Oscillatory traveling waves reveal predictive coding abnormalities in schizophrenia

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Abstract:

The computational mechanisms underlying psychiatric disorders are hotly debated. One hypothesis, grounded in the Bayesian predictive coding framework, proposes that schizophrenia patients have abnormalities in encoding prior beliefs about the environment, resulting in abnormal sensory inference, which can explain core aspects of the psychopathology, such as some of its symptoms. Here, we tested this hypothesis by identifying oscillatory traveling waves as neural signatures of predictive coding. By analyzing a EEG dataset. comprising 146 schizophrenia patients and 96 age-matched healthy controls, we found that schizophrenia patients have stronger top-down alpha-band traveling waves compared to healthy controls during resting state, reflecting stronger precise priors at higher levels of the predictive processing hierarchy. Conversely, we found stronger bottom-up alpha-band waves in schizophrenia patients during a visual task reflecting an alteration of lower sensory priors. Our results yield a novel spatial-based characterization of oscillatory dynamics in schizophrenia, considering brain rhythms as traveling waves and providing a unique framework to study the different components involved in a predictive coding scheme. Altogether, our findings significantly advance our understanding of the mechanisms involved in fundamental pathophysiological aspects of schizophrenia, promoting a more comprehensive and hypothesis-driven approach to psychiatric disorders.

Keywords: Predictive Coding; Schizophrenia; Traveling Waves; Computational Psychiatry

Introduction

Schizophrenia is a severe mental disorder that affects about one percent of the world's population[1], and it is characterized by a large range of psychotic symptoms as well as by strong impairments in mental functioning, including perception, cognition, and personality. Numerous hypotheses and mechanisms have been proposed to explain these abnormalities. One hypothesis is that schizophrenia patients dysfunctionally update their cognitive world model, usually described within the framework of Bayesian inference and predictive coding[2,3]. According to this framework, perception combines incoming sensory evidence with prior information, i.e., beliefs about the world (figure 1, left panel). However, experimental evidence from behavioral studies is mixed, including studies showing that patients rely more on prior beliefs than on sensory information[4,5], studies that found stronger reliance on sensory information in the patients[6,7], and even studies that found intact processing[8–10].

Basic sensory impairments and hallucinations may however rely on abnormalities at different levels of predictive processing. Hence, it has been proposed that schizophrenia patients weigh the prior information more strongly in hierarchically higher regions, but rely more on sensory information in lower hierarchical areas[11,12]. These hierarchical-specific alterations in the priors would explain both impairments in basic sensory processing and more complex phenomena such as hallucinations or delusions [3,13], and may explain the mixed experimental results.

Here, we tested the hypothesis that there are hierarchical-specific alterations in predictive processing from a *neurophysiological* perspective. Recent work showed that oscillatory **alpha-band** (8-12Hz) traveling waves are neural signatures of predictive coding[14–21]. In these studies[14,22], neural activity was measured along the central midline of electrodes (Oz-Fz) to determine how oscillations propagate as traveling waves from occipital to frontal areas (forward waves) or in the opposite direction (backward waves). Based on a model, implementing predictive coding under minimal assumptions[14], the authors proposed that forward traveling waves encode sensory information and prediction-errors (i.e., the difference between top-down predictions and the actual activity), while backward waves carry the prior information [23].

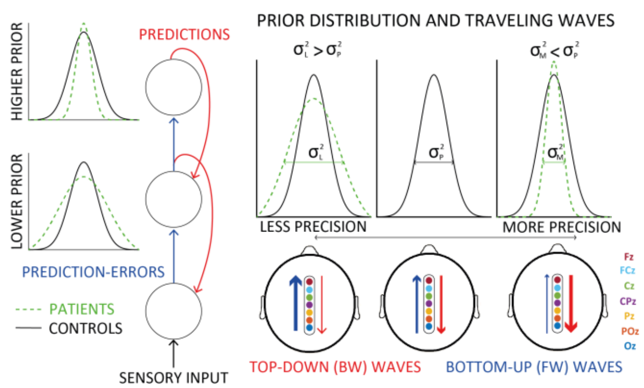

Figure 1- In the Bayesian predictive coding perspective, predictions are generated by prior distributions in higher brain regions, prediction-errors are computed to update the prior based on the sensory evidence (i.e., the likelihood). Recently, it was proposed that hierarchical-specific abnormalities of the priors' precision in schizophrenia, have better precision in higher areas and worse precision in lower, sensory-related areas[11]. Considering backward (BW) and forward (FW) waves as proxies of predictions and prediction-errors[14], one would expect different patterns of traveling waves depending on the precision of the prior: more precise prior (rightmost panel) generate stronger predictions, and in turn stronger backward waves, whereas less precise prior information (leftmost pattern) generates inaccurate predictions, hence higher prediction-errors, reflected by stronger forward waves.

Here, we used the same analysis to test whether patients rely more on prior beliefs than sensory evidence during eyes-closed, resting-state EEG and a visual backward masking task. Following the Bayesian framework, we expect stronger alpha-band backward waves during resting state in schizophrenia patients than in healthy controls due to more precise high-order priors; on the other hand, we expect stronger forward alpha-band waves during a visual task, reflecting an increase in the weighting of the sensory information. (figure 1). We analyzed a large EEG dataset comprising 146 schizophrenia patients and 96 age-matched healthy controls to test these predictions.

Results

We re-analyzed EEG data from previous studies with eye-closed resting state data[24,25] and a visual backward masking task[26,27]. In both dataset, we quantified brain oscillations along the central electrodes' mid-line (from Oz to Fz, figure 1), as in our previous work[14,22]. We considered sliding time windows of 1 and 0.5 seconds from two different datasets, one eyes-closed resting state and one visual backward masking (VBM) task. The waves' amount is expressed as a log-ratio in decibels [dB] between the data and a baseline accounting for fluctuations in the overall power unrelated to the traveling waves (i.e., without the spatial information of the electrodes). See [28] for more details.

Traveling waves during rest. In the resting state dataset, we analyzed FW and BW waves via a two-factor ANCOVAs, considering GROUP (control and patients) and BAND (θ, α, low and high β, and γ) as factors and GENDER, AGE, and EDUCATION as covariates. As showns in figure 2, we found a strong effect for the BAND factor (BF_{10}>>10^{11} for both FW and BW waves) but mild to no effect in the GROUP factor (BW waves, BF_{10}=7.519; FW waves, BF_{10}=0.514) for both FW and BW waves; however, in both directions, we found a very robust GROUP x BAND interaction (for both FW and BW waves BF_{10}>>400), revealing significant differences between the two groups. We then focused specifically on the alpha-band by performing Bayesian ANOVAs considering as factors GROUP and DIRECTION (either forward or backward). Importantly, the results show a strong interaction between GROUP and DIRECTION (BF_{10}>>500), which, in line with our hypothesis, reveals distinct oscillatory dynamics between the patient and the control group.

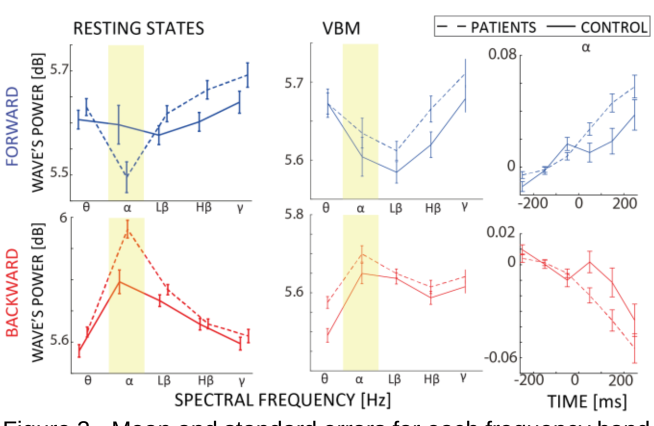

Figure 2 - Mean and standard errors for each frequency band in both dataset for forward (blue) and backward waves. The rightmost panel represents alpha-band waves over time, with stimulus onset at 0ms

Traveling waves for backward masking. According to the proposed Bayesian framework, schizophrenia patients have less precise priors at hierarchically lower sensory areas, thus weighing more sensory information than healthy controls[11,12]. Accordingly, we expect an increase in alpha-band forward waves in patients following visual stimulation, in line with the hypothesis that alpha-band forward waves reflect precision-weighted sensory information[18,20]. To test this hypothesis, we analyze a visual task (the Visual Backward Masking (VBM) dataset, in which a mask follows a briefly presented target). Specifically, we analyzed the changes in FW and BW waves with respect to the onset of the stimulus in each frequency band (i.e., applying a baseline correction computed on the 200ms before stimulus onset, figure 2 right panel). Considering specifically alpha-band waves, our results reveal a difference between GROUP in the forward waves (α, BF_{10}=21.52): patients reveal an increase in alpha-band FW after stimulus onset. Not surprisingly, in both FW and BW waves we found an effect of the TIME factor (FW, BF_{10}=8.12, BW, BF_{10}>10^{14}), and an interaction between GROUP and TIME in FW (BF_{10}>5) but not in BW waves (BF_{10}=0.015). All in all, these results confirm the hypothesis that the patient group show higher FW waves specifically in the alpha-band range, in line with the hypothesis that they rely more on precision-weighted sensory information.

Conclusion

Analyzing EEG recordings in schizophrenia patients and healthy controls[24–27], we found evidence for a dysfunctional updating of beliefs about the world in schizophrenia patients[30]. Previous studies have shown indirect evidence in favor of this interpretation[31–33]. In our study, we quantified oscillatory traveling waves, which reflect the flow of information in predictive processes[14,20]. Unlike previous work, our analysis allowed us to disentangle the different actors involved in the predictive coding process, focusing on their propagation direction. Our results reveal a substantial increase in top-down and a decrease in bottom-up alpha-band traveling waves in schizophrenia patients compared to healthy participants during resting state, and the opposite pattern of results in a visual task, demonstrating that schizophrenia patients have more precise priors (i.e., smaller variability) than healthy participants at hierarchically higher prior but less precise priors in lower sensory areas[5,11,34]. Importantly, these findings describe not only the temporal but also the spatial component of brain rhythms, supporting the key idea that oscillations are best understood when interpreted as traveling waves propagating across cortical regions, coordinating and synchronizing different brain regions[35,36].

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References

1. McCutcheon, R. A., Reis Marques, T. & Howes, O. D. Schizophrenia—An Overview. *JAMA Psychiatry* **77**, 201–210 (2020).
2. Corlett, P. R., Frith, C. D. & Fletcher, P. C. From drugs to deprivation: a Bayesian framework for understanding models of psychosis. *Psychopharmacology* **206**, 515–530 (2009).
3. Krystal, J. H. *et al.* Computational Psychiatry and the Challenge of Schizophrenia. *Schizophrenia Bulletin* **43**, 473–475 (2017).
4. Cassidy, C. M. *et al.* A Perceptual Inference Mechanism for Hallucinations Linked to Striatal Dopamine. *Curr Biol* **28**, 503-514.e4 (2018).
5. Powers, A. R., Mathys, C. & Corlett, P. R. Pavlovian conditioning–induced hallucinations result from overweighting of perceptual priors. *Science* **357**, 596–600 (2017).
6. Stuke, H., Weilnhammer, V. A., Sterzer, P. & Schmack, K. Delusion Proneness is Linked to a Reduced Usage of Prior Beliefs in Perceptual Decisions. *Schizophr Bull* **45**, 80–86 (2019).
7. Weilnhammer, V. *et al.* Psychotic Experiences in Schizophrenia and Sensitivity to Sensory Evidence. *Schizophrenia Bulletin* **46**, 927–936 (2020).
8. Choung, O.-H. *et al.* Intact and deficient contextual processing in schizophrenia patients. *Schizophrenia Research: Cognition* **30**, 100265 (2022).
9. Kaliuzhna, M. *et al.* No evidence for abnormal priors in early vision in schizophrenia. *Schizophrenia Research* **210**, 245–254 (2019).
10. Tibber, M. S. *et al.* Visual Surround Suppression in Schizophrenia. *Front Psychol* **4**, 88 (2013).
11. Corlett, P. R. *et al.* Hallucinations and Strong Priors. *Trends Cogn Sci* **23**, 114–127 (2019).
12. Sterzer, P. *et al.* The Predictive Coding Account of Psychosis. *Biol Psychiatry* **84**, 634–643 (2018).
13. Friston, K., Brown, H. R., Siemerkus, J. & Stephan, K. E. The dysconnection hypothesis (2016). *Schizophr Res* **176**, 83–94 (2016).
14. Alamia, A. & VanRullen, R. Alpha oscillations and traveling waves: Signatures of predictive coding? *PLOS Biology* **17**, e3000487 (2019).
15. Arnal, L. H. & Giraud, A.-L. Cortical oscillations and sensory predictions. *Trends in Cognitive Sciences* **16**, 390–398 (2012).
16. Bastos, A. M. *et al.* Canonical Microcircuits for Predictive Coding. *Neuron* **76**, 695–711 (2012).
17. Bastos, A. M. *et al.* Visual Areas Exert Feedforward and Feedback Influences through Distinct Frequency Channels. *Neuron* **85**, 390–401 (2015).
18. Friston, K. J. Waves of prediction. *PLOS Biology* **17**, e3000426 (2019).
19. Michalareas, G. *et al.* Alpha-Beta and Gamma Rhythms Subserve Feedback and Feedforward Influences among Human Visual Cortical Areas. *Neuron* **89**, 384–397 (2016).

20. Alamia, A., Timmermann, C., Nutt, D. J., VanRullen, R. & Carhart-Harris, R. L. DMT alters cortical travelling waves. *eLife* **9**, e59784 (2020).

21. Alamia, A. & VanRullen, R. A Traveling Waves Perspective on Temporal Binding. *J Cogn Neurosci* 1–9 (2023) doi:10.1162/jocn_a_02004.

22. Pang (庞兆阳), Z., Alamia, A. & VanRullen, R. Turning the Stimulus On and Off Changes the Direction of α Traveling Waves. *eNeuro* **7**, ENEURO.0218-20.2020 (2020).

23. Rao, R. P. N. & Ballard, D. H. Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects. *Nat Neurosci* **2**, 79–87 (1999).

24. da Cruz, J. R. *et al.* EEG microstates are a candidate endophenotype for schizophrenia. *Nat Commun* **11**, 3089 (2020).

25. Gordillo, D. *et al.* The EEG multiverse of schizophrenia. *Cerebral Cortex* **33**, 3816–3826 (2023).

26. da Cruz, J. R. *et al.* Neural Compensation Mechanisms of Siblings of Schizophrenia Patients as Revealed by High-Density EEG. *Schizophrenia Bulletin* **46**, 1009–1018 (2020).

27. Garobbio, S. *et al.* Electrophysiological correlates of visual backward masking in patients with bipolar disorder. *Psychiatry Research: Neuroimaging* **307**, 111206 (2021).

28. Alamia, A., Terral, L., d'Ambra, M. R. & VanRullen, R. Distinct roles of forward and backward alpha-band waves in spatial visual attention. *Elife* **12**, e85035 (2023).

29. Herzog, M. H., Kopmann, S. & Brand, A. Intact figure-ground segmentation in schizophrenia. *Psychiatry Research* **129**, 55–63 (2004).

30. Fletcher, P. C. & Frith, C. D. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. *Nat Rev Neurosci* **10**, 48–58 (2009).

31. Ellson, D. G. Hallucinations produced by sensory conditioning. *Journal of Experimental Psychology* **28**, 1–20 (1941).

32. Kafadar, E. *et al.* Conditioned Hallucinations and Prior Overweighting Are State-Sensitive Markers of Hallucination Susceptibility. *Biological Psychiatry* **92**, 772–780 (2022).

33. Kot, T. & Serper, M. Increased susceptibility to auditory conditioning in hallucinating schizophrenic patients: a preliminary investigation. *J Nerv Ment Dis* **190**, 282–288 (2002).

34. Friston, K. J. Hallucinations and perceptual inference. *Behavioral and Brain Sciences* **28**, 764–766 (2005).

35. Alexander, D. M. *et al.* Spatio-temporal EEG waves in first episode schizophrenia. *Clinical Neurophysiology* **120**, 1667–1682 (2009).

36. Muller, L., Chavane, F., Reynolds, J. & Sejnowski, T. J. Cortical travelling waves: mechanisms and computational principles. *Nat Rev Neurosci* **19**, 255–268 (2018).