Discussion

Petersen (2016): https://doi.org/10.1212/CON.0000000000000313

In DSM5 -> now include a predementia phase called mild neurocognitive disorder

MCI reflects a change in cognitive functioning for this individual person, not a lifelong low cognitive function.

If time allows can MoCA be used for assessment, but clinican must be mindful that these screening instruments are insufficient to make the diagnosis; nevertheless they can be important to isolate domains of impairment and advise the clinician on further assessments (32,33).

In addition, some aspects of psychiatric conditions such as major depression or generalized anxiety disorder can have cognitive components, and consequently, in the early stages of these disorders, cognition may be impaired. The clinician must always consider other medical conditions such as uncompensated heart failure, poorly controlled diabetes mellitus, or chronic obstructive pulmonary disease as contributors to cognitive impairment.

Petersen (2004): https://doi.org/10.1111/j.1365-2796.2004.01388.x

As the field matures, we will learn more about the various subtypes of MCI and their ability to predict various forms of cognitive impairment. Hopefully, as therapeutic interventions become available, we will be able to tailor treatments for specific prodromal forms of cognitive impairment and dementia.

Claus et al. (2000): https://doi.org/10.1159/000017219

Slowing on the electroencephalogram (EEG) in patients with Alzheimer's disease (AD), compared to normal control subjects, evidenced by increase of theta activity and decrease of beta or alpha power, is a uniform finding in previous studies [1–5].

More impairment in overall cognitive function was most strongly reflected in loss of parieto-occipital and fronto-central alpha activity.

Detailed analysis of cognitive domains in relation to localized EEG values also revealed most consistently associations with decrease in alpha activity. Lower temporal and parietal rCBF were significantly associated with lower parieto-occipital alpha activity, while presence of leukoaraiosis was significantly associated with lower relative beta activity and higher absolute delta and theta activity.

Commented [JH1]: @article{petersen2016mild, title={Mild cognitive impairment}, author={Petersen, Ronald C}, journal={CONTINUUM: lifelong Learning in Neurology}, volume={22}, number={2}, pages={404--418}, year={2016}, publisher={LWW} }

Commented [JH2]: Interesting for discussion, that we just have total score of cognitive impairment. So I don't knnow in which domaine patients are better or worse

Commented [JH3]: 32. Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005; 53(4): 695– 699. doi:10.1111/j.1532-5415.2005.53221.x. [DOI] [PubMed] [Google Scholar]
33. Kokmen E, Naessens JM, Offord KP. A short test of mental status: description and preliminary results. Mayo Clin Proc 1987; 62(4): 281– 288. doi:10.1016/S0025-6196(12)61905-3. [DOI] [PubMed] [Google Scholar]

Commented [JH4]: MCI

Commented [JH5]: @article{petersen2004mild, title={Mild cognitive impairment as a diagnostic entity}, author={Petersen, Ronald C}, journal={Journal of internal medicine}, volume={256}, number={3}, pages={183--194}, year={2004}, publisher={Wiley Online Library} }

Commented [JH6]: EEG in cognitive impairment in AD

Commented [JH7]: @article{claus2000determinants, title={Determinants of quantitative spectral electroencephalography in early Alzheimer's disease: cognitive function, regional cerebral blood flow, and computed tomography}, author={Claus, JJ and Ongerboer de Visser, BW and Bour, LJ and Walstra, GJM and Hijdra, A and Verbeeten Jr, B and Van Royen, EA and Kwa, VIH and Van Gool, WA}, journal={Dementia and geriatric cognitive disorders}, volume={11}, number={2}, pages={81--89}, year={2000}, publisher={S. Karger AG Basel, Switzerland} }

Commented [JH8]: 88 Dement Geriatr Cogn Disord 2000;11:81–89 Claus/Ongerboer de Visser/Bour/Walstra/ Hijdra/Verbeeten/Van Royen/Kwa/ van Gool
References
1 Coben LA, Danziger W, Storandt M: A longitudinal EEG study of mild senile dementia of Alzheimer type: Changes at 1 year and at 2.5 years. Electroencephalogr Clin Neurophysiol 1985;61:101–112.
2 Penttila M, Partanen JV, Soininen H, Riekkinen PJ: Quantitative analysis of occipital EEG in different stages of Alzheimer's disease. Electroencephalogr Clin Neurophysiol 1985;60:1–6.
3 Soininen H, Partanen J, Laulumaa V, Paakkonen A, Helkala EL, Riekkinen PJ: Serial EEG in Alzheimer's disease: 3-year follow-up and clinical outcome. Electroencephalogr Clin Neurophysiol 1991;79:342–348.
4 Schreiter-Gasser U, Gasser T, Ziegler P: Quantitative EEG analysis in early onset Alzheimer's disease: Correlations with severity, clinical characteristics, visual EEG and CCT. Electroencephalogr Clin Neurophysiol 1994;90: 267–272.

General level of cognitive function, assessed in several previous studies with the MMSE, is most consistently related to alpha activity on EEG in AD patients [8, 13, 16 17, 46], in agreement with our findings. However, also correlations between overall cognitive function and delta and theta activity were observed in our study and in previous reports [13–16].

Alpha power as strongest correlate of cognitive domains finds support in the study of Jelic et al. [19], where visuospatial functions were strongly related to alpha power in left parieto-occipital and right temporal regions. In the study by Jelic et al. [19] measures of frontal lobe function, including attention and abstraction, were significantly related to fronto-central theta activity. We also found that, in addition to alpha activity, fronto-central theta activity was selected as a significant predictor of performance in attention and abstraction.

Interestingly, our relative beta activity, but also absolute theta and delta activity, were significantly related to leukoaraiosis on CT. This analysis may demonstrate that increase of absolute theta and delta power is sometimes less clearly reflected in the relative power values.

This is probably due to the fact that theta and also delta power determine the main part of the total power. As, for instance, theta or delta increases, the total power more or less increases proportionally. An increase in theta or delta may then be reflected by the absolute power, rather than by the relative EEG values. The preclinical finding that beta activity is found in subcortical or lower cortical structures [51–53] may either suggest that neuronal function of these brain structures is compromised by the presence of leukoaraiosis or that leukoaraiosis results in disconnection of subcortical and cortical structures.

Thus, the results suggest that leukoaraiosis in AD patients is related to slowing of the EEG, evidenced mainly by increase of theta and loss of beta activity.

In conclusion, alpha activity may be closely associated with cognitive function and rCBF, while beta and theta activity are related to lower cortical or subcortical changes. Our study therefore suggests that the EEG bands reflect differential pathophysiologic changes in AD.

Babiloni (2015): https://doi.org/10.1016/j.ijpsycho.2015.02.008

Power density of the resting state EEG rhythms does not capture one of the main features of the AD process, namely the impairment of functional or effective connectivity within long range brain networks underlying the cognitive dysfunction in prodromal and manifest AD patients. Indeed, the majority of the cognitive processes are highly distributed and dynamic processes, depending on the selective interplay among many neural populations distributed across several cortical and sub-cortical regions. In the same line, it is expected that

Commented [JH9]: 8 Kuskowski MA, Mortimer JA, Morley GK,
Malone SM, Okaya AJ: Rate of cognitive decline in Alzheimer's disease is associated with EEG alpha power. Biol Psychiatry 1993;33: 659–662.
13 Dierks T, Frolich L, Ihl R, Maurer K: Correlation between cognitive brain function and electrical brain activity in dementia of Alzheimer type. J Neural Transm 1995;99:55–62.
16 Sloan EP, Fenton GW: EEG power spectra and cognitive change in geriatric psychiatry: A longitudinal study. Electroencephalogr Clin Neurophysiol 1993;86:361–367.
17 Wada Y, Nanbu Y, Jiang ZY, Koshino Y, Yamagushi N, Hashimoto T: Electroencephalographic abnormalities in patients with presenile dementia of the Alzheimer type: Quantitative analysis at rest and during photic stimulation. Biol Psychiatry 1997;41:217–225.
Primavera A, Novello P, Finocchi C, Canevari E, Corsello L: Correlation between Mini-Mental State Examination and quantitative electroencephalography in senile dementia of the Alzheimer type. Neuropsychobiology 1990;23:74–78

Commented [JH10]: 13 Dierks T, Frolich L, Ihl R, Maurer K: Correlation between cognitive brain function and electrical brain activity in dementia of Alzheimer type. J Neural Transm 1995;99:55–62.
14 Elmstahl S, Rosen I, Gullberg B: Quantitative EEG in elderly patients with Alzheimer's disease and healthy controls. Dementia 1994;5: ...

Commented [JH11]: Jelic V, Shigeta M, Julin P, Almkvist O, Winblad B, Wahlund LO: Quantitative electroencephalography power and coherence in Alzheimer's disease and mild cognitive impair- ...

Commented [JH12]: Jelic V, Shigeta M, Julin P, Almkvist O, Winblad B, Wahlund LO: Quantitative electroencephalography power and coherence in Alzheimer's disease and mild cognitive impair- ...

Commented [JH13]: Might also be relevant for discussion

Commented [JH14]: discussion

Commented [JH15]: 51 Leung LS: Fast (beta) rhythms in the hippocampus: A review. Hippocampus 1992;2:93–98.
52 Riekkinen PJ, Riekkinen M, Sirvio J, Mietti- ...

Commented [JH16]: EEG in MCI and AD
EEG introduction, why it's great to use

Commented [JH17]: Good paper!

Commented [JH18]: @article{babiloni2016brain, title={Brain neural synchronization and functional coupling in Alzheimer's disease as revealed by resting state EEG rhythms}, author={Babiloni, Claudio and Lizio, Roberta and Marzano, Nicola and Capotosto, Paolo and Soricelli, Andrea ...

temporally-coordinated brain networks underpinning cognitive functions do become more and more abnormal along the progression of AD neurodegeneration, so that AD can be viewed as a disconnection syndrome (Bokde et al., 2009). An ideal methodological approach is, therefore, the extraction of some functional indexes of the abnormalities of the functional brain connectivity across long term neural networks Q24 (Varela et al. 2001;Q25 Le Van Quyen et al. 2003; Börner et al. 2007).

Conclusion, the resting state EEG makers are promising to unveil abnormal functional connectivity and neuroplasticity of neurotransmission in the brain of AD patients.

Sun, Sun, Chen, Wang & Gao (2024): https://doi.org/10.1186/s12916-024-03481-1

Brain network source connectivity analysis in the spatial domain

Source connectivity analysis is a critical technique using neuroimaging data for examining complex interactions between brain regions [23]. Its main goal is to identify functional or effective linkages among cerebral sources that reflect cognitive shifts in conditions like depression and schizophrenia [24, 25]. Among various functional connectivity metrics, coherence is a key measure, calculating the linear correlation between two signals in the frequency domain. However, coherence measurements can be affected by volumetric conduction, causing misleading pseudo-coherent values [26, 27].

Age-related differences in the impact of SARS-CoV-2 were also apparent. Young adults showed the most significant cognitive impact, followed by adults and adolescents, while children under 10 exhibited the least effect, with significantly fewer link reductions compared to young adults. These findings suggest that the cognitive resilience varies with age, with the brain networks of young adults being notably more vulnerable to disruption by SARS-CoV-2. This vulnerability could be influenced by factors such as the stage of brain development, life-style, or pre-existing health conditions. Adults and adolescents displayed moderate resilience, while the minimal impact on children could indicate more robust brain networks or compensatory mechanisms that protect against connectivity loss.

Significantly, the young adult group demonstrated the highest prevalence of cognitive dysfunctions, closely followed by the adult cohort.

In contrast, the adolescent and child groups showed a lower probability of exhibiting cognitive-related symptoms.

The outcomes of this study distinctly highlight the amplified susceptibility of young adults to cognitive deficits following a SARS-CoV-2 infection, a demographic that has traditionally not been considered as high risk.

Commented [JH19]: Discussion (further research)

Commented [JH20]: EEG in COVID and COVID in general

Commented [JH21]: Important paper

Commented [JH22]: Read again, to see if all is relevant for discussion

Commented [JH23]: @article{sun2024eeg, title={EEG signatures of cognitive decline after mild SARS-CoV-2 infection: an age-dependent study}, author={Sun, Yike and Sun, Jingnan and Chen, Xiaogang and Wang, Yijun and Gao, Xiaorong}, journal={BMC Medicine}, volume={22}, number={1}, pages={257}, year={2024}, publisher={Springer} }

Commented [JH24]: Schoffelen JM, Gross J. Source connectivity analysis with MEG and EEG. Hum Brain Mapp. 2009;30(6):1857–65

Commented [JH25]: Olbrich S, Tränkner A, Chittka T, Hegerl U, Schönknecht P. Functional connectivity in major depression: increased phase synchronization between frontal cortical EEG-source estimates. Psychiatry Research: Neuroimaging. 2014;222(1–2):91–9.
Article Google Scholar
Di Lorenzo G, Daverio A, Ferrentino F, Santarnecchi E, Ciabattini F, Monaco L, et al. Altered resting-state EEG source functional connectivity in schizophrenia: the effect of illness duration. Front Hum Neurosci. 2015;9:234

Commented [JH26]: 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):1178–93.
Article PubMed PubMed Central Google Scholar
Xie W, Toll RT, Nelson CA. EEG functional connectivity analysis in the source space. Dev Cogn Neurosci. 2022;56: 101119

Commented [JH27]: discussion

Commented [JH28]: Connectivity

Our findings propose a more profound impact of SARS-CoV-2 on young adults in comparison to adolescents and children. This insight can potentially steer the formulation of rehabilitation strategies tailored for long COVID patients.

The diminished connectivity in specific brain regions, such as electrode T5, which in temporal lobe, may reflect disruptions in neural networks that are crucial for cognitive functions [54]. This aligns with existing studies that link changes in brain connectivity to various cognitive impairments [55]. The persistence of connectivity reductions primarily within hemispheres further underscores the targeted impact of SARS-CoV-2 on brain function. The increase in the HA parameter within the theta band post-infection in adults suggests subtle yet discernible changes in EEG activity, potentially reflecting alterations in cognitive states. The heightened complexity in EEG patterns post-recovery, particularly in the delta band, might indicate a compensatory neural mechanism or an altered state of brain activity in response to the infection.

The observed concentration of alterations within the delta frequency band presents a pioneering insight, proposing that this band may be particularly susceptible to the neurological impacts of SARS-CoV-2 [56].

Traditionally, it is recognized that delta wave activity is diminished when the eyes are open. However, the findings of this study suggest that delta waves can also reflect changes in subject states to a certain degree.

Allthough none of the participants in this study was clinically diagnosed with “brain fog,” the EEG changes noted bear resemblance to those associated with “brain fog,” hinting at a potential underlying neurological impact of the infection [58].

Results indicate a gradation in susceptibility to cognitive impacts post-SARS-CoV-2 infection across different age groups. The most substantial cognitive changes were observed in young adults, a demographic that is not typically considered at high risk for severe COVID-19 implications. While previous studies have also shown that infection has a greater impact on young adults [59], the results of the present study provide additional evidence at the electrophysiological level for this conclusion.

We endeavored to include as broad a population as possible, yet our study did not encompass all age groups, particularly the elderly. This omission means that the effects of the coronavirus on the neurological systems of older individuals remain unknown, given that some studies suggest this demographic may be more susceptible to such impacts [60].

In essence, this research furthers the existing knowledge on the neurological implications of SARS-CoV-2, underscoring the urgent requirement for a more profound understanding of the

Commented [JH29]: de Schotten MT, Foulon C, Nachev P. Brain disconnections link structural connectivity with function and behaviour. Nature Communications. 2020;11(1):5094.

Commented [JH30]: Klaassens BL, van Gerven JMA, van der Grond J, de Vos F, Möller C, Rombouts S. Diminished posterior precuneus connectivity with the default mode network differentiates normal aging from Alzheimer’s disease. Front Aging Neurosci. 2017;9:97.

Commented [JH31]: Valsamis H, Baki SA, Leung J, Ghosn S, Lapin B, Chari G, et al. SARS-CoV-2 alters neural synchronies in the brain with more severe effects in younger individuals. Sci Rep. 2023;13(1):2942

Commented [JH32]: Aghajani Mir M. Brain Fog: a Narrative Review of the Most Common Mysterious Cognitive Disorder in COVID-19. Mol Neurobiol. 2023. https://doi.org/10.1007/s12035-023-03715-y. Epub ahead of print.

Commented [JH33]: Alradhi MA, Moore J, Patte KA, O’Leary DD, Wade TJ. Adverse childhood experiences and COVID-19 stress on changes in mental health among young adults. Int J Environ Res Public Health. 2022;19(19):12874.

Commented [JH34]: Ciarambino T, Para O, Giordano M. Immune system and COVID-19 by sex differences and age. Women’s health (London, England). 2021;17:17455065211022262

virus's enduring effects on cognition. Particularly, it focuses on its impact on younger demographics, encompassing children and adolescents.

The results intimate that the influence of SARS-CoV-2 is amplified within the younger populace. Although children and adolescents were relatively less affected, they exhibited noteworthy neurophysiological markers of abnormality, suggesting possible risk. This study, therefore, serves as a groundwork for more extensive research into potential therapeutic interventions and strategies to alleviate these cognitive alterations.

Perez, Duque, Hidalgo & Salvador, 2024:

https://doi.org/10.1016/j.biopsycho.2024.108823

However, measuring brain activity at rest has limitations. One of these limitations is continuous cognitive engagement during rest, including processes such as mind wandering and inter-oception. Moreover, without specific instructions, there is no control over what individuals are actually doing while they are at rest. Additionally, resting-state brain activity may not entirely reflect the cognitive and functional capacity during active situations or specific tasks.

The incorporation of spectral power measures across frequency bands in rsEEG as enriching neurophysiological biomarkers in the assessment and monitoring of SCD should be based on an initial demonstration that these measures are reliable, consistent, and sensitive.

Addressing these limitations is crucial for the progression of EEG research and its effective application in the study of SCD.

Although the rsEEG frequency bands are universally identified using Greek letters (e.g., delta, theta, alpha, beta, and gamma), different classifications of their frequency limits were observed in the reviewed studies. To address this lack of consensus, on the one hand, the International Pharmaco-EEG Society recommends the following frequency limits: delta (1.5-<6), theta (6-<8.5), alpha1 (8.5-<10.5), alpha2 (10.5-<12.5), beta1 (12.5-<18.5), beta2 (18.5-<21), beta3 (21.0-<30), gamma (30-<40). For gamma, they empirically choose the following ranges: gamma1 (30-<65), gamma2 (65-<90), and gamma3 (90->135) (Jobert et al., 2012). On the other hand, the International Federation of Clinical Neurophysiology (IFCN) proposes another classification, which is the one most commonly used in clinical EEG (Kane et al., 2017): delta (0.1-<4), theta (4-<8), alpha (8 13), beta (14 30), and gamma (>30–80).

In understanding the distribution of electrical activity across different frequency bands, the reviewed studies have presented analyses of power density (the amount of electrical energy in a specific frequency band per unit of frequency), absolute power (the total amount of

Commented [JH35]: EEG in SCD

Commented [JH36]: @article{perez2024eeg, title={EEG Frequency Bands in Subjective Cognitive Decline: A Systematic Review of Resting State Studies}, author={Perez, Vanesa and Duque, Ar{\'a}nzazu and Hidalgo, Vanesa and Salvador, Alicia}, journal={Biological Psychology}, pages={108823}, year={2024}, publisher={Elsevier} }

Commented [JH37]: limitations

electrical energy in a specific frequency band, disregarding other frequencies), and relative power (the proportion of power in a specific frequency band relative to the total power across all frequencies) (Babiloni et al., 2020; Singh & Krishnan, 2023). The choice of each of these measures to assess brain electrical activity depends on the objectives or the specific analyses being conducted. However, when examining the resting state, it would be advisable to employ relative power, given that it provides information about the proportional distribution of electrical activity in different frequency bands in relation to the total EEG activity. This information can yield valuable insights into potential changes in resting-state brain activity in individuals with SCD.

In conclusion, this systematic review reveals a general tendency toward EEG alterations in the context of SCD. However, specific results indicate noteworthy discrepancies that highlight significant variability.

This complexity underscores the need for a thorough exploration of the underlying factors that contribute to divergence in the results of frequency bands, even within the context of the overall EEG alteration observed. Despite the promising potential of analyzing resting-state frequency bands, further refinement is required for their implementation as early biomarkers of brain activity changes or as complementary information in the neuropsychological evaluation of SCD cases. Additionally, this review exclusively reports group-level differences. Further research is needed to better understand how these findings would translate into an individual diagnostic context. Adherence to the latest guidelines, such as those of the IFCN (Babiloni et al., 2020) or the American Clinical Neurophysiology Society (ACNS) (Sinha et al., 2016), is recommended for proper implementation. Constant and uniform research on these frequency bands, guided by these established protocols, can facilitate the identification of consistent patterns and provide a robust foundation for early diagnosis and the development of more effective treatment strategies. Ultimately, it is crucial to emphasize the importance of adhering to the SCD-I criteria in order to ensure the comparability and reliability of the results across various studies.

Commented [JH38]: discussion

Fröhlich, Kutz, Müller & Claudia Voelcker-Rehagen (2021):

Commented [JH39]: EEG in MCI and AD

https://doi.org/10.3389/fnagi.2021.675689

Commented [JH40]: @article{frohlich2021characteristics, title={Characteristics of resting state EEG power in 80+-year-olds of different cognitive status}, author={Fr{\"o}hlich, Stephanie and Kutz, Dieter F and M{\"u}ller, Katrin and Voelcker-Rehage, Claudia}, journal={Frontiers in aging neuroscience}, volume={13}, pages={675689}, year={2021}, publisher={Frontiers Media SA} }

In this study, the synchronized activity at rest while eyes are open and closed in the classical broad bands delta, theta, alpha, and beta was compared between cognitively healthy OA and individuals with MCI of the same age. The sample included OA, 80 years or older, which are often not enough represented in studies on early detection of dementia. Groups were

Commented [JH41]: Could be somehow the start for my discussion section

compared with respect to mean absolute power, relative power, and reactivity to eyes opening separately in each band.

No significant differences between any of the groups of different cognitive status (CHI, pMCI, naMCI, and aMCI) were detected. Overall, specific topographical patterns were present, which will be compared with results from other age groups later. In addition, EEG reactivity was also present in each of the four frequency bands with overall greater power during EC compared with EO and a few focal increases in the beta band. The topography of reactivity for the most part related to the topography found in the EC condition.

Babiloni et al. (2011): https://doi.org/10.3233/JAD-2011-0051

Recently, greater attention has been focused on the application of quantitative EEG (qEEG) and/or event-related potentials (ERPs) as suitable clinical markers of early stage of disease or its progression [4–6]. It has been reported that a positive ERP peaking 600 ms after the zerotime of stimuli to be encoded (P600) was reduced in patients with AD and mild cognitive impairment (MCI), particularly in those MCI patients who subsequently converted to AD [7, 8]. Furthermore, a positive ERP peaking 300 ms after the zerotime of oddball stimuli (P300) was reduced in amplitude in AD patients [5, 9], even during its early stages [10].

Despite the evidence of abnormal cortical rhythms in MCI and AD subjects, EEG analysis alone is unable to allow a diagnosis of disease.

The hypothesis of some strict relationships between brain activity in MCI and AD subjects implies the prediction of similar features of resting state EEG rhythm in MCI and AD subjects as a function of genetic risk factors.

Kim et al., 2023: https://doi.org/10.3389/fpsyt.2023.1231861

EEG spectral power captures the amplitude of oscillations in each frequency band and can be used as a potential biomarker to differentiate AD from normal aging (25–28). In spectral analysis, it has been predominantly observed that the dementia stages of AD are associated with slowing oscillations caused by increasing low-frequency and decreasing high-frequency band power (24).

However, other studies found no or minimal differences between the MCI and healthy control (HC) groups (29–31), suggesting that the neurophysiological changes underlying MCI may not always be apparent in spectral power owing to the complex and heterogeneous conditions of MCI. Therefore, it is important to combine multiple biomarkers such as complexity

Commented [JH42]: Same, that's how the start of discussion section should look like

Commented [JH43]: EEG in MCI and AD

Commented [JH44]: @article{babiloni2011resting, title={Resting state cortical rhythms in mild cognitive impairment and Alzheimer's disease: electroencephalographic evidence}, author={Babiloni, Claudio and Vecchio, Fabrizio and Lizio, Roberta and Ferri, Raffaele and Rodriguez, Guido and Marzano, Nicola and Frisoni, Giovanni B and Rossini, Paolo M}, journal={Journal of Alzheimer's Disease}, volume={26}, number={s3}, pages={201--214}, year={2011}, publisher={IOS Press} }

Commented [JH45]: [4] Celesia GG, Kaufman D, Cone S (1987) Effects of age and sex on pattern electroretinograms and visual evoked potentials. Electroencephalogr. Clin Neurophysiol 68, 161-171.
[5] Rossini PM, Rossi S, Babiloni C, Polich J (2007) Clinical neurophysiology of aging brain: from normal aging to neurodegeneration. Prog Neurobiol Epub 2007 Aug 8. Review 83, 375-400.
[6] Rossini PM (2009) Implications of brain plasticity to brain-machine interfaces operation a potential paradox? Int Rev Neurobiol 86, 81-90. Review.

Commented [JH46]: [7] Olichney JM, Morris SK, Ochoa C, Salmon DP, Thal LJ, Kutas M, Iragui VJ (2002) Abnormal verbal event related potentials in mild cognitive impairment and incipient Alzheimer's disease. J Neurol Neurosur Ps 73, 377-384.
[8] Olichney JM, Iragui VJ, Salmon DP, Riggins BR, Morris SK, Kutas M (2006) Absent event-related potential (ERP) word repetition effects in mild Alzheimer's disease. Clin Neurophysiol 117, 1319-1330

Commented [JH47]: 5] Rossini PM, Rossi S, Babiloni C, Polich J (2007) Clinical neurophysiology of aging brain: from normal aging to neurodegeneration. Prog Neurobiol Epub 2007 Aug 8. Review 83, 375-400. ...

Commented [JH48]: Polich J, Corey-Bloom J (2005) Alzheimer's disease and P300: review and evaluation of task and modality. Curr Alzheimer Res 2, 515-525

Commented [JH49]: EEG in MCI and AD

Commented [JH50]: @article{kim2023resting, title={Resting-state electroencephalographic characteristics related to mild cognitive impairments}, author={Kim, Seong-Eun and Shin, Chanwoo and Yim, Junyeop and Seo, ...

Commented [JH51]: 25. Monllor P, Cervera-Ferri A, Lloret MA, Esteve D, Lopez B, Leon JL, et al. Electroencephalography as a non-invasive biomarker of Alzheimer's disease: a ...

Commented [JH52]: 24. Cassani R, Estarellas M, San-Martin R, Fraga FJ, Falk TH. Systematic review on resting-state EEG for Alzheimer's disease diagnosis and progression assessment. Dis ...

Commented [JH53]: 29. Van der Hiele K, Vein A, Reijntjes R, Westendorp R, Bollen E, Van Buchem M, et al. EEG correlates in the spectrum of cognitive decline. Clin Neurophysiol. (2007) ...

measures, functional connectivity, and graph-based network analyses, to enhance MCI detection.

3. Results

3.1. Power spectral properties

Topographic plots were computed for the delta (0.1–4 Hz), theta (4-8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–45 Hz) frequency bands in the HC and MCI groups. In both groups, delta oscillations were dominant in the frontal area (Fp1 and Fp2) (Figure 2A). Theta and alpha oscillations were prominent in occipital regions (O1 and O2) in two groups (Figures 2B, C). Beta and gamma activities remained negligible across all brain regions (Figures 2D, E). However, no significant differences were found between the HC and MCI groups in any of the frequency bands and channels after FDR correction.

Our findings indicated that the power spectrum analysis did not yield any significant differences between the HC and MCI groups. However, when analyzing the multiscale SE, we observed that the MCI group exhibited lower complexity.

In addition, the MCI group demonstrated higher wPLI values than the HC group. Further examination using graph theory analysis revealed that the MCI group predominantly displayed lower global efficiency in the theta band and higher local efficiency in the gamma band relative to the HC group. Moreover, nodal efficiency was reduced in the frontal region of the MCI group.

Finally, in the small-world analysis, the MCI group exhibited a lower small-world coefficient when compared to the HC group.

In the power spectral analysis, no significant differences were found between the HC and MCI groups in any frequency band (delta, theta, alpha, beta, or gamma). This suggests that there were no significant differences in the overall power of the EEG signals between the two groups. These results are consistent with those of the recent studies suggesting that PSD had a limited ability to distinguish between HC and MCI groups (30, 77).

However, some prior findings have revealed that MCI can be characterized by lower alpha and beta power as well as stronger delta and theta power (26). This contradiction may be because the neurophysiological changes associated with MCI may not always be apparent in spectral power, suggesting that the power spectral analysis is relatively insensitive to network changes resulting from MCI progression.

Our findings suggest that alterations in functional connectivity and graph theory-based measures, particularly in the theta band associated with memory and attention processes,

Commented [JH54]: 30. Yan Y, Zhao A, Ying W, Qiu Y, Ding Y, Wang Y, et al. Functional connectivity alterations based on the weighted phase lag index: an exploratory electroencephalography study on Alzheimer's Disease. Curr Alzheimer Res. (2021) 18:513–22. doi: 10.2174/1567205018666211001110824

Commented [JH55]: 77. Fröhlich S, Kutz DF, Müller K, Voelcker-Rehage C. Characteristics of resting state EEG power in 80+-year-olds of different cognitive status. Front Aging Neurosci. (2021) 13:675689. doi: 10.3389/fnagi.2021.675689

Commented [JH56]: 26. Kwak YT. Quantitative EEG findings in different stages of Alzheimer's disease. J Clin Neurophysiol. (2006) 23:457–62. doi: 10.1097/01.wnp.0000223453.47663.63

may serve as important clinical biomarkers for detecting and monitoring cognitive decline in individuals with MCI. Small sample size.

Jelic et al., 2000: https://doi.org/10.1016/S0197-4580(00)00153-6

Another potential explanation of our results could be that the use of relative power is compromised by the fact that all other bands are interrelated. An increase in, for example, theta power will also cause a decrease in relative alpha power even if there was no change in the amount of alpha absolute power. However, the main interest of this study was to find sensitive neurophysiological indices of disease prediction and progression in subjects at risk and not to draw any stronger inferences about the biological significance of different frequency bands. The separate reliability part of this study, performed as repeated measurements on healthy subjects, showed in general higher intraindividual temporal variability for absolute power values, which was especially marked for the slow frequency bands. Therefore, the use of relative power values was justified.

Commented [JH57]: EEG in MCI and AD

Commented [JH58]: @article{jelic2000quantitative, title={Quantitative electroencephalography in mild cognitive impairment: longitudinal changes and possible prediction of Alzheimer's disease}, author={Jelic, Vesna and Johansson, Sven Erik and Almkvist, Ove and Shigeta, Masahiro and Julin, Per and Nordberg, Agneta and Winblad, Bengt and Wahlund, Lars Olof}, journal={Neurobiology of aging}, volume={21}, number={4}, pages={533--540}, year={2000}, publisher={Elsevier} }

Commented [JH59]: discussion

Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari & Lönnqvist, 2008: https://doi.org/10.1016/j.jad.2007.06.006

There is growing evidence for cognitive dysfunction in depressive and anxiety disorders. Nevertheless, the neuropsychological profile of young adult patients has not received much systematic investigation. The following paper reviews the existing literature on cognitive impairments in depressive and anxiety disorders particularly among young adults. Additionally, the focus of young adult age group and the effect of confounding variables on study results are discussed.

Cognitive impairments are common in young adults with major depression and anxiety disorders, although their nature remains partly unclear. Accordingly, executive dysfunction is evident in major depression, but other more specific deficits appear to depend essentially on disorder characteristics. The profile of cognitive dysfunction seems to depend on anxiety disorder subtype, but at least obsessive–compulsive disorder is associated with deficits in executive functioning and visual memory. The conflicting results may be explained by heterogeneity within study participants, such as illness status, comorbid mental disorders, and medication, and other methodological issues, including inadequate matching of study groups and varying testing procedures.

Cognitive impairments are common in major depression and anxiety disorders. However, more research is needed to confirm and widen these findings, and to expand the knowledge

Commented [JH60]: Cognitive impairments in depressive and anxiety disorders with a focus on young adults

Commented [JH61]: @article{castaneda2008review, title={A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults}, author={Castaneda, Anu E and Tuulio-Henriksson, Annamari and Marttunen, Mauri and Suvisaari, Jaana and L{\"o}nnqvist, Jouko}, journal={Journal of affective disorders}, volume={106}, number={1-2}, pages={1--27}, year={2008}, publisher={Elsevier} }

into clinical practice. Controlling of confounding variables in future studies is highly recommended

- ➔ But all with objective cognitive impairment and therefore probably not relevant for my discussion

Grant, Thase & Sweeney, 2001: https://doi.org/10.1016/s0006-3223(00)01072-6

The most striking finding from the current study was the absence of significant cognitive impairment on the majority of both standardized neuropsychologic tests and experimental computerized cognitive measures in younger am bulatory adults with major depression. Intact atentional, memory, and motor functioning were noted across batteries, with some suggestion of impaired executive functioning provided by the WCST. These findings from a large sample of younger (average age 39.0 years), unmedicated depressed patients using a comprehensive neurocognitive assessment indicate that major depressive disorder per se in young ambulatory adults is associated with only minimal cognitive deficits. These findings are consistent with those of several other recent studies of smaller samples of younger medicated depressed patients (Fossati et al 1999; Purcell et al 1997) but are notably different from the more consistent findings of cognitive impairments reported among older depressed patients (Beats et al 1996; Elliott et al 1996; Harvey et al 1997; Palmer et al 1996).

Commented [JH62]: Cognitive impairment in depression

Commented [JH63]: @article{grant2001cognitive, title={Cognitive disturbance in outpatient depressed younger adults: evidence of modest impairment}, author={Grant, Merida M and Thase, Michael E and Sweeney, John A}, journal={Biological psychiatry}, volume={50}, number={1}, pages={35--43}, year={2001}, publisher={Elsevier} }

Newson & Thiagarajan (2019): https://doi.org/10.3389/fnhum.2018.00521

Depression: The dominant result for depression was an increase in the absolute power in both theta and beta bands for both eyes open and eyes closed conditions (eyes closed consistency 1.8, validation 880; eyes open consistency 2.0, validation 337) with average magnitudes of 48%. However, these increases were no longer visible when considering relative power where most studies failed to find any significant differences across any band (Knott et al., 2001b; Morgan et al., 2005; Korb et al., 2008; Cook et al., 2014). The largest study (Arns et al., 2015) consisting of 1,344 participants showed increases in theta power across frontal regions of the brain using the eLORETA source localized signal which is methodologically different from most other depression studies identified for this review which perform their analysis in electrode space. Other disorders such as bipolar disorder (Clementz et al., 1994; El-Badri et al., 2001; Bas¸ar et al., 2012; Kam et al., 2013; Narayanan et al., 2014; Moeini et al., 2015), anxiety (Sachs et al., 2004; Oathes et al., 2008; Xing et al., 2017) and panic disorder (Knott et al., 1996; Gordeev, 2008; Wise et al., 2011; de Carvalho et al., 2015) are included here for completeness.

Commented [JH64]: EEG Frequency bands in psychiatric disorders

Commented [JH65]: @article{newson2019eeg, title={EEG frequency bands in psychiatric disorders: a review of resting state studies}, author={Newson, Jennifer J and Thiagarajan, Tara C}, journal={Frontiers in human neuroscience}, volume={12}, pages={521}, year={2019}, publisher={Frontiers Media SA} }

However generally there was no more than one or two studies for any one condition (eyes closed, eyes open, relative power, absolute power), which was too few for the inference of any trends or for the calculation of consistency scores. Nonetheless we show these results as part of our table with the caveat that they are generally poorly validated.

Schreiter-Gasser, Gasser & Ziegler (1993) : https://doi.org/10.1016/0013-4694(94)90144-9

The delta band is by far the best indicator for the degree of dementia. The theta band, which best separated patients from controls (Schreiter-Gasser et al. 1993), separates poorly different stages of dementia. This can be explained by the fact that theta activity is greatly increased already in mild to moderate cases. In the delta band, on the other hand, mild to moderate cases are intermediate between severe cases and controls. Thus, progression of Alzheimer's disease goes along with gradual increase of delta power. This is in general agreement with the literature (Cohen et al. 1985; Penttilfi et al. 1985; Soininen and Partanen 1988; Soininen et al. 1991), but the relationships are more clear-cut in our Study.

Farina et al., 2020: https://doi.org/10.1016/j.neuroimage.2020.116795

Higher delta power in left temporo-parietal areas was also indicative of patient status, though to a lesser degree, consistent with evidence that delta changes occur later (Roh et al., 2011).

Jelic, Shigeta, Julin, Almkvist, Winblad & Wahlund (1996): https://doi.org/10.1159/000106897

The lack of clear qEEG changes in the present study in subjects with MCI can have at least two explanations. 1. Group is heterogeneous and, according to some follow-up studies, only a proportion of them will show further cognitive decline and develop manifest disease (4,9). 2. Some of these subjects have preclinical AD with pathology still restrictred to medial temporal lobes, which cannot be detected as changes in EEG power.

Claus et al. (2000): https://doi.org/10.1159/000017219

This analysis may demonstrate that increase of absolute theta and delta power is sometimes less clearly reflected in the relative power values.

Commented [JH66]: EEG in dementia and AD (what's the difference?)

Commented [JH67]: @article{schreiter1994quantitative, title={Quantitative EEG analysis in early onset Alzheimer's disease: correlations with severity, clinical characteristics, visual EEG and CCT}, author={Schreiter-Gasser, Ursula and Gasser, Theo and Ziegler, Peter}, journal={Electroencephalography and clinical Neurophysiology}, volume={90}, number={4}, pages={267--272}, year={1994}, publisher={Elsevier} }

Commented [JH68]: EEG in MCI and AD

Commented [JH69]: @article{farina2020comparison, title={A comparison of resting state EEG and structural MRI for classifying Alzheimer's disease and mild cognitive impairment}, author={Farina, Francesca R and Emek-Sava{\c{s}}, DD and Rueda-Delgado, L and Boyle, Rory and Kiiski, Hanni and Yener, G{\"o}rsev and Whelan, Robert}, journal={Neuroimage}, volume={215}, pages={116795}, year={2020}, publisher={Elsevier} }

Commented [JH70]: discussion

Commented [JH71]: EEG in AD and MCI / objective and subjective decline

Commented [JH72]: @article{jelic1996quantitative, title={Quantitative electroencephalography power and coherence in Alzheimer's disease and mild cognitive impairment}, author={Jelic, Vesna and Shigeta, Masahiro and Julin, Per and Almkvist, Ove and Winblad, Bengt and Wahlund, Lars-Olof}, journal={Dementia and Geriatric Cognitive Disorders}, volume={7}, number={6}, pages={314--323}, year={1996}, publisher={S. Karger AG Basel, Switzerland} }

Commented [JH73]: EEG in cognitive impairment in AD

Commented [JH74]: @article{claus2000determinants, title={Determinants of quantitative spectral electroencephalography in early Alzheimer's disease: cognitive function, regional cerebral blood flow, and computed tomography}, author={Claus, JJ and Ongerboer de Visser, BW and Bour, LJ and Walstra, GJM and Hijdra, A and Verbeeten Jr, B and Van Royen, EA and Kwa, VIH and Van Gool, WA}, journal={Dementia and geriatric cognitive disorders}, volume={11}, number={2}, pages={81--89}, year={2000}, publisher={S. Karger AG Basel, Switzerland} }

This is probably due to the fact that theta and also delta power determine the main part of the total power. As, for instance, theta or delta increases, the total power more or less increases proportionally. An increase in theta or delta may then be reflected by the absolute power, rather than by the relative EEG values.

Schreiter-Gasser, Gasser & Ziegler (1993) : https://doi.org/10.1016/0013-4694(94)90144-9

The degree of dementia is strongly reflected by an increase of power in the delta frequency band, accentuated on the left hemisphere.

The quantitative EEG shows a surprising power in reflecting stages of AIzheimer's disease and indeed the most striking associations occurred between the degree of dementia and delta power. The delta band is by far the best indicator for the degree of dementia. The theta band, which best separated patients from controls (Schreiter-Gasser et al. 1993), separates poorly different stages of dementia. This can be explained by the fact that theta activity is greatly increased already in mild to moderate cases. In the delta band, on the other hand, mild to moderate cases are intermediate between severe cases and controls. Thus, progression of Alzheimer's disease goes along with gradual increase of delta power. This is in general agreement with the literature (Cohen et al. 1985; Penttilfi et al. 1985; Soininen and Partanen 1988; Soininen et al. 1991), but the relationships are more clear-cut in our Study. This may be attributed to using absolute rather than relative power and also to LOG artifact correction.

Elmståhl, Rosen & Gullberg (1994): https://doi.org/10.1159/000106706

Not only theta power but also delta power is significantly increased. This is most likely due to the fact that our patient sample is one of late-onset AD in a rather advanced stage. In studies of the progress of the FEG with increasing severity of AD theta power is increased, followed by a decrease in beta power and later by an increase in delta power and a decrease in alpha power (3. 25]. Our group of elderly institutionalized patients had obviously reached a stage of marked delta power increase.

The topographical analysis showed a widespread increase in delta and theta power over most cortical areas, whereas the decrease in beta power was more restricted to posterior temporoparietal areas. Delta waves are considered to reflect primarily abnormalities of connections between subcortical and cortical areas whereas the beta power decrease is considered to reflect cortical degenerative changes [26, 27]. The results of our study would

Commented [JH75]: EEG in dementia and AD (what's the difference?)

Commented [JH76]: @article{schreiter1994quantitative, title={Quantitative EEG analysis in early onset Alzheimer's disease: correlations with severity, clinical characteristics, visual EEG and CCT}, author={Schreiter-Gasser, Ursula and Gasser, Theo and Ziegler, Peter}, journal={Electroencephalography and clinical Neurophysiology}, volume={90}, number={4}, pages={267--272}, year={1994}, publisher={Elsevier} }

Commented [JH77]: akzent

Commented [JH78]: EEG in AD

Commented [JH79]: @article{elmstaahl1994quantitative, title={Quantitative EEG in elderly patients with Alzheimer's disease and healthy controls}, author={Elmst{\aa}hl, S{\"o}lve and Ros{\'e}n, Ingmar and Gullberg, Bo}, journal={Dementia and Geriatric Cognitive Disorders}, volume={5}, number={2}, pages={119--124}, year={1994}, publisher={S. Karger AG Basel, Switzerland} }

Commented [JH80]: 3 Cobcn LA. Danziger W. Storandt M: A longitu
dinal EEG study of mild senile dementia of
Alzheimer type: Changes at 1 year and at 2.5
years. J Electrocncephalogr Clin Neurophvsiol
1985:61:101-112.
25 Soinincn H. Partanen J. Laulumaa V. Paak-
konen A. Helkala EL. Riekkinen P: Serial EEG
in Alzheimer's disease: 3 year follow-up and
clinical outcome. J Electrocncephalogr Clin
Ncurophysiol 1991;79:342-348.

Commented [JH81]: 26 Kcllawav P; An orderly approach to visual
analysis: Parameters of the normal EEG in
adults and children; in Klass DW, Daly DD
(eds): Current practice of Clinical Electroen
cephalography. New York, Raven Press. 1979.
pp 69-148.
27 Gloor P, Ball G. Schaull N: Brain lesions that
produce delta waves in the EEG. Neurology
(Minncap) 1977;27:326-333

therefore indicate a profound derangement of subcortical function in combination with degeneration of posterior cortical areas.

Dringenberg (2000): https://doi.org/10.1016/S0166-4328(00)00261-8

Some EEG changes, such as the increase in theta power, occur together with the earliest signs of cognitive deterioration, while others are associated with more advanced cognitive decline (e.g. increased delta power [71,74]). The close relation between EEG slowing and the severity of cognitive symptoms suggests that a disruption of processing in cortical networks contributes importantly to the behavioral disorganization present in AD.

Schild et al., 2022: https://doi.org/10.1007/s00415-022-11444-w

The post-COVID-19 syndrome is a multifaceted condition, which may affect cognition [4, 19]. We focused on patients reporting cognitive impairment among other symptoms at least three months after an asymptomatic to mild/moderate acute COVID-19 disease course. We conducted an extensive neuropsychological assessment, including cognitive screening tests and psychiatric assessments in 52 patients. In 60% of the patients, subjective cognitive impairment was objectified, of which the majority (around 87%) displayed an impairment in more than one domain. Significant group differences between patients with no, minor, or major NCD were found in all cognitive domains and global cognitive performance as expressed by the GCCS. Neither depression, anxiety, fatigue, sleep quality, nor total general health status differed significantlybetween the groups. Only daytime sleepiness was reported significantly less in patients with minor NCD compared with patients with major NCD.

The patient demographics of our study cohort were similar to other studies on the post-COVID-19 syndrome, with an average age of 46.5 years and a high educational level (15.9 years [9, 12, 19, 35, 36]).

The MMSE that is usually administered for the detection of dementia was not sufficiently sensitive to detect cognitive

Commented [JH82]: EEG in AD

Commented [JH83]: @article{dringenberg2000alzheimer, title={Alzheimer's disease: more than a 'cholinergic disorder'—evidence that cholinergic--monoaminergic interactions contribute to EEG slowing and dementia}, author={Dringenberg, Hans C}, journal={Behavioural brain research}, volume={115}, number={2}, pages={235--249}, year={2000}, publisher={Elsevier} }

Commented [JH84]: [71] Penttila¨ M, Partanen JV, Soininen H, Riekkinen PJ. Quantitative analysis of occipital EEG in different stages of Alzheimer's disease. Electroencephalogr Clin Neurophysiol 1985;60:1–6. [74] Prichep LS, John ER, Ferds SH, Reisberg B, Almas M, Alper K, Cancro R. Quantitative EEG correlates of cognitive deterioration in the elderly. Neurobiol Aging 1994;15:85–90.

Commented [JH85]: @article{schild2023multidomain, title={Multidomain cognitive impairment in non-hospitalized patients with the post-COVID-19 syndrome: results from a prospective monocentric cohort}, author={Schild, Ann-Katrin and Goereci, Yasemin and Scharfenberg, Daniel and Klein, Kim and L{\"u}lling, Joachim and Meiberth, Dix and Schweitzer, Finja and St{\"u}rmer, Sophie and Zeyen, Philip and Sahin, Derya and others}, journal={Journal of neurology}, volume={270}, number={3}, pages={1215--1223}, year={2023}, publisher={Springer} }

impairment in our patients, confirming findings by Mattioli et al. [37]. It showed a ceiling effect with small standard deviation and range. The target population of such screening tests usually is older than the patients included in this study which might serve as explanation [38]. The MoCA is more sensitive for the detection of mild cognitive impairment [39]. It was frequently administered in post-COVID-19 patients, where it was able to detect impairment [40, 41]. The MoCA scores in our study indicated impairment in 13 patients. However, the comprehensive neuropsychological assessments revealed impairment in 31 patients indicating still limited sensitivity of the MoCA for post-COVID cognitive dysfunction.

It is
critical to point out that we required self-reported cognitive impairment as the inclusion criterion in our study.

Psychological
approaches like the recently proposed network perspective on neuropsychiatric and cognitive symptoms of the post-COVID-19 syndrome in combination with neurological mechanisms may contribute to explain the variety and persistence of such symptoms after COVID-19 [49].
The patients in our study showed elevated fatigue, poor sleep quality, and increased daytime sleepiness as well as screening scores for depression and anxiety at the borderline to clinical significance at the group level. However, we did not find an association of these assessments with cognition with the exception of higher daytime sleepiness in those with major NCD. Other studies in post-COVID-19 syndrome after mild COVID-19 infection also failed to show associations between cognition and fatigue or depression [14]. This is in contrast with one other study that reported correlations between global cognitive impairment and anxi-

ety and depression in previously hospitalized patients [50].

Also other aspects, like increased self-reflec-
tion or specific personality traits in those with subjective impairment only, may contribute to this finding.

There is much more that I need to look at!!!!!!!!!