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Classification of mild cognitive impairment EEG using combined recurrence and cross recurrence quantification analysis

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ABSTRACT

The present study is aimed at the classification of mild cognitive impairment (MCI) EEG by combining complexity and synchronization features based on quantifiers from the common platform of recurrence based analysis. Recurrence rate (RR) of recurrence quantification analysis (RQA) is used for complexity analysis and RR of cross recurrence quantification analysis (CRQA) is used for synchronization analysis. The investigations are carried out on EEG from two states (i) resting eyes closed (EC) and (ii) short term memory task (STM).The results of our analysis show lower levels of complexity and higher levels of inter and intra hemispheric synchronisation in the MCI EEG compared to that of normal controls (NC) as indicated by the statistically significant higher value of RQA RR and CRQA RR. The results also evidence the effectiveness of memory activation task by bringing out the characteristic features of MCI EEG in task specific regions of temporal, parietal and frontal lobes under the STM condition.A new approach of combining complexity and synchronization features for EEG classification of MCI subjects is proposed, based on the geometrical signal separation in a feature space formed by RQA and CRQA RR values. The results of linear classification analysis of MCI and NC EEG also reveals the effectiveness of task state analysis by the enhanced classification efficiency under the cognitive load of STM condition compared to that of EC condition.

1. Introduction

Dementia caused by Alzheimer's disease (AD) is one of the most common cognitive disorders in geriatric population. Mild Cognitive Impairment (MCI), which is generally considered as an early stage of AD, is defined as a condition with memory deficits greater than normal elderly, but do not fulfil the criteria for clinically probable AD (Petersen et al., 1999). MCI is considered as a challenging condition as it is characterised by only memory impairment, leaving functions involving daily activities unaffected (Petersen et al., 2001; Petersen et al., 2009). MCI subjects are at increased risk of developing AD with a conversion rate of 12% per year (Petersen, 2004). Hence, preclinical discrimination of MCI from normal subjects has great significance in current research scenario and deserves much attention.

EEG signals are the representation of the complex electrical activity of the brain and hence they have the potential of providing useful information about the various dynamical features of the underlying cortical process.Conventional linear analyses of EEG signals have identified characteristic features of different brain states as well as various pathological conditions like seizures, psychiatric disorders,Alzheimer's and Parkinson's disease and toxic states (Rice et al., 1990; Bennys et al., 2001). However, considering the complex interconnections and interactions of the underlying neuronal networks and the identification of nonlinear nature of EEG signals, nonlinear analysis is found to provide important supplementary information in most of these cases (Park et al., 2007; Faust and Bairy, 2012; Stam, 2005; Jelles et al., 2008;Kannathal et al., 2005).

In the case of AD, the established methods of spectral analysis have identified characteristic features of decreased mean frequency and coherence (Jeong, 2004; Dauwels et al., 2010a). Taking into account the nonlinear and nonstationary nature of the EEG signals, dynamical systems theory based methods are successfully applied to EEG signals for effective characterisation of AD and MCI condition. Various entropy measures like Renyi's entropy, Shannon spectral entropy, Approximate entropy, Transfer entropy, Tsalli's entropy, Lempel Ziv's complexity have indicated lower level of complexity of the EEG in MCI and AD patients compared to age matched subjects (Dauwels et al., 2011; Faust and Bairy, 2012; Abasolo et al., 2005; McBride et al., 2015; Sneddon et al., 2004; Labate et al., 2013). Entropy measures characterise the

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diversity in patterns generated over space and time and hence the complexity of evolution. Entropy of a time series characterise its information capacity and thereby its level represents the related predictability. Complexity of EEG as evidenced by entropy measures are characteristic of the number of underlying independent neural sources (Stam, 2005; Ibáñez-Molina and Iglesias-Parro, 2016), thereby indicating its level of dynamic richness. Thus the observed reduction in complexity of AD/MCI EEG are suggested as due to the lowering of dynamism or loss of brain responsivity, caused by neuronal death, cholinergic deficits and other network disconnections (Jeong, 2004; Jeong, 2002; McBride et al., 2014).

Spectral analysis of AD EEG using coherence has reported a decrease in coherence of fast bands as well as an increase in coherence of slow bands indicating disruption of long cortico-cortical cholinergic connections (Jeong, 2004; Jeong, 2002). Resting state studies using nonlinear measures of synchronisation like synchronisation likelihood, omega complexity, S estimator and phase synchronisation measures like phase coherence, imaginary coherence, global field synchronisation (GFS) and phase lag index (PLI) have indicated lowered synchrony in AD EEG compared to that of controls indicating impaired neuronal coordination (Dauwel et al., 2009; Dauwels et al., 2010b; Ma et al., 2014). Loss of synchronisation between different cortical regions is the mainly observed EEG feature in AD condition (Stam et al., 2003; Kramer et al., 2007) and is considered as the outcome of structural/functional disconnections among cortical areas (Delbeuck et al., 2003; Stam et al., 2006) resulting from axonal pathology or death of cortical neurons (Jeong, 2002 and Jeong, 2004).

Nonlinear analysis applied to study the synchronisation or rather the relationship between two or more EEG, can reveal to some extent the cognitive dynamics with respect to functional connectivity and thereby provide information on functional interactions between different brain regions (Stam, 2005). In the case of MCI EEG, the synchronisation pattern is usually found to show high variability with respect to frequency bands, cortical regions and cognitive states. Resting state EEG studies of MCI have indicated a decrease of mean frequency and associated decrease in synchronisation (Stam et al., 2003; Koenig et al., 2005; Moretti et al., 2008; Gómez et al., 2009; Zeng et al., 2015), whereas other studies found no significant difference in synchronisation patterns between MCI and normal subjects (Jiang, 2005). Studies based on state space measures have found a loss of synchrony in resting state, which were found to be nonsignificant after statistical correction (Tao and Tian, 2005; Dauwels et al., 2010b). Several EEG/MEG studies have indicated higher synchronisation levels between different cortical regions in MCI compared to normal subjects under short term memory conditions (Dauwels et al., 2010b; López et al., 2014; Pijnenburg et al., 2004; Jiang and Zheng, 2006), suggestive of a compensatory mechanism in their cortical dynamics (Bajo et al., 2010; Bajo et al., 2012; Cantero et al., 2009). Even in the resting state, a few studies have identified hypersynchronisation in the posterior networks which overlapped with regions of decreased oxygen and glucose metabolism (Knyazeva et al., 2013). The synchronisation of cerebral activity is an important physiological mechanism for the functional integration of different brain regions (Vysata et al., 2014) and the main basic functions of such synchronous activity of neuronal oscillators are neural communication and plasticity (Fell and Axmacher, 2011). Thus functional connectivity methods identify brain regions that possess correlated activity which can help in investigation of pathological connectivity in neurological disorders (Bowyer, 2016).

EEG analysis of cognitive deficit conditions of AD and MCI have been conducted using complexity and synchronisation measures and these features are found to be the most significant ones to characterise such EEG (Abasolo et al., 2006; Stam et al., 2003).However, the focus of these studies was either on complexity or on synchronisation analysis. No studies have been carried out based on the combined use of complexity and synchronisation characteristics on a single platform for any application. EEG complexity is found to be related to the amount of independent cortical generators and therefore, can be sensitive to cortical synchrony (Stam, 2005; Ibáñez-Molina and Iglesias-Parro, 2016). In the neural context, dynamical complexity is interpreted as randomness or lack of interaction between the elements of the dynamical system, hence related to lack of functional sources (Stam, 2005). Considering these interrelations and the fact that complexity and synchronisation are the most important characteristic features of AD/MCI EEG, we propose to investigate the effectiveness of the combined use of complexity and synchronisation features to form a common platform of recurrence quantification methods for the purpose of classification of MCI EEG. The recurrence based quantification methods are found to be highly efficient in characterising nonlinear system dynamics (Kurths et al., 1994). These methods do not require the assumption of stationarity of the data and are highly effective for short noisy signals (Zbilut et al., 1998) making them ideal for the dynamical analysis of real-world signals. Due to these significant characteristics, recurrence methods have found applications in varied fields like engineering, biomedical, geophysics, astrophysics, and economics (Nichols et al., 2006; Rangaprakash and Pradhan, 2014; Marwan et al., 2002; Zolotova and Ponyavin, 2006; Holyst et al., 2001).

The present study aims at classification of MCI EEG based on the combined use of recurrence quantification analysis (RQA) and the cross recurrence quantification analysis (CRQA). The recurrence rates (RR) of RQA and CRQA analysis which are efficient indicators of complexity and synchronisation levels are suitably chosen from the common platform of recurrence based dynamical analysis. The recurrence rate of RQA is the measure of the density of the recurring points in a recurrence plot and hence represents the probability of repetition of a dynamical state. CRQA is the bivariate extension of RQA and recurrence rate of CRQA is the density of cross recurrence points, which is the probability of occurrence of similar states in two systems. These measures have found applications in characterisation of epileptic, anaesthetic, multiple sclerotic EEG, as well as climatological and behavioural signals. RQA measures of RR and DET are effectively used to identify loss of complexity in EEG of multiple sclerosis (Carrubba et al., 2012) and in pre-ictal state of epileptic EEG (Zhang et al., 2008). Similarly, CRQA measures are applied to characterise the effect of anaesthesia on coupling relationships in EEG (Nicolaou and Georgiou, 2014) and the detection of increased synchronisation between thumb and index finger caused by peripheral median nerve block (Li and Li, 2013). CRQA is also used for quantifying the temporal organization of interacting behavioural signals, thus identifying the temporal phases during which interactions take place (Coco and Dale, 2014) and in the analysis of climatological signals for the investigation of palaeo-climatic conditions (Marwan and Kurths, 2004).

Here, classification of MCI EEG is carried out using RQA RR and CRQA RR independently as well as in a combined manner by including both these measures collectively in the classification procedure. In addition, these two features are projected onto a feature space wherein support vector machine (SVM) is applied for classification procedure. The method of using feature space for signal separation has earlier been applied for vocal disorders (Matassini et al., 2000; Manfredi and Matassini, 2002) and fault in induction motors (Stefan and Holger, 2000). To study the effectiveness of the proposed method, EEG analysis is carried out in MCI and normal subjects under resting eyes closed (EC) and a cognitively active state of short term memory task (STM). From the present results, it is found that with the inclusion of complexity and synchronisation features into a single analysis, the classification efficiency is enhanced especially in the STM condition. The present study supports the effectiveness of recurrence based methods for EEG signal analysis and moreover the efficiency of combining the two characteristic features of complexity and synchronisation for enhanced classification efficiency. The study also indicates the effectiveness of applying such methods under the cognitively active state of short term memory task condition.

2. Materials and methods

2.1. Participants

Eighteen MCI patients with mean age 67.1 ± 7.2 years, (seven females) participated in the study. Eighteen age matched elderly subjects with mean age 65.1 ± 5.6 years (five females) consisted the normal control (NC) group. All participants are right handed and native language speakers. Screening for cognitive impairment of the subjects is carried out using the best known and most widely used measure of cognition viz. mini-mental state examination (MMSE) (Tsoi et al., 2015; Sheehan, 2012).The MMSE score of the MCI group is 26.2 ± 1.4 and that of the NC group is 30. Age, MMSE and gender composition are assessed using appropriate parametric/non-parametric tests and it is found that the age and sex ratio did not differ significantly between the groups as indicated by $p > 0.05$, $\chi^2(16) = 15.000$. The MMSE scores were significantly different between the two groups ($p < 0.05$). All NC subjects gave informed written consent to voluntarily participate in the study. Care-givers of MCI subjects also gave informed written consent of participation of their wards in the study with full knowledge of nature of the procedure. The Medical Ethical Committee of Welcare Hospital approved the study.

Diagnostic testing of MCI was performed by clinical evaluation, biochemical screening, radiological and neuropsychological testing. The MCI subjects enrolled for the study were affected only in the memory domains while attention, language and other cognitive functions were normal. Inclusion criteria for the patient group were (i) subjective memory complaint as per medical history (ii) independent activities of daily living as per the information provided by the caregivers (iii) normal general cognitive performance other than memory loss (iv) no dementia according to DSM IV criteria (diagnostic and statistical manual of mental disorders, IVed.) (v) absence of psychiatric history (vi) a cut off of MMSE ≥ 24. Exclusion criteria were (i) history of head trauma (ii) substance abuse (iii) seizure/epilepsy (iv) delirium (v) dementia (vi) clinical signs of anxiety or depressive illness on evaluation by a clinical neurophyscian (vii) focal lesions in gray or white matter on radiological evaluation using resonance imaging (MRI)/ computed tomography (CT) (viii) use of psycho pharmacological treatment.

2.2. EEG recording and preprocessing

EEG signals were recorded under two different cognitive states viz. (i) resting eyes closed (EC) (ii) short term memory task (STM) each lasting for a duration of five minutes. The subjects were seated in an armchair in a semi reclined position. Initially, a brief demo of the memory activation task is given to familiarize the subjects with the task. They were asked to remain relaxed but alert with eyes closed and minimum movements for five minutes of EEG recording.An interstate interval of 60 s was given for the subjects to open their eyes and stretch arms and legs. After this interval, the audio track of small story narration was played back while the subjects remained in EC state. Following this, ten different questions based on the story were asked in a monotonous tone with 10 s gap. The subjects were instructed to give the answer in this gap. This is repeated for two more sessions. Fig. 1 shows the flow of events occurring during the experiment.

Thirty two channel EEG are acquired according to the international 10–20 system with the electrodes referenced to linked earlobes. EEG signals are recorded using Digital Wingraph EEG system (Neurocare, Model Number 13000). The electrodes are placed at the following nineteen locations viz. A1, A2, Cz, Fp1, Fp2, F3, F4, F7, F8, T3, T4, T5, T6, C3, C4, P3, P4, O1 & O2. The signals are digitized at a rate of 128 samples per second with a 16-bit analog to digital converter. The recorded EEG was digitally filtered using a band pass filter of cut-off frequencies at 0.4 and 60 Hz and a 50 Hz notch filter. Artifact free epochs of 10s duration were chosen and stored in a PC for further off-line analysis.The signals from the channels Fp1 and Fp2 are not included in the study, as these channels are the most affected ones by ocular artifacts.

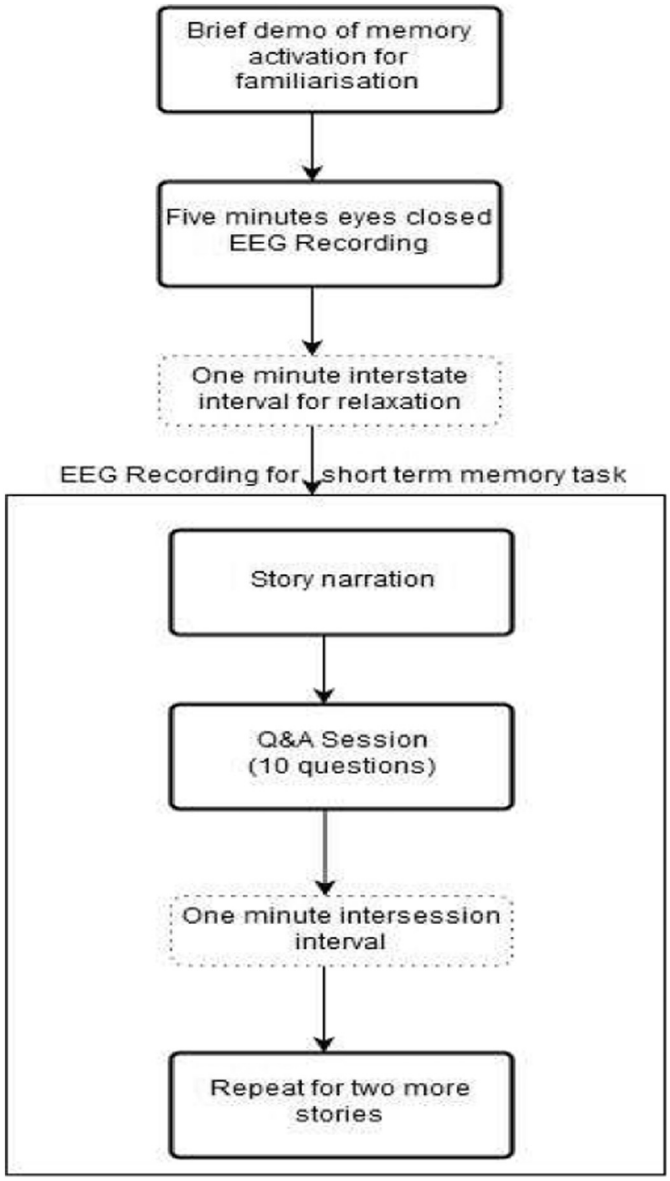

Fig. 1. Flow chart of various events during the experiment.

2.3. Recurrence quantification analysis (RQA)

RQA is an effective technique which extracts and characterises various aspects of a nonlinear system. RQA is based on the recurrence or repetition of state points in the state space. It quantifies the information about the recurrence of different states of a system at different times from a given time series. Unlike other conventional nonlinear measures, RQA is efficient in characterising changes in dynamical features from real world signals which are short, noisy and nonstationary (Romano et al., 2005). RQA provides several measures, among which the recurrence rate (RR) is an efficient indicator of the regularity or predictability of a given time series. For highly complex systems, the RR values are very low indicating low regularity and predictability whereas the RR values are very high for periodic systems which are highly predictable.

Table 1
Mean values of RQA and inter and intra lobar CRQA RR for NC and MCI groups under the two cognitive states of resting EC and STM. The '*' indicates the regions where statistically significant differences are higher for MCI.

			F	T	P	O
RQA	EC	NC	0.6823	0.5118	0.5956	0.4742
		MCI	0.7389	0.6151	0.7844*	0.5833
	STM	NC	0.4311	0.3323	0.3930	0.3439
		MCI	0.5431	0.5143*	0.6282*	0.5423

			FT	FP	FO	TP	TO	PO
Inter lobar CRQA RR	EC	NC	0.6312	0.6641	0.6109	0.5823	0.5180	0.5523
		MCI	0.7303	0.7928*	0.7166	0.7417*	0.6359	0.7198*
	STM	NC	0.4656	0.5115	0.4604	0.4509	0.3809	0.4330
		MCI	0.6390*	0.6838*	0.6387*	0.7016*	0.6520*	0.6789*

			F	T	P	O
Intra lobar CRQA RR	EC	NC	0.7000	0.5373	0.6017	0.4866
		MCI	0.7815	0.6510	0.7993*	0.6475*
	STM	NC	0.5156	0.3936	0.4880	0.3725
		MCI	0.6590	0.6536*	0.7156*	0.3675

2.4. Cross recurrence quantification analysis (CRQA)

CRQA is a bivariate extension of recurrence method for determining the similarity of states between dynamical systems (Marwan and Kurths, 2002). CRQA also provides a recurrence rate (RR) which quantifies similarity between any two systems. CRQA RR is an indicator of the probability of occurrence of similar states in the two systems (Marwan and Kurths, 2002). High value of CRQA RR represents high probabilities of occurrence of the same state in both systems. CRQA measures are being applied for synchronisation analysis of real world signals like, EEG, geophysical and electrochemical data (Rangaprakash and Pradhan, 2014; Marwan et al., 2002; Romano et al., 2005).

2.5. EEG analysis

RQA and CRQA analysis are carried out on the artifact free epochs obtained from 14 locations, viz. F3, F4, F7, F8, T3, T4, T5, T6, C3, P3, C4, P4 O1 and O2.Signals from two locations Fp1and Fp2 are not considered for the analysis due to relatively high artifact contaminated epochs. An average number of 32 ± 4.8 and 26 ± 2.05 artifact free epochs per channel per subject are used correspondingly from EC and STM states for the analysis. No significant difference ($p > 0.05$) is observed between the number of epochs in each case.

The complexity analysis is carried out using recurrence quantification method. Mean values of RQA RR of all the artifact free epochs from each channel are calculated. The RQA RR values are further averaged for each of the four regions, frontal, temporal, parietal and occipital so as to represent the dynamical state of each of these regions. For example, RQA RR values from the channels F3, F4, F7, F8 are averaged for frontal, T3, T4, T5, T6 are averaged for temporal, C3, C4, P3, P4 for parietal and O1, O2 for occipital regions.

The synchronisation analysis is carried out using the cross recurrence method on the EEG signals from the 14 locations. The analysis is carried on two different levels (i) inter lobar and (ii) intra lobar.In inter lobar analysis, the CRQA RR is evaluated for all pairs of channels. Mean values of these variables are calculated for every region pair like frontal-temporal, frontal-parietal, frontal-occipital, temporal-parietal, temporal-occipital, parietal-occipital. For this, the CRQA RR variables are averaged for every pair of channels between the chosen pair of regions. For example, in the case of frontal- temporal inter lobar analysis the CRQA RR is averaged over all the pairs of channels from frontal (F3, F4, F7, F8) and temporal (T3, T4, T5, T6). This is repeated for remaining pairs. In the intra lobar case, the CRQA RR is averaged for every pair of channel within a particular region. For example, in the frontal region, CRQA RR is averaged over all the pairs between F3 F4, F3 F7, F3 F8, F4 F7, F4 F8 and F7 F8. Similarly, averaged CRQA RR is evaluated for temporal, parietal and occipital regions.

2.6. Statistical analysis

IBM SPSS Statistics for Windows, version 20 is used for statistical analysis and multivariate ANOVA is used for the comparison of RQA RR and CRQA RR for different pairs of regions. Average RQA RR values of each of the four regions are compared between the two groups of NC and MCI under the two cognitive states of resting EC and STM. Follow up analyses are carried out using individual ANOVA with bonferroni post correction applied to p-values. Similar comparisons are carried out on averaged inter lobar CRQA RR and intra lobar CRQA RR values of

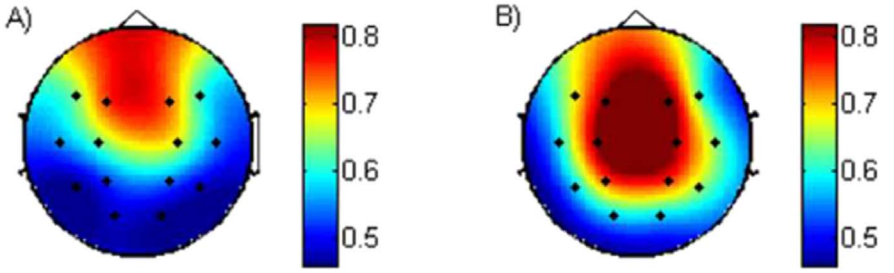

Fig. 2. Scalp maps of RQA RR of A) NC B) MCI in resting EC state for all 14 channels.

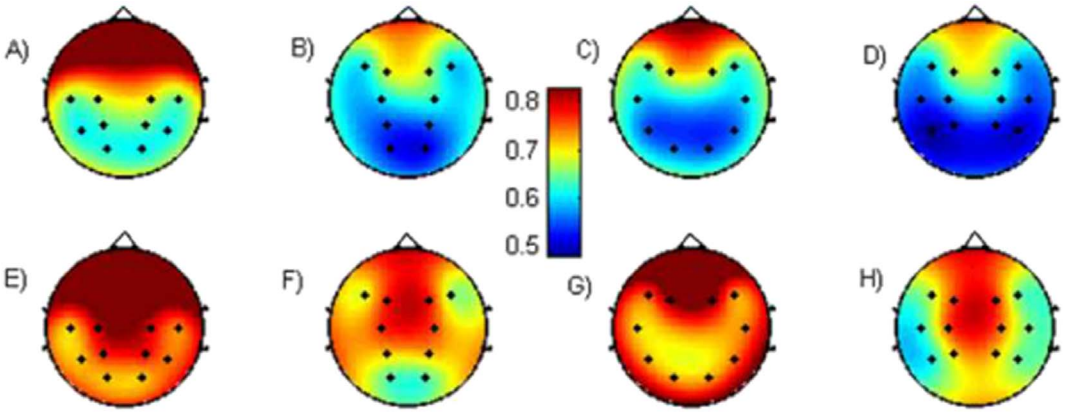

Fig. 3. (A–D) the inter lobar CRQA RR of NC group in resting EC state for A) frontal B) temporal C) parietal and D) occipital regions with all other regions and 3 (E–H) inter lobar CRQA RR of MCI group for(E) frontal (F) temporal (G) parietal and (H) occipital regions with all other regions.

each of these regions. The ability of these measures to discriminate the MCI EEG from that of NC is tested using linear discriminant analysis and support vector machine (SVM). The classification rates are obtained through leave-one-out-cross validation.

2.7. Feature space

Considering the efficiency of RQA and CRQA RR values in identifying the characteristic differences of MCI EEG from that of normal subjects, these two features are used to form a feature space for better classification of MCI EEG based on recurrence features. The feature vector entries representing the subjects from the two groups are constructed using average values of RQA RR and CRQA RR of all the four regions. Separate feature spaces are formed by combining RQA RR with inter and intra lobar CRQA RR values. In the first case, each feature vector is formed by using average RQA RR values of all regions and average of inter lobar CRQA RR values of all region pairs. In the second case, the feature vectors are formed by using average RQA RR values and average of intra lobar CRQA RR values of all the four regions. The feature vectors of the two groups are expected to occupy different regions of the feature space due to the characteristic differences in their complexity and synchronisation levels. Thus classification of MCI EEG can be successfully performed on a common platform based on recurrence quantification.

3. Results

The mean values of RQA RR and inter and intra lobar CRQA RR for the NC and MCI groups under the two cognitive states of resting EC and STM are shown in Table 1. Statistical analyses are carried out for identifying the group differences in the complexity and synchronisation values in each of these two states.

3.1. Resting eyes closed (EC) condition

Fig. 2A and B show the scalp maps of RQA RR of NC and MCI respectively. From this figure and Table 1, it can be observed that, in the resting EC condition, the RQA RR values of MCI group is generally higher than that of NC group in all the four regions. MANOVA analysis revealed an overall significant effect of group on the regions, $F(4,31) = 5.833$, $p < 0.005$ partial $\eta^2 = 0.43$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.00125$) between the NC and MCI groups are indicated by '*' in Table 1.From these results, it can be observed that statistically significant differences in the RQA RR values are observed between the two groups only in the parietal region.

Fig. 3A–D show scalp maps of inter lobar CRQA RR values of the frontal, temporal, parietal and occipital regions respectively of the NC group, each of which shows the synchronisation strength of the particular region with all the other three regions. Similarly, Fig. 3E–H show inter lobar CRQA RR values of MCI group for frontal, temporal, parietal and occipital regions respectively. MANOVA analysis revealed an overall significant effect of group on the regions, $F(6,29) = 4.423$, $p < 0.005$ partial $\eta^2 = 0.48$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.0008$) between the NC and MCI groups are indicated by '*' in Table 1.

Fig. 4A and B show scalp maps of the intra lobar CRQA RR values of frontal, temporal, parietal and occipital regions of NC and MCI groups respectively. MANOVA analysis revealed an overall significant effect of group on the regions, $F(4,31) = 4.564$, $p < 0.005$ partial $\eta^2 = 0.37$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.00125$) between the NC and MCI groups are indicated by '*' in Table 1.

Linear discriminant analysis (LDA) shows best separation between NC and MCI by including RQA RR values of parietal region ($\lambda = 0.645$, $\chi^2 = 14.702$, sensitivity: 55.6%, specificity: 88.9%, correctly classified cases: 72.2%, $p < 0.005$). Leave-one-out cross validation method is applied to obtain the classification results.

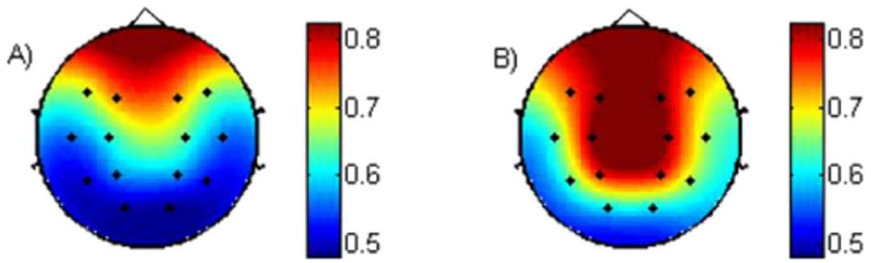

Fig. 4. The intra lobar CRQA RR of the frontal, temporal, parietal and occipital regions of A) NC B) MCI under resting EC state.

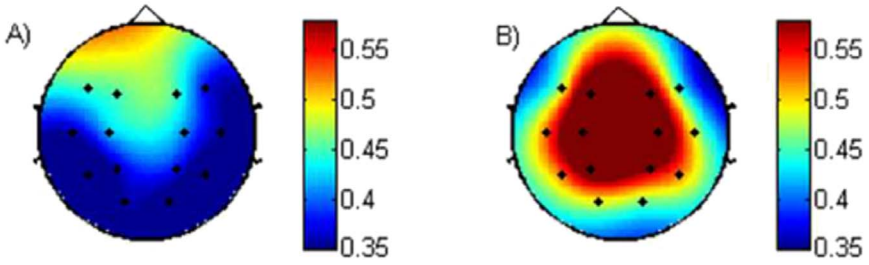

Fig. 5. Scalp maps of RQA RR of A) NC B) MCI under STM state for all 14 channels.

3.2. Short term memory task (STM)

Fig. 5A and B show the scalp map of RQA RR of NC and MCI respectively. MANOVA analysis revealed an overall significant effect of group on the regions, $F(4,31) = 4.585$, $p < 0.005$ partial $\eta^2 = 0.37$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.00125$) between the NC and MCI groups are indicated by '*' in Table 1.

Fig. 6A–D show inter lobar CRQA RR values of the NC group for the frontal, temporal, parietal and occipital regions in the STM condition. These figures represent the synchronisation strength of a particular region with each of the other three regions. Similarly, Fig. 6E–H shows inter lobar CRQA RR values of MCI group. MANOVA analysis revealed an overall significant effect of group on the regions, $F(6,29) = 4.444$, $p < 0.005$ partial $\eta^2 = 0.48$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.0008$) between the NC and MCI groups are indicated by '*' in Table 1.

Fig. 7A and B show the intra lobar CRQA RR values of NC and MCI groups respectively. MANOVA analysis revealed an overall significant effect of group on the regions, $F(4,31) = 8.056$, $p < 0.005$ partial $\eta^2 = 0.51$. Follow up analysis is carried out with multiple ANOVA using bonferroni correction for multiple comparisons. Regions where this analysis with multiple ANOVAs revealed significant differences ($p < 0.00125$) between the NC and MCI groups are indicated by '*' in Table 1.

In the STM condition, LDA shows best separation between the two groups by including RQA RR values of occipital region,inter lobar CRQA value of temporal-occipital region and intra lobar CRQA value of occipital region ($\lambda = 0.405$, $\chi^2 = 29.403$, sensitivity: 100%, specificity: 83.3%, correctly classified cases: 91.7%, $p < 0.005$). Leave-one-out cross validation is applied to obtain the classification results.

3.3. Feature space

Fig. 8A and B show the feature space formed using RQA RR and inter and intra lobar CRQA RR values respectively, in the EC condition. Fig. 8A shows the feature space at inter lobar level wherein SVM is applied for classification analysis. The results of SVM applied to the couplets of RQA RR and inter CRQA RR values used in the above feature space show a clear separation between the groups ($y = -0.7338x + 1.1153$). Similarly, Fig. 8B shows the same analysis in the intra lobar level where also the groups are well separated ($y = -0.6331x + 1.0506$).

Fig. 9 shows the feature space formed using RQA RR and inter and intra lobar CRQA RR values, in the STM condition. Fig. 9A and B show the results of linear classification analysis using SVM applied to the couplets of RQA RR and CRQA RR values at both inter and intra lobar levels respectively, in the STM condition. The results reveal that the two groups are linearly separated at both inter lobar ($y = -0.5023x + 0.8147$) and intra lobar ($y = -0.6869x + 0.8602$) levels.

4. Discussion

The present study aims at classifying MCI EEG by applying complexity and synchronisation measures based on the common platform of recurrence analysis. The couplets of RQA RR and CRQA RR are used to form the feature space, to discriminate the EEG features of MCI from that of NC. The results of our studies show that the combined use of RQA and CRQA measures enhances the efficiency of the group classification between EEG of MCI and NC.

In the resting EC condition, MCI EEG shows a general trend of decreased complexity compared to that of NC as indicated by the high RQA RR values. However, statistically significant higher value of RQA RR is observed only in the parietal region. In the cognitive state of STM also, there is a general trend of decreased complexity in the MCI group as indicated by the high RQA RR values. Compared to the resting condition, statistically significant higher RQA RR values are observed in the temporal as well as parietal regions, in the STM condition. These higher RQA RR values suggest significant lower levels of complexity of EEG from these regions. The significant difference in complexity in EEG of temporal region is made evident under STM condition. This suggest that administration of STM will be more effective in bringing out the early changes in cortical dynamics of MCI subjects. Similar changes in

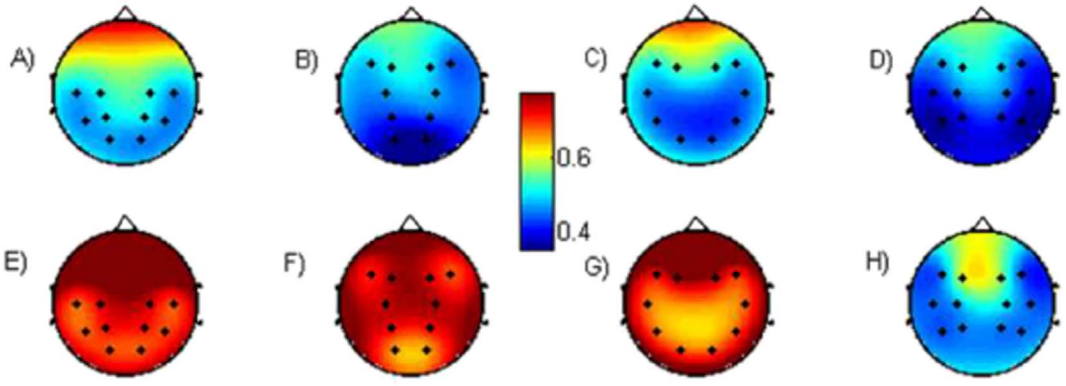

Fig. 6. (A–D) the inter lobar CRQA RR of NC group in STM state for A) frontal B)temporal C) parietal and D) occipital regions with all other regions 5(E–H) inter lobar CRQA RR of MCI group for E) frontal F) temporal G) parietal and H) occipital regions with all other regions.

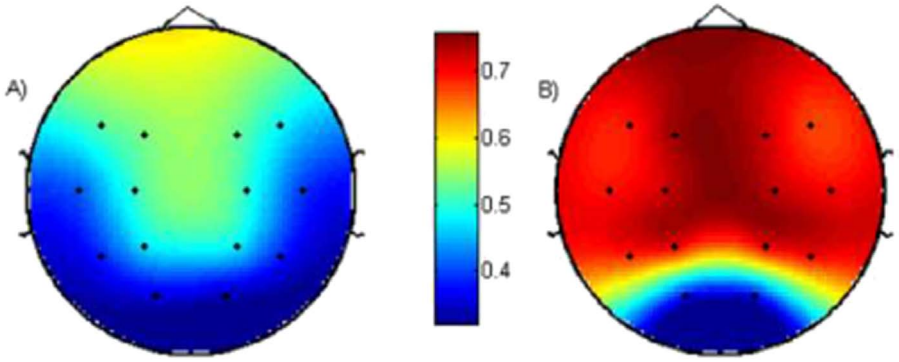

Fig. 7. The intra lobar CRQA RR of the frontal, temporal, parietal and occipital regions of A) NC B) MCI under STM state.

the resting electromagnetic activity of AD subjects had earlier been explained by neurophysiological changes in the temporal and parietal regions (Hornero et al., 2007; Nestor et al., 2004; Rossini et al., 2007). The results of present investigations using RQA RR supports earlier observations of decreased complexity and thereby the loss of dynamical brain responsivity to stimuli (Jeong, 2002). These findings indicate the efficiency of RQA RR in differentiating MCI EEG from that of NC. The differences in the dynamical complexity of MCI EEG from that of NC are better revealed in more regions in the STM condition.

The results of CRQA analysis of EEG under resting EC and STM conditions show higher levels of synchronisation in MCI EEG compared to NC. This increased level of synchronisation in MCI EEG which is better revealed under memory activation supporting earlier observations of similar hypersynchronisation dynamics of MCI EEG (Cantero et al., 2009; Knyazeva et al., 2013). Inter lobar synchronisation analysis in resting EC condition, shows significant hypersynchronisation between the frontal-parietal, temporal-parietal and parietal-occipital region pairs, indicated by the high CRQA RR values. The hypersynchronisation of MCI EEG is better revealed under the STM condition wherein significantly higher synchronisation levels are observed in all region pairs compared to the specific three region pairs observed in the resting EC condition. Intra lobar synchronisation revealed significant differences in parietal and occipital regions under resting EC condition whereas temporal and parietal regions in STM condition. Compared to the resting EC condition, the memory activation state of STM is found more useful in evidencing the characteristic difference in inter and intra hemisphere synchronisation levels of MCI group with respect to that of controls. Cross recurrence analysis is found to be an efficient tool for the study of nonlinear interdependencies in bivariate series. These higher CRQA RR in MCI EEG is suggestive of increased functional interconnections. These results of higher degree of inter and intra hemispheric synchronisation in MCI subjects especially in memory activation condition are in concurrence with earlier observations of higher synchronisation in MCI EEG. The result of the present study supports the earlier suggestions of compensatory cortical activities in central cortex in response to task demand. This reveals the effectiveness of CRQA measures in the analysis of synchronisation dynamics. The method of CRQA analysis effectively identified the importance of the task state studies to evidence the dynamical changes occurring in the MCI EEG.

Consolidating the above results from the present study, we can observe that investigation of EEG dynamics of MCI subjects can be made effective under memory activation task condition. In general, memory and cognitive processes are known to be mediated by highly interconnected neuronal networks between different cortical regions (Hogan, 2003). The temporal lobes are associated with the perception of different input signals and is also the seat of memory association and formation. The parietal region is the site of multimodal afferent integration for collating multiple information (Ropper and Samuels, 2009) and thus plays an important role in cognitive functioning. Short term memory task activities specifically requires the coordinated function of language area in the temporal region, the association cortex in the parietal region and the prefrontal cortex which are mainly associated with attention activity, working as a slave for higher mental

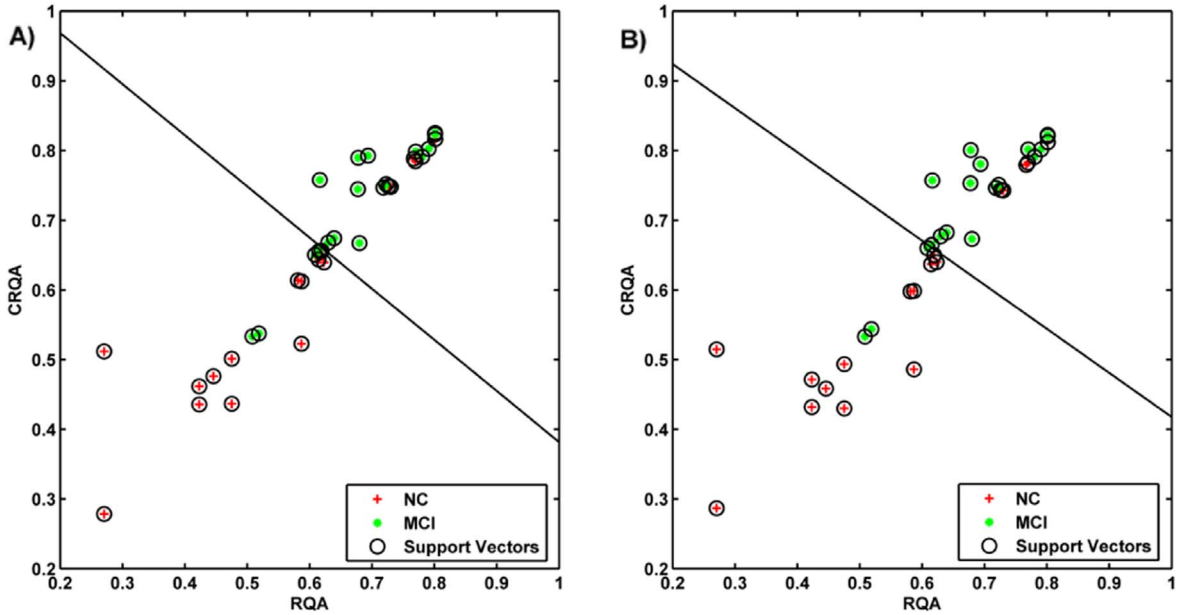

Fig. 8. NC and MCI classification in resting EC state with A) RQA RR and inter lobar CRQA RR B) RQA RR and intra lobar CRQA RR using support vector machine.

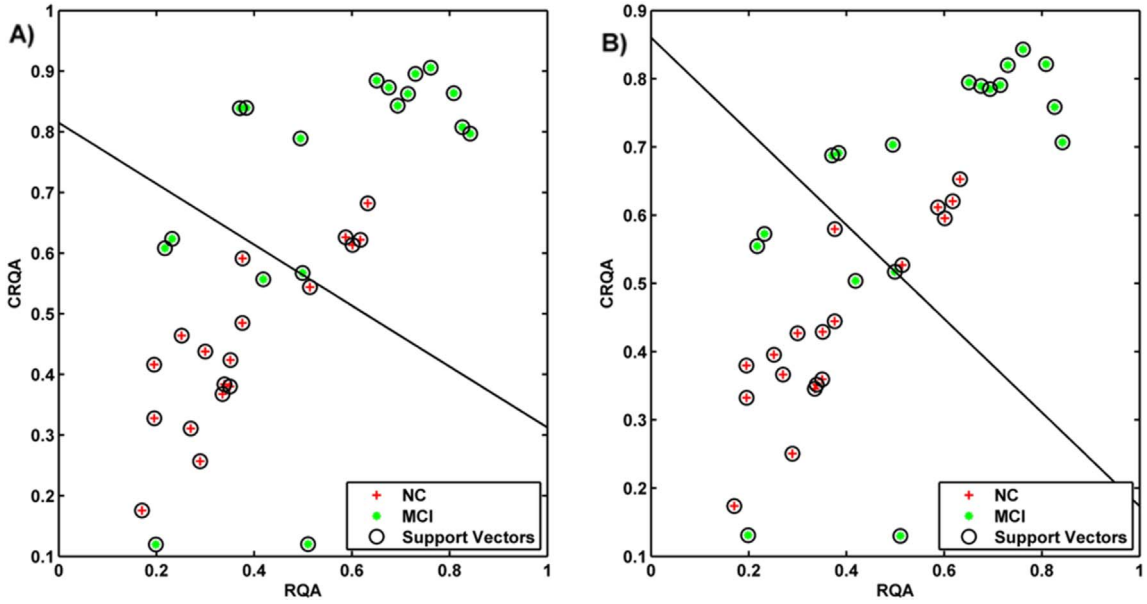

Fig. 9. NC and MCI classification in STM state with A) RQA RR and inter lobar CRQA RR B) RQA RR and intra lobar CRQA RR using support vector machine.

functioning. It is also noteworthy that the temporal lobe, hippocampus and other related cortices play an important role in cholinergic activity in the central nervous system (Ropper and Samuels, 2009; Jiang and Zheng, 2006). In the light of the fact that AD is a disease condition mainly affected by cholinergic deficits, it is hence reasonable to assume that in cognitive disease condition, early changes in the cortical dynamic responsivity and interconnectivity in the early stage of AD can be better observed under memory activation task states. The present results supports the above assumption by revealing lower dynamic activity and higher compensatory connection in task specific locations under the STM condition.

Considering the effectiveness of RQA and CRQA measures in revealing the characteristic changes in synchronisation and complexity of MCI EEG, these two features are combined to form a feature space.In both EC and STM conditions, MCI group is visibly separated from the NC group in the feature space as can be inferred from the Figs. 7 and 8. Even though individually these two measures can be utilised for the identification of the characteristic features of MCI EEG, better results are obtained by combining these two measures to form the feature space. In the resting EC condition, the two groups are well separated in the feature space at both inter and intra levels as shown in Fig. 7A and B. Here, LDA applied to RQA RR values provides classification efficiency of 80.6%. Similarly LDA applied to CRQA RR values provides classification efficiency of 72.2%. The corresponding value of the classification efficiency is 72.2% when LDA is applied to combined RQA and CRQA RR in the resting EC condition. However, the group separation is better revealed by the LDA in the STM condition.Herein, the individual classification efficiency of LDA applied to RQA and CRQA RR values are observed to be 72.2% and 86.1% respectively. In this cognitively active state, classification efficiency of 91.7% is obtained with the combination of RQA and CRQA measures. From the results of LDA applied to the couplets of RQA and CRQA RR, a better classification of 91.7% is obtained under the STM condition compared to 72.2% of EC condition. The feature space shown in Fig. 8A and B also indicates a clear separation between the groups in the STM condition at both inter and intra levels.

This study reveals the effectiveness of combining the RQA and CRQA measures for classification of MCI EEG and also the effectiveness of such investigations in the cognitively active state of STM. The results of our investigation using combined RQA and CRQA RR values support previous results of decreased complexity and the presence of a compensatory mechanism in the MCI brain (Bajo et al., 2010). The importance of task state studies for better classification is also evidenced by the present findings as it can be observed by comparing the classification efficiency of the LDA between the EC and STM condition. The difference in the complexity is mainly observed in the temporal and parietal regions whereas the synchronisation differences are observed in all regions under the task condition. The results of our investigation combining the complexity and synchronisation features of EEG can effectively distinguish the MCI subjects from NC.

5. Conclusion

The present study is aimed at the classification of MCI EEG based on the combined use of complexity and synchronisation characteristics as inferred from recurrence analysis. For this purpose, EEG analysis is carried out using recurrence rates of RQA and CRQA under resting eyes closed and short term memory task condition. EEG classification is carried out using the complexity feature of RQA RR and synchronisation feature of CRQA RR independently as well as jointly. These measures are used to form a feature space wherein further signal separation and classification are carried out.

From the results of the current study, it is observed that the recurrence based methods can effectively differentiate the MCI EEG based on complexity and synchronisation features. The MCI EEG shows a general trend of lowered complexity indicated by high RQR RR values compared to that of NC in both EC and STM conditions. Similarly, the MCI EEG shows hypersynchronisation indicated by high values of CRQA RR. The results indicate that task state studies can clearly bring out the dynamical difference of MCI EEG. These features are more evident under the task condition of STM. The results of linear discriminant analysis also support the importance of task state studies as revealed by the better classification efficiency obtained under STM condition. The combined use of RQA and CRQA feature vectors provides a visual platform for geometrical separation of MCI EEG from that of NC. The results of our analysis show that the MCI and NC EEG occupy different regions of the feature space with clear separation. Support vector machine applied to the couplets of these feature vectors shows that the MCI group can be differentiated from the NC group in the proposed feature space. Thus the present work provides a new outlook of using recurrence and cross recurrence quantification (RQA and CRQA) features of MCI EEG for achieving enhanced classification efficiency and the use of a visual platform of feature space for better indication of the differences in the EEG features which contribute to further enhancement of the classification efficiency.

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