EEG in SCD

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Recognizing that preventive interventions are typically more effective in preclinical stages, current research endeavors to focus on identifying early biological markers of SCD using resting-state electroencephalogram (rsEEG) methods (Perez et al., 2024). The review emphasizes patterns in frequency band activity, revealing that individuals classified as SCD exhibited increased theta power than healthy controls, but decreased than MCI (Perez et al., 2024). However, findings for the alpha, delta, and beta bands were inconsistent, demonstrating variability across studies and highlighting the need for further research (Perez et al., 2024).

Although there has been extensive recent research on the use of frequency bands in individuals with SCD to investigate and understand changes in brain activity associated with early MCI and the risk of progression to neurodegenerative diseases such as AD, the findings have not yet been fully integrated (Perez et al., 2024). This is probably due to the heterogeneity of the methodological approaches and criteria used to characterize SCD.
Four studies documented alterations in the rsEEG delta frequency band in people with SCD. Sibilano et al. (2023), Iliadou et al. (2021), and Gouw et al. (2017) conducted a thorough investigation of frequency band changes by comparing individuals with SCD to those with MCI.
Additionally, Sibiliano included a group of healthy controls in their analysis. In Iliadou's (2021) study, the MCI group exhibited a significant increase in overall delta power compared to the SCD group, highlighting distinctive spectral alterations. Moreover, in their spectral analysis comparing SCD and MCI, Sibilano et al. (2023) identified higher spectral power in the delta band that was associated with the clinical progression from SCD to MCI. In a longitudinal study exploring the gradual progression towards AD, Gouw et al. (2017) identified alterations in spectral power in individuals with SCD who eventually advanced to MCI.
The study reported heightened delta activity throughout the cortex.
Finally, Jeong et al. (2021) reported increased delta activity in the frontal cortex in individuals with SCD compared to healthy controls. Six studies reported an abnormal rsEEG of theta power in people with SCD compared to MCI and healthy control groups. Three studies

specifically explored rsEEG in individuals with SCD along the MCI continuum. Iliadou et al. (2021) observed lower spectral power in theta in SCD compared to individuals with MCI. Sibilano et al. (2023) utilized rsEEG to discriminate between SCD and MCI, identifying the delta and theta bands as discriminating the most between SCD and MCI. We identified six articles that reported alterations in alpha power in individuals with SCD compared to those with MCI and healthy control groups. Iliadou et al. (2021) observed a decrease in alpha spectral power in individuals with SCD compared to those with MCI. Additionally, a decrease in spectral power across the entire alpha band was noted in individuals with SCD who progressed to MCI in the study conducted by Gouw et al. (2017). When comparing people with SCD to the healthy control group, Jeong et al. (2021) found a decrease in alpha1, specifically in the occipital regions, whereas Prichep et al. (2006) observed a decrease in the alpha band. In contrast, Alexander et al. (2006) reported an increase, rather than a decrease, in the alpha band in individuals with SCD compared to the healthy control group. In the case of the beta band, three studies reported noteworthy changes. Iliadou et al. (2021) observed a decrease in beta spectral power in individuals with SCD compared to those with MCI. Additionally, Mazzon et al. (2018) identified a decrease in beta power in the left frontal regions when comparing the SCD group to the MCI group. In the study by Alexander et al. (2006), which compared individuals with SCD to a healthy control group, increased beta power was observed in the central, parietal, and frontal regions in individuals with SCD. None of the studies included in this review reported significant changes in the groups in the gamma frequency band.

Overall, individuals with SCD exhibited a pronounced increase in theta spectral power compared to healthy controls, whereas those with MCI showed a further increment compared to individuals with SCD, indicating alterations across the MCI continuum. Similar alterations across the MCI continuum were observed in alpha spectral power.

Specifically, individuals with SCD displayed decreased alpha spectral power compared to healthy controls, but higher levels than in individuals with MCI. However, this trend is inconsistent because two studies reported increases, rather than decreases, in this band in both SCD and MCI. Additionally, findings for the delta and beta frequency bands are rather inconclusive, given that half of the studies did not identify significant effects within these bands. In the studies that did observe effects, an increase in delta was noted in individuals with SCD compared to healthy controls, as well as in individuals with MCI compared to individuals with SCD. The findings related to beta band activity are also unclear. Whereas one study reported an increase in beta band activity when comparing SCD and healthy controls, an

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examination of the MCI continuum reveals a tendency towards decreased beta band activity in individuals with MCI compared to those with SCD.

Despite this overarching trend, variability in the studies' results was evident, probably stemming from variations in measurement and analysis methodologies and discrepancies in the diagnostic criteria used to define SCD.

Overall, most of the consulted studies reported an alteration in the EEG associated with SCD, as evidenced by an increase in spectral power in the low-frequency bands and a decrease in spectral power in the high-frequency bands.

Most of the analyzed studies reported abnormal rsEEG activity in individuals with SCD compared to healthy control groups. Furthermore, studies contrasting SCD and MCI reveal that rsEEG abnormalities persist and intensify as cognitive decline progresses. Our review revealed the following evidence: 1) increased delta power in individuals with SCD compared to both healthy controls and people with MCI, although these findings were not consistently reported across all the studies; 2) a progressive increase in theta frequency bands in individuals with SCD compared to healthy controls, which intensified when comparing MCI to SCD; 3) a decrease in the alpha frequency band in individuals with SCD compared to healthy controls, with this decrease being more pronounced in those diagnosed with MCI compared to SCD. However, this trend was not observed in two studies that compared individuals with SCD to healthy controls and individuals with MCI, respectively. In these studies, unexpected increases, rather than decreases, in alpha and beta frequency band spectral power were reported in the SCD groups compared to healthy controls, and in the MCI groups compared to the SCD groups; 4) a decrease in beta band activity was only noted in studies that compared MCI with SCD. Conversely, the other two studies reported increases in the frequency of this band.

What is the physiological significance of the changes observed in the spectral power of delta, theta, alpha, and beta rhythms in individuals with SCD? The alterations in the high and low components of the delta rhythms, indicative of a healthy brain, are thought to be influenced by inhibiting oscillators within the reticulo-thalamic (7–14 Hz), thalamo-cortical (1–4 Hz), and intracortical (<1 Hz) neural circuits (Steriade, 2006). Moreover, it has been proposed that thalamo-cortical circuits play a role in the generation and modulation of theta rhythms. Thus, it is plausible to hypothesize that diminished activation of neurons, possibly due to acetylcholine reduction or synaptic damage, can impact inhibitory and excitatory cortical feedback interactions that are crucial for generating cortical rsEEG rhythms. This disruption may influence the regulation of overall brain arousal, the balance of cortical

inhibition/excitation, and vigilance, potentially resulting in a decrease in spectral power across the delta and theta bands. The crucial implication of cholinergic deficiency is further corroborated by EEG investigations using scopolamine, a non-selective antagonist of muscarinic receptors that hinders stimulation of postsynaptic receptors. Following scopolamine administration, healthy subjects show increased delta and theta power, along with decreased alpha and beta power (Ebert et al., 2001).

Furthermore, beta rhythms may be associated with the regulation of thalamocortical flow, encompassing commands, images, and motor plans through the basal ganglia and motor thalamus (Oswal et al., 2013). As mentioned previously, Alexander et al. (2006) and Iliadou et al. (2021) found distinct alpha and beta rhythm patterns from those found in other studies reviewed. These authors suggested that the psychophysiological changes observed in the SCD in their study may reflect an initial compensatory process in response to early cognitive impairment.

Notably, theta and gamma bands are recognized for their involvement in memory (Klimesch, 1999; Nyhus & Curran, 2010), whereas delta bands play a role in maintaining focused attention (Harmony, 2013). The alpha band has been associated with attention and memory processes (Klimesch, 1999, 2012). Although the role of beta oscillations in the cognitive process has been explored less, some evidence suggests that they are related to the state of attention (Güntekin et al., 2013). Third, because SCD often precedes more severe conditions, such as MCI or AD, analyzing the rsEEG may be crucial in identifying early markers of changes in brain activity, making earlier interventions possible.

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 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.

Therefore, it would be beneficial to investigate early and reliable biomarkers for the detection and treatment of SCD in an attempt to maintain cognitive health and delay or prevent the progression to AD (Abdulrab & Heun, 2008).