Editorials

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Advances in EEG-based functional connectivity approaches to the study of the central nervous system in health and disease

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Abstract

Functional brain connectivity is closely linked to the complex interactions between brain networks. In the last two decades, measures of functional connectivity based on electroencephalogram (EEG) data have proved to be an important tool for neurologists and clinical and non-clinical neuroscientists. Indeed, EEG-based functional connectivity may reveal the neurophysiological processes and networks underlying human cognition and the pathophysiology of neuropsychiatric disorders. This editorial discusses recent advances and future prospects in the study of EEG-based functional connectivity, with a focus on the main methodological approaches to studying brain networks in health and disease.

Key words: EEG, brain connectivity, brain oscillations, central nervous system, clinical neuroscience

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The "old but gold" electroencephalogram

Ever since the German psychiatrist Hans Berger discovered human brainwaves in 1920, the electroencephalogram (EEG) has remained an essential tool for assessing the pathophysiology and brain functions associated with cognitive processes and behavior, as well as brain disorders. The EEG is one of the most frequently used high-temporal resolution techniques in different but convergent scientific fields, including neuroscience, neurology and psychiatry.[1] Indeed, EEG systems are low-cost, non-invasive, can be implemented at the bedside of patients, and have been shown to have high test–retest reliability, sensitivity and specificity.[2–6] Thus, EEG is considered a valuable method for studying temporal hierarchy and dynamics of neurocognitive processes and the central nervous system in health and disease.[7–11] In particular, EEG-based measurements can capture fast cognitive dynamics and the temporal progression of cognitive events in the timeframe in which cognition occurs.[12–19]

Although the use of the EEG in humans for research and clinical purposes is dated, thousands of studies are now described in the scientific literature, and today we can firmly state that EEG is a valuable tool among the neurotechniques that allow the study of brain functions and cognition, as well as their complex interactions. Indeed, due to technological advancements, EEG still represents a valid technique that constantly presents new theoretical, functional and computational challenges. Therefore, in our opinion, we can define it as the 'old but gold' neuroscientific methodology.

EEG technical and methodological promises and pitfalls

Over the last two decades, a growing interest has emerged in quantitative measures of EEG-based connectivity. These quantitative analyses allow for the evaluation of interdependencies between brain signals recorded from the scalp level (i.e., sensor space) or between neural nodes (i.e., source space). Different methodological procedures can be applied to the study of EEG-based connectivity.[20] Nevertheless, many methodological and theoretical problems may arise. For example, volume conduction represents a primary issue when analyzing sensor–space connectivity.[21–23] In this regard, the low spatial resolution of the EEG makes it challenging to interpret connectivity results in relation to brain areas. In particular, common neural sources can influence contiguous electrode activity, which may increase the risk of false positive connectivity for contiguous electrodes.[4,21,24,25] Thus, it is possible to calculate source-level connectivity to reduce the effect of volume conduction.[4,21] However, source-level methods also have some limitations. While connectivity measures from sensor-level EEG recordings have low spatial precision, source-level analysis requires a large number of electrodes or accurate head models to infer how electrical fields propagate through the head at a reasonable spatial resolution.[26] This process is called the inverse problem.[27] Recent studies propose new methodological advances and recommendations to reduce technical and theoretical issues related to EEG analyses.[3,28] Furthermore, the consensus on using EEG-based measurements may have crucial implications for their application in clinical research.

In a clinical context, the ad hoc visual evaluation of EEG data is still an important criterion for the assessment of epilepsies and disorders of consciousness.[29–33] However, new computational advances would allow for a more objective and quantitative EEG data analysis. Indeed, scalp-level EEG visual analysis does not allow estimates of the interconnections between distant brain areas and quantitative data, which differs from visual evaluation, as the latter can be compared with normative data.[7] Finally, these quantitative analyses of EEG data can be used as biomarkers for classifying neuropsychiatric disorders and identifying the psychophysiological correlates of cognition.[20,34–37]

EEG-based functional connectivity

Empirical research and mathematical models in neuroscience propose oscillatory synchronization between brain nodes and networks as a key mechanism for information sharing within neural networks.[38–40] However, complex neural networks implicated in cognitive functions communicate at multiple spatial and temporal scales.[41] Indeed, EEG-based measures of connectivity may reflect diverse aspects of these spatiotemporal relationships between electrodes at the scalp level or between nodes at the source space.[3] In general, EEG-based connectivity can describe either the statistical linear or non-linear covariation between signals (i.e., functional connectivity) or the causal influence of the activity of one signal over another as effective connectivity.[42–44] These computational models may unveil intrinsic brain networks and functional mechanisms underlying sensorimotor, cognitive and affective processes in healthy participants and patients with neurological and psychiatric disorders.

There are several methods for quantifying and evaluating functional connectivity using EEG-recorded data,[45] and each method has its advantages and limitations. Different measures are better suited for specific purposes or assumptions about underlying neurophysiological processes.[46] In particular, functional connectivity measurements can be based on associations between phases (e.g., phase lag index, phase locking values and phase coherence),[25,47,48] between the amplitude of the oscillations in specific frequency bands (e.g., power-based coherence and cross-frequency coupling),[49–52] and in the complexity of the EEG signal (e.g., mutual information and transfer entropy).[20,53] In the subsequent sections, we will briefly describe some of the EEG functional connectivity analyses and recent advances, in the use of these analyses, for the study of the brain functioning in health and disease.

(a) The functional connectivity measures based on the phase of brain oscillatory activity rely on the phase angle distribution between 2 signals. For instance, the phase lag index (PLI and the similar evolutions, namely weighted PLI and squared weighted PLI) evaluates the consistency of the phase differences between 2 EEG signals recorded over specific electrodes or neural nodes.[47] The PLI has been shown to be less influenced by spurious correlations than power coherence measures because of common sources.[47]

(b) Power-based connectivity analyses involve the correlation between 2 signals over time and across frequency amplitudes. These correlations can be computed between activity in the same or different frequency bands (i.e., power coherence (PC)) and between different events (i.e., inter-trial coherence).[49,50] For instance, PC calculates the absolute correlation between amplitudes in specific frequency bands over time.

(c) Mutual information (MI) and related measures such as transfer entropy and joint entropy are based on the concept of entropy, which can be defined as the amount of information within a variable.[24] Mutual information is a functional connectivity index that estimates the level of information shared between 2 variables or time series, and is calculated by adding the individual entropies of the time series and subtracting the joint entropy.

Therefore, EEG functional connectivity measures can provide multidimensional data and largely independent information. However, the cross-validation of results using more than 1 technique is rare in the literature.[3] These evidence-based approaches highlight neural mechanisms of brain plasticity and connectivity in healthy individuals,[54,55] but more importantly, they could also lead to adequate prediction and evaluation of clinical symptoms or treatment improvements.[10,20,30,36,56–60] In particular, a recent study compared different measures to predict clinical outcomes in patients with traumatic or nontraumatic acquired brain injuries.[20] While the PLI connectivity may reflect the typical diffuse axonal damage in trauma patients, the MI and PC predicted long-term clinical outcomes in all patients. Moreover, a larger PC within the fronto-parietal motor network in the first weeks after stroke correlated positively with subsequent motor and cognitive improvements, while connectivity increases were associated with poorer clinical outcomes.[61]

Impaired PLI connectivity within the fronto-parieto-occipital areas can be an accurate biomarker for predicting the future development of psychiatric disorders in subclinical populations.[60,62,63] In addition, large-scale connectivity impairments within the alpha range have been directly associated with the severity of the positive symptoms of schizophrenia.[64] Furthermore, several studies report a decrease in long-range connectivity among the autism spectrum disorder population using different measures,[65–68] while results regarding short-range connectivity are not as clear.[64] Moreover, abnormal lateralization and inter-hemispheric connectivity in autism spectrum disorders have been consistently reported across studies.[64]

Conclusions and future insights

As discussed, EEG-based connectivity is a multifaceted world comprising various methodological approaches with different advantages and limitations.[69,70] There is no optimal brain connectivity measurement, and using one measure should be based on the study hypotheses and the neurophysiological and/or neurological mechanisms behind the specific connectivity. Many recent studies have focused on modeling and estimating EEG-based connectivity, and increasing evidence shows that it can be helpful in investigating and understanding human cognition as well as psychiatric and neurological conditions.[3,45]

After decades of intensive use, there is no doubt that EEG-based research has a great potential, and the study of EEG functional connectivity can have a massive impact with decisive repercussions in research and clinical practice. However, to use connectivity measures in a clinical context, one of the major advances should be the ability to collect normative data to reduce biases and better understand the link between functional networks and cognition.[3] Moreover, although algorithms were implemented to compute functional connectivity measures, technical advances are needed to make those measures reliable and easy to implement in a clinical context. In this view, international cooperation and open data repositories with strict methodological standards should be encouraged among scientists.[71]

In recent years, quantitative EEG measurements, brain connectivity data and clinical data were combined using machine learning algorithms in multicenter studies to improve accuracy in the clinical classification of neuropsychiatric diseases and brain diseases as well as to study complex cognitive functions.[20,57,72] Advances in the application of machine learning algorithms in a clinical context may help with clinical decision-making and the implementation of brain–computer interfaces in neurorehabilitation. Moreover, integrating psychophysiological, structural and functional imaging data with behavioral data using causative statistics can create models of cognitive functions[73] and neuropsychiatric diseases,[10,74–76] and advance our understanding of human cognition.

In the near future, EEG-based connectivity could provide crucial information about neural network functioning in health and disease with high temporal resolution and precision. These EEG measurements may help characterize the psychophysiological correlates of brain diseases and cognitive functions as well as monitor the psychophysiological effects of neurorehabilitative treatments over time. However, current international guidelines do not endorse the use of EEG biomarkers in clinical trials performed in patients, for example, in Alzheimer's disease,[77] autism spectrum disorders,[78] depression,[79] and other neuropsychiatric disorders, despite increasing evidence.[80] Thus, it is currently reasonable, timely and relevant to make a concerted effort to translate scientific advances into clinical practice.

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References

1. Biasiucci A, Franceschiello B, Murray MM. Electroencephalography. *Curr Biol*. 2019;29(3):R80–R85. doi:10.1016/j.cub.2018.11.052
2. Brienza M, Mecarelli O. Neurophysiological basis of EEG. In: Mecarelli O, ed. *Clinical Electroencephalography*. Cham, Switzerland: Springer International Publishing; 2019:9–21. doi:10.1007/978-3-030-04573-9_2
3. Babiloni C, Barry RJ, Başar E, et al. International Federation of Clinical Neurophysiology (IFCN); EEG research workgroup. Recommendations on frequency and topographic analysis of resting state EEG rhythms. Part 1: Applications in clinical research studies. *Clin Neurophysiol*. 2020;131(1):285–307. doi:10.1016/j.clinph.2019.06.234
4. Mahjoory K, Nikulin VV, Botrel L, Linkenkaer-Hansen K, Fato MM, Haufe S. Consistency of EEG source localization and connectivity estimates. *Neuroimage*. 2017;152:590–601. doi:10.1016/j.neuroimage.2017.02.076
5. Cocquyt E, Van Laeken H, Van Mierlo P, De Letter M. Test–retest reliability of electroencephalographic and magnetoencephalographic measures elicited during language tasks: A literature review. *Eur J Neurosci*. 2023;57(8):1353–1367. doi:10.1111/ejn.15948
6. Bareham CA, Roberts N, Allanson J, et al. Bedside EEG predicts longitudinal behavioural changes in disorders of consciousness. *Neuroimage Clin*. 2020;28:102372. doi:10.1016/j.nicl.2020.102372
7. Bolwig TG. EEG and psychiatry: Time for a resurrection. *Acta Psychiatr Scand*. 2008;117(4):241–243. doi:10.1111/j.1600-0447.2008.01172.x
8. Buzsáki G, Wang XJ. Mechanisms of gamma oscillations. *Annu Rev Neurosci*. 2012;35(1):203–225. doi:10.1146/annurev-neuro-062111-150444
9. Gerez M, Tello A. Selected quantitative EEG (QEEG) and event-related potential (ERP) variables as discriminators for positive and negative schizophrenia. *Biol Psychiatry*. 1995;38(1):34–49. doi:10.1016/0006-3223(94)00205-H
10. Di Gregorio F, Petrone V, Casanova E, et al. Hierarchical psychophysiological pathways subtend perceptual asymmetries in neglect. *Neuroimage*. 2023;270:119942. doi:10.1016/j.neuroimage.2023.119942
11. Al-Qazzaz NK, Ali SHBM, Ahmad SA, Islam MS, Escudero J. Discrimination of stroke-related mild cognitive impairment and vascular dementia using EEG signal analysis. *Med Biol Eng Comput*. 2018;56(1):137–157. doi:10.1007/s11517-017-1734-7
12. Di Gregorio F, Maier ME, Steinhauser M. Are errors detected before they occur? Early error sensations revealed by metacognitive judgments on the timing of error awareness. *Conscious Cogn*. 2020;77:102857. doi:10.1016/j.concog.2019.102857
13. Di Gregorio F, Maier ME, Steinhauser M. Early correlates of error-related brain activity predict subjective timing of error awareness. *Psychophysiology*. 2022;59(7):e14020. doi:10.1111/psyp.14020
14. O'Reilly RC. Six principles for biologically based computational models of cortical cognition. *Trends Cogn Sci*. 1998;2(11):455–462. doi:10.1016/S1364-6613(98)01241-8
15. Kahneman D. *Thinking, Fast and Slow*. New York, USA: Farrar, Straus and Giroux; 2013. ISBN:978-0-374-53355-7.
16. Battaglia S, Cardellicchio P, Di Fazio C, Nazzi C, Fracasso A, Borgomaneri S. Stopping in (e)motion: Reactive action inhibition when facing valence-independent emotional stimuli. *Front Behav Neurosci*. 2022;16:998714. doi:10.3389/fnbeh.2022.998714
17. Battaglia S, Thayer JF. Functional interplay between central and autonomic nervous systems in human fear conditioning. *Trends Neurosci*. 2022;45(7):504–506. doi:10.1016/j.tins.2022.04.003
18. Battaglia S, Orsolini S, Borgomaneri S, Barbieri R, Diciotti S, Di Pellegrino G. Characterizing cardiac autonomic dynamics of fear learning in humans. *Psychophysiology*. 2022;59(12):e14122. doi:10.1111/psyp.14122
19. Battaglia S, Cardellicchio P, Di Fazio C, Nazzi C, Fracasso A, Borgomaneri S. The influence of vicarious fear-learning in "infecting" reactive action inhibition. *Front Behav Neurosci*. 2022;16:946263. doi:10.3389/fnbeh.2022.946263
20. Di Gregorio F, La Porta F, Petrone V, et al. Accuracy of EEG biomarkers in the detection of clinical outcome in disorders of consciousness after severe acquired brain injury: Preliminary results of a pilot study using a machine learning approach. *Biomedicines*. 2022;10(8):1897. doi:10.3390/biomedicines10081897
21. Palva JM, Wang SH, Palva S, et al. Ghost interactions in MEG/EEG source space: A note of caution on inter-areal coupling measures. *Neuroimage*. 2018;173:632–643. doi:10.1016/j.neuroimage.2018.02.032
22. Haufe S, Meinecke F, Görgen K, et al. On the interpretation of weight vectors of linear models in multivariate neuroimaging. *Neuroimage*. 2014;87:96–110. doi:10.1016/j.neuroimage.2013.10.067
23. Hipp JF, Siegel M. Accounting for linear transformations of EEG and MEG data in source analysis. *PLoS One*. 2015;10(4):e0121048. doi:10.1371/journal.pone.0121048
24. Cohen MX. *Analyzing Neural Time Series Data: Theory and Practice*. Cambridge, USA: MIT Press; 2014. ISBN:978-0-262-01987-3.
25. Vinck M, Oostenveld R, Van Wingerden M, Battaglia F, Pennartz CMA. An improved index of phase-synchronization for electrophysiological data in the presence of volume-conduction, noise and sample-size bias. *Neuroimage*. 2011;55(4):1548–1565. doi:10.1016/j.neuroimage.2011.01.055
26. Moezzi B, Goldsworthy MR. Commentary: Consistency of EEG source localization and connectivity estimates. *Front Neurosci*. 2018;12:147. doi:10.3389/fnins.2018.00147
27. Van Diessen E, Numan T, Van Dellen E, et al. Opportunities and methodological challenges in EEG and MEG resting state functional brain network research. *Clin Neurophysiol*. 2015;126(8):1468–1481. doi:10.1016/j.clinph.2014.11.018
28. Hallett M, De Haan W, Deco G, et al. Human brain connectivity: Clinical applications for clinical neurophysiology. *Clin Neurophysiol*. 2020;131(7):1621–1651. doi:10.1016/j.clinph.2020.03.031
29. Isaksson A, Wennberg A. Visual evaluation and computer analysis of the EEG: A comparison. *Electroencephalogr Clin Neurophysiol*. 1975;38(1):79–86. doi:10.1016/0013-4694(75)90212-6
30. Bagnato S, Boccagni C, Prestandrea C, Sant'Angelo A, Castiglione A, Galardi G. Prognostic value of standard EEG in traumatic and non-traumatic disorders of consciousness following coma. *Clin Neurophysiol*. 2010;121(3):274–280. doi:10.1016/j.clinph.2009.11.008
31. Duszyk-Bogorodzka A, Zieleniewska M, Jankowiak-Siuda K. Brain activity characteristics of patients with disorders of consciousness in the EEG resting state paradigm: A review. *Front Syst Neurosci*. 2022;16:654541. doi:10.3389/fnsys.2022.654541
32. Smith SJM. EEG in the diagnosis, classification, and management of patients with epilepsy. *J Neurol Neurosurg Psychiatry*. 2005;76(Suppl 2):ii2–ii7. doi:10.1136/jnnp.2005.069245
33. Rossi Sebastiano D, Varotto G, Sattin D, Franceschetti S. EEG assessment in patients with disorders of consciousness: Aims, advantages, limits, and pitfalls. *Front Neurol*. 2021;12:649849. doi:10.3389/fneur.2021.649849
34. Di Gregorio F, Ernst B, Steinhauser M. Differential effects of instructed and objective feedback reliability on feedback-related brain activity. *Psychophysiology*. 2019;56(9):e13399. doi:10.1111/psyp.13399
35. Keser Z, Buchl SC, Seven NA, et al. Electroencephalogram (EEG) with or without transcranial magnetic stimulation (TMS) as biomarkers for post-stroke recovery: A narrative review. *Front Neurol*. 2022;13:827866. doi:10.3389/fneur.2022.827866
36. Kim B, Winstein C. Can neurological biomarkers of brain impairment be used to predict poststroke motor recovery? A systematic review. *Neurorehabil Neural Repair*. 2017;31(1):3–24. doi:10.1177/1545968316662708
37. Al-Qazzaz NK, Ali SHBMd, Ahmad SA, Chellappan K, Islam MdS, Escudero J. Role of EEG as biomarker in the early detection and classification of dementia. *ScientificWorldJournal*. 2014;2014:906038. doi:10.1155/2014/906038

38. Fries P. A mechanism for cognitive dynamics: Neuronal communication through neuronal coherence. *Trends Cogn Sci*. 2005;9(10):474–480. doi:10.1016/j.tics.2005.08.011
39. Salinas E, Sejnowski TJ. Correlated neuronal activity and the flow of neural information. *Nat Rev Neurosci*. 2001;2(8):539–550. doi:10.1038/35086012
40. Singer W. Synchronization of cortical activity and its putative role in information processing and learning. *Annu Rev Physiol*. 1993;55(1):349–374. doi:10.1146/annurev.ph.55.030193.002025
41. Varela F, Lachaux JP, Rodriguez E, Martinerie J. The brainweb: Phase synchronization and large-scale integration. *Nat Rev Neurosci*. 2001;2(4):229–239. doi:10.1038/35067550
42. Valdes-Sosa PA, Roebroeck A, Daunizeau J, Friston K. Effective connectivity: Influence, causality and biophysical modeling. *Neuroimage*. 2011;58(2):339–361. doi:10.1016/j.neuroimage.2011.03.058
43. Friston KJ. Functional and effective connectivity: A review. *Brain Connect*. 2011;1(1):13–36. doi:10.1089/brain.2011.0008
44. Dietz MJ, Friston KJ, Mattingley JB, Roepstorff A, Garrido MI. Effective connectivity reveals right-hemisphere dominance in audiospatial perception: Implications for models of spatial neglect. *J Neurosci*. 2014;34(14):5003–5011. doi:10.1523/JNEUROSCI.3765-13.2014
45. Cao J, Zhao Y, Shan X, et al. Brain functional and effective connectivity based on electroencephalography recordings: A review. *Hum Brain Mapp*. 2022;43(2):860–879. doi:10.1002/hbm.25683
46. Imperatori LS, Betta M, Cecchetti L, et al. EEG functional connectivity metrics wPLI and wSMI account for distinct types of brain functional interactions. *Sci Rep*. 2019;9(1):8894. doi:10.1038/s41598-019-45289-7
47. Stam CJ, Nolte G, Daffertshofer A. Phase lag index: Assessment of functional connectivity from multi channel EEG and MEG with diminished bias from common sources. *Hum Brain Mapp*. 2007;28(11):1178–1193. doi:10.1002/hbm.20346
48. Nolte G, Ziehe A, Nikulin VV, et al. Robustly estimating the flow direction of information in complex physical systems. *Phys Rev Lett*. 2008;100(23):234101. doi:10.1103/PhysRevLett.100.234101
49. Bruns A, Eckhorn R, Jokeit H, Ebner A. Amplitude envelope correlation detects coupling among incoherent brain signals. *Neuroreport*. 2000;11(7):1509–1514. PMID:10841367.
50. Hipp JF, Hawellek DJ, Corbetta M, Siegel M, Engel AK. Large-scale cortical correlation structure of spontaneous oscillatory activity. *Nat Neurosci*. 2012;15(6):884–890. doi:10.1038/nn.3101
51. Canolty RT, Knight RT. The functional role of cross-frequency coupling. *Trends Cogn Sci*. 2010;14(11):506–515. doi:10.1016/j.tics.2010.09.001
52. Allen EA, Liu J, Kiehl KA, et al. Components of cross-frequency modulation in health and disease. *Front Syst Neurosci*. 2011;5:59. doi:10.3389/fnsys.2011.00059
53. King JR, Sitt JD, Faugeras F, et al. Information sharing in the brain indexes consciousness in noncommunicative patients. *Curr Biol*. 2013;23(19):1914–1919. doi:10.1016/j.cub.2013.07.075
54. Battaglia S, Nazzi C, Thayer JF. Fear-induced bradycardia in mental disorders: Foundations, current advances, future perspectives. *Neurosci Biobehav Rev*. 2023;149:105163. doi:10.1016/j.neubiorev.2023.105163
55. Battaglia S, Di Fazio C, Vicario CM, Avenanti A. Neuropharmacological modulation of N-methyl-D-aspartate, noradrenaline and endocannabinoid receptors in fear extinction learning: Synaptic transmission and plasticity. *Int J Mol Sci*. 2023;24(6):5926. doi:10.3390/ijms24065926
56. Bagnato S, Boccagni C, Sant'Angelo A, Fingelkurts AA, Fingelkurts AA, Galardi G. Longitudinal assessment of clinical signs of recovery in patients with unresponsive wakefulness syndrome after traumatic or nontraumatic brain injury. *J Neurotrauma*. 2017;34(2):535–539. doi:10.1089/neu.2016.4418
57. Chennu S, Annen J, Wannez S, et al. Brain networks predict metabolism, diagnosis and prognosis at the bedside in disorders of consciousness. *Brain*. 2017;140(8):2120–2132. doi:10.1093/brain/awx163
58. Di Gregorio F, La Porta F, Casanova E, et al. Efficacy of repetitive transcranial magnetic stimulation combined with visual scanning treatment on cognitive and behavioral symptoms of left hemispatial neglect in right hemispheric stroke patients: Study protocol for a randomized controlled trial. *Trials*. 2021;22(1):24. doi:10.1186/s13063-020-04943-6
59. Di Gregorio F, La Porta F, Lullini G, et al. Efficacy of repetitive transcranial magnetic stimulation combined with visual scanning treatment on cognitive-behavioral symptoms of unilateral spatial neglect in patients with traumatic brain injury: Study protocol for a randomized controlled trial. *Front Neurol*. 2021;12:702649. doi:10.3389/fneur.2021.702649
60. Trajkovic J, Di Gregorio F, Ferri F, Marzi C, Diciotti S, Romei V. Resting state alpha oscillatory activity is a valid and reliable marker of schizotypy. *Sci Rep*. 2021;11(1):10379. doi:10.1038/s41598-021-89690-7
61. Nicolo P, Rizk S, Magnin C, Pietro MD, Schnider A, Guggisberg AG. Coherent neural oscillations predict future motor and language improvement after stroke. *Brain*. 2015;138(10):3048–3060. doi:10.1093/brain/awv200
62. Liu T, Zhang J, Dong X, et al. Occipital alpha connectivity during resting-state electroencephalography in patients with ultra-high risk for psychosis and schizophrenia. *Front Psychiatry*. 2019;10:553. doi:10.3389/fpsyt.2019.00553
63. King S, Holleran L, Mothersill D, et al. Early life adversity, functional connectivity and cognitive performance in schizophrenia: The mediating role of IL-6. *Brain Behav Immun*. 2021;98:388–396. doi:10.1016/j.bbi.2021.06.016
64. Ippolito G, Bertaccini R, Tarasi L, et al. The role of alpha oscillations among the main neuropsychiatric disorders in the adult and developing human brain: Evidence from the last 10 years of research. *Biomedicines*. 2022;10(12):3189. doi:10.3390/biomedicines10123189
65. O'Reilly C, Lewis JD, Elsabbagh M. Is functional brain connectivity atypical in autism? A systematic review of EEG and MEG studies. *PLoS One*. 2017;12(5):e0175870. doi:10.1371/journal.pone.0175870
66. Han J, Zeng K, Kang J, et al. Development of brain network in children with autism from early childhood to late childhood. *Neuroscience*. 2017;367:134–146. doi:10.1016/j.neuroscience.2017.10.015
67. Dickinson A, DiStefano C, Lin YY, Scheffler AW, Senturk D, Jeste SS. Interhemispheric alpha-band hypoconnectivity in children with autism spectrum disorder. *Behav Brain Res*. 2018;348:227–234. doi:10.1016/j.bbr.2018.04.026
68. Zhou T, Kang J, Cong F, Li DrX. Early childhood developmental functional connectivity of autistic brains with non-negative matrix factorization. *Neuroimage Clin*. 2020;26:102251. doi:10.1016/j.nicl.2020.102251
69. Balogh L, Tanaka M, Török N, Vécsei L, Taguchi S. Crosstalk between existential phenomenological psychotherapy and neurological sciences in mood and anxiety disorders. *Biomedicines*. 2021;9(4):340. doi:10.3390/biomedicines9040340
70. Tanaka M, Vécsei L. Editorial of Special Issue 'Dissecting Neurological and Neuropsychiatric Diseases: Neurodegeneration and Neuroprotection.' *Int J Mol Sci*. 2022;23(13):6991. doi:10.3390/ijms23136991
71. Tanaka M, Szabó Á, Vécsei L. Integrating armchair, bench, and bedside research for behavioral neurology and neuropsychiatry: Editorial. *Biomedicines*. 2022;10(12):2999. doi:10.3390/biomedicines10122999
72. Engemann DA, Raimondo F, King JR, et al. Robust EEG-based cross-site and cross-protocol classification of states of consciousness. *Brain*. 2018;141(11):3179–3192. doi:10.1093/brain/awy251
73. Casey CP, Tanabe S, Farahbakhsh Z, et al. Dynamic causal modelling of auditory surprise during disconnected consciousness: The role of feedback connectivity. *Neuroimage*. 2022;263:119657. doi:10.1016/j.neuroimage.2022.119657
74. Tanaka M, Toldi J, Vécsei L. Exploring the etiological links behind neurodegenerative diseases: Inflammatory cytokines and bioactive kynurenines. *Int J Mol Sci*. 2020;21(7):2431. doi:10.3390/ijms21072431
75. Tanaka M, Tóth F, Polyák H, Szabó Á, Mándi Y, Vécsei L. Immune influencers in action: Metabolites and enzymes of the tryptophan–kynurenine metabolic pathway. *Biomedicines*. 2021;9(7):734. doi:10.3390/biomedicines9070734
76. Tanaka M, Szabó Á, Spekker E, Polyák H, Tóth F, Vécsei L. Mitochondrial impairment: A common motif in neuropsychiatric presentation? The link to the tryptophan–kynurenine metabolic system. *Cells*. 2022;11(16):2607. doi:10.3390/cells11162607
77. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):263–269. doi:10.1016/j.jalz.2011.03.005

78. Howes OD, Rogdaki M, Findon JL, et al. Autism spectrum disorder: Consensus guidelines on assessment, treatment and research from the British Association for Psychopharmacology. *J Psychopharmacol*. 2018;32(1):3–29. doi:10.1177/0269881117741766
79. Davidson JRT. Major depressive disorder treatment guidelines in America and Europe. *J Clin Psychiatry*. 2010;71(Suppl E1):e04. doi:10.4088/JCP.9058se1c.04gry
80. Babiloni C, Arakaki X, Azami H, et al. Measures of resting state EEG rhythms for clinical trials in Alzheimer's disease: Recommendations of an expert panel. *Alzheimers Dement*. 2021;17(9):1528–1553. doi:10.1002/alz.12311