Disturbed Beta Band Functional Connectivity in Patients With Mild Cognitive Impairment: An MEG Study

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Abstract—Mild cognitive impairment (MCI) refers to the clinical state of subjects who suffer from some degree of cognitive deterioration but do not meet clinical criteria for dementia. The aim of this study was to analyze the magnetoencephalogram (MEG) background activity in MCI subjects using two connectivity measures: coherence and synchronization likelihood (SL). Our results showed that coherence and SL mean values were lower in the MCI group than in control group at all frequency bands (delta, theta, alpha-1, alpha-2, beta, and gamma). Significant differences were found in the beta frequency band with both measures ($p < 0.05$, Mann–Whitney $U$-test). Coherence analysis also revealed significant differences between controls and MCI in the gamma band. Additionally, coherence and SL mean values at each frequency band were analyzed by means of receiver operating characteristic curves. The highest accuracy (69.8%) was achieved in the beta band with both connectivity measures. Our results suggest that spontaneous MEG rhythms show disconnection problems in MCI, especially in the beta band. In conclusion, both coherence and SL may be useful measures for discriminating MCI patients from control subjects.

Index Terms—Beta frequency band, coherence, functional connectivity, magnetoencephalogram, mild cognitive impairment (MCI), synchronization likelihood (SL).

I. INTRODUCTION

MILD cognitive impairment (MCI) has been interpreted as the clinical condition between normal aging and Alzheimer’s disease (AD) in which persons experience a cognitive deterioration beyond that expected for age and education, yet they do not meet currently accepted criteria for clinically probable AD [1], [2]. Compared with demented people and elderly subjects without cognitive impairment, MCI patients show intermediate amounts of AD neuropathological findings identified by senile plaques containing amyloid-beta-peptide and neurofibrillary tangles in the medial temporal lobe structures [3]. MCI is a heterogeneous clinical entity in which three subtypes can be distinguished [4]: amnestic MCI, multiple-domain slightly impaired, and single-domain nonmemory MCI. The heterogeneity of this group makes very difficult to determine if a potential MCI patient is exhibiting cognitive changes of normal aging or the earliest stages of dementia [1]. To help in the diagnosis, the “Working Group on MCI” of the “European Consortium on Alzheimer’s Disease” has recently defined the criteria for MCI identification [4]: 1) cognitive complaints coming from the patients or their families; 2) the reporting of a decline in cognitive functioning relative to previous abilities during the past year by the patient or informant; 3) cognitive disorders as evidenced by clinical evaluation; 4) absence of major repercussions on daily life; and 5) absence of dementia.

A previous diagnosis of MCI is considered an important risk factor for the development of AD. In fact, the progression rate from MCI to dementia is approximately 12% per year, whereas the conversion rate from normal elderly subjects to demented ones is only of 1–2% [5]. Nevertheless, some MCI patients remain stable or return to normal over time [3]. Recent studies examined the EEG and magnetoencephalography (MEG) activity in MCI patients [6]–[22]. Some of them found significant differences between MCI and AD patients, but only a few studies could distinguish MCI from controls, due to the fact that the gap between these groups is small.

There is evidence that AD includes a disconnection syndrome. This idea is supported by neuropathological, electrophysiological, and neuroimaging studies [23]. Since MCI is frequently considered an intermediate stage between controls and AD patients, such syndrome might also appear in this group. The disconnection syndrome has been studied with linear and nonlinear measures. Coherence is the method most widely used. It is a normalized linear measure of the correlations between two signals as a function of frequency [24], [25]. Several authors have reported a decrease in AD coherence values in alpha and beta bands (for a review, see [26]). This measure has also been used to study the connectivity in MCI. Moretti et al. [15] showed that MCI patients have a decrease of intrahemispheric frontoparietal and an increase of temporal interhemispheric EEG coherence as compared to elderly controls. Other study suggested that coherence analysis might estimate the risk for the progression to AD in MCI subjects [19]. Nevertheless, it should be remarked that...
this method just captures the linear interactions between pairs of EEG or MEG signals. Thus, coherence may fail to detect nonlinear interdependencies between the underlying dynamical systems. To overcome this limitation, Stam and van Dijk [27] proposed the so-called synchronization likelihood (SL), which is sensitive to linear and nonlinear interdependencies. Additionally, SL can be computed with a high time resolution, making it suitable for nonstationary time series. This method has already been employed to study the brain activity in MCI. For instance, Stam et al. [21] reported that the SL was significantly decreased in the 14–18 and 18–22 Hz bands in AD patients compared with both MCI subjects and healthy controls. Nevertheless, the synchronization was similar in controls’ EEGs and those of MCI patients [21]. The typical EEG frequency bands (delta, theta, alpha-1, alpha-2, beta, and gamma) were also analyzed with this measure in patients at rest and during a visual working memory task [17]. Significant differences between MCI and controls were found only in alpha-2 band during the working memory condition [17]. These results may suggest that SL cannot distinguish the brain recordings obtained from controls and MCI patients during a resting-state condition. Nevertheless, MEG may be more suitable than EEG to assess functional connectivity due to the fact that MEG is more sensitive to nonlinear correlations [28]. Furthermore, EEG acquisition can be significantly influenced by technical and methodological issues, like distance between electrodes and the sensor placement. Additionally, MEG offers higher spatial resolution than conventional EEG. Finally, MEG provides reference-free recordings, which are not distorted by the resistive properties of the skull [29], [30]. Due to all these advantages, we have used MEG in our study.

An early diagnosis of AD is critical not only to reduce the damage suffered by the patient’s brain, but also to adopt more efficient therapeutic strategies that could alter the progression of the disease. Since a key factor for an early diagnosis of AD is to distinguish patients with MCI from elderly controls, we have examined the MEG background activity in 18 MCI patients and 25 control subjects by means of coherence and SL. Our purpose was to check the hypothesis that the MEG background activity reflects a disconnection syndrome in MCI patients. Additionally, we wanted to assess which measure shows a better performance for discriminating MCI patients from control subjects.

II. MATERIALS AND METHODS

A. Subjects and MEG Recording

MEGs were recorded using a 148-channel whole-head magnetometer (MAGNES 2500 WH, 4D Neuroimaging) located in a magnetically shielded room. The subjects were in an awake but resting-state with their eyes closed and under vigilance control during the recording. They were asked to avoid eye and head movements. For each subject, 5 min of recording were acquired at a sampling frequency of 678.17 Hz, using a hardware bandpass filter from 0.1 to 200 Hz. Then, the equipment decimated each 5 min dataset. This process consisted of filtering the data to respect the Nyquist criterion, followed by a downsampling by a factor of four, thus obtaining a sampling rate of 169.55 Hz. Finally, four artifact-free epochs (4096 samples) per subject were selected. Offline artifact rejection was performed by an experienced technician who was blind to the patients’ diagnosis. These epochs were copied as ASCII files for further analysis.

MEG data were acquired from 43 subjects: 18 MCI patients and 25 elderly control subjects. Clinical diagnosis was ascertained by means of exhaustive medical, neurological, psychiatric, and neuropsychological examinations. Cognitive status was evaluated with the Mini Mental State Examination (MMSE) of Folstein et al. [31], while functional status was screened by means of the Global Deterioration Scale/Functional Assessment Staging (GDS/FAST) system [32]. All control subjects and patients’ caregivers signed an informed consent for the participation in this research work. The local Ethics Committee approved this study.

The MCI group consisted of 18 patients (eight men and ten women; age = 74.89 ± 5.57 years, mean ± standard deviation, SD) diagnosed following Petersen’s criteria [33]. Two patients met the criteria of amnestic MCI, while the others were included in the multiple-domain category. The mean MMSE score for MCI group was 25.67 ± 1.81 (mean ± SD), whereas the GDS/FAST score was equal to three for all patients. They were free of other significant medical, neurological, and psychiatric diseases. Particularly, in order to prevent the potential confounding influence of depressive symptoms on the individuals’ cognitive status, all participants underwent an evaluation by means of the Yesavage’s geriatric depression scale [34]. Patients with scores above the 0–9 points range were excluded. Moreover, none of the participants in the study used medication that could affect the MEG activity.

MEGs were also obtained from 25 elderly control subjects without past or present neurological disorders (nine men and 16 women; age = 71.92 ± 6.47 years). The difference in the mean age of both populations is not statistically significant (p = 0.12 > 0.05, Student’s t-test). The MMSE and GDS/FAST scores for these controls were 28.84 ± 1.18 and 1.72 ± 0.46 (mean ± SD), respectively.

B. Coherence

Coherence is a normalized linear measure of the correlations between two signals within a certain frequency band [24], [25]. It can be interpreted as a functional measure for information transfer between brain areas [35]. Coherence analysis has been previously used to analyze the brain background activity in AD and MCI [15], [19], [26].

The coherence between two time series of length N, X = (x_1, x_2, ..., x_N) and Y = (y_1, y_2, ..., y_N), is defined as the cross-spectrum normalized by the product of the two power spectra. Its mean overall frequencies can be computed via the mean over time of the corresponding analytical signals [36]

$$\text{Coherence}_{XY} = \frac{\langle A_X A_Y e^{i\Delta\varphi} \rangle}{\sqrt{\langle A_X^2 \rangle \langle A_Y^2 \rangle}}$$

(1)

where A_X and A_Y are the amplitudes of the two time series and $\Delta\varphi$ is the instantaneous phase difference between the time series. This equation returns a value between 0 and 1, indicating the amount of correlation between X and Y. The end result
of computing the coherence for all pairwise combinations of MEG channels is an \( B \times B \) matrix with \( B = 148 \) (number of channels), where each entry \( B_{i,j} \) contains the coherence value for channels \( i \) and \( j \).

C. Synchronization Likelihood

SL is a general measure of the correlation or synchronization between two time series, which is sensitive to linear as well as nonlinear interdependencies [27]. It can be computed with a high time resolution, making it suitable for nonstationary time series [27]. SL takes on values between \( P_{\text{ref}} \) (a small number close to 0) in case of independent time series and 1 in case of fully synchronized time series. This measure has already used to study the generalized synchronization in EEG/MEG signals in MCI and AD [6], [8], [17], [21], [37].

For two signals of length \( N \) (\( X \) and \( Y \)), the algorithm to calculate the SL between them is the following [27], [37]:

1) Given an embedding dimension \( m \) and a time delay \( \tau \), the embedded vectors for each time series are reconstructed using the Takens’ theorem [38]

\[
X_i = \{x_i, x_{i+\tau}, x_{i+2\tau}, \ldots, x_{i+(m-1)\tau}\} \quad \text{(2)}
\]

\[
Y_i = \{y_i, y_{i+\tau}, y_{i+2\tau}, \ldots, y_{i+(m-1)\tau}\}. \quad \text{(3)}
\]

2) The choice of \( \tau \) and \( m \) was based upon the frequency content of the signals [39]. \( \tau \) is chosen small enough to oversample the highest frequencies present in the time series, whereas the embedding window \( \tau \times m \) is selected long enough to capture the period of the slowest frequency. Thus, for a signal recorded at a sampling frequency \( f_s \) and band-pass filtered between a low frequency \( f_{LF} \) and a high frequency \( f_{HF} \) (all these frequencies expressed in hertz), \( \tau \) and \( m \) (expressed in samples) are chosen such that [37]

\[
\tau = \frac{f_s}{f_{HF} \times 4} \quad \text{(4)}
\]

\[
m = \frac{f_s}{f_{LF} \times \tau}. \quad \text{(5)}
\]

3) SL is defined as the conditional likelihood that the distance between \( Y_i \) and \( Y_j \), will be smaller than a cutoff distance \( r_y \), given that the distance between \( X_i \) and \( X_j \) is smaller than a cutoff distance \( r_x \). In the case of maximal synchronization, this likelihood is 1; in the case of independent systems, it is a small but nonzero number, namely \( P_{\text{ref}} \). The value of \( P_{\text{ref}} \) can be set at an arbitrarily low level (\( P_{\text{ref}} \ll 1 \), and does not depend on the properties of the time series, nor it is influenced by the embedding parameters [27]. In our study, a value of \( P_{\text{ref}} = 0.01 \) was used [37].

4) In practice, the cutoff distances are calculated such that the likelihood of random vectors being close is fixed at \( P_{\text{ref}} \), which is the same value for \( X \) and \( Y \). In order to fix the \( r_x \) and \( r_y \) values, the correlation integral \( C_r \) is used

\[
C_r = \frac{2}{M \times (M - w)} \sum_{i=1}^{M} \sum_{j=i+w}^{M} \theta (r \|X_i - X_j\|)
\]

where \( M \) is the number of reconstructed vectors, \( w \) is the Theiler correction for autocorrelation [40], \( \| \cdot \| \) is the Euclidean distance, and \( \theta \) is the Heaviside function: \( \theta (a) = 0 \), if \( a \leq 0 \), and \( \theta (a) = 1 \), if \( a > 0 \). Now, \( r_x \) and \( r_y \) are chosen such that \( C_{r_x} = P_{\text{ref}} \) and \( C_{r_y} = P_{\text{ref}} \).

5) Finally, the SL between two signals \( X \) and \( Y \) can be formally defined as

\[
SL_{X,Y} = \frac{2}{M \times (M - w) \times P_{\text{ref}}} \times \sum_{i=1}^{M} \sum_{j=i+w}^{M} \theta (r_x \|X_i - X_j\|) \times \theta (r_y \|Y_i - Y_j\|). \quad \text{(7)}
\]

SL was computed for all pairs of channels, obtaining a 148 \( \times \) 148 matrix, as described for the coherence analysis. As SL is a symmetric measure of the strength of synchronization (\( SL_{X,Y} = SL_{Y,X} \)), a symmetric matrix is obtained.

D. Spectral Analysis

The power spectral density for each signal was estimated as the Fourier transform of the autocorrelation function. The power was calculated as the definite integral of the power spectral density function in the following frequency bands: delta (0.5–4 Hz), theta (4–8 Hz), alpha-1 (8–10 Hz), alpha-2 (10–13 Hz), beta (13–30 Hz), and gamma (30–45 Hz). Next, the relative power for each frequency band was computed by dividing the integrated value by the total power in the 0.5–45 Hz frequency band. Finally, the mean relative power spectra for all channels in each group (MCI and controls) were calculated.

III. RESULTS

We applied coherence and SL to measure the statistical interdependencies between MEG channels in MCI patients and elderly controls. Because there is strong evidence that synchronization in different frequency bands may be related to different functions in the brain [41], these measures were computed for all pairwise combinations of MEG channels in six bands: delta, theta, alpha-1, alpha-2, beta, and gamma. Since four artifact-free time segments of 4096 samples for each subject were selected, the results were averaged over these four epochs. Therefore, a 148 \( \times \) 148 coherence matrix and a 148 \( \times \) 148 SL matrix were obtained per subject and frequency band.

In order to reduce the dimension of the results, further averaging over all pairs of channels was done, obtaining one coherence value and one SL value per subject and frequency band. With both measures, mean values were lower in the MCI group than in control group at all frequency bands. Afterwards,
Fig. 1. ROC curves showing the discrimination between MCI patients and control subjects with coherence at (a) delta, theta, and alpha-1 bands, and (b) alpha-2, beta, and gamma bands.

Fig. 2. ROC curves showing the discrimination between MCI patients and control subjects with SL at (a) delta, theta, and alpha-1 bands, and (b) alpha-2, beta, and gamma bands.

the Kolmogorov–Smirnov test was used to verify normality of distributions. As the connectivity values did not meet parametric test assumptions, the nonparametric Mann–Whitney $U$-test was used for the statistical comparison between control subjects and MCI patients. Significant differences with both measures were found only in the beta band ($p$-value = 0.04 with coherence; $p$-value = 0.03 with SL). Additionally, coherence values significantly decreased in the gamma band of MCI patients ($p$-value = 0.04). Correlations between connectivity values and MMSE and GDS/FAST scores were also computed for all the frequency bands, although no significant correlations were found.

Receiver operating characteristic (ROC) curves were used to assess the ability of coherence and SL to discriminate MCI patients from control subjects in the aforementioned frequency bands. An ROC curve summarizes the performance of a two-class classifier across the range of possible thresholds. It is a graphical representation of the tradeoffs between sensitivity and specificity. Sensitivity is the true positive rate whereas specificity is equal to the true negative rate. Accuracy is the percentage of subjects (MCI patients and controls) correctly recognized. The area under the ROC curve (AROC) indicates the probability that a randomly selected MCI patient has a connectivity value lower than a randomly chosen control subject. The highest accuracy (69.8%) and AROC (0.69) values were reached in the beta band using both coherence and SL. Figs. 1 and 2 illustrate the ROC curves, whereas the sensitivity, specificity, accuracy, AROC, and $p$-values obtained with these measures at each frequency band are displayed in Tables I and II.

Additionally, the relative power in six frequency bands (delta, theta, alpha-1, alpha-2, beta, and gamma) was calculated. The relative power values (mean ± SD) in each frequency band for MCI patients and controls are shown in Table III. No significant differences between these groups were found in any frequency band, as Table III shows. Moreover, Fig. 3 illustrates the mean relative power in MCI and control groups.
TABLE I
SENSITIVITY, SPECIFICITY, ACCURACY, AROC, AND P-VALUES OBTAINED WITH COHERENCE AT EACH FREQUENCY BAND

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>AROC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>55.5</td>
<td>52.0</td>
<td>53.5</td>
<td>0.54</td>
<td>0.66</td>
</tr>
<tr>
<td>Theta</td>
<td>66.7</td>
<td>56.0</td>
<td>60.5</td>
<td>0.61</td>
<td>0.21</td>
</tr>
<tr>
<td>Alpha-1</td>
<td>66.7</td>
<td>60.0</td>
<td>62.8</td>
<td>0.62</td>
<td>0.19</td>
</tr>
<tr>
<td>Alpha-2</td>
<td>50.0</td>
<td>72.0</td>
<td>62.8</td>
<td>0.63</td>
<td>0.14</td>
</tr>
<tr>
<td>Beta</td>
<td>72.2</td>
<td>68.0</td>
<td>69.8</td>
<td>0.69</td>
<td>0.04</td>
</tr>
<tr>
<td>Gamma</td>
<td>72.2</td>
<td>60.0</td>
<td>65.1</td>
<td>0.69</td>
<td>0.04</td>
</tr>
</tbody>
</table>

TABLE II
SENSITIVITY, SPECIFICITY, ACCURACY, AROC, AND P-VALUES OBTAINED WITH SL AT EACH FREQUENCY BAND

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>AROC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>66.7</td>
<td>48.0</td>
<td>55.8</td>
<td>0.53</td>
<td>0.74</td>
</tr>
<tr>
<td>Theta</td>
<td>61.1</td>
<td>72.0</td>
<td>67.4</td>
<td>0.61</td>
<td>0.22</td>
</tr>
<tr>
<td>Alpha-1</td>
<td>66.7</td>
<td>64.0</td>
<td>65.1</td>
<td>0.62</td>
<td>0.17</td>
</tr>
<tr>
<td>Alpha-2</td>
<td>77.8</td>
<td>52.0</td>
<td>62.8</td>
<td>0.62</td>
<td>0.18</td>
</tr>
<tr>
<td>Beta</td>
<td>72.2</td>
<td>68.0</td>
<td>69.8</td>
<td>0.69</td>
<td>0.03</td>
</tr>
<tr>
<td>Gamma</td>
<td>61.1</td>
<td>56.0</td>
<td>58.1</td>
<td>0.59</td>
<td>0.32</td>
</tr>
</tbody>
</table>

TABLE III
RELATIVE POWER VALUES (MEAN ± SD) FOR MCI PATIENTS AND CONTROL SUBJECTS IN EACH FREQUENCY BAND

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>MCI patients</th>
<th>Control subjects</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>0.20 ± 0.08</td>
<td>0.22 ± 0.16</td>
<td>0.45</td>
</tr>
<tr>
<td>Theta</td>
<td>0.18 ± 0.06</td>
<td>0.17 ± 0.05</td>
<td>0.96</td>
</tr>
<tr>
<td>Alpha-1</td>
<td>0.12 ± 0.06</td>
<td>0.09 ± 0.04</td>
<td>0.06</td>
</tr>
<tr>
<td>Alpha-2</td>
<td>0.13 ± 0.04</td>
<td>0.12 ± 0.05</td>
<td>0.38</td>
</tr>
<tr>
<td>Beta</td>
<td>0.33 ± 0.11</td>
<td>0.34 ± 0.13</td>
<td>0.89</td>
</tr>
<tr>
<td>Gamma</td>
<td>0.04 ± 0.02</td>
<td>0.05 ± 0.03</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Fig. 3. Mean relative power spectra for all channels in MCI and control groups.

IV. DISCUSSION AND CONCLUSION

We analyzed the MEG background activity from 18 MCI patients and 25 control subjects by means of coherence and SL. Our purpose was to test the hypothesis that the brain activity recorded in MEG signals can reflect a disconnection syndrome in MCI patients. Additionally, the results obtained with these connectivity measures have been compared.

Coherence and SL have proven to be effective in discriminating MCI patients from controls subjects. Our study revealed that MCI subjects have lower connectivity values than controls in all frequency bands. Our findings support the notion that MCI involves a loss of functional connectivity. Moreover, significant statistical differences were found in the beta band with both measures ($p < 0.05$, Mann–Whitney $U$-test). Coherence analysis also revealed significant differences in the gamma band. Therefore, coherence seems a better tool than SL for differentiating both groups. However, these findings are preliminary and require replication in a larger patient population before any conclusion can be made about the clinical diagnostic value of these measures.

ROC curves were used to assess the ability of mean coherence and SL values at different frequency bands to classify MCI patients and control subjects. At beta band, an accuracy of 69.8% (72.2%, sensitivity; 68.0% specificity) was achieved with both measures. This value is lower than the accuracy obtained using neural networks in a previous EEG study: 93.5% [20]. Nevertheless, it is noteworthy that in the current study both groups were carefully matched for age, whereas a difference of more than 12 years in the mean age of MCI and controls exists in the previous one.

Several studies have documented the loss of brain functional connectivity in AD using EEG and MEG data. Most of these studies were carried out using the well-known coherence [24], [25]. The main finding is a lower synchronization level in alpha and beta bands. Nevertheless, contradictory results have been found in the other frequency bands [26]. Recently, other synchronization methods have been used to analyze the EEG/MEG activity in AD, such as cross-mutual information [42], global field synchronization [14], and SL [8], [37]. The connectivity loss in AD may be due to the fact that neuritic plaques appears organized in AD patients’ brains, affecting the ends of corticocortical connections [43]. In the current MCI study, coherence and SL values were significantly decreased in the beta band of MCI patients. Our results suggest that the neurodegenerative processes may affect brain synchronization first in this band.

Although MCI plays an important role in the investigation of AD, only a few studies have analyzed the brain background activity in MCI patients using connectivity measures [6], [7], [14], [15], [19], [21]. For instance, Rossini et al. [19] suggested that EEG coherence analyses may estimate the risk for the progression from MCI to AD patients. Another EEG study showed that MCI subjects have a decrease of intrahemispheric frontoparietal and an increase of temporal interhemispheric coherence [15]. Significant differences between both groups were found only in beta band in [14], as in this research. Another study revealed that lower beta band synchronization is correlated with lower MMSE scores, suggesting that this frequency band may be of diagnostic importance in dementia, especially in early stages [21]. Nevertheless, some EEG studies have shown significant differences also in other frequency bands [6], [7]. Babiloni et al. [7] suggested that parietal to frontal direction...
of the information flux within EEG functional coupling was stronger in controls than in MCI, principally at alpha and beta rhythms. Using SL, significant differences between MCI subjects and elderly controls were found in delta and alpha bands at frontoparietal electrode pairs [6]. The differences in the results of all these research works (previous EEG papers and the current MEG study) may be due to the following reasons: 1) MEG is not distorted by the resistive properties of the skull, whereas high-frequency signals with small amplitude may be attenuated by the inhomogeneous boundaries of the brain and the skull, and often cannot be detected by EEG [29]; 2) the important differences in the patient populations analyzed in these studies (age, sex, MCI subtype, etc.); 3) the heterogeneity of MCI group [2]; 4) finally, several connectivity measures (coherence, SL, global field synchronization, directed transfer function, . . . ), which may reflect different properties of the signals, have been employed.

The current study was carried out during a resting-state condition (eyes closed). Nevertheless, van der Heijl et al. [22] suggested that memory activation reveals EEG differences between MCI patients and controls while EEG background activity does not. Additionally, Pijnenburg et al. [17] found significant differences between both groups in alpha-2 band during a visual working memory task. Other investigations have used evoked potentials to differentiate controls and MCI patients, but this aim was not always achieved. For instance, Püregger et al. [18] analyzed MEG data during an episodic word recognition test to differentiate MCI patients from control subjects. Although their results showed reaction times in MCI patients compared to controls, no significant differences were found [18]. In another study, electrophysiological responses to specific sensory inputs were used, concluding that brain potentials in MCI subjects during target detection have certain features similar to controls and other features similar to AD patients [11]. In any case, our results suggest that MEG resting-state background activity could be useful to differentiate MCI patients from elderly controls.

Some limitations of our study merit consideration. First, the sample size is small to prove the usefulness of coherence and SL as diagnostic tools. Thus, a larger database including recordings from the three MCI subtypes is needed to confirm the performance of these methods. Second, no significant correlations between the connectivity values and the MMSE scores were found, suggesting that these measures cannot detect a gradation in MCI subjects. Further work should be attempted to follow the MCI patients who have taken part in this study to investigate whether MCI patients with the lowest coherence and SL values suffer from AD in the future.

In summary, our work presents the coherence and the SL as methods to study the brain connectivity in MCI patients. Our results provide evidence of disconnection problems in MCI, especially in the beta frequency band. Additionally, an accuracy of 69.8% was achieved in this band in the classification of MCI patients’ MEG recordings and control subjects’ ones. Our findings show the usefulness of coherence and SL to detect the brain dysfunction in MCI.

**References**


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Dr. Maestú has been a member of the Board of the Spanish Psychophysiology Society.