input processing and, more specifically temporal integration or segregation of different inputs [21–23]. The longer the time windows of the neural activity of a region, the more inputs at multiple distant points in time can be summed and pooled together under the umbrella of one temporal window and subsequently elicit one (rather than multiple) neural activity change, i.e., task-related activity [24].

These timewindow lengths can be quantified via the autocorrelation window (ACW). By correlating the signal with temporally shifted versions of itself, one can measure the moment when the correlation decays below a certain value, usually when $r < 0.5$. This threshold can be reached earlier (shorter window) or later (longer window) in time. Shorter ACW reflect faster neural fluctuations while longer ACW are linked to slower fluctuations. Hence, the ACW can give insight in the intrinsic neural timescales.

Given the role of the insula and the right insula in particular in mediating integration of intero- and exteroceptive inputs [15,16], we assume longer INT, i.e., longer ACW, in the right insula than the left insula. Intero- and exteroceptive, proprioceptive, and even internal cognitive/mental inputs may be temporally integrated to a higher degree by the longer time windows of the right insula (than the shorter ones of the left insula). This suits the right insula ideally to provide the “dynamic or temporal glue” or connection between the three layers of self [17].

2. Materials and Methods

Our investigation comprised different steps and methods. First, we focused on an fMRI sample to investigate the spatial topography of right vs. left insula. Secondly we focused on an EEG to investigate the temporal dynamic of right vs. left insula. Moreover,

we further investigated the role of right vs. left insula in different states, that are the resting- and the task-state in both fMRI and EEG.

2.1. fMRI

2.1.1. fMRI Sample

The fMRI sample was constituted by 32 right-handed male participants (age 21–33; mean = 25.4; standard deviation = 2.82). They are the same as those included in previous studies (for more detail see [8,9]). All participants had normal or corrected-to-normal vision capabilities. None of the participants reported a history of neurological or psychiatric disease, or substance abuse. Written informed consent was obtained from all participants after full explanation of the study procedure, in line with the Declaration of Helsinki. The Ethics Committee for Biomedical Research of the provinces of Chieti and Pescara approved the experimental protocol.

2.1.2. Resting State fMRI

A total of 32 subjects completed resting state fMRI acquisition (2 resting state of 6 min each, eyes open and fixation cross).

2.1.3. Task fMRI

In total, 21 out of the 32 participants (age 21–30; mean = 24.9; standard deviation = 2.45) also completed task fMRI acquisition. During the task fMRI runs (8 runs of 7.8 min each), a wooden table was placed on the participant's legs. An inanimate target (mannequin hand) and an animate target (the hand of another volunteer who was standing next to the scanner) were both placed next to the participant's hand. The participant completed a series of active touch and no-touch trials. Active touch was performed through an object to avoid the direct physical sensation of touching the different targets, that is, the hand of a volunteer (animate target) or a mannequin hand (inanimate target; for more details on the task see [8]). For the purpose of our investigation, we focused specifically on active touch trials and on animate and inanimate conditions. The different targets were used as a proxy of self-relatedness and non-self relatedness (respectively) since our previous findings [8] showed, at a behavioral and neuronal level, how the active touch towards the animate stimuli is featured by higher degree of self-relatedness vs. lower degree of self-relatedness as linked with the inanimate target. Thus, our task showed the intimate link between actively touch another animate target and self-relatedness.

2.1.4. fMRI Data Acquisition and Preprocessing

For each participant, BOLD contrast functional imaging was performed with a Philips Achieva scanner (Andover, MA, USA) at 3 T at the Institute of Advanced Biomedical Technologies, Chieti, Italy. An initial T1-weighted anatomical (3D TFE pulse sequence) was acquired with the following parameters: field of view = 240 mm; voxel size = (1 mm × 1 mm × 1 mm); TR 8.1; TE 3.7. Two resting-state fMRI runs (number of fMRI frames/run: 180) and 8 task fMRI runs (number of fMRI frames/run: 235) were acquired in a single fMRI session (T2* weighted EPI sequence with TR = 2000 ms; TE = 35 ms; 31 slices; slice thickness = 3.5 mm; in-plane voxel size = 2.875 × 2.875; field of view = 230 mm; flip angle = 90°). Preprocessing procedures of the fMRI data were implemented in Analysis of Functional NeuroImages software (AFNI; [25]; <http://afni.nimh.nih.gov/afni> accessed on 28 August 2021) including: (1) slice timing correction; (2) rigid body correction/realignment within and across runs. Six head motion parameters, 3 translational and 3 rotation parameters, were estimated and frame-wise realignment was performed using AFNI's 3dvolreg command. After the estimated motion parameters were visually inspected, participants with head motion larger than ±2 mm translation or ±2.5° rotation were eliminated [26]; (3) co-registration with high-resolution anatomical images; (4) spatial normalization into Talairach stereotactic space; (5) resampling to 3 × 3 × 3 mm³ voxels; and (6) regression of linear and nonlinear drift (equivalent to a high-pass filtering of

0.0067 Hz), head motion and its first-order temporal derivative, and mean time series from the white matter (WM) and cerebrospinal fluid (CSF) to control for non-neural noise [27]. The WM and CSF masks were eroded by one voxel [28] to minimize partial voluming with gray matter; (7) spatial smoothing with an 8 mm fullwidth at half-maximum isotropic Gaussian kernel.

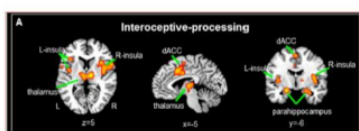
2.1.5. Definition of Regions/Nodes of Interest (ROIs)

In order to investigate the spatial configuration of the three layers of self [17] in spontaneous activity of the brain (during resting state fMRI) regions of interest (ROIs) were taken from each layer of self of the hierarchical model proposed recently by Qin et al. [17] i.e., (a) the interoceptive self; (b) the extero- proprio-ceptive self and (c) the mental self (see Figure 1 for a list of regions included in each layer of self). All the regions were created with a 10 mm diameter (spherical) centered using the coordinates reported in [17]. According to our aim we focused especially on the role of right anterior insula (vs. the role of left anterior insula).

2.1.6. Resting State Analysis

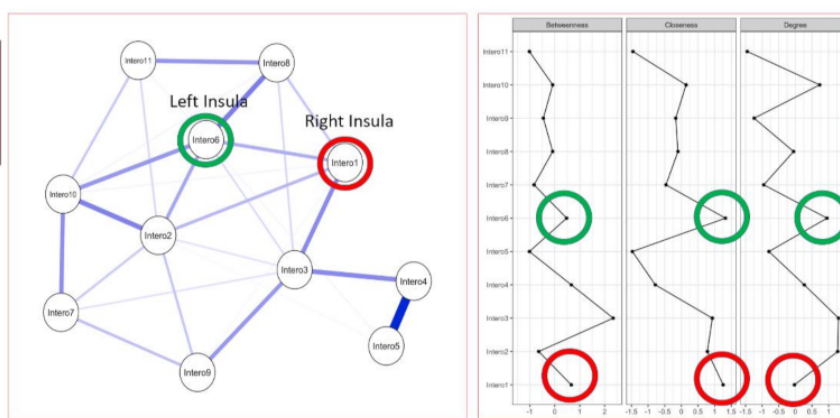
The same preprocessing steps described above were performed on resting state data with the addition of temporal band-pass filtering ($0.01 < f < 0.1$ Hz) to reduce low-frequency drift and high-frequency respiratory/cardiac noise [29,30]. Given the methodological issues recently raised [19,31,32], global signal regression (GSR) was not included in the preprocessing of the resting state fMRI data. In graph theory, a complex system is modelled as a “graph”, which is defined as a set of “nodes” (each ROI) linked by “edges” (regularized partial correlations between pairs of nodes controlling for all other nodes in the network). To investigate the relationship between the different regions-nodes of each layer of self [17] a network approach analysis (performed in JASP) was used in order to investigate *Closeness* (the inverse of the sum of all shortest paths from the node of interest to all other nodes), *Betweenness* (the number of shortest paths that pass through the node of interest), *Degree* (nodal strength: the sum of the absolute input weights of that node). In general, a higher *Degree* measure indicates that this node has a central role in the network). We used EBICglasso technique (computing a sparse gaussian graphical model with the graphical lasso [33]. Tuning parameter was set at 0.5 using the Extended Bayesian Information criterium (EBIC) this 0.5 indicate that more parsimonious models with fewer edges are preferred—This method provides a network of partial correlation coefficients with a limited number of spurious edges [34,35]. Centrality indices are plotted using standardized z-scores in order to facilitate interpretation.

INTEROCEPTIVE PROCESSING



Interoceptive-processing

1	R	Insula
2	L	Dorsal anterior cingulate cortex
3	R	thalamus
4	R	Parahippocampal Gyrus
5	L	Parahippocampal Gyrus
6	L	Insula
7	L	Insula
8	R	Inferior parietal lobule
9	R	Superior frontal gyrus
10	L	Superior temporal gyrus
11	L	Postcentral gyrus



(a)

Figure 1. Cont.

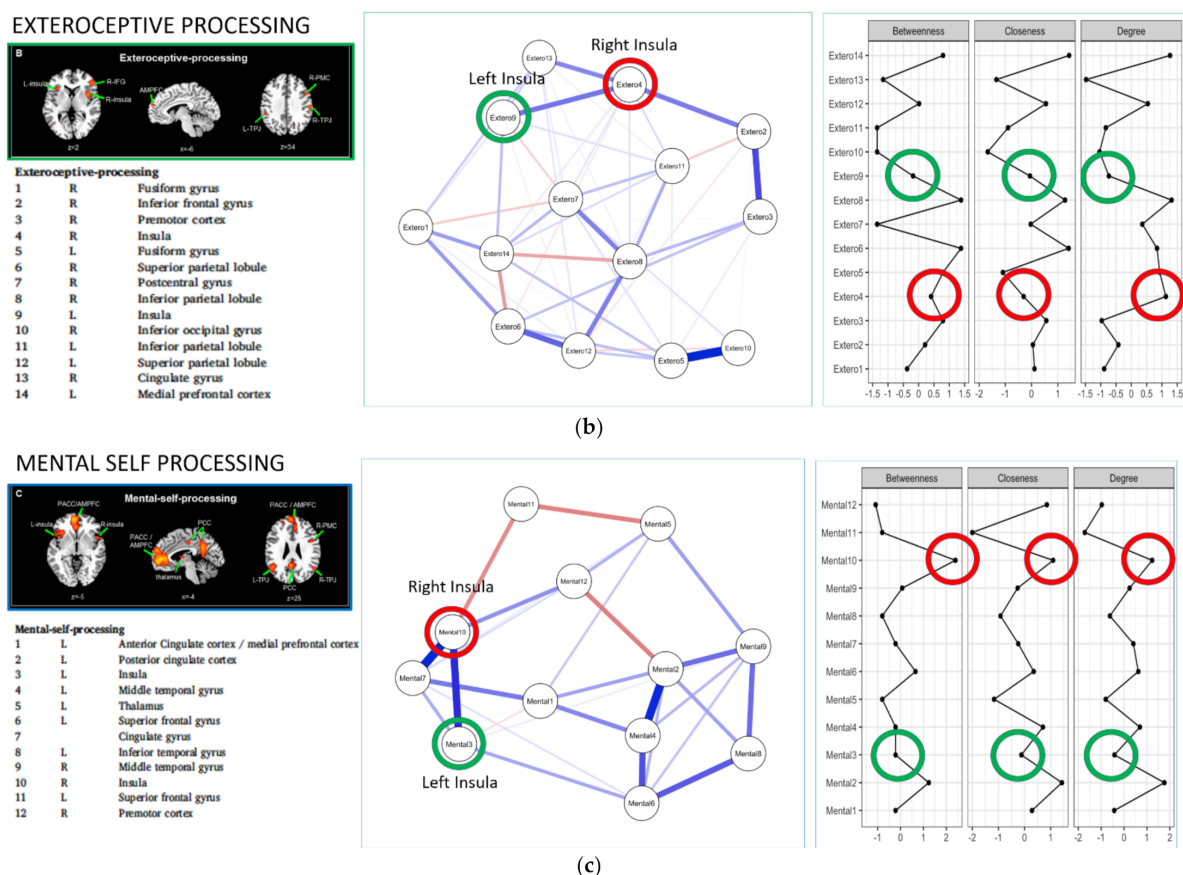


Figure 1. Resting state network analyses of the Three Layers Model of Self. (a) Interoceptive processing level; (b) exteroceptive processing; (c) mental self-processing. Blu lines indicate positive relation between nodes. Red lines indicate negative relation between nodes. The thickness of the lines indicates the degree of relation between nodes.

2.1.7. Task Functional Connectivity—gPPI

The generalized procedure of psychophysiological interactions [36] was used to calculate the condition-specific FC of regions of interest. According to our aim we used as seed regions for the gPPI the right anterior insula (MNI; C_{mass} $x = 40$, $y = 19$, $z = -6$) and the left anterior insula (MNI; C_{mass} $x = -40$, $y = 19$, $z = -6$) (see Figure 2). The gPPI procedure consisted in the following steps: (1) physiological seeds were obtained extracting the mean activity from non-zero voxels included in each ROI; (2) psychological variables for each regressor were created as vectors with the same temporal length as the seeds, and with a binary value of 1 or 0 for each TR, depending if the condition represented by the regressor was or was not active at that TR; (3) for each seed, extracted activity was deconvolved with a standard gamma function, and (4) multiplied with the psychological vector of each regressor; (5) each resulting vector, for each condition+, was re-convolved with the gamma function, and used as a PPI regressor. Nuisance regressors for motion, WM, and CSF were also included in the model. At the single subject level, a general linear model was performed for each ROI. At the group level, a whole brain measures $2 \times 2 \times 2$ ANOVA with factors seed-ROI (levels: right and left anterior insula) target (levels: self-related and non self-related) and valence (levels: pleasant and unpleasant) was run in AFNI to study the context-dependent FC (β_{fc}) of each ROI. Results were corrected via Monte Carlo simulation (using 3dClustSim), setting a threshold of $p < 0.005$ and a cluster size > 40 voxels, to obtain a corrected significance level of $\alpha < 0.05$. Post-hoc analysis focused predominantly on the comparison between right anterior insula and left anterior insula specifically for the self-related context-dependent FC in accordance with our hypotheses.

Task context dependent functional connectivity

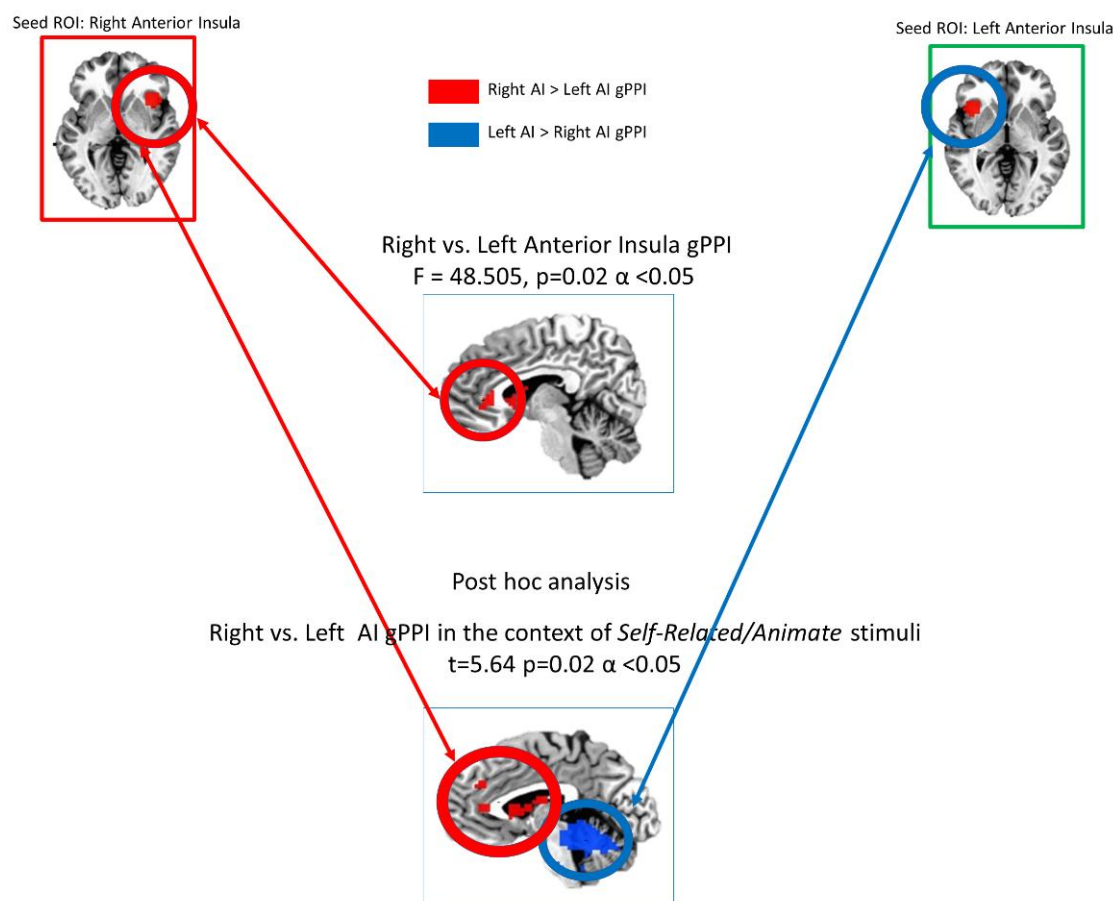


Figure 2. Task context-dependent functional connectivity—Generalized Psychophysiological Interaction—gPPI.

2.2. EEG

2.2.1. EEG Sample

Twenty-seven participants were recruited. None of them had current or a history of psychiatric or neurological disorders and normal or corrected-to-normal vision. We excluded two participants due to technical problems while EEG recordings and one subject due to extreme results. Our final sample consists of 24 subjects (14 women, 10 men) with a mean age of 22.33 years (SD: 4.49, range: 19 to 36). Written informed consent was obtained. The study was approved by the local Ethics committee (REB # 2018054).

2.2.2. Resting State

For the EEG recordings, participants performed 7 min of resting state with eyes open, fixing a screen with a black cross on a grey background.

2.2.3. Stimuli

Our paradigm uses the well-known face-morphing technique [37–41]. Prior to the EEG recordings, pictures were taken from each of the participants with a Samsung A50 phone. Participants were asked to show a neutral facial expression, mouth closed. The pictures were then prepared in the free and open-source graphics editor GIMP (2.10.12) [42]. All faces were turned in black and white and cut in an oval circle, remaining only the eyes, nose and mouth areas on a black background. Then, each face was morphed with

a same-sex and same-race face from the NimStim facial pictures set [43]. In addition, a same-sex famous face was morphed with an unknown face. Morphings were realized with the Abrosoft Fantamorph 5 Software [44] in 1% steps (from 0% to 100% self-face or 0% to 100% famous face).

2.2.4. Morphing Task

Pictures were presented in a continuous manner to create the experience of a morphed movie between the two faces. A total of four morphing conditions were created based on the order and the identity depicted on the pictures: Self-conditions: (1) from 'self' to 'other' face, (2) from 'other' to 'self' face. Control conditions: (3) from 'famous' to 'unknown' and (4) from the 'unknown' to the 'famous' face. The order of presentation was randomized.

Participants were instructed to press a key when they stop to see the first face and to give a second keypress when they started to see the second face. To ensure that the moment of the keypress was time-independent, we randomly varied the movie length between 10 to 15 s. In addition, the intertrial interval was jittered between 4 to 6 s (Figure 3a). In total there were 200 trials, 50 trials per condition in 8 blocks. But for the purpose of these analyses, we only used 7 min of continuous recording that were extracted from the second block. Also, we were interested in the general activity in task, therefore we do not distinguish between the conditions in future analyses.

2.2.5. EEG Data Acquisition and Preprocessing

EEG data was recorded using Ag/AgCl electrodes through a 64-channel Brain Vision EasyCap (according to the International 10–20 System) referenced to the right mastoid. The data was sampled at 1000 Hz with DC recording. The EEG data preprocessing was performed using the EEGLAB toolbox for MATLAB (R2017b; [45], RRID:SCR_007292). The data was downsampled to 500 Hz and filtered with a low-pass filter at 50 Hz and a high-pass filter at 1 Hz. With a customer script, noisy channels (defined as 4 interquartile above or below each channels mean) have been determined and spherically interpolated before re-referencing to the average. Further, artifacts were removed using independent component analysis (ICA) performed using the EEGLAB software creating 64 independent components. Next, we used MARA implementation to automatically reject noisy components [46].

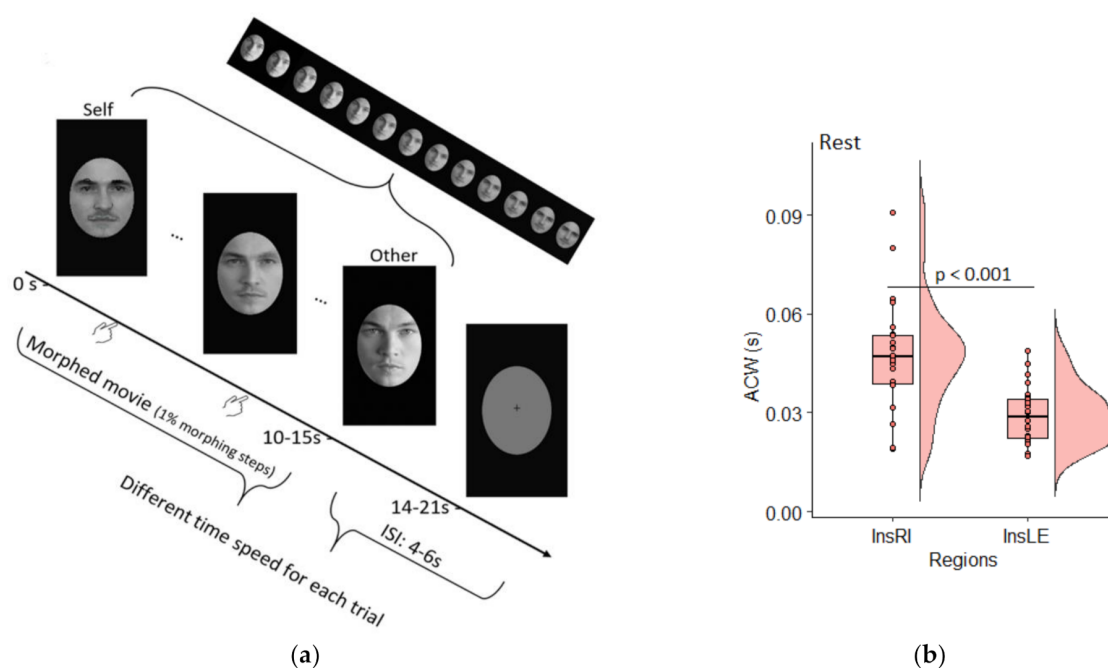


Figure 3. Cont.

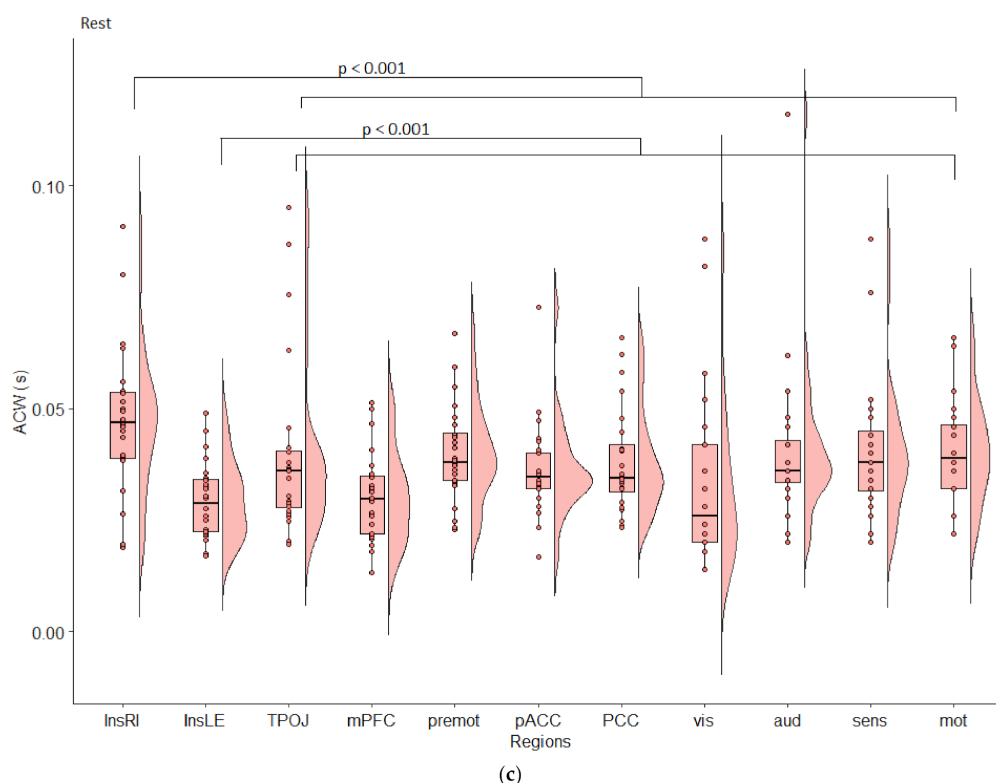


Figure 3. Autocorrelation calculated on the estimated activity per region in resting state. (a) Morphing task. Depicted is a schematic representation of the first condition ‘self to other’. Identity and order of faces vary depending on condition; (b) Longer ACW were found in the right Insula compared to the left insula; (c) The insula in comparison to primary sensory and motor regions as well as the regions implicated in the three layers model of the self. *p*-values are Bonferroni-corrected post hocs. Aud = primary auditory cortex, InsLE = left Insula, InsRI = right Insula, mot = primary motor cortex, mPFC = medial prefrontal cortex, pACC = perigenual anterior cingulate cortex, PCC = posterior cingulate cortex, premot = premotor cortex, sens = primary somatosensory cortex, TPOJ = temporo-parieto-occipital junction, vis = primary visual cortex.

2.2.6. ROIs and Source Localization eLORETA

We defined our ROIs for the EEG analysis based on six main regions implicated in the three layers of the self as emphasized in the meta-analysis of Qin et al. [17] (Figure 4a). These regions are the insula, the temporo-parieto-occipital junction (TPOJ), the anteromedial prefrontal cortex (amPFC), the premotor cortex (PMC), the perigenual anterior cingulate cortex (pACC) and the posterior cingulate cortex (PCC). As a control, we also included the primary motor, primary visual, primary auditory and primary somatosensory cortex. Regions were defined according to the Glasser parcellations [47].

Exact Low Resolution Electromagnetic Tomography (eLORETA, [48]) was performed by estimating the virtual-channel source for each region of the Glasser atlas in FieldTrip [49]. The output is a timeseries of estimated source level activity for each region. We investigated the right and left insula separately while averaging the right and left parts of the other regions (See Supplementary Table S1). On these timeseries, we calculated ACW.

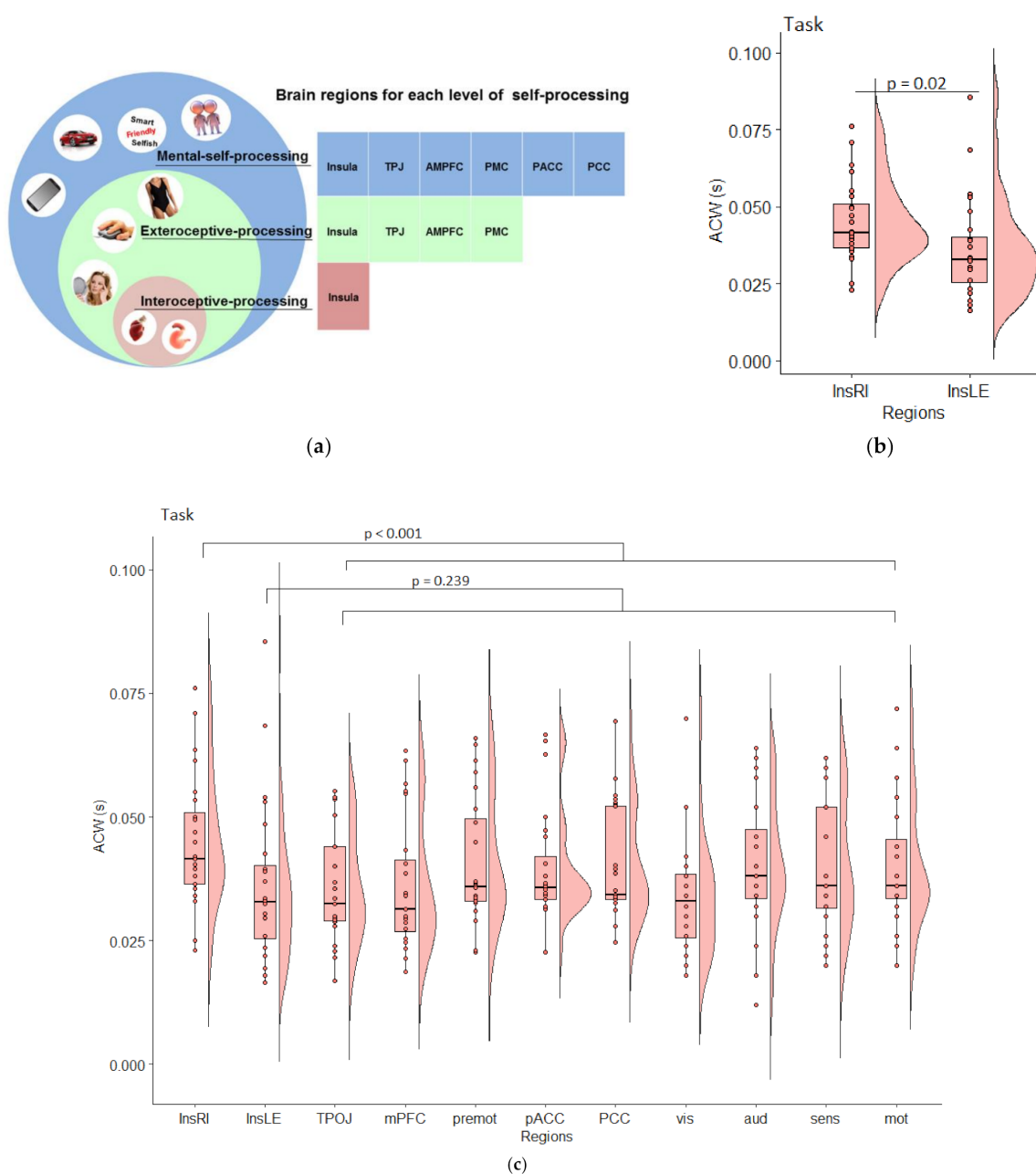


Figure 4. Autocorrelation calculated on the estimated activity per region in task state. **(a)** ROIs for the EEG study. Graph reproduced from Qin et al. (2020) with the kind permission of the authors; **(b)** Comparison of the left and right insula task state.; **(c)** Raincloud plots of ACW in task state in all ROIs. p -values represent Helmert contrasts. Aud = primary auditory cortex, InsLE = left Insula, InsRI = right Insula, mot = primary motor cortex, mPFC = medial prefrontal cortex, pACC = perigenual anterior cingulate cortex, PCC = posterior cingulate cortex, premo = premotor cortex, sens = primary somatosensory cortex, TPOJ = temporo-parieto-occipital junction, vis = primary visual cortex.

2.2.7. Autocorrelation Window

The autocorrelation window (ACW) is defined as full-width-at-half-maximum of the temporal autocorrelation function of a time series and plays an important role in information integration [50,51]. It was calculated in python 3 using the autocorrelation function with the statmodels package on the regional activity extracted via eLORETA. The ACW is in units of s, that is to say, an ACW of 0.06 s indicates that the correlation between the estimated timeseries with itself is correlated with an $r = 0.5$ at a temporal shift of 0.06 s.

2.2.8. Statistical Analysis

Due to multiple measures per subject on different brain regions in two different states (rest and task state), we computed repeated measures ANOVA with a Greenhouse-Geisser correction when sphericity was violated. Helmert contrasts for either the right or left insula against all other regions, in resting as well as in task state, mark the special role of the insula. Analyses were run in R and JASP.

3. Results

3.1. Resting State fMRI Analysis

In order to estimate the centrality of the insula in the spontaneous activity of the brain, we applied a network analysis approach using as nodes of each network the ROIs related to the three different layers of self, as recently proposed by [17], i.e., (a) interoceptive self, (b) extero-ceptive self, (c) mental self (See Figure 1a–c).

For the intero-ceptive self network as shown in Figure 1a, we can observe that the nodes showing stronger *Degree (nodal strength)* are the dorsal anterior cingulate cortex, the thalamus, the left insula, and the superior temporal gyrus. The stronger *Betweenness* is represented by the thalamus while the stronger *Closeness* is represented by both right and left anterior insula.

For the extero- proprio-ceptive self network as shown in Figure 1b, we can observe that the nodes showing stronger *Degree (nodal strength)* are right insula, inferior parietal lobule, and the medial prefrontal cortex. The stronger *Betweenness* and *Closeness* is represented by superior parietal lobule, inferior parietal lobule and medial prefrontal cortex. As it can be observed in this layer of self, right insula showed a significant higher degree of centrality in comparison with left insula.

For the mental self network as shown in Figure 1c, we can observe the central role of right insula together with posterior cingulate cortex for all three measures *Degree (nodal strength)*, *Betweenness* and *Closeness*. As it can be observed left insula did not show any significant centrality role within this network.

Altogether these findings show the increasing “integrative role” (higher centrality metrics reflect how connected and potentially relevant a node is within a network) of the right insula over the increased hierarchical layer of self: (a) the right insula shows a significant closeness centrality role (i.e., the average distance of a node to all the other nodes in the network) together with the left insula (showing also higher DC) in the interoceptive layer of self; (b) the right insula shows a strong degree (nodal strength) in the exteroceptive layer of self (i.e., the sum of the absolute value of the edge weights) and (c) the right insula has a prominent role in all the three measures of centrality (degree, closeness and betweenness) in the mental layer of self while the left anterior insula does not show a central role in the network. To put it simple, the centrality of the right vs. the left insula already in resting state fMRI increases together with the hierarchical increase of self-processing showing the most prominent role within the mental self-network.

3.2. Task Context-Dependent Functional Connectivity

To evaluate the context-dependent connectivity (self-related context and non self-related context), gPPI was performed using as seed a right and a left anterior insula regions of interests. This allowed to identify voxel clusters whose functional connectivity with the seeds ROIs was significantly modulated by the different contexts during the task. At a group level no significant effects were found for the factor valence, and for the interaction between target and valence for both seed ROIs. Thus, we focused our investigation on seed ROI level (right and left anterior insula) and on the target level (self-related context and non self-related context). A repeated measures ANOVA showed highly significant differences between seed ROIs ($F = 48.505$, $p = 0.02$, $\alpha < 0.05$) indicating that the right anterior insula is more connected with pACC. Post-hoc analysis revealed a significant difference ($t = 5.64$; $p = 0.02$, $\alpha < 0.05$) between right and left anterior insula FC during the context of self-related processing with right AI > left AI for regions like PACC (MNI

$x = 8, y = -41; z = -9$) and right caudate nucleus, middle right insula (MNI $x = 40, y = 11; z = -13$) and left middle temporal gyrus while left > right in regions like left cerebellum cortex (MNI $x = -40, y = -58, z = -32$). No significant difference with the same threshold were found between right and left insula for the non self-related context (See Figure 2).

In sum these gPPI findings show the increased context dependent FC between Right Anterior Insula (but not Left AI) and typical self regions like pACC during self-related processing (vs. non self-related). This confirms the functional integrative role of the right AI in self-specific task.

3.3. Temporal Analyses in EEG

In order to estimate the length of the INTs in the insula, we compared the ACW on the estimated activity in the left and right Insula in resting state (Figure 3b). Results indicate a highly significant difference ($t(24) = 5.21, p < 0.001$) with a longer ACW in the right ($m = 0.048, SD = 0.017$) compared to the left insula ($m = 0.029, SD = 0.009$).

Does this difference in the INT remain in comparison to other self-related and unisensory areas? A repeated measures ANOVA showed highly significant differences between regions ($F(4.7, 108.21) = 5.26, p = 0.0003$). A Helmert contrast revealed significant differences in ACW for the right ($p < 0.001$) and left ($p < 0.001$) insula compared to the self and unisensory regions (Figure 3c). Interestingly, the left insula is significantly shorter than the other self- and unisensory regions. This confirms our hypothesis of longer INT in the right insula in resting state. Does this difference between right and left insula maintain in a self-task? And does the right insula maintain the longer INT compared to the other regions in the task?

To answer this question, we ran a repeated measures ANOVA between left and right insula in task and can confirm a significant difference between these two regions ($F(1, 23) = 6.224, p = 0.020$; Figure 4b). Next, we investigated the left and right insula in the context of the other regions (Figure 4c) and found a significant effect of the region ($F(1.07, 24.65) = 64.327, p < 0.001$). Helmert contrasts confirm that the right ($p < 0.001$) but not the left insula ($p = 0.239$) is significantly longer compared to the unisensory or self [17] regions. This confirms the special role of the right insula.

4. Discussion

We here investigated the neural topography and dynamic of right and left insula with respect to those regions implicated in the different layers of self. Our main findings are: (i) significant higher degree (nodal strength and other network-related measures) of the right anterior insula than left insula over the hierarchical layers of self; (ii) higher context dependent functional connectivity between right anterior insula (vs. left) and other regions implicated in the context of self-related processing; (iii) significantly longer temporal windows, i.e., autocorrelation window, in the neural activity of the right anterior insula than the left anterior insula during both rest and self-specific task; (iv) significantly longer autocorrelation window during a self-specific task in right anterior insula compared to the other regions implicated in the three layers of self. Together, our findings show special topographic and dynamic features in the neural activity of the right insula compared to both left insula and other self-specific regions. This renders neural activity in the right insula highly suitable to serve as topographic and dynamic glue or node for integrating different layers of self.

4.1. From Functional Connectivity over Functional Integration to Spatial Nestedness of Self

Using resting state fMRI, we show that the right anterior insula exhibits increasing centrality indices over the three hierarchical layers of self in comparison with all other regions implicated. Our findings extend previous imaging studies that demonstrate strong recruitment of the right anterior insula during self-referential tasks [6–11,14,17,52]. These studies usually demonstrate the conjoint recruitment of right/left anterior insula with the cortical midline structures (CMS) and potentially other regions implicated in self. Our

findings provide the topographic substrate of such conjoint activation of right (and left) insula and CMS: this, as we propose, is due to the increasing centrality and functional connectivity of the right insula to other regions like the CMN over the hierarchical self-networks. Intriguingly our findings don't deny the role of the left insula, which showed significant centrality indices especially for the intero-ceptive self processing network. This might be in line with the fact that many studies on self-referential tasks [6–11,14,17,52] usually demonstrate the conjoint recruitment of right and left anterior insula together with the CMS.

High centrality and functional connectivity mean that the right insula integrates the activity of the other regions of the self-networks. Functional connectivity allows for functional integration, that is, the degree to which a region pools or sums the activity of other regions within its own neural activity [53,54]. The high degree of functional integration enables the right insula to integrate interoceptive, exteroceptive, proprioceptive, and cognitive/mental information from the three layers of the self-networks. That, in turn, allows for an intrinsic link or connection between the three layers of self-specific information which are thereby spatially or topographically nested within each other [17]. We hypothesize that the right insula's key role in constituting spatial nestedness on the neuronal level, i.e., among the three layers of self-networks may also be manifest on the psychological level: self-specific interoceptive information may be contained and nested within the layer of self-specific proprio- and exteroceptive information which, in turn, may be nested and contained within the even more extended layer of self-specific mental or cognitive information. That remains to be investigated though. If true, spatial nestedness may provide a shared feature of neural and mental levels of self, i.e., their "common currency" [20,21].

4.2. From Autocorrelation Window over Temporal Integration to Temporal Continuity of Self

Our second main finding consists in the observation of longer INT in the right insula compared to the left insula and the other regions implicated in the three layers of self. This was already present during the resting state and carried over to the task states during the processing of self-specific information, i.e., the own face. The involvement of longer INT in right insula complements recent resting state findings that show a relationship of ACW and self-consciousness: the longer the ACW in the resting state, the higher degree of self-consciousness [55] and the better self-specificity of information is integrated and preserved across different temporal delays [56].

INT are key in the temporal integration and segregation of inputs at different points in time [22–24]. The longer the time windows of the neural activity of a region, the more inputs at different even distant points in time can be lumped and pooled together under the umbrella of one temporal window and subsequently elicit one (rather than multiple) neural activity change, i.e., task-related activity [57]. The right insula's longer ACW may thus suit ideally to integrate, i.e., pool and sum different inputs occurring at different points in time: the different time points of intero-, extero, and proprioceptive and cognitive/mental inputs are subsumed within one temporal window on the basis which they induce one integrated (rather than two or several parallel) activity change within the right insula.

How is such high degree of temporal integration on the neural level manifest on the psychological level of self? Neuronally, different inputs at distinct time points are integrated within the neural activity of the right insula and the regions of the three layers of self-specific networks. Temporal integration of different time points' inputs in neural activity means that those temporally distinct inputs are connected to each other within the duration of the integrating temporal window. This constitutes temporal continuity between the originally temporally distinct inputs. The long time windows of right insula compared to both left insula and other self-specific regions suit it ideally for constituting a high degree of temporal continuity among the three distinct layers of self, i.e., interoceptive, extero-proprioceptive, and mental/cognitive. Such temporal continuity may amount to what is described by the concept of personal identity [58,59]. Temporal continuity may

thus provide a shared feature of neural and psychological levels of self/personal identity, i.e., their “common currency” [20,21]. Figure 5 resumes the roles of the right insula (glue between the three layers of the self) with its spatial (upper row) and temporal (lower row) processes.

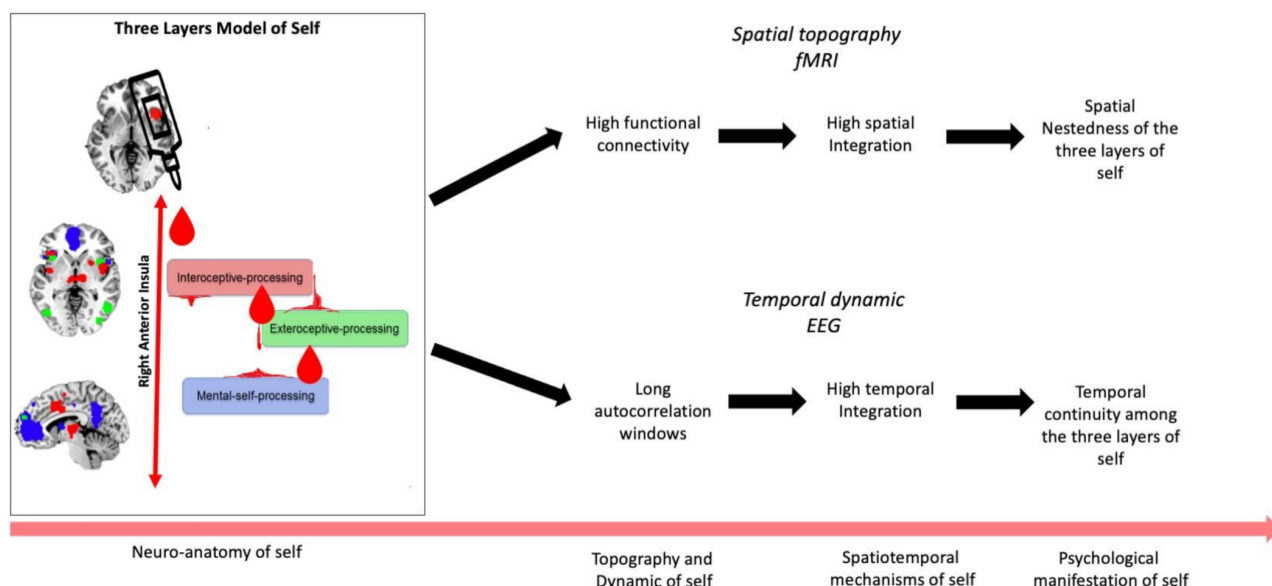


Figure 5. Visual representation of spatial and temporal mechanisms of the three layers of self. The left part of the figure shows that the glue (drops) provided by the right anterior insula joins all the networks, e.g., interoceptive- exteroceptive- and mental-self processing in accordance with Qin et al. 2020. The right side of the figure highlights the key role of right anterior insula for functional/spatial and temporal integration in our fMRI and EEG findings. Overall, this figure represents how neuronal data might translate in spatio-temporal mechanism and psychological manifestation of self.

4.3. Methodological Limitations

One limitation is that we did not recruit the same subjects for fMRI and EEG. Moreover, different paradigms like self-related/animate vs. non-self-related/inanimate and self-enfacement were run in fMRI and EEG respectively. While this is clearly a limitation, it can also be taken as litmus test for the validity of our findings. Despite different paradigms and different subjects, both modalities show analogous converging findings, the topographic and dynamic specialness of right insula compared to left insula.

Yet another limitation is that we did not go into detail about the neuro-anatomical differentiations within the insula itself. This concerns anterior and posterior as well as dorsal and ventral parts of the insula [60–62]. Instead, we here focused only on mainly the anterior insula as this is the region of interest we obtained from the Qin et al. [17] meta-analyses. Particularly in EEG is to consider that the insula is a deeply located structure and the recorded activity may be contaminated by the temporal and frontoparietal opercula.

One can also argue that we here focused only on those regions implicated in the three layers of the self-networks defined by Qin et al. [17]. This carries the advantage that we can really make specific assumption of the right insula with respect to specifically the three layers of the self-networks. While the disadvantage consists in the fact that we cannot make any assumptions about the particular role of the right insula for the brain’s global activity and its topography [63]. That was not our aim, though, as our focus was mainly on the special role of the right insula for the self. Moreover, another limitation is represented by the fact that those *a priori* defined regions are dysbalanced in terms of laterality. For instance, for the exteroceptive-self layer 9 regions on 14 (64%) are located on the right side of the brain while for the mental-self only 3 regions on 12 (25%) are located at the right side of the brain. However, in both cases right anterior insula showed higher centrality indices when compared to the left one. Considering the intrinsic limitation represented

by the laterality disbalance and the different number of regions/nodes for each network that might affect the analysis, this seems to tentatively suggest that nor the prevalence of right regions in exteroceptive-self processing network nor the prevalence of left regions in mental-self processing network affect the role of right insula within the networks.

Furthermore, the fMRI sample is composed only by men. This limits the generalizability of our findings and leave open the question whether there are functional brain differences between males and females across the different networks. Future research needs to confirm these data on other samples including both men and women to further support our interpretations and extend the generalizability of our findings.

Finally, we did not directly investigate familiarity. We can only infer from the Qin et al. study that the key difference between self-specificity and familiarity consists in the absence of the right/left insula in familiarity. One major psychological difference between familiarity and self-specificity is that only the latter but not the former involves the own body including intero- and proprioceptive feelings/sensations. Given its role in interoceptive and proprioceptive processing as well as intero-exteroceptive integration [15,16,64–66], the right insula may be key in yielding a particular feeling or subjective experience, a sense of self, whereas such feeling is not present in familiarity.

5. Conclusions

What renders neural activity in the right rather than left anterior insula more suitable to take on a special role in mediating self-specificity? We here show that neural activity in the right insula exhibits special topographic and dynamic features compared to the left insula. The right insula shows higher degree of functional integration with respect to other regions implicated in the different layers of self. Moreover, the right insula exhibits longer time windows in its neural activity than both the left insula and the other regions of the different layers of self. Together, these findings suggest higher degrees of both functional and temporal integration in the neural activity of the right insula. This suits the right insula ideally to serve as topographic and dynamic node or glue between the distinct layers of self ensuring their high degrees of spatial nestedness and temporal continuity.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/brainsci11101312/s1>, Table S1: Composition of ROIs for the EEG analyses. ACW was calculated on each region individually and then average to build the ROIs.

Author Contributions: Conceptualization, A.S. and G.N.; methodology, A.S. and A.W.; software, A.C. and A.W.; validation, A.S., A.W. and G.N.; formal analysis, A.S. and A.W.; investigation, A.S. and A.W.; resources, A.S., A.W. and G.N.; data curation, A.S. and A.W.; writing—original draft preparation, A.S., A.W. and G.N.; writing—review and editing, A.S., A.W. and G.N.; visualization, A.S., A.W. and G.N.; supervision, G.N.; project administration, G.N.; funding acquisition, A.S., G.N. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of the University of Ottawa (#2018054, 10 September 2019) for the EEG part and approved by Ethics Committee of the University of Chieti-Pescara (#1015, 1 October 2015) for the fMRI recordings.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data are not publicly available due to restrictions e.g. their containing information that could compromise the privacy of research participants. The data that support the findings of this study can be requested to the corresponding author.

Acknowledgments: This project/research was supported by the Michael Smith Foundation Canada Research Chair, by the grant from the Ministry of Science and Technology of China, National Key R&D Program of China (2016YFC1306700), from the European Union's Horizon 2020 Framework Program for Research and Innovation under the Specific Grant Agreement No. 785907 (Human Brain Project SGA2), the ERANET grant, NFRF grant, Team grant from uOMBRI to GN and by "Search

for Excellence—UdA” (University G. d’Annunzio of Chieti Pescara) to A.S. for the project SYNC (The Self and its psYchological and Neuronal Correlates—Implications for the understanding and treatment of disorders of Self).

Conflicts of Interest: The authors declare no conflict of interest.

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Repertoire of timescales in uni – and transmodal regions mediate working memory capacity

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ARTICLE INFO

Keywords:

Timescales
Working memory
Cognitive capacity
Core-periphery

ABSTRACT

Working memory (WM) describes the dynamic process of maintenance and manipulation of information over a certain time delay. Neuronally, WM recruits a distributed network of cortical regions like the visual and dorsolateral prefrontal cortex as well as the subcortical hippocampus. How the input dynamics and subsequent neural dynamics impact WM remains unclear though. To answer this question, we combined the analysis of behavioral WM capacity with measuring neural dynamics through task-related power spectrum changes, e.g., median frequency (MF) in functional magnetic resonance imaging (fMRI). We show that the processing of the input dynamics, e.g., the task structure's specific timescale, leads to changes in the unimodal visual cortex's corresponding timescale which also relates to working memory capacity. While the more transmodal hippocampus relates to working memory capacity through its balance across multiple timescales or frequencies. In conclusion, we here show the relevance of both input dynamics and different neural timescales for WM capacity in uni – and transmodal regions like visual cortex and hippocampus for the subject's WM performance.

Significance statement

Working memory (WM) describes the dynamic process of maintenance and manipulation of information over a certain time delay. This time delay suggests the involvement of the brain's neural timescales. How are these neural timescales related to WM capacity?

We show that it is particularly a balanced power across multiple timescales in the transmodal regions like the hippocampus that is related to WM capacity. While uni-modal regions like the primary visual cortex are related to WM capacity through their sensitivity to input dynamics. Taken together, we here for the first time show a direct link between neural and cognitive levels of working memory.

1. Introduction

Within our daily activities we perform many different cognitive operations on various inputs, for instance manipulating, monitoring and storing specific stimuli in working memory. Working memory (WM) describes the dynamic process of maintenance and manipulation of information over short time delays despite new incoming interfering information (Li et al., 2022; Sreenivasan and D'Esposito, 2019). One key feature is WM capacity or WM span which has been conceptualized as a containment ability referring to the amount of information a system (e.g. short-term memory buffer) can possibly process and gather (Atkinson and Shiffrin, 1968). While in a more dynamic conceptualization, capacity is compared to a system's robustness, that is, how much the system can be loaded before it breaks down; or bandwidth, e.g., how much information can be processed or transmitted in a unit of time (Wenger and Townsend, 2000). Accordingly, a person with a higher capacity can easily manipulate higher and lower cognitive loads in working memory compared to a low-capacity person. The dynamic

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<https://doi.org/10.1016/j.neuroimage.2024.120602>

Received 18 February 2024; Received in revised form 1 April 2024; Accepted 2 April 2024

Available online 3 April 2024

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processes on the neural level that mediate working memory capacity remain yet unclear. Addressing this gap in our knowledge is the goal of our study.

Working memory operates through a neuronally distributed network of brain regions (Berger et al., 2019; Christophel et al., 2017; de Mooij-van Malsen et al., 2023; Li et al., 2022; Owen et al., 2005; Rose, 2020). Higher-order regions like the parietal or dorsolateral prefrontal cortex (DLPFC) as well as lower-order regions like visual cortex (Borders et al., 2022; Christophel et al., 2017; Gayet et al., 2018; Yonelinas, 2013; Zhao et al., 2022) are associated with WM performance. The role of the hippocampus in WM has been a subject of extensive research and debate, with multiple studies providing evidence both for and against its involvement in WM processes (Borders et al., 2022; Leszczynski, 2011; Shavitt et al., 2020; Tambini et al., 2023; Yonelinas, 2013). While visual WM as assessed in the visual match-to-sample task recruits the hippocampus (Von Allmen et al., 2013), the implication of the hippocampus in working memory in other tasks remains highly contentious, primarily attributed to its relatively low activation levels during various WM tasks (Courtney, 2022; Kessels and Bergmann, 2022; Peters and Reithler, 2022; Rose and Chao, 2022; Slotnick, 2023; Stern and Hasselmo, 2022; Wood et al., 2022).

Specific temporal patterns of neural activity have been described as characteristic in WM (Bhattacharya et al., 2022; Liu et al., 2023; Wasmuht et al., 2018). One process, key in mediating actual WM performance, is delay activity. Delay activity is a sustained neural activity over the retention delay (Christophel et al., 2017; Curtis and D'Esposito, 2003; D'Esposito and Postle, 2015; Li et al., 2022; Sreenivasan and D'Esposito, 2019). This delay activity is mainly found in parietal and frontal cortices (Li et al., 2022). Another dynamic process reported in WM literature is cortical short-term plasticity where the information is temporally maintained through synaptic weight changes. This dynamic neural functioning is referred to as 'activity-silent WM' (Beukers et al., 2021; Courtney, 2022) as it does not appear as blood-oxygenation-level-dependent (BOLD) signal increase as commonly measured via general linear modeling (GLM) of hemodynamic signal. To specify the activity-silent neural dynamics in more detail, we suggest the implication of a variety of neural dynamics during WM. Neural dynamics operate on various timescales, ranging from milliseconds over seconds (Cavanagh et al., 2020; Golesorkhi et al., 2021; Huang et al., 2018; Murray et al., 2014; Wengler et al., 2020). Different mental processes have been related to the recruitment of varying ranges of timescales (Wolff et al., 2022; Zilio et al., 2021). For instance, a shift towards slower timescales have been related to the loss of consciousness (Wolff et al., 2022; Zilio et al., 2021, 2023) while the recruitment of multiple timescales has been shown in cognitive processes like attention (Zeraati et al., 2023). How the multiple timescales of the brain's neural activity mediate working memory capacity remains to be explored.

In addition to the brain's neural timescales, working memory capacity may also be mediated by the timescales of the inputs themselves, e.g., input dynamics. One key feature shaping neural activity is the task design (Mumford et al., 2014). External stimuli are typically presented with a certain temporal structure (e.g., longer or shorter, regular or irregular trial durations or intertrial intervals (Fiveash et al., 2020; Rhodes and Di Luca, 2016; Thunell and Thorpe, 2019; Zeithamova et al., 2017). The emerging temporal structure over the duration of a task with a series of trials is here referred to as 'task-periodicity'. Its regularity and frequency may be processed and ultimately encoded by the brain's neural activity in a corresponding frequency range, leading to periodic activations (Fiveash et al., 2020; Huettel et al., 2014; Klar et al., 2023b, 2023a). Specifically, two recent studies demonstrated that inter-trial or inter-stimulus-intervals in the infra-slow frequency range (periods of 15.5 to 60 s) yield power increases in corresponding frequency ranges of the brain's power spectrum density (PSD) (Klar et al., 2023b, 2023a). They show that the loss of consciousness in anesthesia goes along with the loss of task-periodic power peaks in the brain's PSD (Klar et al.,

2023b, 2023a). This leaves open whether such task-periodicity in specific single frequencies also modulates cognitive functions like working memory on both neural and behavioral levels.

To capture the implication of different timescales of neural dynamics, we will here focus on the frequency domain of the fMRI signal. The frequency domain is displayed using a power spectral distribution (PSD). The PSD is the distribution of power of different frequencies obtained via Fourier transformation of the signal. Hence it indicates if there is one predominant or multiple equally strong frequencies implicated. An important measure of summarizing this information is the median frequency (MF; for studies applying MF in fMRI, see (Golesorkhi et al., 2022a; Huang et al., 2018; Klar et al., 2023b, 2023a)). MF divides the power spectrum into two halves with an equal area under the curve and indicates the frequency of that dividing line – it thus provides an estimate of whether the PSD is tilted more towards the slower or faster frequency ranges (Golesorkhi et al., 2022a). Reflecting the power balance within the whole or global PSD across both slower and faster frequencies (measured in broadband), MF indexes the global range of the power spectrum (Huang et al., 2018). Is such range of the brain's PSD related to the range of WM capacity?

Considering the temporal nature of working memory (see above), we think that dynamic neural measures should yield important insights. Therefore, the goal of our fMRI study was to investigate how WM capacity is related to the brain's neural dynamics, that is its single and multiple timescales. For this, participants performed a working memory task with regularly presented trials. We will explore the task induced frequency power within the single more local PSD (narrowband), as well as the multiple timescales of the global power distribution across the whole frequency range as measured by MF in the PSD (broadband). We performed these analyses in typical working memory regions like DLPFC and hippocampus, as well as sensory regions like the primary visual area and the motor cortex (as reaction time was required inducing a regular motor response).

Our first specific aim consisted in investigating single (task-periodicity induced, narrowband) and multiple frequency power indices based on the PSD. Task-periodicity is estimated via the power at the frequency corresponding to the trial duration while the multiple frequencies are indexed by the MF which tests for the balance between slow and fast frequency power. Given the previous observations of task-periodicity (Fiveash et al., 2020; Klar et al., 2023b, 2023a), we hypothesized a single power peak in specifically the visual cortex changes in a frequency range that corresponds to the trial durations of the VSTM task but not in the control recording. This would illustrate that the task-periodicity impacts neural activity in the same frequency in which the task was presented. The second specific aim was to link the neuronal dynamics to behavior. We hypothesized that the task-induced single power PSD peak and the global PSD characteristics are related to WM capacity. Specifically, we hypothesized that subjects with higher WM capacity show a better neural alignment to the task-periodicity as manifest in higher PSD peak in visual cortex. Secondly, these same subjects are expected to show a particular balance of slow and fast frequency power on the global PSD in especially those regions typically associated with WM, that is, hippocampus and DLPFC.

2. Methods

2.1. Participants

The inclusion criteria for participants are described in (Steffener et al., 2022). 40 young and 40 old participants have been recorded in functional magnetic resonance imaging (fMRI). The final sample includes 36 subjects (18 female; Age: $m = 36.1$, $SD = 23$, $min = 19.2$, $max = 80.8$). The high exclusion was necessary due to motion-censoring as the time dependent measures like MF highly sensitive to atypical fluctuations. (See Section 2.8. pre-processing). The study received ethical approval from the Research Ethics Board (REB) of the University of

Ottawa, and all participants signed informed consent forms.

2.2. Task administration in MRI

The VSTM task, a delayed matching task as in (Nagel et al., 2009), consists of regularly presented trials and was chosen to study the relationship between the task's periodicity effect and memory capacity. One or several dots are presented for 2.5 s at random position on the screen. The number of dots presented varies in each block. Next, a mask is shown for 0.3 s before the participant is to keep the locations of the dots in memory for 3.2s. Then, a single dot was shown at one position of the screen for 2.5s and the participant was asked to indicate with a button press if there has been a dot at this location during the encoding period. The task is presented in blocks of 6 trials (each 9.5 s). The inter-block-interval is 23 s (20 s break, 3 s countdown before the next block). The whole task takes 329.5 s (with a TR of 1.11, this makes $362TR + 2TR$ at the end to capture the rather slow BOLD activity). Hence, working memory is solicited periodically every 9.5 s (0.105Hz).

The load level is adapted to each subject's capacity. The capacity was assessed in an earlier, purely behavioral staircase procedure (see Steffener et al., 2022). The task was implemented in PsychoPy2 (Peirce et al., 2019). All software to deliver this task is publicly available at: <https://github.com/NCMLab/CognitiveTasks>.

To assure that the periodicity peak is related to the task structure and not to scanner noise or other nuisances, we chose another recording of the same subject and same recording session. This recording of similar duration and does not follow a periodic trial presentation of 9.5 s. Hence, we do not expect to find a task-periodicity peak at this frequency in the control task.

Two identical runs for each task were administered within the MRI.

2.3. Assessment of working memory capacity

Capacity was determined with a staircase method via the VSTM task before participants entered the scanner (Fig. 1A). Capacity was defined as the level with 80 % correct trials using a 3-up/1-down staircase. For details on the procedure, see (Steffener et al., 2022). Subsequently, the difficulty of the VSTM task in the scanner was adapted to each subject's capacity. Hence, capacity here is considered as cognitive repertoire (McIntosh and Jirsa, 2019). Hence, when faced with a specific trial, each participant realizes the task based on their own range or repertoire of behaviors (here WM capacity). For instance, a load level of 3 dots will be perceived as much more challenging for a participant with a low capacity while the same stimuli is perceived as simple for a participant with a capacity of 12. Within the same load level, one's ease to give the correct response is fluctuating due to dynamic nature of brain fluctuations. If not apparent in accuracy, it commonly emerges in reaction time

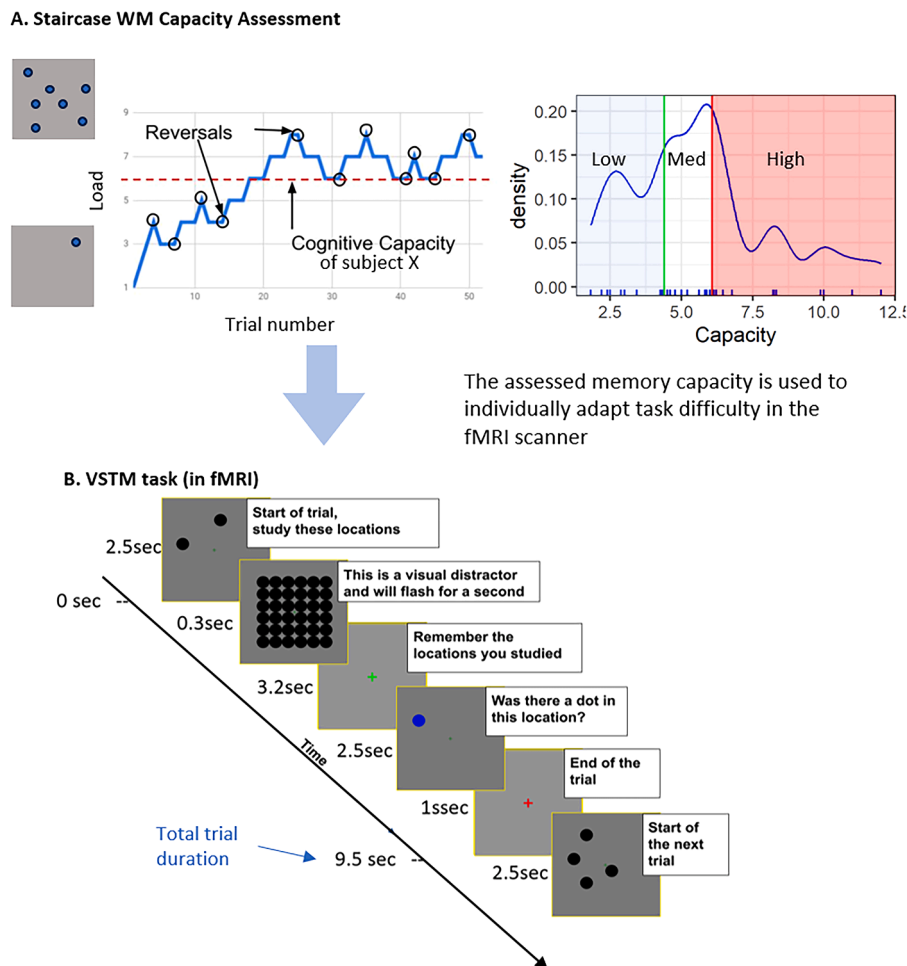


Fig. 1. Behavioral procedure. **A** Participants WM capacity was assessed with the VSTM task before entering the scanner in a staircase procedure. **B** The difficulty of the VSTM task in the scanner was adapted to each participant based on their capacity. Participants were asked to remember the position of one or several dots before they were to indicate if the dot probe is at a position where a dot appeared during the encoding period. One trial takes 9.5 s. The VSTM is presented in blocks of 6 trials (each 9.5 s). The inter-block-interval is 23 s (20 s break, 3 s countdown before the next block). Hence, memory is solicited every 9.5 s (0.105Hz). Hence, the VSTM task has a very rhythmic structure with a response expected every 9.5 s.

(RT). Longer RT is evidence of a current higher difficulty compared to shorter RT.

For some analysis we categorized the variable capacity. For this, we split the capacity in high, medium and low values. Groups were defined by to have an equal size to avoid groups with a very low sample size.

2.4. MRI data collection parameters

All neuroimaging used the 3T Siemens Biograph mMR MR-PET scanner at the Brain Imaging Centre (BIC) at the Royal Ottawa Mental Health Centre (ROMHC). Participants wore protective earplugs during the scans and held a squeeze ball they could activate if they felt uncomfortable and wished to terminate the scan. A multi-band accelerated EPI sequence (Moeller et al., 2010) using an acceleration factor of 6, TR = 1110ms, TE = 16.6ms, 52-degree flip angle, phase partial Fourier 6/8, 56 slices collected in an alternating increasing slice order, 2.5×2.5 mm in-plane resolution, slice thickness = 2.75 mm, field of view: 220×200 mm (Steffener et al., 2022). A total of 365 volumes were recorded per run.

2.5. Pre-processing

All image preprocessing has been done in AFNI using `afni_proc.py` (<https://afni.nimh.nih.gov>) (Cox, 1996). For each task and subject, we applied slice timing correction. We applied motion censoring of volumes with Enorm (Euclidean norm of first differences of motion parameters) > 0.25 mm. Anatomical scans were normalized into MNI152 2009c stereotactic space and regression of linear and non-linear drift, and regression of local white matter signals to reduce non-neuronal noise (Jo et al., 2013). Finally, we applied a spatial smoothing using an 8 mm full-width at half-maximum isotropic Gaussian kernel and a bandpass between 0.01 and the Nyquist frequency of 0.45 Hz. The censored volumes were interpolated with a polynomial of degree 3.

If more than 10 % of data was removed during the preprocessing due to motion, the run was discarded. This strict removal is important because our measures are very timeseries sensitive. If several timepoints are missing in a row, the interpolation creates a smoothed section which impacts strongly measures like MF.

2.6. Definition of ROIs

ROIs were extracted based on Glasser et al. (Glasser et al., 2016). The primary visual area (V1) and the primary motor area (M1) were chosen in regard to the visual nature of the task requiring a motor response. The hippocampus and dorsolateral prefrontal cortex (DLPFC) were chosen due to their implication in WM (Borders et al., 2022; Christophel et al., 2017; Gayet et al., 2018; Yonelinas, 2013; Zhao et al., 2022; Courtney, 2022; Kessels and Bergmann, 2022; Peters and Reithler, 2022; Rose and Chao, 2022; Slotnick, 2023; Stern and Hasselmo, 2022; Wood et al., 2022). Voxels of these regions were extracted and calculations were computed on these voxels before averaging across voxels per ROI.

2.7. Periodogram

First, we computed the power spectrum for each voxel in the desired ROIs before it was averaged into one PSD per ROI and per subject. The PSD was computed via the `signal.periodogram` function with a hamming window in python 3.10.

2.8. Task-periodicity peak: a measure of a single timescale

The peak indicates the area under the curve of the narrowband power spectrum between 0.1 to 0.11Hz (9 to 10 s period, 4 frequency sampling points). This surrounds the frequency of the task periodicity of 9.5s. It was estimated with an integral approximation of the spectrum using Simpson's rule with the `scipy.integrate.simps` function in python.

This measure considers only a part of the power spectrum. Hence, we call it a local variable.

2.9. Median frequency: a measure of multiple timescales

The PSD was calculated as described in Section 2.10. MF indicates the frequency that divides the area under the curve of the PSD into 2 equal halves (total PSD from 0.01 to 0.45Hz, 176 frequency sampling points (Golesorkhi et al., 2022b)). In this way, it indicates the relationship of power between slow and fast frequencies. A low MF corresponds to stronger power in slow frequencies. In contrary, a high MF is an indicator of a shift of power towards faster frequencies (Golesorkhi et al., 2022b). In the frequency domain, timescales as indexed by MF have been related to consciousness (Bergamasco et al., 2021; Chen et al., 2021; Jacob et al., 2022; Kumar et al., 2022; McDonald et al., 1999), epilepsy (Elsherif and Esmail, 2022; Vlachou et al., 2022), motricity (Balbinot et al., 2023; Cavalcante et al., 2022; Ettema et al., 2022; Gaspar-Junior et al., 2022; Gizzi et al., 2021; Ortega-Becerra et al., 2021; Silva et al., 2022; Sozzi and Schieppati, 2022) and fatigue (De la Fuente et al., 2021; Ebenbichler et al., 2023; Ettema et al., 2022; Florencio et al., 2021; Habets et al., 2021; Hou et al., 2021; Jurasz et al., 2022; Lowery et al., 2002; Moll et al., 2022; Puce et al., 2021; Tang et al., 2022). In the cognitive domain, MF has been linked to cognitive decline (Benz et al., 2014; Choi et al., 2019; Hoshi et al., 2022; Ruiz-Gómez et al., 2018; Verrusio et al., 2015). For instance, MF in resting-state EEG and MEG has been proposed as predictor of Mini-Mental State Examination (MMSE) (Choi et al., 2019; Hoshi et al., 2022) and Frontal Assessment battery (FAB) scores (Hoshi et al., 2022). A slowing in neural activity has been associated with a higher cognitive decline.

2.10. MF-post

To capture the global MF independent of the power peak, we computed MF on the section of the PSD following the periodicity-peak, hence in the Hz range from 0.11 to 0.45Hz (136 frequency data points). The section on the PSD before the peak was too small for MF calculation.

2.11. Functional connectivity

To compute functional connectivity (FC) between the selected ROIs, mean time-series of each ROI were extracted from the pre-processed data. Next, we extracted the correlation coefficient between each ROI with the hippocampus, subject-based.

2.12. Statistical analyses

Mixed effect models were used to account for the repeated measures nature of ROI, hemisphere and run. Hence, these factors were always included as fixed effects, while subjects were considered as random factor. Linear mixed models with repeated measures were computed with the `r` package 'lme4' and the `lmer()` function (`model <- lmer(DV ~ ROI*side*Run + (1|Subject), df)`). Further, Wilcoxon tests were chosen to compare the groups 'high' vs. 'low' due to their unequal variances.

3. Results

3.1. Behavioral

We first show large inter-individual differences in both capacity and RT (Fig. 2A+B). Next, we correlated the capacity with RT across all runs and load levels. In both runs, RT relates similarly to the capacity (Run1: $r = -0.52$, $p = 0.0027$; Run2: $r = -0.53$, $p = 0.0029$; Fig. 2B). We conclude that both recorded runs are equivalent on the behavioral side. As in the literature, this sample also presents a faster RT with a higher capacity (Unsworth and Engle, 2005).

To specify the link between RT and capacity in relation to the load

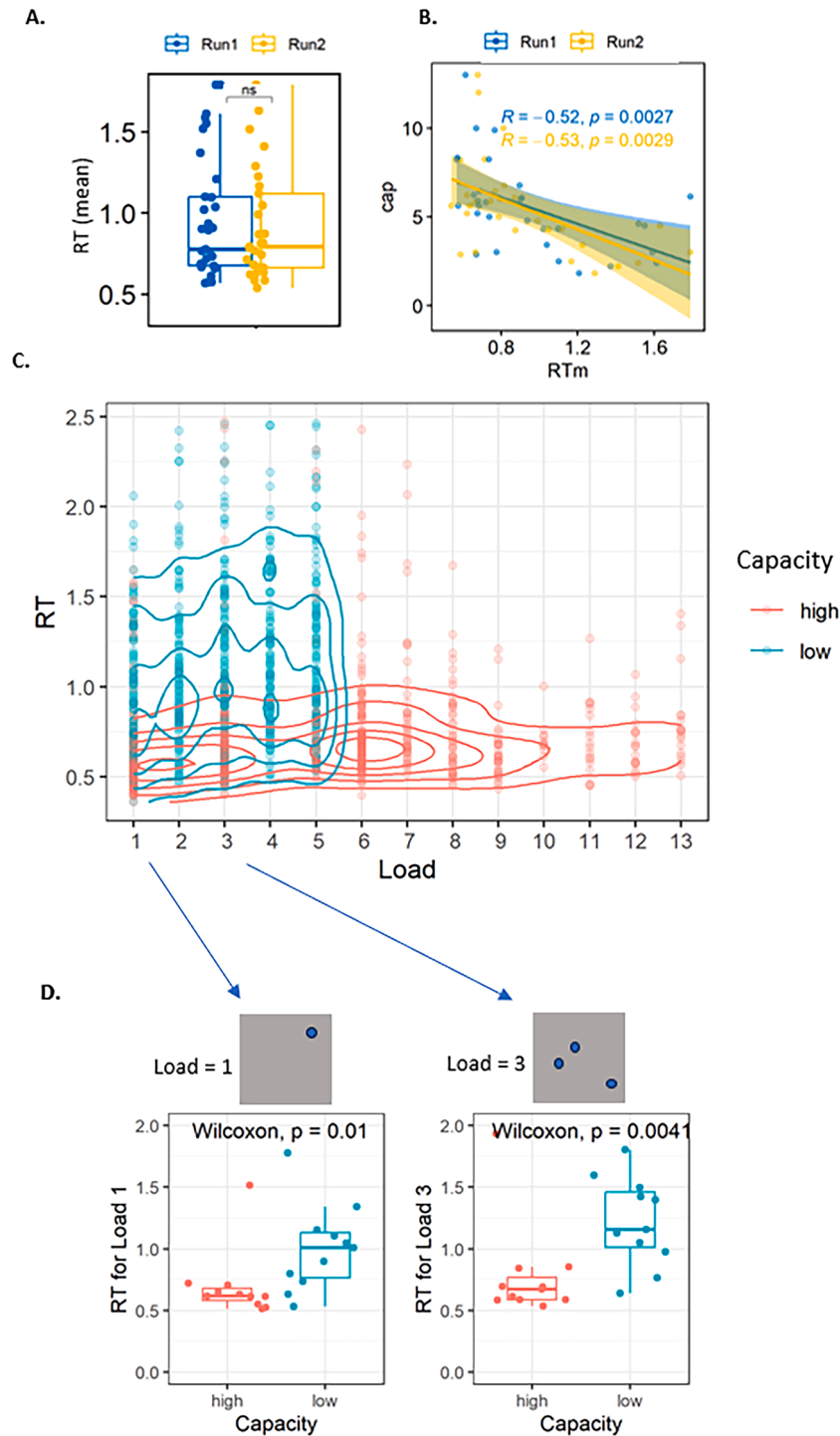


Fig. 2. Behavioral results. **A** Boxplots of RT in the VSTM task. RT does not differ between runs. **B** Similar correlations between RT and capacity can be observed in both runs. **C** Relationship between RT and load level, colored by high and low capacity for simplicity. Participants with a lower capacity range have a longer RT on low load trials compared to subjects with a high capacity. **D** Load levels 1 and 3 are shared across all subjects. We observe significant differences in RT between participants with high compared to low capacity in terms of their mean RT to load levels 1 and 3. This indicates that participants respond differently to the same stimulus based on their own repertoire of capacity.

level, we defined equally sized groups into high, medium, and low based on their capacity (Fig. 1A right). Descriptively, Fig. 2C depicts how participants with high vs. low capacity respond to different degrees of task-difficulty (Load). Each participant was presented with five different load levels. We observe how participants with low capacity take a long RT on simple load levels while high-capacity participants show a short RT for these same load levels. To confirm this observation statistically,

we found significant Wilcoxon signed-rank tests ($p < 0.05$) between high - and low-capacity participants for load levels 1 and 3 (Fig. 2D). Load levels 1 and 3 were presented to all participants, independent of their capacity level, hence they offer a possibility for direct comparison of all subjects. It is clearly visible that high-capacity participants respond faster to the same load levels than low-capacity participants. This indicates that the extend of the working memory capacity also affects the

processing of low load items. Finally, it shall be mentioned that, as the VSTM task was administered twice in the scanner, we also investigated if both trials were equivalent in terms of response time (RT). No significant differences were found ($p > 0.05$, Fig. 2A).

3.2. Neuronal data – single and multiple components of the power spectrum

3.2.1. Single Timescale (task-periodicity peak)

To assess the impact of the temporal structure of the task, e.g., task-periodicity on neural activity, we compare the power spectrum density (PSD) from the VSTM task with the one of the control recording (Fig. 3A + B, non-log transformed PSD are in the supplements) at $\log(0.105\text{Hz})$ (peak). The interaction effect of task and ROI on the peak of the mixed model was significant ($F(3,766.93) = 63.244$, $p < .000$). Post-hoc pairwise comparisons indicate a significantly stronger peak in V1 during the VSTM task compared to the control ($p < .0001$; Fig. 3C). Next, we shuffled the timeseries of the BOLD activity of both tasks and all ROIs and computed the peak. No significant difference between VSTM and control recording was found for any of the ROIs ($p > .05$; see supplements). This indicates a clear effect of the task-periodicity on neural activations in the sensory region V1.

Multiple Timescales (MF): To capture properties of a wider range of neural fluctuations, we computed the PSD and extracted MF across all frequencies (broadband; Fig. 4A). MF is an indicator of the distribution of power between faster and slower frequencies. A mixed model indicates a significant main effect of ROI on MF ($F(3,432.47) = 161.99$, $p < .0000$). Bonferroni-corrected pairwise comparisons show significant differences between all ROIs except for M1 and DLPFC (Fig. 4B). V1 To test if this difference remains without the task-induced periodicity in the lower frequency of 0.105Hz, we computed the MF on the section of the PSD after the task-induced power peak (0.11–0.45Hz). Results remain consistent when excluding the slower frequencies (see supplements). Together, this indicates that regions clearly differ in their balance of higher and lower frequencies, with V1 demonstrating the strongest and the hippocampus weakest tendency towards higher power in slow frequencies.

3.3. Neuronal-behavioral relationships – linking single and multiple timescales to capacity and reaction time

In the previous section we showed a clear impact of the task-periodicity on neural BOLD-fluctuations in V1. The impact is centered to a single, local frequency (0.105Hz) of the PSD. Secondly, we investigated the global power distribution over the full PSD via the MF and observed clear differences between regions in their fast-slow frequency balance. Here, V1 and the hippocampus position themselves at the extremes, with the V1 demonstrating the highest expression of slow frequencies. How are these dynamic neuronal features related to behavior?

3.3.1. Single timescale and behavior

First, we will investigate the relationship between the task-periodicity effect and behavior. For this, we computed several mixed models (see methods). Capacity and RT are related to the peak via an interaction effect with ROI while controlling for the effect of hemisphere and run (Capacity: $F(3,418.67) = 4.96$, $p = .002$; RT: $F(3, 418.51) = 6.828$, $p = .000$). A higher peak in the visual cortex is related to a better capacity and a faster RT (In Fig. 5A). Hence, the more the power spectrum in V1 adapts to the task periodicity, the better the subjects' performance. Or in other terms, a more adaptive V1 to external temporal information is related to a better memory capacity.

3.3.2. Multiple timescales and behavior

Next, we associated behavioral variables with the global PSD measure MF. A significant interaction effect between ROI and MF has been found for capacity ($F(3,417.34) = 4.034$, $p < .007$) and RT ($F(3,417.20)$

$= 4.603$, $p < .003$). In Fig. 5B we observe the strongest link between MF and capacity as well as between MF and RT in the hippocampus. We confirm this by investigating MF on the PSD after the periodicity-related power peak (post-MF, 0.11–0.45Hz) to verify that this effect is not due to the peak itself (Fig. 5B.b). And indeed, the results with post-MF confirm those on the global MF. A higher MF in this study means a median frequency at about half of the total spectrum. This indicates that a more equilibrated relationship between the power in low and high frequencies goes jointly with better WM capacity.

Together, we observe differential regional involvement of single and multiple neuronal timescales in WM capacity. The sensory region V1 is related to WM capacity and RT via the encoding of the task-periodicity while the hippocampus relates to the WM variables via its balance of fast and slow frequencies.

3.4. Functional connectivity

WM has a cue or input component, a delay or maintenance component and an response or output component (Curtis and D'Esposito, 2003). These components need to coordinate among each other. We hypothesize that a better motor-hippocampus coordination/synchrony leads to faster RT.

To further established and support that the Hippocampus is really involved in WM, we conducted FC, indicating the degree of synchronization, between the hippocampus and the other three ROIs (Fig. 6, see supplements for correlation table). Next, we correlated the individual association strength between ROIs with the behavioral RT and capacity. And indeed, a highly significant correlation was found between the left hippocampus-left motor cortex synchronization with RT ($r = -0.546$, $p < .001$) and marginally with capacity ($r = 0.327$, $p = 0.072$). This indicates that a higher motor-hippocampus synchrony is associated with faster RT and better capacity. We conclude that the hippocampus is implicated in WM.

3.4.1. Hierarchy of timescales in WM

So far, we could show that capacity and RT are linked to the task-periodicity (b95rel) via V1 and to the fast-slow frequency power balance (MF) in the hippocampus. Do both regions with their respective timescale impact working memory capacity equally? To answer this question, we computed a stepwise regression with RT as dependent, MF in hippocampus (MF_hippo) and the task-periodicity peak in V1 (peak_V1) as independent variable. Both independent variables have a significant effect on RT (MF_hippo: $p < .001$; peak_V1: $p = .008$) with an R^2 of 0.203 for MF_hippo and of 0.046 for peak_V1 (the full results of this regression are in the supplements). We computed the same analysis with capacity as dependent variable and found similar results (MF_hippo: $p < .001$, $R^2 = 0.149$; peak_V1: $p = 0.013$, $R^2 = 0.44$; full results are in the supplements). In this sense, the global distribution of power in faster and slower frequencies in the hippocampus is the main factor predicting RT and WM capacity. The stronger task-periodicity effect in V1 may rather play a role as a facilitator.

3.4.2. Mediation model

WM capacity was assessed before the main recording. RT indicates the actual performance on each trial, capturing trial-to-trial variations reflecting the dynamic repertoire of brain dynamics. Hence, we placed capacity as independent and RT as outcome variable (Fig. 7). As mediator we included the MF of the hippocampus and the power spectrum peak in V1. Run and hemisphere were added as background confounders. The indirect path of the model with peak_V1 as mediator was not significant ($p = 0.127$). Instead, the mediative character of MF_hippo between the global capacity and the actual RT is significant ($p = .005$). Neither of the confounders influenced the model. (Full results of the model and the non-significant results of the indirect path $RT \rightarrow MF_hippo \rightarrow capacity$ can be found in supplements).

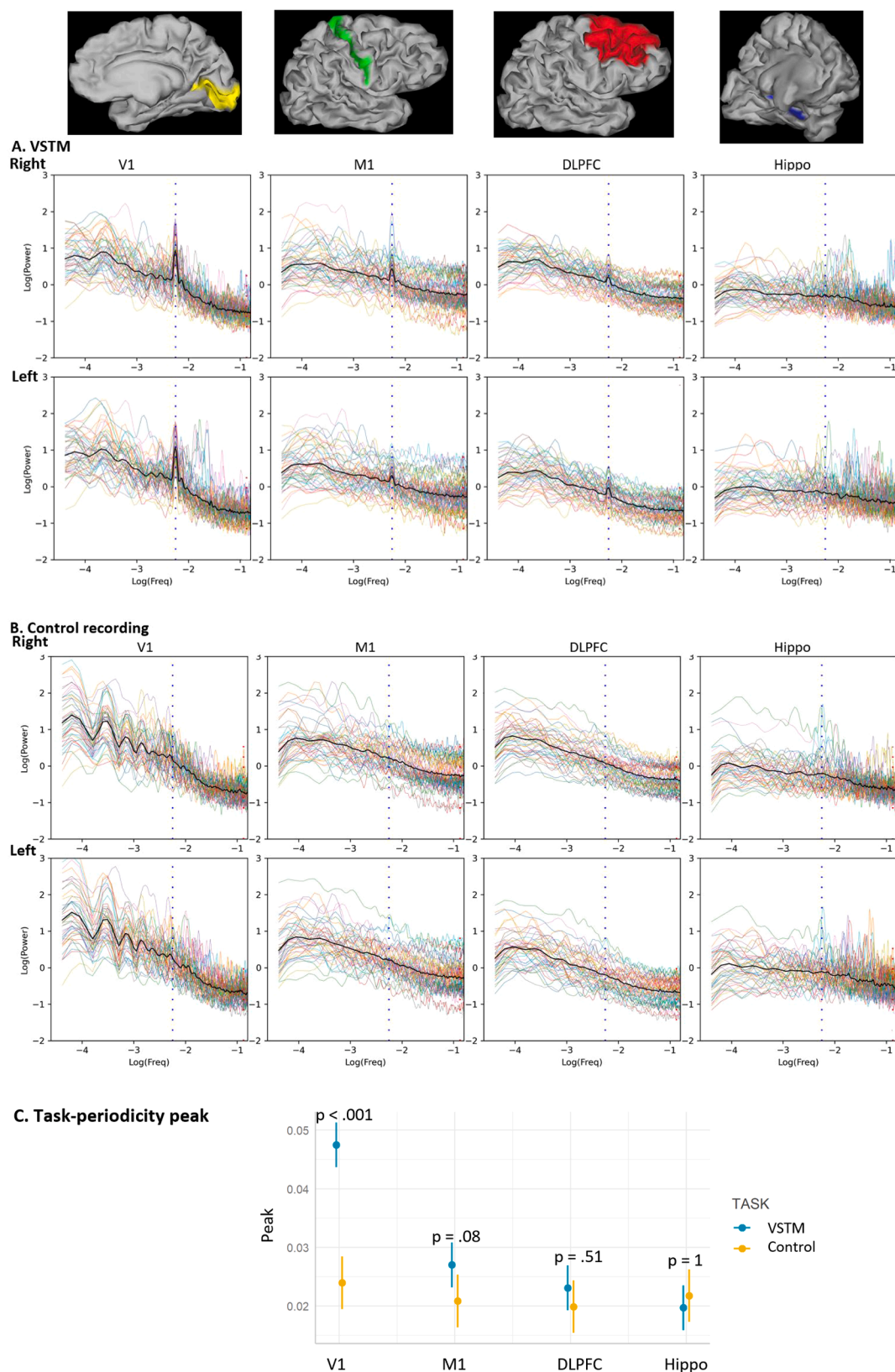
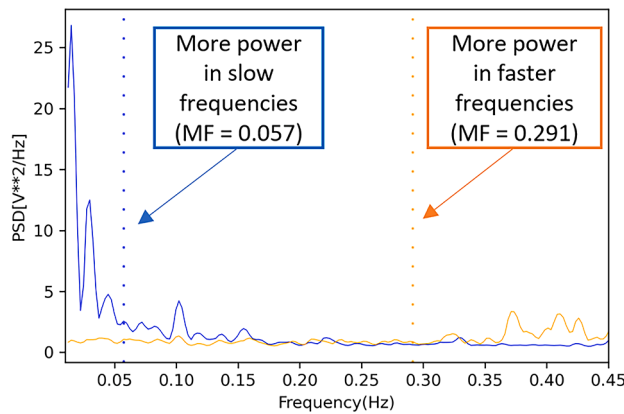


Fig. 3. **A+B** Power spectra of each ROI (in log scale for better visibility of the peak. See supplements for PSDs in linear scale). Each line depicts one subject, the black line indicates the average of all subjects. The upper row depicts the right hemisphere, the lower row the left hemisphere. The blue vertical dotted line indicates 0.105Hz (9.5 s), the red one 0.416Hz (2.5 s), indicative of the expected trial periodicity for the VSTM and Control recording, respectively. By visual inspection we remark a power peak at the expected task-periodicity for the VSTM task but not for the Control recording. **C** Boxplot of the peak measuring the relative power between 0.1-0.11Hz that corresponds to the frequency of the task-periodicity in the VSTM task. Significant differences (Bonferroni corrected) indicate a higher power peak in the VSTM than the Control recording. This indicates that we find the expected effect of the task-periodicity in our dataset.

A. Illustration of median frequency (MF)



B. Global: Descriptive plot MF

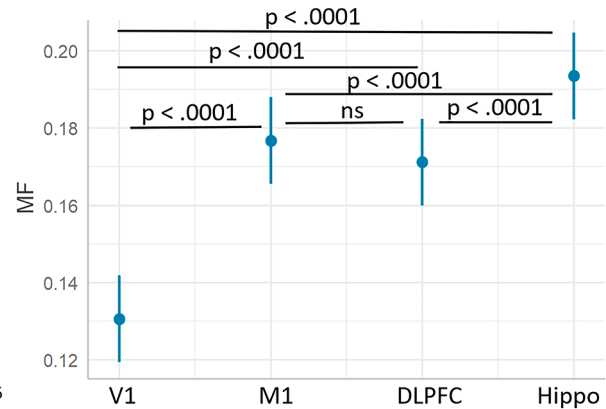


Fig. 4. **A** Illustration of MF calculated on the PSD in linear space. Lower values of MF indicate higher power in slow frequencies, hence a particular importance of slow frequencies components in the measured BOLD activity. Depicted are extreme (highest/lowest) power distributions observed in fMRI. **B** Descriptive plot for the multiple timescale measure Median Frequency in the VSTM task. We observe a low MF for V1 and a medium MF with a high variability in the hippocampus.

4. Discussion

Different mental processes have been related to the recruitment of varying ranges of timescales (Wolff et al., 2022; Zilio et al., 2021, 2023). For instance, the recruitment of multiple timescales has been shown in cognitive processes like attention (Zeraati et al., 2023) while EEG studies indicate a shift towards slower timescales during the loss of consciousness (Wolff et al., 2022; Zilio et al., 2021, 2023). In this study, we aimed to elucidate neural timescales implicated in WM. First, we showed that a higher memory capacity is related to a faster response time averaged across all load levels. This is commonly observed in memory tasks and hence validates our task administration (Bo et al., 2019).

Next, we tested for the implication of the hippocampus in WM (Schneider et al., 2017) via functional connectivity and found the synchrony between the left motor cortex and the left hippocampus to be significantly related to behavior. This validates the further inclusion of the hippocampus in the analysis.

Our first specific aim was the investigation of dynamic BOLD fluctuations implicated in WM capacity and the influence of the tasks' periodic structure on these dynamic fluctuations. Both neural measures were considered to provide information about the probabilistic functional modes underlying brain dynamics and behavior (McIntosh and Jirsa, 2019). Here we provide first evidence that the temporal characteristics of the task design plays a role in WM performance during input processing. Results showed that the regular task structure of 9.5 s (0.105Hz) clearly elicited repeatedly single BOLD fluctuations at 9.5 s as indexed by the local power peak. This predominantly affected the primary visual area. This is not surprising (Huettel et al., 2014) given that we have a visual task. Indeed, music studies and neural oscillators provide evidence of the ability of the brain to synchronize to a rhythmic external stimulation like tones (Doelling and Assaneo, 2021; Fiveash et al., 2020; Rhodes and Di Luca, 2016). Strikingly, the observed task-induced power peak was not independent of task performance. Here, a stronger neural response in the primary visual area to the task periodicity was observed in subjects with a higher memory capacity, suggesting its role in input processing.

The second aim of this study was to investigate if WM capacity is reflected in the dynamic neuronal fluctuations of multiple timescales as measured by MF. Different neural fluctuations have been linked to WM in different frequency bands (e.g., theta, gamma), inter-peak-intervals (Noguchi and Kakigi, 2020), delay activity (Christophel et al., 2017; Curtis and D'Esposito, 2003; D'Esposito and Postle, 2015; Li et al., 2022;

Sreenivasan and D'Esposito, 2019) or activity-silent processes (Beukers et al., 2021; Courtney, 2022; Rose, 2020). These studies provide evidence of the importance of neural fluctuations in WM. Our results extend these findings by showing a close relationship between WM capacity and the balance of power between higher and lower frequencies in the hippocampus. Higher capacity and faster RT were found to be associated with a rather balanced power distribution across all frequencies, e.g., MF, in the hippocampus. Higher power in slower frequencies was linked to a decreased capacity and longer RT. This is in line with findings related to activity-silent WM (Beukers et al., 2021; Rose, 2020; Rose and Chao, 2022) where processes operate which are invisible to BOLD amplitude measures. We can conclude on a close relationship between the recruitment of multiple neural timescales in the hippocampus and fluctuations in the WM repertoire.

This work focused on the timescale of 9.5 seconds per trial. Future directions which alter the stimulus duration and retention duration will help tease apart what aspect of the task periodicity is the "most" important. The other line of evidence implies the global power spectrum's balance of slow and fast frequency power, e.g., MF in the hippocampus, suggesting its role in information storage or maintenance in shaping WM capacity via multiple timescales.

4.1. Limitations

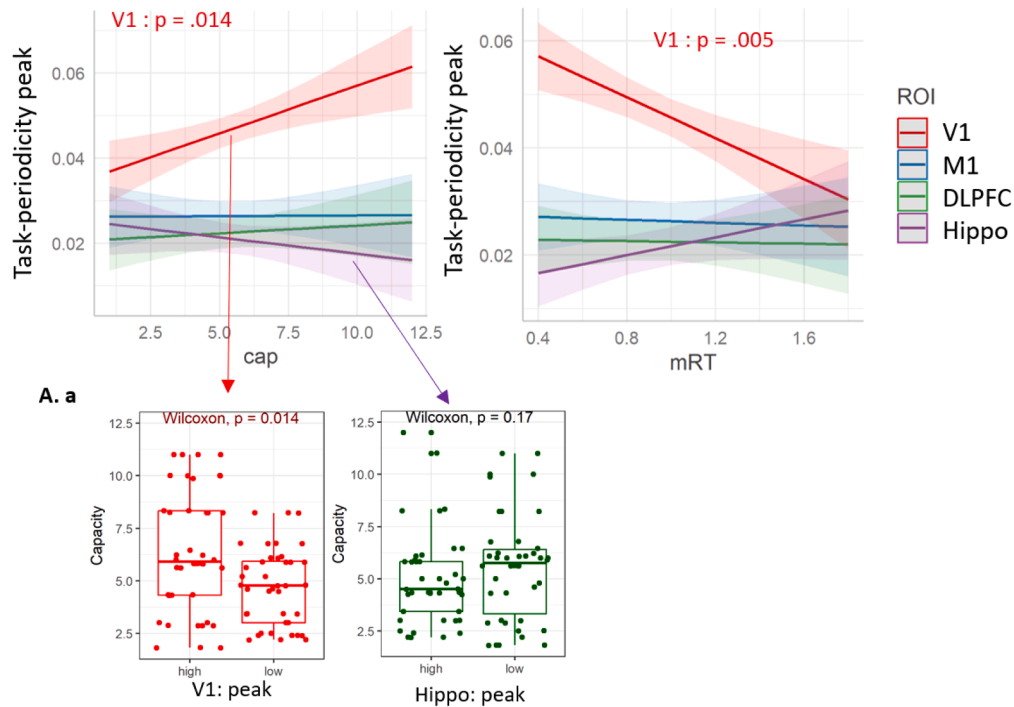
Even though opting for a frequency domain approach instead of investigating task activations in the time domain is still quite rare in the field of neuroscience, it offers some interesting advantages. Power spectra analyses allow the investigation of recurrent fluctuations at specific frequencies and the relationship among them. This additional level of abstraction has great potential for new measures of neural dynamics and a new understanding of how brain and behavior are related.

5. Conclusion

We demonstrate how the input dynamics with its single timescales in the task's periodicity is processed in a unimodal region like the visual cortex and, importantly, relates to working memory capacity. While the more transmodal hippocampus relates to working memory capacity through multiple timescales with their balance of shorter and longer ones. This underscores the key relevance of the brain's different timescales for working memory capacity which, as our data show, interact in especially unimodal sensory regions with the timescales of the input itself, e.g., task periodicity. Timescales may thus provide the bridge or

Neuro-behavioral relationship

A. Local PSD index Task-periodicity power peak:



B. Global PSD index MF:

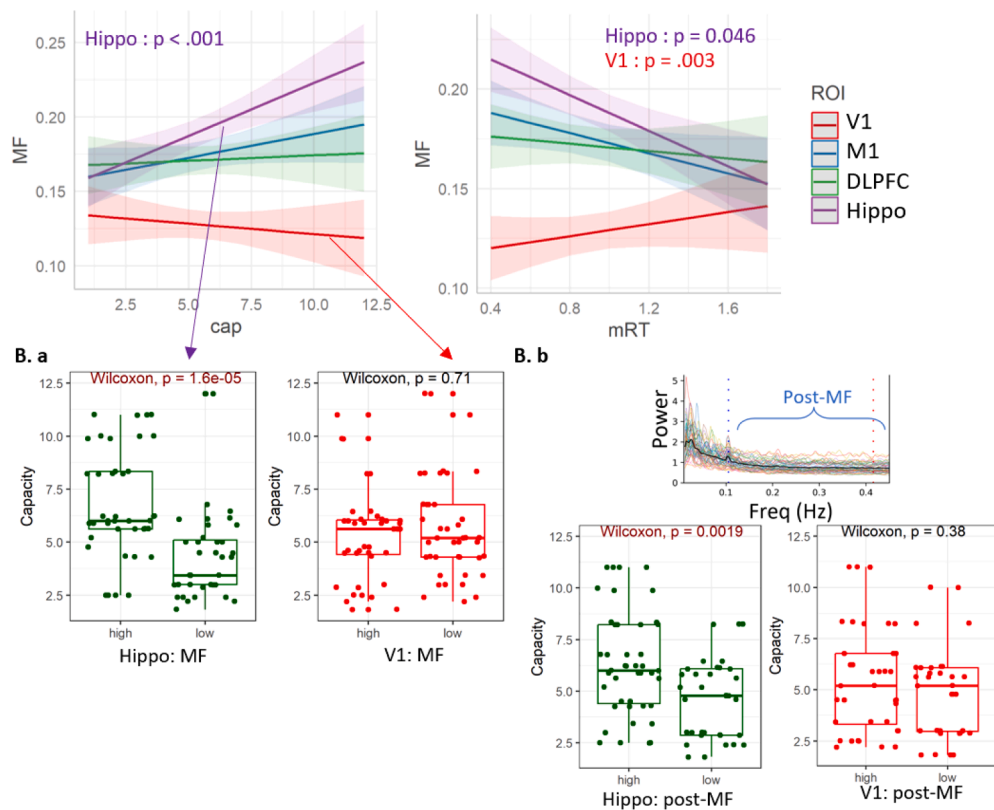


Fig. 5. Single and multiple timescale measures in relation to behavior. **A** Capacity and RT relate to the single timescale task-periodicity peak in V1. P-values indicate a significant difference in the slope of V1 compared to M1. In **A.a**, we confirm that participants with a higher peak in V1 activity also have a higher capacity. This is not the case for the peak in the hippocampus. **B** Relationship between multiple timescales (MF) and behavioral measures. Here, these are the multiple timescales in the hippocampus which are related to WM. **B.b** Relationship between capacity and post-MF.

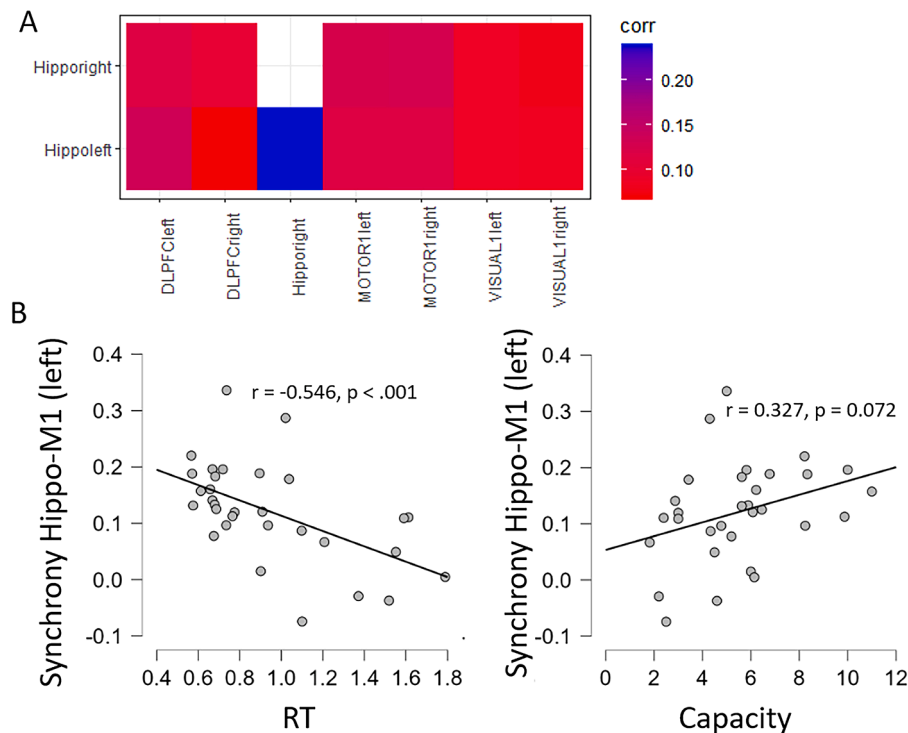


Fig. 6. Heatmap of the synchronization strength between the mean timeseries of the hippocampus with the other ROIs. B Correlation between M1-Hippocampus synchronization and behavioral measures RT and capacity.

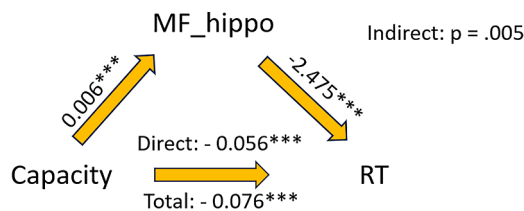


Fig. 7. Mediation model suggesting that the global factor capacity influences RT via an equilibrated balance of faster and slower fluctuations in the hippocampus.

connection from the input dynamics over the neural dynamics to the output's cognitive function, e.g., working memory capacity. Accordingly, the dynamics of both input and brain shape the output, e.g., working memory which is seemingly shared by all three as their “common currency” as suggested in Spatiotemporal Neuroscience (Northoff et al., 2020a; Northoff et al., 2020b).

Finally, one important methodological implication of our results is that the study of cognitive processes and neural activities should adopt a broader view of the dynamics of both task and brain. This, for instance, means to incorporate multifaceted temporal and thus dynamic features of the task structure itself, e.g., its periodicity. While on the neural level both single more local (narrowband) timescales as well as more global timescales need to be distinguished and thus measured separately. This is further reiterated by our results showing a complex cognitive process like working memory requires both single and multiple timescales at different processing states.

CRedit authorship contribution statement

Angelika Wolman: Writing – review & editing, Writing – original draft, Visualization, Software, Project administration, Methodology, Investigation, Formal analysis. **Yasir Çatal:** Writing – review & editing, Software, Methodology. **Philipp Klar:** Writing – review & editing,

Software. **Jason Steffener:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Data curation. **Georg Northoff:** Writing – original draft, Supervision, Funding acquisition, Conceptualization, Writing – review & editing.

Declaration of competing interest

The authors declare no conflicts of interest.

Data availability

Data will be made available on request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.neuroimage.2024.120602](https://doi.org/10.1016/j.neuroimage.2024.120602).

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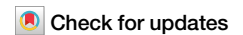
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<https://doi.org/10.1038/s42003-024-07235-w>

From the brain's encoding of input dynamics to its behavior: neural dynamics shape bias in decision making



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The human brain is tightly connected to the individual's environment and its input dynamics. How the dynamics of periodic environmental stimuli influence neural activity and subsequent behavior via neural entrainment or alignment is not fully clear yet, though. This study explores how periodic environmental stimuli influence neural activity and behavior. EEG data was collected during a Go-NoGo task with a periodic intertrial interval (ITI) of 1.3 s (0.769 Hz). Results showed that the task's temporal structure increased power spectrum activity at 0.769 Hz, which showed high intersubject variability. Higher task-periodicity effects were linked to stronger phase-based intertrial coherence (ITC) and reduced neural complexity, as measured by lower Lempel-Ziv Complexity (LZC). Additionally, higher periodicity in the power spectrum correlated with faster reaction times and stronger response bias. We conclude that the encoding of the inputs' dynamics into the brains power spectrum shapes subsequent behavior, e.g., RT and response bias, through reducing neural complexity.

Events in our environment enroll dynamically on different timescales. One rhythmic process which we all are subjected to is the circadian cycle operating on a timescale of 24 h. But others may occur based on our specific environment, like a train passing by every 10 min or the (ir)regular flickering of an electronic device nearby. The brain exhibits its own very complex intrinsic dynamic activity changes over time¹. How the brain and its intrinsic neural dynamics encode the external inputs' dynamics and how that impacts subsequent behavior remains to be elucidated.

Behavioral task design used in neuroscientific research significantly influences neural activity². External stimuli are typically presented with a particular temporal structure, i.e., rhythmic or periodic, including trial durations and intertrial intervals^{3–6}. We will refer to 'task-periodicity' as the temporal pattern that emerges over the whole course of a task, involving a series of trials presented at a certain more or less regular timescale. For instance, it is known that the brain processes and encodes the inputs' regularity and frequency within a corresponding frequency range, resulting in periodic activations^{3,7–10}. Recent studies indicate that inter-trial or inter-stimulus-intervals in the infra-slow frequency range (periods of 15.5 to 60 s) lead to power increases in the corresponding frequency ranges of the brain's power spectrum density (PSD)^{8–11}. Behaviorally, a recent study shows that

this power increase in the sensory region V1 influences WM performance¹⁰. These findings suggest that the task periodic power peak modulate behavior. The neural mechanisms of this modulation remain unclear, though. Addressing this gap in our knowledge is the goal of our study.

The impact of the brain's encoding of a regular task-periodic input on neural activity in the shorter timescale of single trial durations can be subsumed under the term of neural entrainment^{12,13}. Neural entrainment can be measured via different neural indices¹². For instance, intertrial phase coherence (ITC) measures the temporal recurrence in the phase angles of a signal at each time point over several trials as for instance during repeated auditory stimuli¹⁴. This makes ITC a promising candidate to measure the effects of auditory task periodicity on phase angles.

The temporal dynamics of neural activity can also be measured in terms of Information processing through its degree of complexity by the Lempel Ziv complexity (LZC, Lempel & Ziv, 1976). LZC provides a tool to estimate the compressibility of a signal¹⁵ and has widespread use in EEG^{16,17}. A lower LZC indicates higher degree of signal compression and thus reduced neural complexity. How the encoding of the task periodicity impacts information processing and its neural complexity as well as its relation to behavior remains unclear.

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The goal of this study is to investigate the neural mechanism by which task periodicity impacts behavior. We assume that the neural encoding of the task's overall periodic structure in a corresponding frequency of the power spectrum modulates behavior through the neural dynamics as manifest in its information processing, i.e., LZC, and entrainment with ITC. For that purpose, we apply an auditory Go NoGo task which, presenting a high number of repeated stimuli, is well suited for investigating task periodicity effects in the power spectrum. While this task is usually used to measure attention and inhibition when comparing Go and NoGo trials¹⁸, we here shift the focus to assess how the neural encoding of the periodic Go stimuli within the power spectrum modulates subjects' behavior, i.e., their decision making bias in response to the Go NoGo stimuli, through neural complexity (LZC) and entrainment (ITC). Given that the LZC measures the degree of the compression of the signal, one may expect that higher encoding of the task's periodic structure within the power spectrum allows for better signal compression resulting in less complexity, e.g., lower LZC.

Our first specific aim is to investigate whether the regularly presented input dynamics of the external stimuli, i.e., task periodicity is neurally processed and encoded within the power spectrum. Based on previous data^{8–11}, we hypothesize that the frequency of the task's regular temporal structure featured by its intertrial intervals will lead to a power increase in the corresponding frequency of the PSD. Moreover, we expect considerable intersubject variability in the degree of that power peak as that may relate to intersubject variability in subsequent behavior, i.e., reaction times and decision making bias (see below for details).

Our second specific aim is to test how the neural encoding of the task-periodicity within the power spectrum peak relates to the neural dynamics of entrainment, i.e., ITC, and the complexity or information processing, i.e., LZC. Given that the ITC indicates phase synchrony across averaged trials, we expect a higher ITC in participants with a high task-periodicity power peak. In this sense, the ITC is a validation measure of the task-periodicity peak. Previous research showed that neural variability is reduced with stronger stimulus strength¹⁹. Therefore, we hypothesize that subjects with high values in both ITC and PSD peak exhibit less neural complexity reflecting higher signal compression, i.e., low LZC.

Finally, the third goal is to assess if the neural encoding of the inputs' dynamics through the task-periodicity in the power spectrum peak and the two measures of event related dynamics, e.g., ITC and LZC, also impacts the participants' behavior, e.g., output dynamics. Embracing specific decision biases enables organisms to customize their choices according to the environmental requirements which can be measured by Signal detection theory (SDT²⁰, see also ref. 21). For instance, opting for a liberal response strategy proves beneficial when accurate target detection is paramount, while a conservative approach becomes optimal for minimizing the risk of false alarms^{20,22}. We therefore expect that a highly regular task-structure favors high degrees of anticipation which would be observable in increased false alarms and a faster RT. Hence, we hypothesize that a higher neural encoding of the input dynamics into the PSD peak, a higher ITC, and lower LZC facilitates faster RT and higher false alarm rate, that is, a more liberal bias as measured by the Criterion C in SDT.

Method

Participants

Twenty-six healthy volunteers (16 males; age: $m = 26.869$, $sd = 6.628$) participated in this study. Due to technical difficulties, one subject was excluded. The subjects gave written informed consent and the study protocol was approved by the Royal Institute of Mental Health Ethics Committee (REB # 2019004). All ethical regulations relevant to human research participants were followed.

Task design

Participants completed a Go-NoGo task (Fig. 1). High pitch (1500 Hz), low pitch (1000 Hz), and 'silent' tones were randomly presented to participants for 150 ms. Participants were instructed to respond to each high tone as quickly as possible by pressing a button. Additionally, they were asked to

abstain from responding during the low pitch and "silent" tones. High tones were presented for 70% of the trials, while low tones and 'silent' tones were presented for 15% of trials each. Each trial was separated by an intertrial interval of exactly 1.3 s and a total of 520 trials were presented.

EEG data acquisition and preprocessing

EEG data was recorded during a 5-min resting state with eyes open and a task state of 11 min. To have comparable recording lengths, only the middle 5 min of the task state were considered for statistical comparisons between rest and task conditions.

EEG data was recorded using Ag/AgCl electrodes through a 64-channel Brain Vision EasyCap (according to the International 10–20 System) and was sampled at 1000 Hz with DC recording. The EEG data preprocessing was performed using the EEGLAB toolbox for MATLAB (R2022a). The data was downsampled to 500 Hz and filtered with an FIR zero-phase low-pass filter at 50 Hz and a high-pass filter at 0.1 Hz²³. With a custom script, noisy channels (defined as 5 interquartiles above or below each channel's mean) were spherically interpolated (amount of channels per subject: mean = 0.444, $sd = 1.086$) before re-referencing to the average. Further, artifacts were identified using independent component analysis (ICA) via the EEGLAB software (infomax) creating 63 independent components. Finally, we used MARA implementation to automatically reject noisy components. We defined a threshold of artifact probability to 0.75. The number of removed components varied across subject (amount of components removed per subject: mean = 37.259, $sd = 11.93$).

Neurodynamic measures

Channel selection. All subsequent analyses are calculated on the channel Cz due to its implication in auditory processing²⁴.

Task-periodicity. Neural alignment to the temporal envelope of the task is quantified with the power amplitude of the power spectrum (PSD) at exactly the stimulus presentation frequency (1.3 s/0.769 Hz). We refer to this measure hereafter with 'peak' or 'peak at 0.769 Hz'. The PSD was calculated with the signal.periodogram function from scipy in python 3.10 with a hamming window and a frequency resolution of 0.00333 Hz ($f_2 - f_1$).

Intertrial Phase Coherence (ITC). The ITC indicates the phase-synchronization across trials. We computed it in mne via the `tfr_morlet` function from 2 to 4 Hz. Number of cycles was for half of each frequency respectively. To extract a single ITC value per subject, we averaged the ITC for each condition in the theta range from 3 to 10 Hz and from 0.2 to 0.5 s after stimulus onset (see black box in each of the subplots in Fig. 4). This window showed the strongest differentiation between conditions.

Lempel-Ziv-Complexity (LZC). LZC is an indicator of signal compression by measuring its complexity^{15,25}. It is based on the regularity/irregularity of the signal. LZC measures the number of distinct patterns in a binary sequence which reflects the number of bits required to reconstruct a signal^{15,25}. Low values reflect high degrees of regularity, entailing a high degree of signal compressibility. A low LZC indicate high irregularity and low compressibility (see Fig. 1B). We computed it in python 3.10 following the description of²⁵ for pre- and post-stim activity separately. The length of pre- and post-stimulus activity was of 0.5 s respectively which is long enough for LZC computation but short enough to avoid an overlap of pre- from post-stimulus activity.

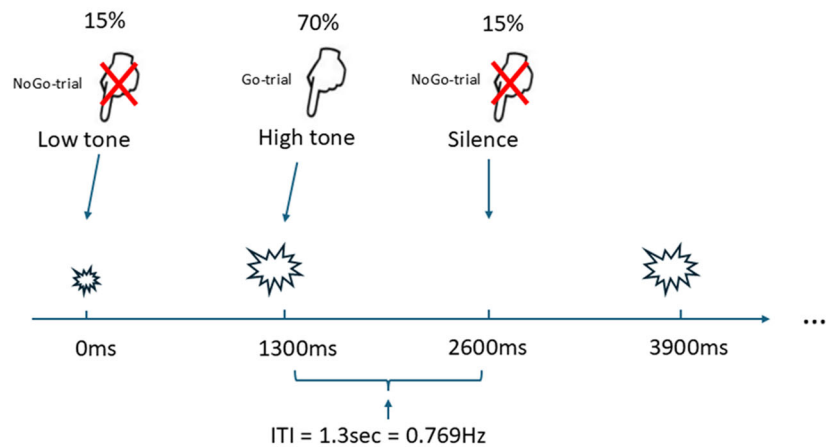
Behavioral measures

Signal detection theory. The Go-NoGo task was analysed with SDT²⁰ because it yields separate indicators for the accuracy in form of the cognitive bias Criterion C and sensitivity d' .

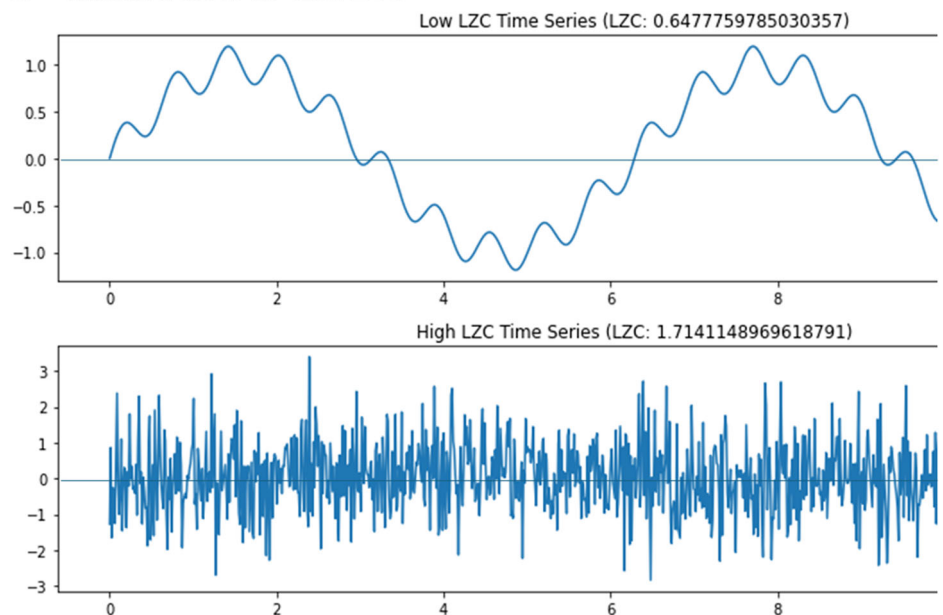
Criterion C. The criterion C of the signal detection theory²⁰ indicates a predominance of the participant to commit rather one than the other of the two error types (false alarms or misses). It is calculated based on the Hit and

Fig. 1 | Task design. **A** Task design. Participants are asked to give a button press to the frequent high tone and to inhibit a response after the low tone and the silence. The ITI was of 1.3 s, which corresponds to a frequency of 0.769 Hz. **B** Illustration of the LZC measure. The upper timeseries has a low LZC (0.648). The lower timeseries has a high LZC (1.714).

A Go/No-Go Design



B Illustration of the LZC



False alarm rate as follows²⁶:

$$\text{Criterion } C = -0.5 * (z\text{Hit} + z\text{FA})$$

Considering the facilitation of false alarms (FA) in Go-NoGo tasks, the bias is commonly negative, indicating a predominance of FA¹⁸. Still, the principle of the Criterion C remains in this task as it situates each individual on a continuum of response bias. Hence, a Criterion C close to zero indicates a rather equal number of false alarms and misses while an increase in FA is indicated by a more negative Criterion C.

Sensitivity d' . Sensitivity d' is a measure of discriminability and indicates the ability of a participant to distinguish between two stimuli. In our case, it indicates how well the participant achieved to behaviorally distinguish Go vs NoGo trials. It is calculated based on the hit and false alarm rate (Anderson, 2015).

$$\text{Sensitivity } d' = z\text{Hit} - z\text{FA}$$

A hit rate that equals the false alarm rate ($d' = 0$) is indicator of an inability to discriminate between the two stimuli. A higher d' corresponds to less errors.

Statistical analysis

A Wilcoxon rank test was used to compare the task-periodicity peak during rest and task. Repeated measures ANOVA is used to compare ITC and LZC across all three conditions. Correlations were employed to assess the co-occurrence of effects. For the correlations with the ITC and LZC, we did not distinguish between conditions.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Results

Behavioral analysis: reaction time and decision making bias

To assess behavior, we computed SDT indices Criterion C ($m = -0.594$, $SD = 0.243$, $\text{max} = -0.066$, $\text{min} = -1.124$) and Sensitivity d' ($m = 3.669$, $SD = 0.854$, $\text{max} = 1.138$, $\text{min} = 5.213$; Fig. 2A) as well as response time ($m = 0.421$, $SD = 0.080$, $\text{max} = 0.335$, $\text{min} = 0.675$; Fig. 2C). A general lower percentage of correct trials ($m = 3.669$, $SD = 0.854$, $\text{max} = 1.138$, $\text{min} = 5.213$) was found for the low NoGo condition compared to the high (Go) condition ($p < 0.001$) and silence ($p < 0.001$; high vs silent: $p = 0.156$). Criterion C and RT correlated ($r = 0.620$, $p < 0.001$), indicating that faster

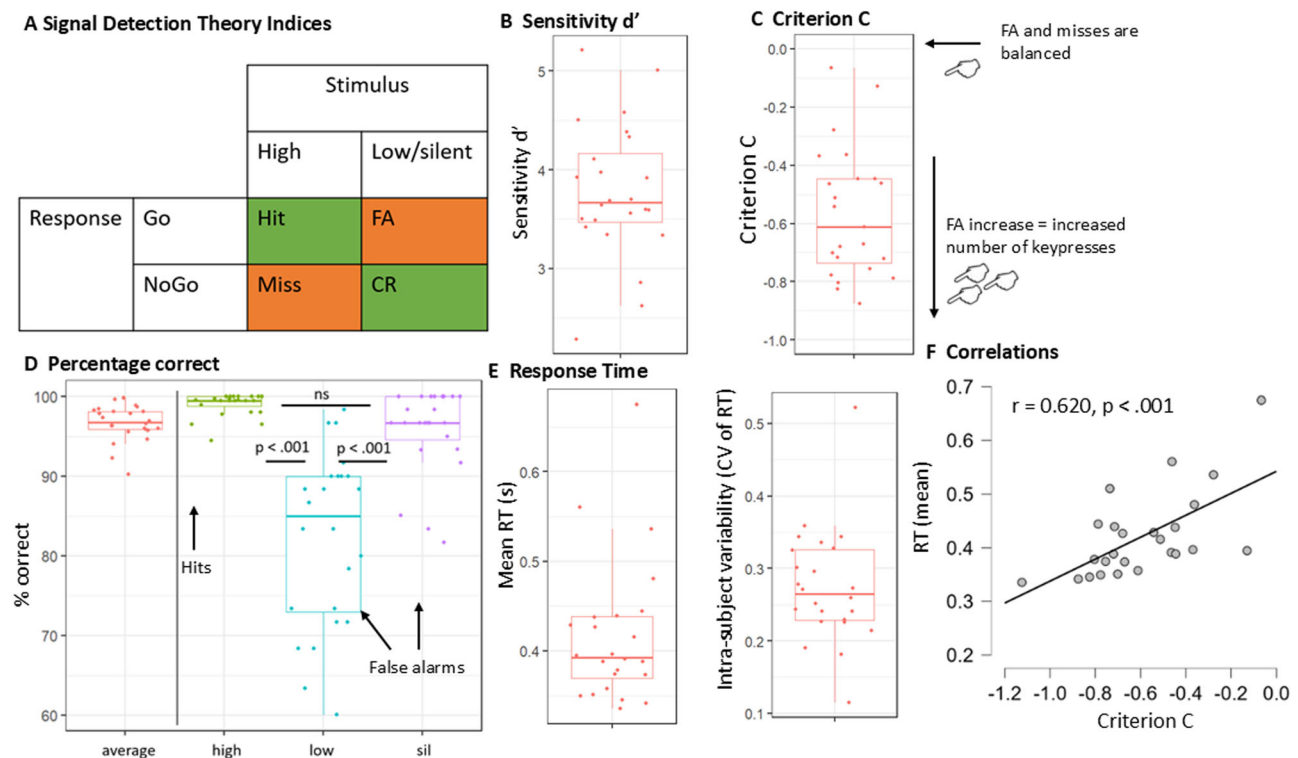


Fig. 2 | Illustration of the principle of Signal detection theory. **A** Illustration of the principle of Signal detection theory. **B** Sensitivity d' and **(C)** Criterion C are calculated based on the Hit and Miss rate. A higher d' indicates better performance while

lower Criterion C indicates a stronger preference for false alarms compared to misses. **D** Percentage correct. **E** Response time of correct trials (high tones) and its intra-subject variability. **F** Correlation between response time and Criterion C.

responding leads to a higher FA rate. Moreover, we observed high inter-subject variability in both RT (SD = 0.080) and Criterion C (SD = 0.243) as visualized by the extension of our violin plots in Fig. 2.

Encoding of input dynamics into neural dynamics: task periodicity peak in the power spectrum

To respond to our first aim, we computed the PSD over 5 min resting state and 5 min task state (Fig. 3). A significant power increase was found during the task-state compared to resting state at exactly the frequency of the task's ITI (0.769 Hz; $t(25) = 5.930, p < 0.001, d = 1.163; z = 4.051, p < 0.001, \text{matched rank biserial correlation} = 0.909$). We exclude the possibility that this power increase is due to motor activity related to button presses as they occur with irregular time intervals (see intra-subject variability of RT, Fig. 2C). In contrast to the power of the peak at the specific frequency of the task's periodicity, the total power of the whole PSD was equivalent in rest and task ($p > 0.8$). While the ratio of the peak in relation to the total power at 0.769 Hz was significantly higher in task than in rest ($t(25) = 5.677, p < 0.001, d = 1.113; z = 4.432, p < 0.001, \text{matched rank biserial correlation} = 0.994$).

Interestingly, the power increase observed in task state was related to a significant increase in intersubject variability (F-test to compare two variances: $F(25,25) = 0.027, p < 0.001$) reflecting the neural differences in the participants' capacity to process and encode the input dynamics, i.e., its overall temporal structure. Together, these results provide strong evidence that the periodic nature of the task design, the input dynamics, impact neural dynamics in a highly intersubjectively variable way.

Event related neural dynamics I: Intertrial coherence

Next, we analysed event-related neural dynamics. First, we computed the ITC (Fig. 4) for each condition between 0.3–0.5 sec and 3–10 Hz. A repeated measures ANOVA yielded a significant main effect for condition ($F(1.62, 40.61) = 59.184, p < 0.001$). Pairwise comparisons indicated a significant higher ITC for the low condition than for silent and high tones (Fig. 2B;

tukey hsd: high vs. low: 0.143, $p < 0.001$; high vs. silence: ns, low vs. silence: $-0.181, p < 0.001$).

Event related neural dynamics II: Lempel-Ziv complexity in pre- and post-stimulus activity

Next, we computed LZC on 500 ms long pre- and post-stimulus section of the EEG signal. Significant differences were found for the post-stimulus period ($F(2,50) = 25.451, p < 0.001$) in the low vs high ($p < 0.001$) and low vs silent ($p < 0.001$) conditions (high vs low: $p = 0.5$). Together, the event related measures were sensitive to the condition, particularly to the low tone condition which tests for response inhibition (Fig. 5A).

In general, pre-stimulus activity yielded a significantly higher LZC than during the post-stimulus interval, this indicates that the processing in the post-stimulus period exhibits higher compression of the signal (Fig. 5B; $t(25) = 5.909, p < 0.001, d = 1.159; z = 4.026, p < 0.001, \text{matched rank biserial correlation} = 0.903$). Finally, the pre-post-stimulus difference of LZC was significantly higher for the low tone condition compared to the high ($p = 0.001$) and silent ($p < 0.001$) condition (high vs silent: $p = 0.363$, Fig. 5C, see supplementary Fig S2 for pre-post differences in the PSD).

From the encoded input dynamics to the event related neural dynamics

We next investigated how the encoded input dynamics relate to our measures of the event related neural dynamics. For this, we computed the correlation between the task-periodicity power peak and both ITC and LZC (Fig. 6; see supplementary table S1 for further links between neural variables). As a reminder, for the correlations, we averaged the ITC and LZC across conditions as the peak is condition unspecific. Indeed, the peak correlated with both ITC and post-stimulus LZC as well as marginally with the LZC pre-post difference ($r = -0.386, p = 0.052$). A higher peak was related to a higher ITC ($r = 0.409, p = 0.038$), a lower pre-stimulus LZC ($r = -0.413, p = 0.036$), and lower post-stimulus LZC ($r = -0.476,$

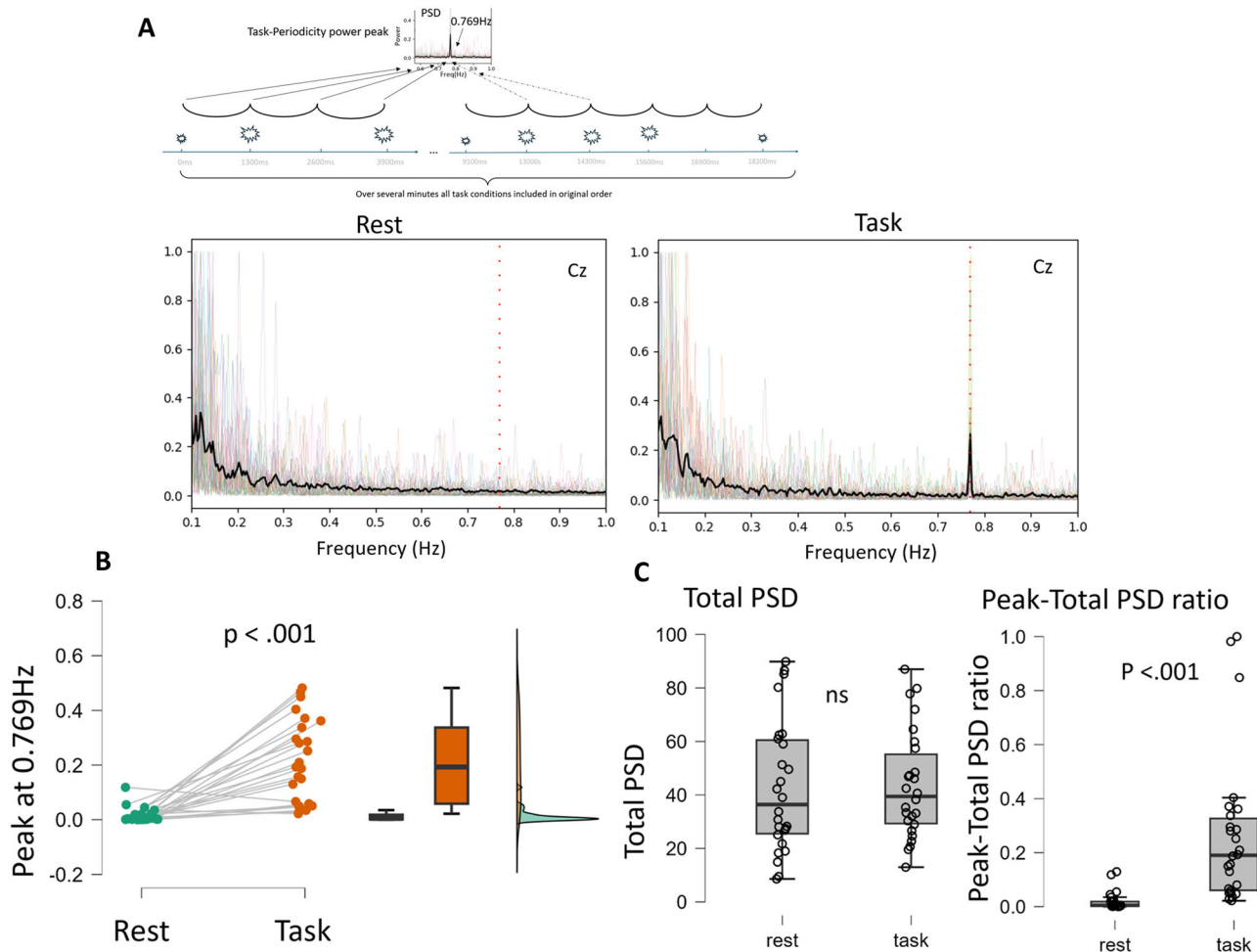


Fig. 3 | Task-periodicity. The top row is a schematic representation of the underlying task structure resumed in the power peak. **A** Power spectrum for rest and task EEG activity. Colored lines indicate individual subjects while the thick black line indicates the group average. At the 0.769 Hz, a clear power increase is visible for the

task compared to the resting state. **B** Quantification of the peak by extracting its amplitude in rest and task for each subject. The significant difference between rest and task comes jointly with a higher variability of the peak during task (left). **C** The total PSD remains stable from rest to task. (n = 25).

$p = 0.014$). This suggests that the degree of the encoded input dynamics through the power spectrum peak strongly modulate the subsequent event related neural dynamics, e.g., ITC and LZC.

From the encoded input dynamics to behavior

Above, we could show the strong impact of the external stimulus dynamics on the event-related dynamics. Does the input dynamics as processed by the brain modulate the subsequent behavioral responses? To answer this question, we correlated the task-periodicity peak with our behavioral measures (Fig. 7A). We observed that a higher peak comes with a faster RT ($r = -0.479$, $p = 0.015$) and a stronger Criterion C ($r = -0.657$, $p < 0.001$). In contrast, no relationship was found with sensitivity d' ($r = 0.078$, $p = 0.711$). Together, this shows that the input dynamics do indeed modulate, through the encoded task-periodicity, the subsequent behavioral responses, i.e., the bias in the decision.

From the event related neural dynamics to behavior

Next, we investigated the relationship of both ITC (Fig. 7B) and the LZC (Fig. 7C, D) with the behavioral measures. The ITC correlated with RT ($r = -0.66$, $p < 0.001$) and Criterion C ($r = -0.553$, $p = 0.004$) but not with sensitivity d' ($r = 0.211$, $p = 0.311$). Pre-stimulus LZC correlates with RT only ($r = 0.465$, $p = 0.019$; Criterion C: $r = 0.320$, $p = 0.118$; Sensitivity d' : $r = -0.027$, $p = 0.899$). Post-stimulus LZC correlated with RT only ($r = 0.535$, $p = 0.006$; Sensitivity d' : $r = -0.014$, $p = 0.948$) and marginally with Criterion C ($r = 0.387$, $p = 0.056$). The Pre-Post-Stimulus LZC difference correlated

with both RT ($r = -0.468$, $p = 0.018$) and Criterion C ($r = -0.438$, $p = 0.029$) but not with accuracy (Sensitivity d' : $r = -0.077$, $p = 0.715$).

Together, we repeatedly observed a strong link of the neural measures, ITC and LZC with the behavioral measures, i.e., RT and Criterion C. Interestingly, unlike the decision making bias Criterion C, the accuracy index d' was not related to any of the neural measures. Albeit tentatively, this suggests that the degree of the neuronally encoded input dynamics modulates the direction or type of errors (bias) but not the accuracy itself (the total number of errors).

Discussion

How does neural entrainment in form of task-periodicity impact neural activity and behavior? First, we observed a strong power increase at the frequency corresponding to the task structure (trial duration = 1.3 s). The same peak was not observed during the resting state which allows us to exclude the possibility that this strong power increase during the task might be due to noise sources external or internal to the participant. The observation of such task-periodicity effect on the PSD is not new⁷. Indeed, music studies and neural oscillators provide evidence of the ability of the brain to synchronize to a rhythmic external stimulation like tones^{3,4,27}. However, our results go beyond the simple observation of such task periodicity effect by relating it to behavior.

Extending these findings, we observed high intersubject variability in the degree of the encoded power peak which is related to intersubject differences in behavior, e.g., decision making bias and reaction time. We

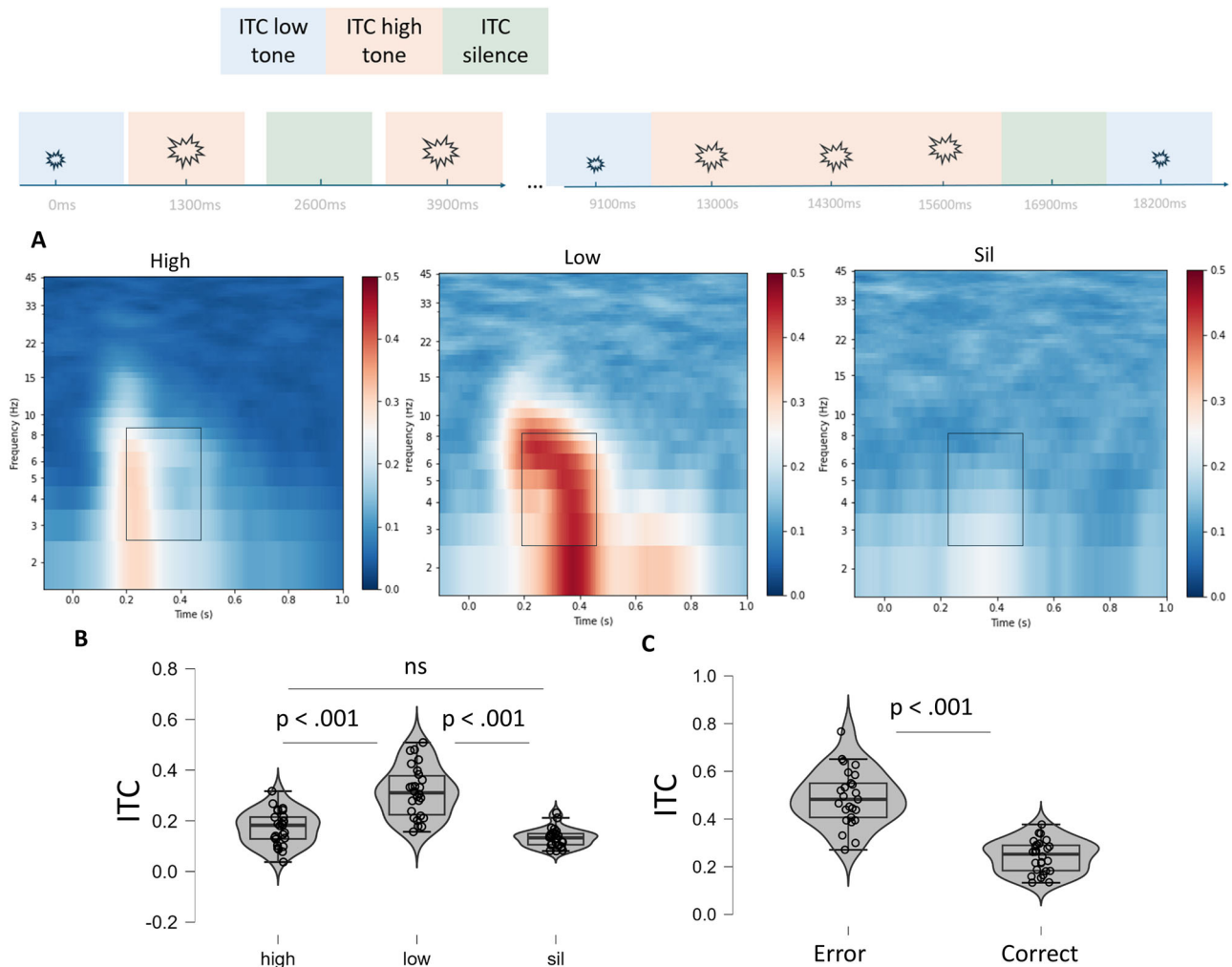


Fig. 4 | ITC. **A** ITC average across subjects for each condition. **B** Descriptive plots for the ITC. For further analyzes, the average was computed between 0.2 and 0.5 s in the frequency range from 3 to 10 Hz (black rectangle). **C** A significantly higher ITC is observed for incorrect trials (average ITC of all conditions). ($n = 25$).

observed that subjects with a higher power peak, reflecting better encoding of the task's overall temporal structure, exhibit faster reaction time and a stronger liberal bias in their decision making, as measured by Criterion C. This suggests that higher degrees of neural entrainment or alignment¹³ to the external task's temporal structure, i.e., its input dynamics, modulates subsequent behavior, i.e., output dynamics.

Following these findings, we asked ourselves about the neural dynamics of such effects of the encoded task periodicity on behavior. We observed increased ITC in subjects with a high peak in their PSD. That suggests that the encoded task periodicity of the input dynamics modulates event related dynamics on the phase level as measured by the ITC. Further, we also observed that the PSD peak modulated information processing as measured by LZC, an index of neural complexity^{15,25,28} was higher during the pre-stimulus than the post-stimulus period²⁹. This suggests a decrease of neural complexity with higher signal compression after stimulus onset. That is in line with various findings of decreased post-stimulus trial-to-trial variability during the post-stimulus period^{29–35}. Extending these findings, we show that such decrease also holds for signal complexity, e.g., LZC. Extending one recent finding about pre and post-stimulus difference in LZC²⁹, we demonstrate that the LZC decrease is negatively related to the degree of the power peak in the PSD with a higher peak leading to lower LZC. This suggests that the better encoding of the task's overall temporal structure, as indexed by a higher power peak, reduces neural complexity through higher degrees of signal compression, e.g., low LZC.

The analysis of behavior revealed that an increase in false alarms (FA) is associated with a faster response time (RT). In simpler terms, a faster RT indicates difficulty in inhibiting responses during rare NoGo trials and may suggest relatively stronger alignment with the temporal task structure. This alignment is substantiated by a significant correlation between the amplitude of the task periodicity peak within the power spectrum and the subjects' RT. Intriguingly, the accuracy of subjects' decision making measured by sensitivity d' does not exhibit a correlation with either RT or the peak in the power spectrum, suggesting that a stronger task alignment does not impact the overall error count but rather influences the type of errors committed, that is the decision making bias as measured by Criterion C. The Inter-Trial Coherence (ITC), a neural measure indexing entrainment¹² or alignment¹³ to the trial structure, yields similar outcomes: higher ITC, indicating greater alignment with the trial structure, correlates with faster response times and an increase in false alarms.

Together, our findings show how different measures of the processing and encoding of input dynamics relate to and shape the output, that is, behavior. The input dynamics as encoded in the PSD peak and the ITC shape both reaction time and decision bias. The same applies to the LZC. This raises the question what connects these different measures across the boundaries of input, brain, and output. Albeit tentatively, we assume that their timescales and thus, more generally their dynamics, connect and differentiate them. The peak of the PSD is measured over the whole task duration without any averaging into event-related activity, this entails a rather long timescale of the whole task duration. While the ITC is measured in the post-stimulus period

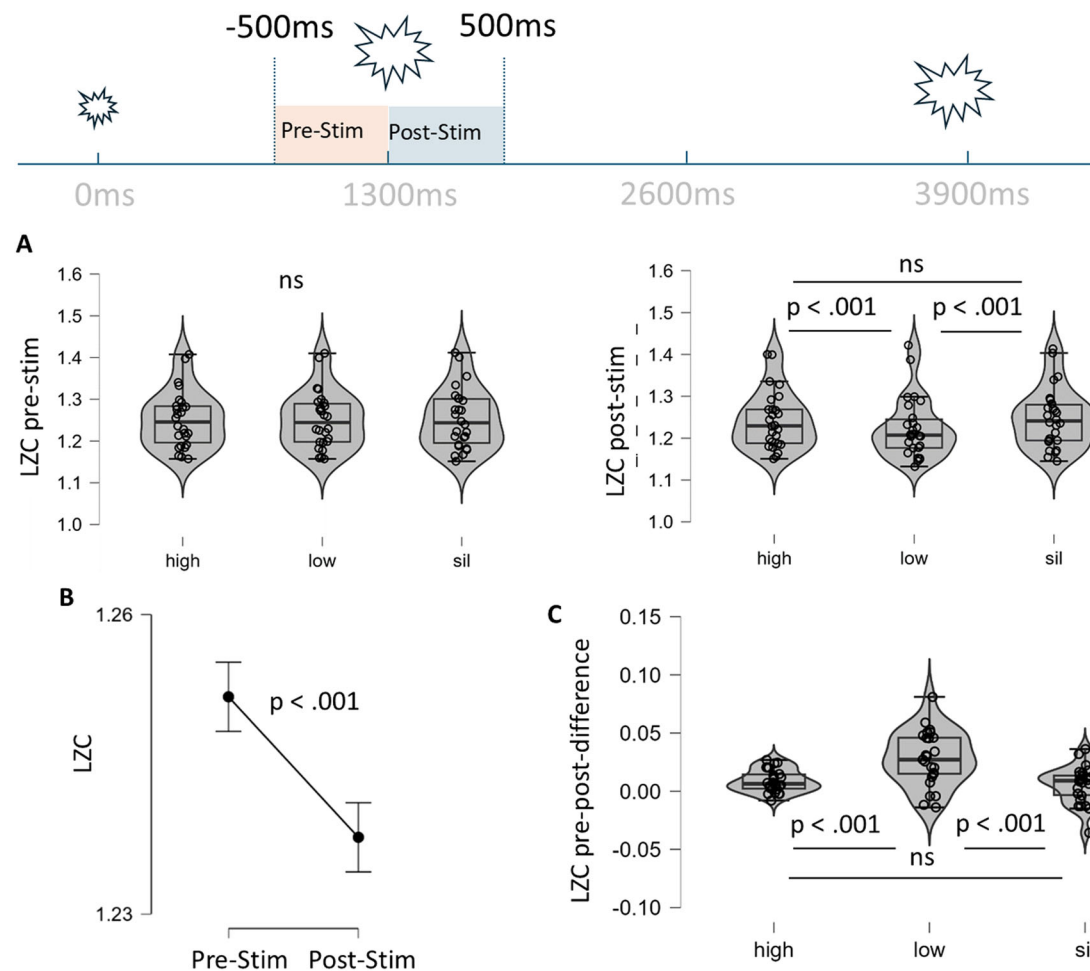
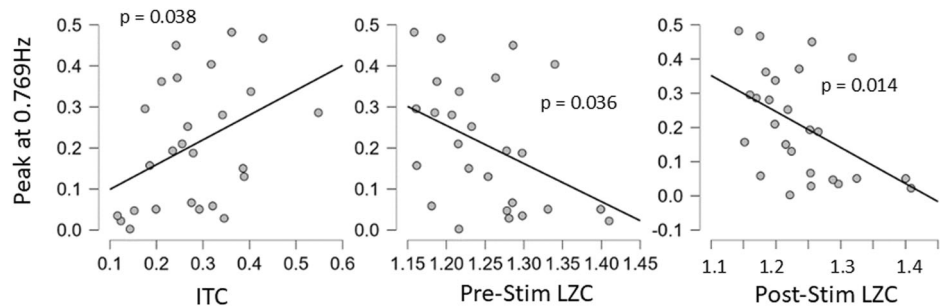


Fig. 5 | LZC. **A** Descriptive plots for pre (left) – and post (right) – stimulus LZC. **B** Pre- and Post LZC comparison, conditions averaged. **C** Pre-Post stimulus LZC difference for each condition. ($n = 25$).

Fig. 6 | Impact of task-periodicity on neuronal dynamics. Impact of task-periodicity on neuronal dynamics (averaged over conditions). A higher peak comes with an increased ITC. Further, a stronger peak is related to a higher degree of compression (pre and post stimulus LZC), indicating a reduction of complexity. The correlation between peak and LZC pre-post stimulus difference was marginally significant and showed that a higher difference might be linked to a higher peak. ($n = 25$).



over the short duration of single repeated and thereby averaged trials. Finally, the LZC takes on an intermediate timescale as measured over the continuum of 500 ms pre-stimulus and post-stimulus periods respectively. Albeit tentatively, our findings support the relevance of the brain's multiple timescales including longer and shorter ones for yielding behavior and decision making. What we observe on the level of behavior as complex amalgam of different timescales in the output dynamics, may be the result of the brain's neural processing of the external inputs' timescales within the inputs, e.g., input dynamics, through its own internal neural dynamics featured by its multiple timescales^{25,35,36}. As evidenced by our results, behavior and cognition may then be strongly shaped by the brain's neural dynamics and its various timescales just as suggested in Spatiotemporal Neuroscience^{37,38} and its Dynamic Layer Model (DLB) of the brain³⁶.

Some limitations of this study shall be mentioned. Even though we can exclude the relevance of motor activity in the task-periodicity power increase due to its variability in occurrence (RT are sometimes faster, sometimes slower, see supplementary Fig. S1), it could be of interest to add a recording of the Go-NoGo task without requiring any motor response. Further, additional studies will be necessary to estimate the impact of different forms of task-periodicity like slower or faster on subsequent behavior. The effect of task-periodicity on the behavior should also be investigated in different task-designs demanding different cognitive functions. Further, refined behavioral analysis may be warranted. For instance, in our case stronger alignment to the task-structure did not impact the number of errors but the type of error (Criterion C). Hence future studies are warranted to

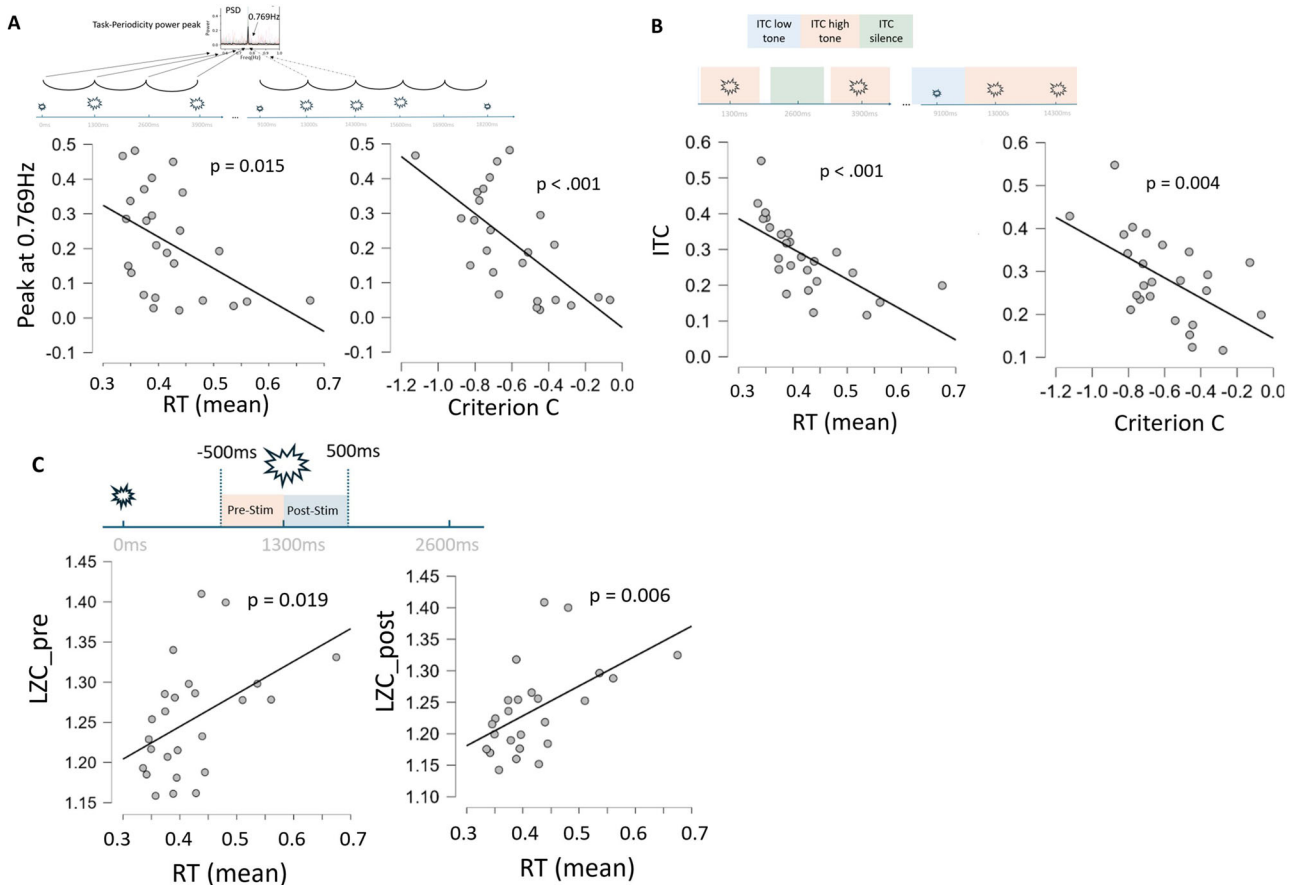


Fig. 7 | Task-periodicity and behavior. **A** Correlation between the peak and behavior. **B** Correlation between the ITC and behavior. **C** Correlation between the pre- and post-stimulus LZC and behavior. ($n = 24$).

investigate the impact of different forms of task periodicity on distinct features of cognition and behavior.

In conclusion, we demonstrate how the neural encoding of the input dynamics like its periodicity into the brain's power spectrum shapes subsequent behavior, e.g., decision making bias and reaction time. This is mediated by neural entrainment, e.g., ITC, and information processing, e.g., LZC, in event related dynamics. Our findings demonstrate direct relationship of input encoding with subsequent output behavior through shared neural dynamics as their “common currency”^{37,38}. This further highlights the key role of the brain's neural dynamics in shaping our behavior and its mental features as suggested in Spatiotemporal Neuroscience^{37,38} and its DLB of the brain³⁶.

Data availability

Data is available on request. Data as plotted in this manuscript and its scripts are available at https://drive.google.com/drive/folders/1hj-LEBXQ-Qb3MSVC0XOZvr6R_kX_IDXf?usp=sharing.

Code availability

Code is available on request.

Received: 30 April 2024; Accepted: 7 November 2024;

Published online: 19 November 2024

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Author contributions

A.W.: data recording, conception, analysis, first draft, revisions, figures; S.L.: revision; L.L.A.: data recording; J.G.: conception; G.N.: Supervision, conception, funding, first draft, revision.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s42003-024-07235-w>.

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Peer review information *Communications Biology* thanks the anonymous reviewers for their contribution to the peer review of this work. Primary Handling Editors: Christian Beste and Benjamin Bessieres.

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<https://doi.org/10.1038/s42003-024-06642-3>

Dynamic mechanisms that couple the brain and breathing to the external environment

Check for updates

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Brain and breathing activities are closely related. However, the exact neurophysiological mechanisms that couple the brain and breathing to stimuli in the external environment are not yet agreed upon. Our data support that synchronization and dynamic attunement are two key mechanisms that couple local brain activity and breathing to external periodic stimuli. First, we review the existing literature, which provides strong evidence for the synchronization of brain and breathing in terms of coherence, cross-frequency coupling and phase-based entrainment. Second, using EEG and breathing data, we show that both the lungs and localized brain activity at the Cz channel attune the temporal structure of their power spectra to the periodic structure of external auditory inputs. We highlight the role of dynamic attunement in playing a key role in coordinating the tripartite temporal alignment of localized brain activity, breathing and input dynamics across longer timescales like minutes. Overall, this perspective sheds light on potential mechanisms of brain-breathing coupling and its alignment to stimuli in the external environment.

Oscillations in breathing are linked to oscillations in neural activity^{1–6}, arousal^{7–12}, and cognitive function^{13–18}, although the exact mechanisms have not been agreed upon. Our perspective paper highlights two mechanisms in the coupling of the brain, breathing, and external inputs from the environmental context. First, reviewing recent literature, we show that synchronization is key in directly connecting brain and breathing activity across shorter timescales from milliseconds to seconds. This includes different facets of synchronization like coherence, cross-frequency coupling, and entrainment. Then, using breathing and EEG data recorded in a small sample of subjects ($N = 21$), we demonstrate a temporal alignment of EEG data at the Cz electrode and breathing to the speed and variability of external inputs across longer timescales like minutes. Specifically, the data show that the input temporal structure manifests in corresponding temporal changes in the power spectra of both brain and breathing leading to their increased synchronization at specifically the intertrial interval of the task.

We describe the phenomenon of specific power spectral adaptations as dynamic attunement which can be seen as a subset mechanism of the more general feature of temporospatial alignment¹⁹. Dynamic attunement, taken in the present context, describes the adaptation of the temporal structure of both neural and respiratory activities to the temporal structure of the input over longer periods of time like minutes. The tight link between the temporal

structures of both brain activity at the Cz channel and breathing with one of the external inputs suggests that the dynamics themselves (i.e., the complex temporal properties of signals and inputs across shorter and longer timescales) may provide the direct connection between the brain, breathing, and the environment.

Results

Mechanism one—synchronization of brain and breathing

Emerging evidence suggests that breathing and brain activity may be synchronized with each other at relatively short timescales, for instance, at the level of the millisecond-to-second^{3,20,21}. To underscore the robustness of these effects, we review evidence from the current literature in humans that aligns with data first discovered in animal models. Cross-species representation of these mechanisms is crucial as it implies the fundamental and intrinsic nature of the coupling between activity in the brain and lungs.

Oscillations in breathing activity are coupled to oscillations in neural activity within the same frequency range (see ref. 22 for a recent review). In 1942, Edgar Adrian was the first to show breathing-synchronous oscillations in the local field potential of the olfactory bulb in the hedgehog²³. Further experiments have revealed that these oscillations are present in other species. For instance, coherence between breathing and neural time series was

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demonstrated by Ito et al., 2014. The authors mounted intracranial recording devices to the somatosensory whisker barrel cortices while simultaneously monitoring breathing. The authors reported that oscillations in the local field potential (LFP) within the delta band (1–4 Hz) were phase-locked to the breathing cycle²⁴ (see ref. 25 for a review).

Research in this field has since made the jump to human models. For instance, Herrero et al.²⁶ used intracranial recordings and cross-spectral analysis of resting-state breathing and brain data to demonstrate a high degree of brain-breathing coherence across a widespread network of cortical (i.e., prefrontal, parietal, cingulate) and limbic regions (i.e., amygdala, insula, hippocampus) in the slow cortical potential range (i.e., 0.1–1 Hz). The authors indicated that the highest peak in the neuronal power spectrum in frequencies analyzed between 0–1 Hz occurred precisely at the breathing rate²⁶. Collectively, these findings suggest that the lungs and the brain couple their activity across relatively short timescales (i.e., at the level of the second-to-millisecond) through the synchronization of their slow wave activities (see Fig. 1).

Given the direct coupling of breathing and brain activity in the same frequency range, a logical progression is to ask whether breathing's slow frequency activity is also related to the activity of the brain in faster frequency ranges. In the context of breathing, it has been demonstrated that different breathing speeds (slow or fast) yield vastly different mental effects. For instance, periods of slow breathing have been demonstrated to promote feelings of general wellbeing^{27–29} while periods of faster breathing tend to increase feelings of anxiety^{29–33}. The coupling of breathing speeds to a wide range of mental effects suggests that characteristics of the breathing waveform may be directly coupled to a multitude of frequencies in the brain^{34–37}.

To examine the relationships between two oscillators at different speeds, researchers analyze how the phase of the slower oscillator relates to the phase, frequency, or amplitude of faster ones^{38–40}. Ito et al.²⁴ provided evidence using mice for cross-frequency coupling between breathing and brain time series. The authors demonstrated that the amplitude of local field potentials in the gamma frequency band (30+ Hz) changes in tandem with the breathing phase with bursts of activity occurring during the early part of breathing exhalation. Using similar cross-frequency models, Tort et al., 2021 showed that breathing rate strongly correlates with the neural peak frequency and amplitude of gamma oscillations (30+ Hz). The phase locking of breathing to higher-order frequency ranges in the brain has also been shown in work by Cavelli et al., 2018 who demonstrated in cats that the beginning of exhalation was associated with bursts of gamma activity within a widespread network of regions (i.e., olfactory bulb, prefrontal cortex, and parietal cortex; see ref. 41 and see Fig. 1).

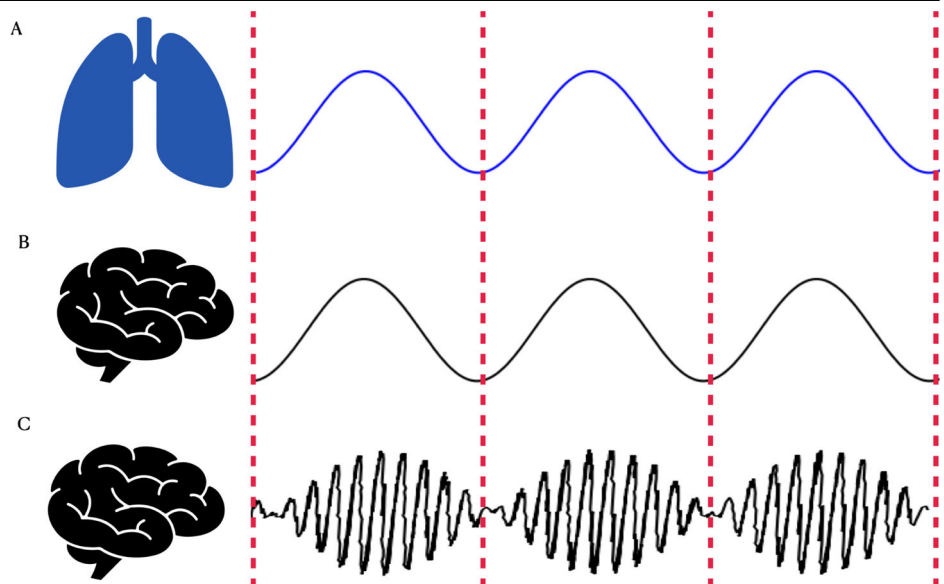
Cross-frequency coupling between breathing and brain activity has been replicated in humans. For instance, Herrero et al.²⁶ reported bursts of neural gamma activity in the hippocampus tended to occur during the early part of the breathing exhalation. Cross-frequency coupling between breathing and neuronal time series extends beyond the gamma band. For example, Kluger and Gross¹ used magnetoencephalography (MEG) resting state brain data from human participants while breathing was simultaneously recorded—their goal was to investigate whether breathing in the frequency range of 0.1–0.3 Hz is related to the amplitudes of neuronal activity in the 2–150 Hz frequency range. Kluger and Gross's results indicate the relationship between breathing and neural oscillations is significant across all commonly measured neural frequency ranges (i.e., delta, alpha, beta, and gamma) and is widely distributed across the brain. Collectively, these findings indicate that the brain and breathing coordinate their activities at relatively short timescales using synchronization as indexed by coherence and cross-frequency coupling.

Mechanism two—the dynamic attunement of brain and breathing to external input streams in a small dataset

The relationship between breathing and brain signals interacts across all frequencies (0–30+ Hz; see section 2.0). This leads us to wonder if external factors including their specific frequencies can influence the patterns of brain-breathing coupling for instance previously demonstrated with auditory^{42,43} and visual stimuli^{44,45}. The influence of external factors on bodily rhythms has been described as 'alignment' which, roughly, refers to how the brain's neural activity or the lungs' respiratory activity adapts their temporal structure to one of the external input streams like their power spectra, speed and variability¹⁹.

Alignment between systems and stimuli operates on multiple timescales, from shorter to longer ones¹⁹. Presupposing a very short timescale, a single external event can lead to a synchronized change in the wavelength and phase angle of an oscillating system at the moment the event occurs. However, without repeated input, the system will return to its intrinsic oscillatory activity, a process known as "resetting"⁴⁵. Resetting has been observed in the brain and breathing in response to a variety of stimuli, including sensory, cognitive, and somatic stimuli^{44–46} (for a recent review see ref. 47). The alignment to a sequence of rhythmic stimuli (i.e., at a slightly longer timescale) is described as entrainment. Entrainment is described as when neural activity synchronizes its wavelength and phase with the timing of external stimuli⁴⁵ (see Fig. 2). Entrainment, therefore, may indicate that dynamical features of the input itself may play a key role in shaping the activity within bodily oscillators such as the lungs or brain^{19,48–50}. In essence,

Fig. 1 | Illustration of brain-breathing synchronization at shorter timescales. Panels (A) and (B) illustrate coherence between brain and breathing activity in the same frequency range as demonstrated by Ito et al. and Herrero et al.^{24,26}. Panels (A) and (C) illustrate cross-frequency coupling between faster frequency activity of the brain and breathing.



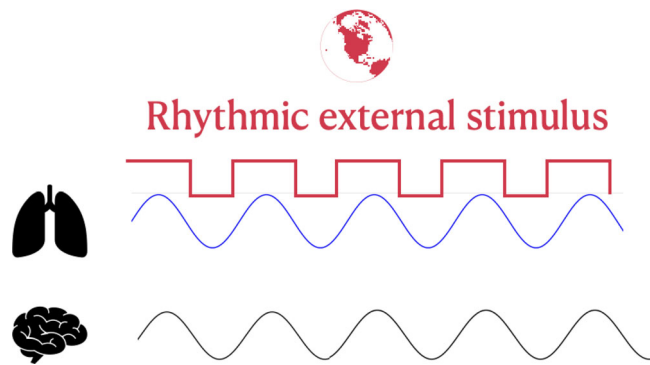


Fig. 2 | Illustration of entrainment. Entrainment results in stable wavelength, phase, and amplitude synchronization through a series of rhythmic phase resets. As entrainment is measured across a sequence of multiple external inputs, entrainment links breathing and brain activity to external inputs on a longer timescale than a phase reset.

by examining the dynamic changes between bodily signal temporal characteristics (i.e., in the power spectra) and the corresponding attributes of the inputs like their respective frequency ranges, we can gain insight into the system's overall adaptability and flexibility toward the inputs' dynamics.

The breathing rhythm has the remarkable capacity to adapt to different environmental contexts over shorter and longer timescales. For example, during the physical act of running fast, breathing also becomes fast⁵¹. Coupling between breathing and rhythmic inputs has also been shown in more complex situations, for instance when listening to music, dancing, or playing an instrument^{42,52,53}. Here the coupling occurs over longer timescales lasting several minutes if not longer. The observed alignment of the breathing waveform and various internal and external rhythms raises the question of the neural mechanisms that enable the alignment of the lungs and brain to the environmental context over longer timescales. To distinguish such alignment on a longer timescale from the ones operating on shorter timescales (i.e., synchronization), we coin the term 'dynamic attunement'.

Together, the remarkable adaptability and flexibility of both brain and breathing to their respective environmental context seem to operate over different timescales. These may include shorter ones as in phase reset in response to single stimuli, intermediate ones like in entrainment of the phase in response to multiple repeated stimuli, and longer timescales operating across several minutes if not hours (see ref. 54 in fMRI). Our focus here is on the last one, the longer timescales, namely dynamic attunement. The main question is how both the brain and lungs adapt the temporal structure of their activities to that of the inputs over longer periods. We now present breathing and EEG data supporting exactly this coupling of the brain, breathing, and inputs over a longer timescale, that is, dynamic attunement.

Twenty-one participants ($N = 21$) underwent 5 min of resting state and a go/no-go task where they were asked to respond to auditory inputs by pressing a key (see supplemental material for full details about the methods). Breathing data acquired using a pneumatic belt at the level of the diaphragm, and EEG activity at the Cz channel, due to its relevance for auditory processing⁵⁵, were compared during rest and task states to quantify local brain-breathing coupling and its dynamic attunement to external stimuli. As indicated above, dynamic attunement refers to the adaptation of the temporal structures of both neural and respiratory activities to one of the inputs themselves over longer periods like multiple minutes entailing alignment over a longer timescale (as distinguished from the shorter timescales of entrainment and even shorter of a "reset").

Using EEG data from the Cz electrode and corresponding breathing data, we explore how localized neural activity may align with breathing in response to rhythmic stimuli. Our data showed that both breathing and neural signals were dynamically attuned to the temporal structure of the external stimuli by both showing power spectra peaks in exactly that

frequency range in which the external stimuli were presented. Accordingly, the findings support localized brain-breathing attunement to the longer-term temporal structure of the external stimuli as evidenced by specific changes in their power spectrum (PSD). This is supported by increases in the amount of coherence between breathing and EEG time series at the Cz electrode during the task relative to the resting state.

To quantify the effect of the task on breathing at the group level, we compared traditional breathing signal metrics such as breathing rate (breaths per minute; bpm), variability (standard deviation of the breath-to-breath intervals in milliseconds; SDBBI) and phase lengths (inspiration and expiration in seconds; s) between rest and task conditions. Significant changes in these signal characteristics would indicate adaptations of the breathing rhythm to the external input.

There was a significant increase in breaths per minute during the task ($M = 20.28$, $SD = 3.55$) as compared to the resting state with a large effect size. ($M = 14.34$, $SD = 3.91$; $z = 3.841$, $p < 0.001$, *matched rank biserial correlation* = 0.957). Consequently, significant reductions in inspiration phase lengths were also observed during the task ($M = 1.14$, $SD = 0.27$) as compared to the resting state with a large effect size ($M = 1.83$, $SD = 0.74$, $z = -3.841$, $p < 0.001$, *matched rank biserial correlation* = -0.957). In a similar fashion, expiration phase lengths significantly decreased during the task ($M = 1.73$, $SD = 0.31$) as compared to resting conditions with a large effect size ($M = 2.59$, $SD = 0.85$, $z = -3.702$, $p < 0.001$, *matched rank biserial correlation* = -0.922); see Fig. 3).

Given the correspondence in the temporal structure of breathing with that of the external input streams, we next investigated the effects of the task on breathing variability. If the breathing is indeed modulated by the durations of the external tones' intertrial intervals, one would expect a decrease in breathing variability during task states. To quantify the effect of the task on breathing variability, we compared the average variability of the breath-to-breath intervals between rest and task conditions. Results indicated a significant reduction in the standard deviation of the breath-to-breath intervals during the task ($M = 551.35$, $SD = 302.44$) as compared to the resting state ($M = 1429.78$, $SD = 781.27$); $z = -3.597$, $p < 0.001$, *matched rank biserial correlation* = -0.896; see Fig. 3). Collectively, an increase in breathing speed and a simultaneous reduction in its variability indicates a temporally organizational effect of the task's periodic structure on the breathing rhythm.

It is worth noting that inspiration and expiration phase lengths approached the intertrial interval of the task (1.3 s; see Fig. 3 and Fig. 4). To illustrate the alignment of inspiration and expiration phase lengths to the intertrial interval of the task, we have included a visualization of the changes in the distribution of inspiration and expiration times across participants for each condition. Results indicate that participants' inspiration and expiration phases approach 1.3 seconds in length during the task state (see Fig. 4).

In addition, F-tests revealed significant decreases in intersubject variability in the SDBBI ($F(20,21) = 6.67$, $p < 0.001$), inspiration ($F(20,21) = 7.43$, $p < 0.001$), and expiration times ($F(20,21) = 7.46$, $p < 0.001$) were observed in the task as compared to the rest conditions (see Figs. 3, 4). A decrease in the overall distance between subjects during the task compared to rest conditions further supports the temporal alignment of breathing to the external input.

We next raised the question of direct temporal correspondence of the breathing rhythm during the task state by investigating whether the intertrial interval of the task is directly reflected in an analogous temporal structure in the breathing pattern, e.g., in its power spectrum. For that, we recalculated the 1.3 s intertrial intervals as a frequency amounting to 0.769 Hz. To quantify the adaptation of specific temporal characteristics, we compared the size of the power peak at exactly the stimulus presentation frequency (1.3 s = 0.769 Hz) in the breathing power spectrum between rest and task conditions. Results indicated a significant increase in the power peak at 0.769 Hz during the task ($M = 0.029$, $SD = 0.077$) as compared to the resting state ($M = 0.002$, $SD = 0.002$; $z = 3.389$, $p < 0.001$, *matched rank biserial correlation* = 0.844). This large effect size indicates a substantial difference between the two conditions.

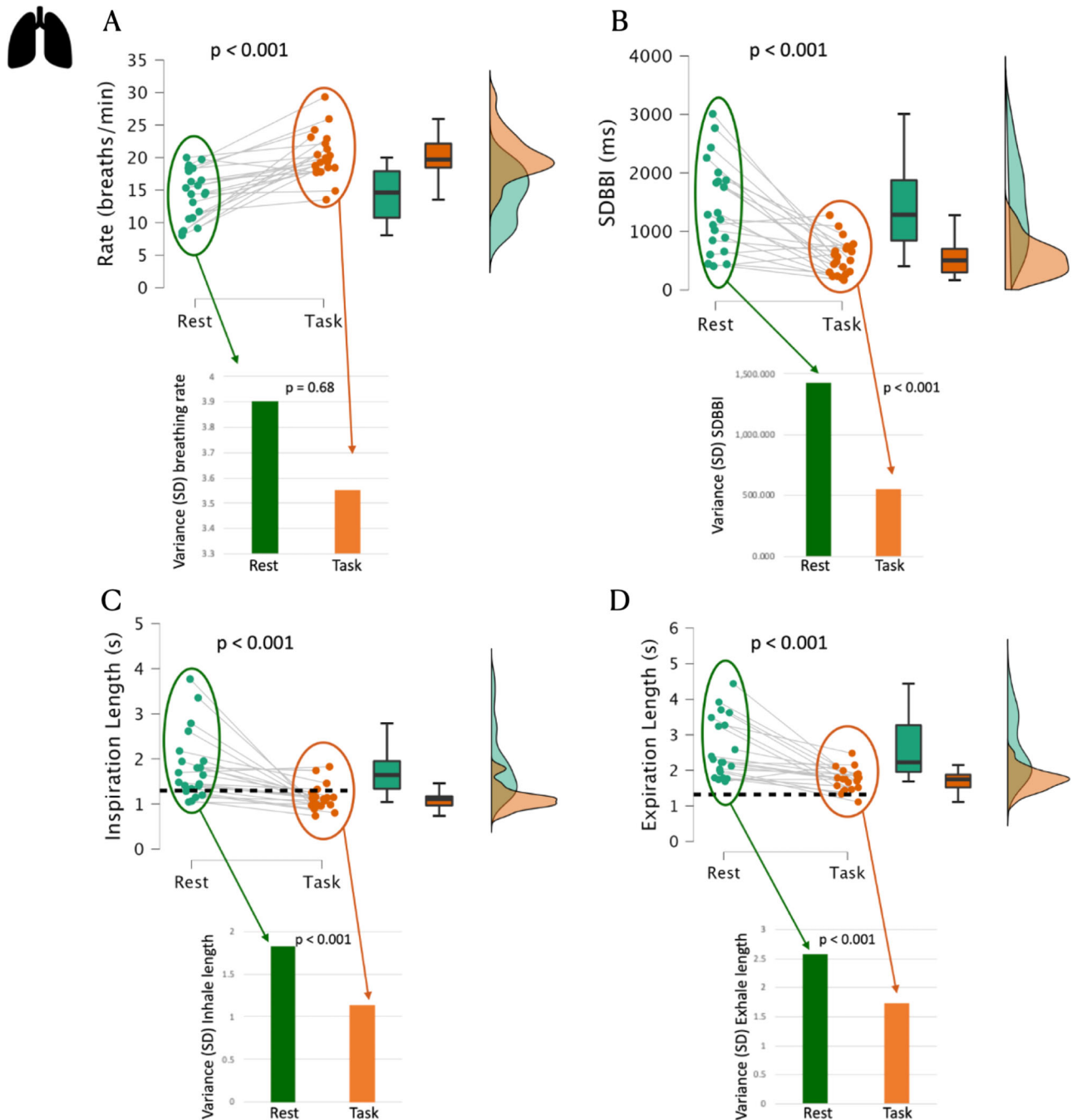


Fig. 3 | Breathing metrics were collected during rest and task conditions ($N = 21$). Results indicate an overall faster (A) and less variable (B) breathing rhythm in the task relative to the resting state. In (C, D), the black dotted line indicates the exact intertrial interval of the task condition (1.3 seconds). Inspiration (C) and expiration times (D) tended to align themselves with these timings. Statistical measures above bar plots indicate results from F-tests. Results indicate significant decreases in the

group variance of the SDBBI, inspiration, and expiration phase lengths during the task compared to resting conditions. A lower amount of intersubject variability during task states indicates that the breathing rhythm shapes itself to match the temporal structure of the external input. SDBBI = standard deviation of the breath-to-breath intervals. Error bars represent the 95% confidence interval.

Together, reductions in breathing variability and increases in the breathing power spectrum at exactly the stimulus presentation's frequency indicate an overall dynamic attunement of the breathing's temporal structure to the temporal structure of the external stimuli (i.e., input dynamics).

Given the tight link between breathing and brain activity, one may expect these systems to adapt similarly in their responses to external stimuli. To quantify if the brain adopts specific temporal characteristics of the task,

we compared the size of the power peak at exactly the stimulus presentation frequency (1.3 seconds/0.769 Hz) in the neuronal power spectrum at the Cz channel between rest and task conditions.

Results indicated a significant increase in the power peak during the task (see Fig. 5; $M = 0.480$, $SD = 0.367$) as compared to the resting state with a large effect size ($M = 0.016$, $SD = 0.031$; $z = 4.015$, $p < 0.001$, *matched rank biserial correlation* = 1.00). To investigate this phenomenon further, we computed several additional analyses. First, we checked if the total power

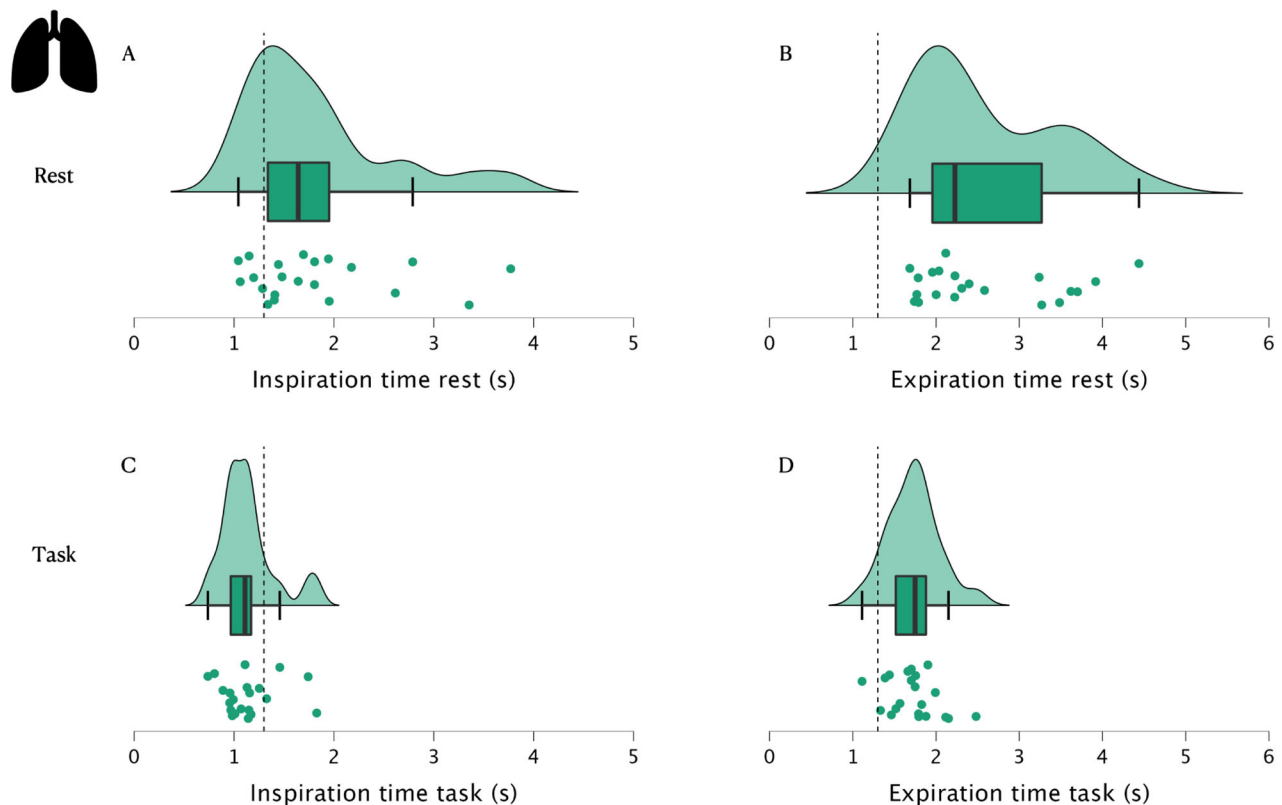


Fig. 4 | Visualization of the differences in the distributions of inspiration and expiration times between rest and task. Panels (A) and (B) represent the rest condition and panels (C) and (D) represent task conditions across participants ($N = 21$). Black dotted lines represent the intertrial interval of 1.3 s (0.769 Hz).

Results indicate that participants' inspiration and expiration times group themselves around the intertrial interval of the task (1.3 s). Error bars represent the 95% confidence interval.

between rest and task changed. Indeed, the task state increased the total power for breathing with a large effect size ($z = -2.242$, $p = 0.024$, *matched rank biserial correlation* = 0.558) and brain ($z = -3.458$, $p < 0.001$, *matched rank biserial correlation* = 0.861) significantly. In this case, is the power peak observed during the task of relevance or could it stem simply from a general increase in power? To answer this question, we computed the ratio between the peak and the total power. Again, we can observe a clear increase in the ratio from rest to tasks in breathing ($z = -2.597$, $p < 0.001$, *matched rank biserial correlation* = -0.896) and brain with large effect sizes ($z = -4.015$, $p < 0.001$, *matched rank biserial correlation* = 1).

To make sure that the power increase observed during the task state is not due to increased motor activity, motor artifacts in all EEG recordings were removed via independent component analysis prior to analyses (see supplemental section 2.1.4 for details on data acquisition and preprocessing). Then, we plotted the response times for each subject over the total duration of the Go-NoGo task. We observed a high inter- and intra-subject variability in response times which do not add up to one specific frequency (see supplemental figure S1 for detailed results). These results suggest that the power peak increase at 0.769 Hz observed during the task in both the brain and breathing is likely to be induced by the dynamic attunement of the Cz channel and breathing to the temporal structure of the task rather than being related to some unspecific factor.

Finally, we investigated if the difference in the peak between rest and task is solely related to an increase in the mean or also via an increased intersubject variability. The F-test to compare two variances is significant for breathing ($F(20,21) = 1001.5$, $p < .001$) and EEG ($F(20,21) = 146.5$, $p < 0.001$), showing a higher intersubject variance of the peak during the task than rest.

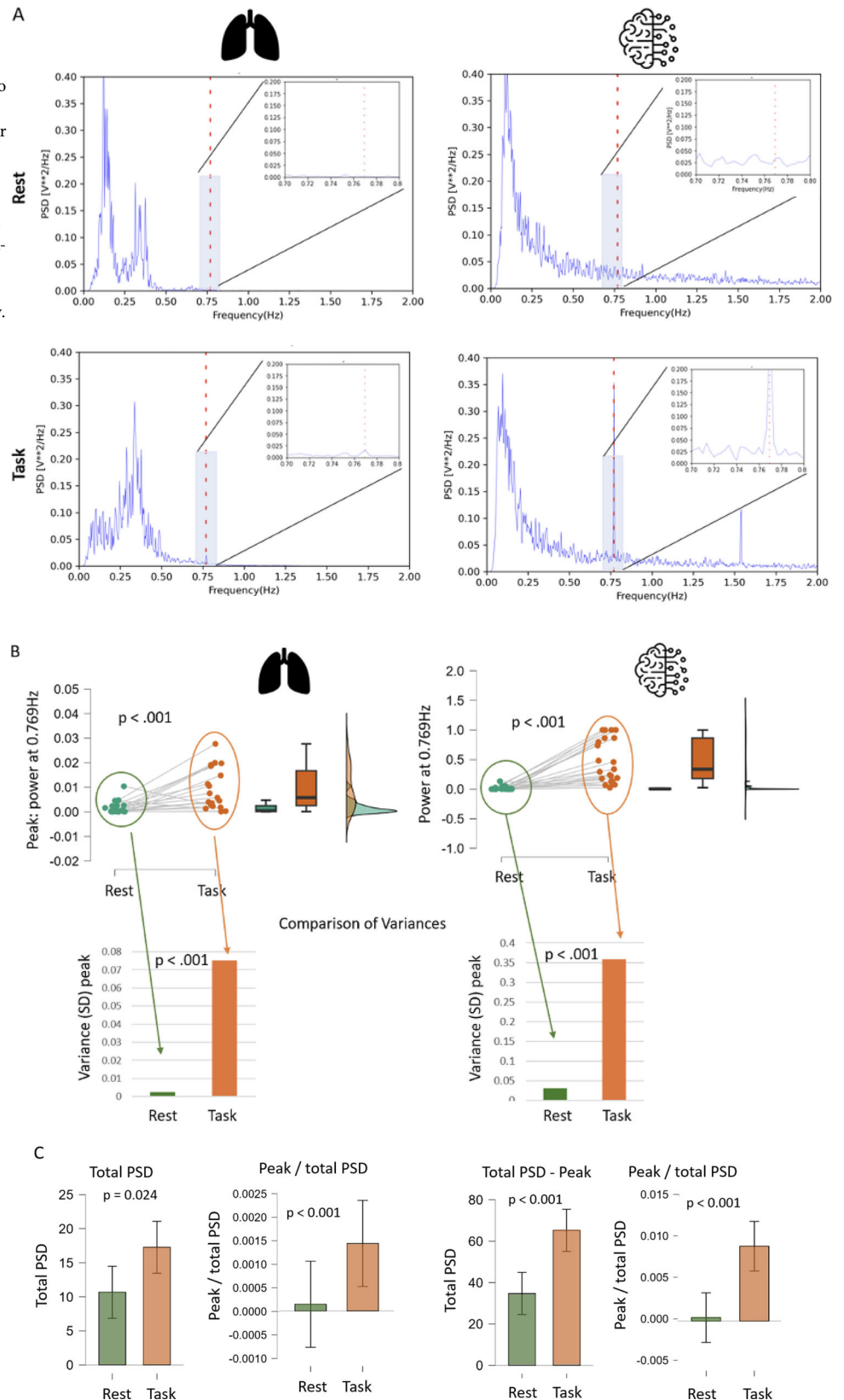
We observe a statistically significant increase in the power spectra of both neural and respiratory activity at exactly the stimulus presentation frequency of the task. As both the Cz channel and breathing show this

periodicity power peak at 0.769 Hz, we hypothesize that a higher degree of synchrony might exist between the Cz channel and breathing in the task than in the rest. To test for this, we computed the coherence between breathing and the Cz channel. A higher degree of coherence would indicate a higher degree of synchronization. Indeed, in Fig. 6, we observe a higher coherence at 0.769 Hz in the task ($M = 0.256$, $SD = 0.150$); than in rest ($M = 0.098$, $SD = 0.097$) with a large effect size ($z = 3.08$, $p = 0.001$, *matched rank biserial correlation* = 0.766).

Finally, we calculated phase-amplitude coupling via the modulation index between breathing and the Cz channel using a previously validated approach^{56,57}. The breathing activity was filtered between 0.5–1 Hz, which is exactly the range including the task's frequency. The neural activity was filtered between 1–4.5 Hz (a higher frequency was not possible due to the low sampling rate of the breathing data—see Methods). A higher modulation index was found in the task ($M = 0.458$, $SD = 0.253$) than in rest ($M = 0.318$, $SD = 0.200$) with a large effect size ($t(20) = 2.27$, $p = 0.034$, $d = 0.495$; $z = 2.033$, $p = 0.042$, *matched rank biserial correlation* = 0.506) which suggests a higher degree of phase amplitude coupling between breathing and the brain during the task compared to the rest. Scaled values for the modulation index are presented in Fig. 6b and raw values can be found in the supplemental information (see supplemental information for a link to the Figshare repository).

Together, our analysis shows evidence of mutually shared information on breathing and localized brain activity patterns including their modulation by the external task periodicity. Hence, it may be the case that neural and respiratory systems adapt the dynamics of their activity in similar ways to the dynamics of inputs in their environment. This suggests that dynamics may provide the direct connection between the brain, breathing and environment over longer timescales, so-called “dynamic attunement”.

Fig. 5 | Visualization of dynamic attunement.
A Power spectrum of respiration and EEG signals averaged across participants ($N = 21$). For the breathing, we observe an overall shift from slower to faster frequencies in task versus resting state conditions. A zoom-in to the light blue shaded area for each subject can be found in the supplemental material. **B** In both breathing and brain, a larger peak is found at the rate of stimulus presentation (0.769 Hz, exact frequency indicated by red dotted line) during the task indicating the presence of task-dependent entrainment (i.e., task periodicity). **C** Total PSD and peak to total PSD ratio for breathing and brain. PSD = power spectral density. Error bars represent the 95% confidence interval.



Discussion

Our main aim of this work was to assess the mechanisms that couple breathing and brain activity to the external environment over shorter and longer timescales. In addition, we sought to investigate whether their activities are coordinated with the input dynamics of external stimuli.

Using existing literature in combination with our data set, our investigations have revealed two potential mechanisms (i.e., synchronization and dynamic attunement) in the coordination of brain activity at the Cz channel and breathing with the environment across shorter and longer timescales.

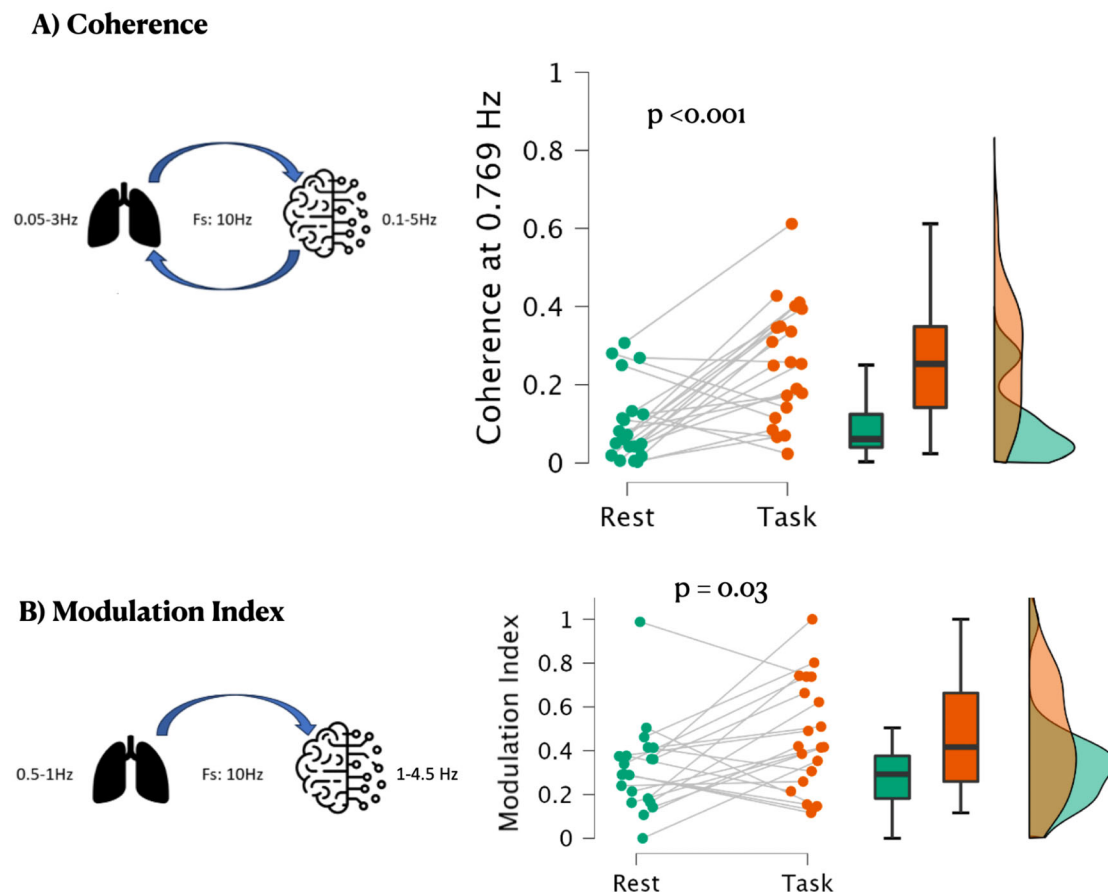


Fig. 6 | Breathing-brain coupling is shaped by the external environment. Synchronization of brain and local breathing to the external temporal stimulus pattern ($N = 21$). **A** Increases in brain-breathing coupling during task conditions are indicated by the increase in coherence at precisely the intertrial interval of the task (i.e., 0.769 Hz). **B** Synchronization of the breathing activity with faster frequencies in the brain. Increases in brain-breathing coupling during task conditions are further

supported by increases in the modulation index. Higher degrees of coherence and modulation indices between breathing and the Cz channel during task conditions suggest that the external task dynamics impact the brain-breathing coupling relationship. Error bars represent the 95% confidence interval.

First, reviewing the literature, we reveal that the lungs and brain exhibit high degrees of coherence in the 0–1 Hz frequency band (see refs. 17,22 for recent reviews). In addition, breathing (0.1–0.3 Hz) shows a high degree of phase-amplitude coupling with faster frequencies in the brain for instance in the gamma band (see refs. 25,39 for reviews). We next asked the question of whether external factors can influence the patterns of brain-breathing coupling for instance as seen with music⁴². Our review of the data shows that the breathing and brain rhythms adapt their activities to the temporal structure of the external input. This can occur over shorter timescales as in phase reset in response to single stimuli as well as over slightly longer timescales with repeated external stimuli for instance as seen in the case of entrainment⁴⁵. Together, these findings support that the brain and breathing may couple their activity together across shorter timescales using various facets of synchronization.

Our first mechanism, namely synchronization, facilitates alignment of the brain and breathing over shorter timescales at the level of the millisecond to a few seconds^{25,26,34,39,41,58}. This, as we would say, reflects the alignment of the brain and breathing at a relatively short timescale, that is, the time point of their mutual synchronization with external stimuli. As described in the previous paragraph, with repeated input the data show that synchronization of brain and breathing can also occur across different timescales for instance seen in the case of entrainment⁴⁵. The coordination of brain and breathing within and across multiple timescales suggests a key role of synchronization in the temporal alignment of brain and breathing over shorter timescales (i.e., milliseconds to several seconds).

This suggests that their rhythmic activity does not occur in isolation but, rather, may be intrinsically connected.

We have so far focused on brain-breathing-environmental coupling at shorter timescales like milliseconds to seconds while leaving open the question of how the brain, breathing, and environmental coordination extend over longer durations like minutes or longer⁵⁴. Our data show that participants' physiological rhythms adopt specific temporal characteristics after several minutes of task engagement. Notably, spectral analysis of breathing and brain activity at the Cz channel demonstrates a significant increase in power peak precisely aligned with the intertrial interval of the task (1.3 s/0.769 Hz; see Fig. 5 and Supplemental Fig. S2 for individual subject results). The existence of a trilateral relationship in the temporal structures of localized brain activity, breathing, and the external inputs is further supported by the observed higher amounts of coherence between the Cz channel and breathing at 0.769 Hz during the task as compared to the resting state (see Fig. 6). The temporal alignment of neural signals and breathing after undergoing several minutes of the task suggests dynamic attunement facilitates coordination of the brain, breathing, and environment across longer timescales like minutes or potentially even longer.

The temporal alignment of brain activity at the Cz channel and breathing with external inputs over shorter and longer timescales suggests a potential bridge between the body and the environment. Such intricate temporal coordination may play a pivotal role in navigating complex environmental contexts over shorter and more extended periods of time, influencing behavioral outcomes (see Fig. 7). Our data support that

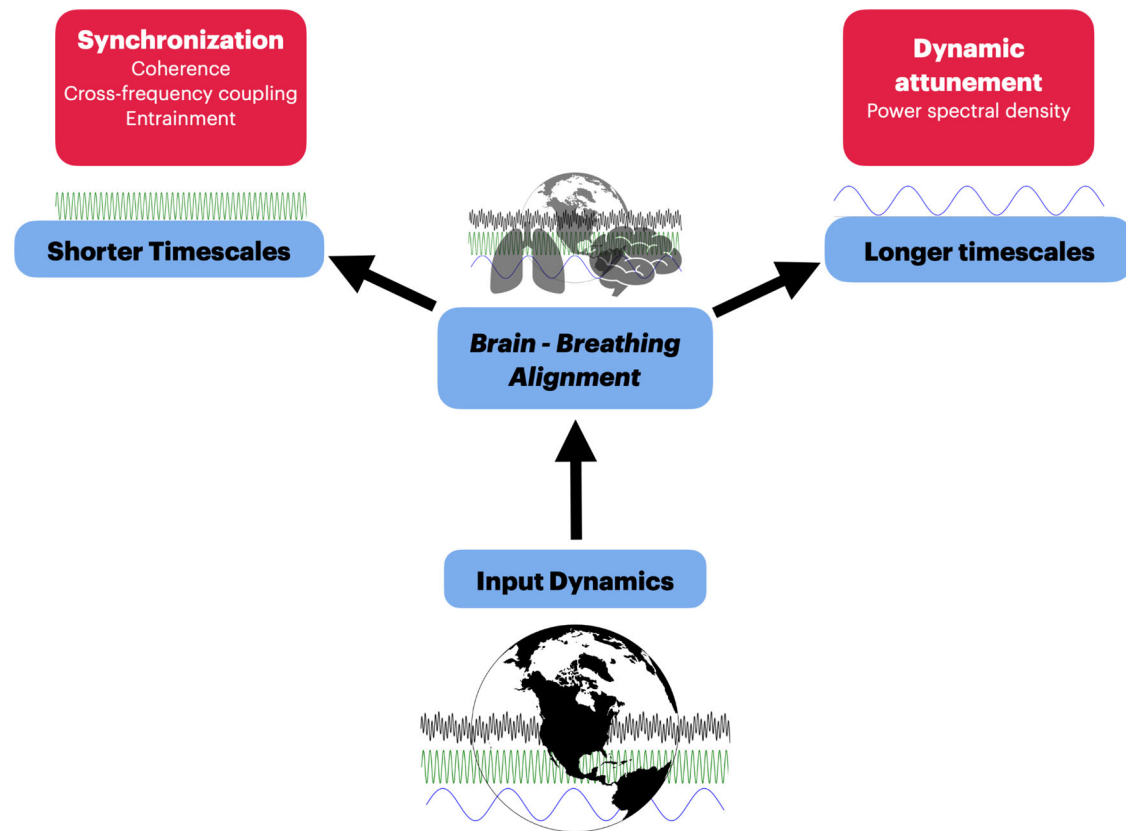


Fig. 7 | Summary of findings. Overall, our findings support two dynamic mechanisms of brain-breathing alignment. First, we show that the lungs and brain synchronize their activity with one another over shorter timescales like milliseconds or seconds as evidenced by coherence, cross-frequency coupling, and entrainment. Second, operating over longer timescales of minutes if not hours, our empirical data suggest that the temporal structure of the environmental inputs shapes the temporal structure of the activities within both lungs and brain activity at the Cz channel. This is indicated by the frequency-specific adaptations in their power spectrums to the exact frequency of the intertrial interval of the task (i.e., dynamic attunement). Dynamic attunement describes a form of alignment in which the lungs and brain adapt the temporal structure of their

activities like in their power spectra to the specific temporal characteristics of the external environmental inputs. Brain-breathing dynamic attunement is further supported by the increase in coherence between the lungs and brain at 0.769 Hz during the task which indicates their common alignment to a shared third party (i.e., the input dynamics). Hence, the observed increases in the amounts of synchrony between the lung and local brain activity during task states, coupled with the increases in their power peak at the exact intertrial interval of the task, suggest that there is a threefold alignment of neural activity, breathing and environment through their timing with dynamics being shared among them as their “common currency”^{59,60}.

dynamical features are shared among localized brain activity, breathing, and environmental stimuli. This allows crossing their internal-external divide by dynamics as their shared feature (i.e., as their “common currency”^{59,60}).

While these data offer valuable insights, the modest sample size in the empirical section of the paper may limit the generalizability of our findings. In addition, we focused on neural activity at the Cz electrode due to its implication in auditory processing⁵⁵. This approach captures localized brain responses that may not be reflective of broader neural dynamics across the entire brain. This limitation restricts our ability to generalize findings to other brain regions and functions. Moreover, while we have provided an overview of the interactions between breathing and local brain activity in response to external auditory inputs, a key feature missing in this work is a link to behavioral outcomes. Future investigations should aim to bridge the gap between the described neurophysiological mechanisms and observed behavior by comparing how the input (the stimulus) directly relates to the output (the behavior) as mediated by what is in between (the physiology).

More specifically, future studies should employ methods that relate how the dynamics of the behavior, e.g., the output, directly relate to the dynamics of the stimulus, e.g., the input, as mediated by the dynamics of the body’s physiology in a given frequency range, e.g., brain and breathing. The elucidation of these techniques may provide key insights into the exact mechanisms by which neurophysiological features of brain breathing coupling are related to behavior.

Conclusion

In conclusion, combining review and empirical data, we demonstrate two potential mechanisms operationalized across different timescales, in coordinating local brain activity at the Cz electrode and breathing as well as their alignment to external inputs. The first mechanism, operating on shorter timescales from milliseconds to seconds, concerns the synchronization of the brain and breathing in terms of coherence, cross-frequency coupling and entrainment. The second mechanism operates over longer timescales from several minutes or potentially even longer and thereby refers to what we describe as dynamic attunement.

Together, these observations attribute a key role of dynamical properties in directly connecting three systems (i.e., brain, lungs and the environment) that, in their timescales, are thought to be very different. Hence, albeit tentatively, we suppose that dynamics are shared by the brain, breathing and environment across shorter and longer timescales providing their “common currency”^{59,60}. Our findings enhance the understanding of brain-breathing coupling in response to external inputs framing their mechanisms including their potential relevance for behavior in terms of “Spatiotemporal Neuroscience”^{59,60}.

Finally, if linked to behavior and cognition in the future, the mechanisms of brain-breathing environment coupling could carry major clinical implications for mental and cognitive disorders where the subjects’ alignment to their respective environmental contexts is severely

compromised⁶¹. Hence, our proposed view of brain-breathing-environment coupling in terms of dynamics featured by and operating across different timescales may allow for novel diagnostic and therapeutic opportunities in the future.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The raw dataset used for analysis during the current study is available from the corresponding author upon reasonable request. The source data underlying Figs. 3,4,5, and 6 can be found in the following Figshare repository <https://doi.org/10.6084/m9.figshare.25429780.v3>

Code availability

The code used for analysis during the current study is available from the corresponding author upon reasonable request.

Received: 14 November 2023; Accepted: 26 July 2024;

Published online: 03 August 2024

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Acknowledgements

This project was supported by an NSERC Discovery Grant (DGECR-2022-00309) and a Canada Research Chair (Tier II, CRC-2020-00174) to JAEA. This project was supplied with equipment for data acquisition by GN (European Union’s Horizon 2020 Framework Program for Research and Innovation No. 785907; Human Brain Project SGA2). GN is also grateful to CIHR, NSERC, and SSHRC for supporting his tri-council grant from the Canada–UK Artificial Intelligence (AI) Initiative The self as agent–environment nexus: crossing disciplinary boundaries to help human selves and anticipate artificial selves’ (ES/T01279X/1) (together with Karl J. Friston from the UK).

Author contributions

J.G. — Conceptualization, data acquisition, analysis, and preparation of the manuscript. A.W. — Conceptualization, data acquisition, analysis, and preparation of the manuscript. L.A. — Data acquisition. AWolf — Conceptualization. J.A. — Conceptualization, preparation of the manuscript, and funding G.N. — Conceptualization, preparation of the manuscript, and equipment.

Competing interests

The authors declare no competing interests

Additional information

Supplementary information The online version contains supplementary material available at <https://doi.org/10.1038/s42003-024-06642-3>.

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Peer review information *Communications Biology* thanks the anonymous reviewers for their contribution to the peer review of this work. Primary Handling Editors: Christian Beste and Manuel Breuer.

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