MEG Bibliography - Alzheimer's

Regional analysis of spontaneous MEG rhythms in patients with Alzheimer's disease using spectral entropies.
Poza J, Hornero R, Escudero J, Fernández A, Sánchez CI
Ann Biomed Eng, 2008;36(1):141-52
Alzheimer's disease (AD) is the most common form of dementia. Ageing is the greatest known risk factor for this disorder. Therefore, the prevalence of AD is expected to increase in western countries due to the rise in life expectancy. Nowadays, a low diagnosis accuracy is reached, but an early and accurate identification of AD should be attempted. In this sense, only a few studies have focused on the magnetoencephalographic (MEG) AD patterns. This work represents a new effort to explore the ability of three entropies from information theory to discriminate between spontaneous MEG rhythms from 20 AD patients and 21 controls. The Shannon (SSE), Tsallis (TSE), and Rényi (RSE) spectral entropies were calculated from the time-frequency distribution of the power spectral density (PSD). The entropies provided statistically significant lower values for AD patients than for controls in all brain regions ($p < 0.0005$). This fact suggests a significant loss of irregularity in AD patients' MEG activity. Maximal accuracy of 87.8% was achieved by both the TSE and RSE (90.0%, sensitivity; 85.7%, specificity). The statistically significant results obtained by both the extensive (SSE and RSE) and non-extensive (TSE) spectral entropies suggest that AD could disturb long and short-range interactions causing an abnormal brain function.

Analysis of the magnetoencephalogram background activity in Alzheimer's disease patients with auto-mutual information.
Gómez C, Hornero R, Abásolo D, Fernández A, Escudero J
Comput Methods Programs Biomed, 2007;87(3):239-47
The aim of the present study was to analyse the magnetoencephalogram (MEG) background activity in patients with Alzheimer's disease (AD), one of the most frequent disorders among elderly population. For this pilot study, we recorded the MEGs with a 148-channel whole-head magnetometer in 20 patients with probable AD and 21 age-matched control subjects. Artefact-free epochs of 3392 samples were analysed with auto-mutual information (AMI). Average AMI decline rates were lower for the AD patients' recordings than for control subjects' ones. Statistically significant differences were found using a Student's t-test ($p<0.01$) in 144 channels. Mean AMI values were analysed with a receiver operating characteristic curve. Sensitivity, specificity and accuracy values of 75%, 90.5% and 82.9% were obtained. Our results show that AMI estimations of the magnetic brain activity are different in both groups, hence indicating an abnormal type of dynamics associated with AD. This study suggests that AMI might help medical doctors in the diagnosis of the disease.

Magnetoencephalographic evaluation of resting-state functional connectivity in Alzheimer's disease.
Stam CJ, Jones BF, Manshanden I, van Cappellen van Walsum AM, Montez T, Verbunt JP, de Munck JC, van Dijk BW, Berendse HW, Scheltens P
Neuroimage, 2006;32(3):1335-1344
Statistical interdependencies between magnetoencephalographic signals recorded over different brain regions may reflect the functional connectivity of the resting-state networks. We investigated topographic characteristics of disturbed resting-state networks in Alzheimer's disease patients in different frequency bands. Whole-head 151-channel MEG was recorded in 18 Alzheimer patients (mean age 72.1 years, SD 5.6; 11 males) and 18 healthy controls (mean age 69.1 years, SD 6.8; 7 males) during a no-task eyes-closed resting state. Pair-wise interdependencies of MEG signals were computed in six frequency bands (delta, theta, alpha1, alpha2, beta and gamma) with the synchronization likelihood (a nonlinear measure) and coherence and grouped into long distance (intra- and interhemispheric) and short distance interactions. In the alpha1 and beta band, Alzheimer patients showed a loss of long distance intrahemispheric interactions, with a focus on left fronto-temporal/parietal connections. Functional connectivity was increased in Alzheimer patients locally in the theta band (centro-parietal regions) and the beta and gamma band (occipito-parietal regions). In the Alzheimer group, positive correlations were found between alpha1, alpha2 and beta band synchronization likelihood and MMSE score. Resting-state functional connectivity in Alzheimer's disease is characterized by specific changes of long and short distance interactions in the theta, alpha1, beta and gamma bands. These changes may reflect loss of anatomical connections and/or reduced central cholinergic activity and could underlie part of the cognitive impairment.

Source estimation of spontaneous MEG oscillations in mild cognitive impairment.
Osipova D, Rantanen K, Ahveninen J, Ylikoski R, Happola O, Strandberg T, Pekkonen E
Neurosci Lett, 2006;405(1-2):57-61
Mild cognitive impairment (MCI) is a memory disorder often preceding Alzheimer's disease (AD). AD has been shown to be associated with abnormal generation of spontaneous electromagnetic activity. We investigated whether the cortical generation of spontaneous brain oscillations in MCI shows changes resembling those observed in AD. A minimum current estimates algorithm was applied to identify cortical sources of magnetoencephalographic (MEG) spontaneous brain oscillations in male MCI patients with a clear memory disorder and in healthy elderly controls. This data was subsequently compared to a male subsample of AD patients from an earlier study. While there were clear oscillatory abnormalities in AD patients, there was no evidence of significant changes in the alpha source distribution in MCI patients as compared to healthy controls. Deficits in the distribution of oscillatory sources in the resting state are thus likely to occur at later stages of cognitive impairment than MCI.

Enhanced magnetic auditory steady-state response in early Alzheimer's disease.
Osipova D, Pekkonen E, Ahveninen J
Clin Neurophysiol, 2006;117(9):1990-1995
OBJECTIVE: Previous studies have reported abnormalities in both spontaneous and evoked electromagnetic brain activity in Alzheimer's disease (AD). We studied the auditory steady-state response (SSR) which represents the net effect of entrained background activity and superimposed cortical evoked responses, in AD patients and healthy controls. METHODS: Whole-head magnetoencephalography (MEG) was used to measure SSR to monaural 40-Hz stimulation in AD patients and age-matched controls. Equivalent current dipoles (ECD) of the SSR were modeled in each hemisphere, and source amplitudes were compared between the two groups using time-varying ECD models. RESULTS: Our results indicate that the SSR is significantly increased in AD patients with mild to moderate cognitive deterioration in comparison with healthy elderly subjects. CONCLUSIONS: Goal-directed functioning requires optimization of inhibitory and excitatory inputs in the cortex, allowing the adaptation of responsiveness to repetitive stimulation with low relevance. The present results suggest that this balance is impaired in AD, manifesting itself in decreased inhibition in cortical auditory processing and impaired adaptation of the stimulus-locked activity, probably due to abnormalities in cholinergic modulation. SIGNIFICANCE: MEG appears to be a sensitive tool to detect abnormalities of auditory processing already in early stages of AD.

Medial temporal lobe neuromagnetic hypoactivation and risk for developing cognitive decline in elderly population: a 2-year follow-up study.
Maestu F, Campo P, Gil-Gregorio P, Fernandez S, Fernandez A, Ortiz T
Neurobiol Aging, 2006;27(1):32-7
Cognition declines as a function of age. However, some elders could develop more severe status such as mild cognitive impairment (MCI). The aim of this study was the early detection of neurophysiological patterns of brain activity that may predict the possibility of certain subjects to develop MCI. Brain magnetic activity was recorded from 15 healthy subjects during a memory task by means of magnetoencephalography. None of the participants could be considered as MCI at the time of the first clinical evaluation. After 2-year follow-up, five subjects developed

MCI and 10 maintained their cognitive status across time. The subjects who developed cognitive decline showed a lower number of activity sources in the left medial temporal lobe between 400 and 800 ms after stimulus onset, as compared to the non-cognitive decline group. These findings may help with the early identification of elderly subjects at high risk of cognitive decline, allowing the possibility of neuropsychological or pharmaceutical treatment that delay or prevent the progression of the cognitive impairment.

Complexity analysis of the magnetoencephalogram background activity in Alzheimer's disease patients.

Gomez C, Hornero R, Abasolo D, Fernandez A, Lopez M

Med Eng Phys, 2006;28(9):851-859

The aim of the present study was to analyse the magnetoencephalogram (MEG) background activity in patients with Alzheimer's disease (AD) using the Lempel-Ziv (LZ) complexity. This non-linear method measures the complexity of finite sequences and is related to the number of distinct substrings and the rate of their occurrence along the sequence. The MEGs were recorded with a 148-channel whole-head magnetometer (MAGNES 2500 WH, 4D Neuroimaging) in 21 patients with AD and in 21 age-matched control subjects. Artefact-free epochs were selected for complexity analysis. Results showed that MEG signals from AD patients had lower complexity than control subjects' MEGs and the differences were statistically significant ($p<0.01$). In order to reduce the dimension of the LZ complexity results, a principal components analysis (PCA) was applied, and only the first principal component was retained. The first component score from PCA was graphically analysed using a box plot and a receiver-operating characteristic (ROC) curve. A specificity of 85.71%, a sensitivity of 80.95% and an area under the ROC curve of 0.9002 were obtained. These preliminary results suggest that cognitive dysfunction in AD is associated with a decreased LZ complexity in the MEG signals.

Functional magnetic resonance imaging and magnetoencephalography differences associated with APOEϵ4 in young healthy adults.

Filbey FM, Slack KJ, Sunderland TP, Cohen RM

Neuroreport, 2006;17(15):1585-1590

Functional neural alterations are present in middle-aged to late-aged healthy individuals carrying the ϵ4 allele of the apolipoprotein E (APOEϵ4) gene, a known risk factor for Alzheimer's disease. Neural activity was measured in young adults with and without the ϵ4 allele (APOEϵ4+ and APOEϵ4-) by functional magnetic resonance imaging and magnetoencephalography while performing a visual working memory task on two separate days. Greater activity was observed in frontal areas and cingulate gyri in APOEϵ4+participants by both functional magnetic resonance imaging and magnetoencephalography with regional blood oxygenation level-dependent responses correlating with increased theta band power. The findings suggest that the presence of the APOEϵ4 allele has physiological consequences before aging that may contribute to risk for Alzheimer's disease.

Magnetoencephalographic parietal delta dipole density in mild cognitive impairment: preliminary results of a method to estimate the risk of developing Alzheimer disease.

Fernandez A, Turrero A, Zuluaga P, Gil P, Maestu F, Campo P, Ortiz T.

Arch Neurol, 2006;63(3):427-30

BACKGROUND: Subjects with mild cognitive impairment (MCI) are at a higher risk of experiencing Alzheimer disease (AD). Magnetoencephalographic temporoparietal dipole densities of low-frequency activity are good predictors of individuals' cognitive status, and might be a useful tool to investigate the conversion from MCI to AD. OBJECTIVE: To investigate the role of low-frequency dipole densities as predictors of the risk of developing AD. DESIGN: Whole-head magnetoencephalographic recordings were obtained from 19 probable AD patients, 17 MCI patients, and 17 healthy control subjects. The generators of focal magnetic slow waves were located using a single moving dipole model. RESULTS: Left parietal delta dipole density permitted a reliable classification of AD and MCI patients. The MCI patients were divided into 2 groups based on the median left parietal delta dipole density, and were followed up for 2 years. The estimated relative risk of conversion to AD was increased by 350% in those MCI patients with high left parietal delta dipole density scores. CONCLUSIONS: Results confirmed the important role of parietal delta dipole density in the evaluation of AD and MCI. A magnetoencephalographic-based assessment of AD and MCI patients might be considered a useful clinical test in the near future.

Quantitative magnetoencephalography of spontaneous brain activity in Alzheimer disease: an exhaustive frequency analys.

Fernandez A, Hornero R, Mayo A, Poza J, Maestu F, Ortiz Alonso T

Alzheimer Dis Assoc Disord, 2006;20(3):153-159

Quantitative magnetoencephalography (qMEG) was used to investigate differences in the 2 to 60 Hz spectral power, between Alzheimer disease (AD) patients and control subjects. Twenty-two AD patients and 21 age-matched control subjects participated in this study. MEG signal analysis comprised the division of the entire 2 to 60 Hz spectrum in 2 Hz-width subbands. Both the relative power and the contribution of each subband to the correct classification of AD patients and controls were calculated. The relative power in 2 bands comprised between 2 to 4 Hz and 16 to 28 Hz was selected by a restrictive multiple-comparison test, among the entire 2 to 60 Hz spectrum. Using 2 to 4 Hz values it is possible to choose a classification rule with an estimate sensitivity and specificity given by 68% and 76% respectively. Alternatively, when 16 to 28 Hz values are used, it is possible to obtain a better classification rule with an estimate sensitivity and specificity given by 81% and 80%, respectively. To the best of our knowledge, this is the first electroencephalography or MEG study where a so exhaustive analysis of the magneto-electric spectrum has been performed. This study supports the notion that more attention should be devoted to the study of beta band in AD.

MEG spectral profile in Alzheimer's disease and mild cognitive impairment.

Fernandez A, Hornero R, Mayo A, Poza J, Gil-Gregorio P, Ortiz T.

Clin Neurophysiol, 2006;117(2):306-14

OBJECTIVE: In this study, we applied a novel procedure to calculate the mean frequency from the Magnetoencephalography (MEG) signals of 22 patients with Alzheimer's Disease (AD), 22 patients with mild cognitive impairment (MCI), and 21 healthy controls. A significant mean frequency decrease was expected in pathological groups. MCI subjects are expected to show intermediate mean frequency values between AD patients and controls. METHODS: MEG signal was obtained from a whole-head 148 channels magnetometer in a resting condition. We estimated the power spectral density from the MEG signal by means of the Fourier transform of the autocorrelation function. Then, we computed the mean frequency for each subject. RESULTS: Mean frequency was higher in controls (12.46 +/- 2.00 Hz, mean +/- SD) than in MCI subjects (10.82 +/- 2.21 Hz) with significant differences ($P < 0.05$). Moreover, mean frequency values in MCI subjects were higher than in AD patients (9.06 +/- 2.48 Hz, $P < 0.05$). We also detected a decrease of 0.17 Hz per year in mean frequency from normal subjects' MEG ($P < 0.05$) CONCLUSIONS: Results demonstrated that the approach adopted for the calculation of a mean frequency score seems to be adequate and sensitive to detect differences between normal aging, cognitive deterioration and AD. In addition, data may contribute to the theoretical discussion on the nature of mild cognitive impairment and its similitudes with Alzheimer's disease. SIGNIFICANCE: This paper may be considered a first step to obtain a reliable measure which summarizes spectral information, and might be of a potential clinical interest.

Using magnetoencephalography to study patterns of brain magnetic activity in Alzheimer's disease.

Criado JR, Amo C, Quint P, Kurelowech L, Otis SM

Am J Alzheimers Dis Other Demen, 2006;21(6):416-23

The use of magnetoencephalography to study neurophysiologic abnormalities associated with Alzheimer's disease is reviewed. The most

consistent observation is that Alzheimer's disease patients exhibit an increase in focal slow-wave activity that covaried with cognitive performance. It is still unclear whether generation of focal slow-wave activity precedes or is a consequence of Alzheimer's disease-related neuropathology. Also reviewed is the use of magnetoencephalography to identify early functional changes preceding the diagnosis of dementia. Magnetoencephalography detected neurophysiologic abnormalities associated with cognitive deficits before the diagnosis of mild cognitive impairment. This is supported by evidence presented suggesting that some patients with subjective cognitive complaints, without evidence of dementia, show an increase in focal slow-wave generators. Further research is needed to determine whether the outstanding spatial and temporal resolution of the magnetoencephalography technique could complement other neuroimaging techniques in identifying neurophysiologic abnormalities preceding the diagnosis of Alzheimer's disease and mild cognitive impairment.

Altered generation of spontaneous oscillations in Alzheimer's disease.

Osipova D, Ahveninen J, Jensen O, Ylikoski A, Pekkonen E

Neuroimage, 2005;27(4):835-41

Slowing of spontaneous alpha oscillations and an anterior shift of a source of alpha activity (8-13 Hz) have been consistently reported in the EEG studies of Alzheimer's disease (AD). It is unknown whether these changes are associated with a gradual shift in location and frequency of existing sources or rather with the involvement of a new set of oscillators. We addressed this question by applying source modeling (minimum current estimates, MCE) to spontaneous alpha activity recorded with a 306-channel MEG system from eleven non-medicated AD patients with mild to moderate cognitive impairment and twelve age-matched controls during the eyes-closed session. AD patients had predominant lower alpha band sources in the temporal regions, whereas in the controls, robust alpha sources were found near the parieto-occipital sulcus. Activation within the parieto-occipital region was significantly weaker, and activation in the right temporal area was significantly enhanced in the AD patients. These results suggest an increased temporal-lobe contribution coinciding with parieto-occipital deficits. We propose that MCE, which provides simultaneous mapping of several oscillatory sources, might be useful for detecting neurophysiological abnormalities associated with AD in combination with other neuropsychological and neurological measures.

Evidence of biochemical and biomagnetic interactions in Alzheimer's disease: an MEG and MR spectroscopy study.

Maestu F, Garcia-Segura J, Ortiz T, Montoya J, Fernandez A, Gil-Gregorio P, Campo P, Fernandez S, Viano J, Portera A

Dement Geriatr Cogn Disord, 2005;20(2-3):145-52

BACKGROUND: Several neuroimaging studies have shown reliable differences between Alzheimer's disease (AD) patients and age-matched controls. However, few studies have demonstrated the interactions between neuroimaging methods for the diagnoses of AD. Objective: In this study, we try to elucidate the complementary nature of magnetoencephalography (MEG) and magnetic resonance spectroscopy (MRS) examinations in the assessmentof AD. METHODS: Ten patients fulfilling the NINCDS-ADRDA criteria of probable AD, and 10 elderly individuals with no history of neurological or psychiatric illness serving as age-matched controls participated in the study. All patients and controls received an MRS, MEG and neuropsychological assessment. MEG data were obtained in the context of a working memory task, previously utilized in a similar sample of patients. RESULTS: The AD group showed a reduced number of activity sources over left temporoparietal areas during the late portion of the evoked magnetic field (between 400-800 ms), as well as a bilateral temporoparietal increase in creatine and myoinositol concentrations, and in the myoinositol/N-acetyl-aspartate ratio. The combination of the variables 'number of dipoles during the late portion of the evoked magnetic field' and 'myoinositol/N-acetyl-aspartate ratio' accounted for 65% of the variance of the Mini Mental State Examination scores. Conclusions: These results highlight the importance of assessing the complex brain pathology underlying AD by utilizing multiple brain examination modalities in a coordinate approach.

Proton magnetic resonance spectroscopy and magnetoencephalographic estimation of delta dipole density: a combination of techniques that may contribute to the diagnosis of Alzheimer's disease.

Fernandez A, Garcia-Segura JM, Ortiz T, Montoya J, Maestu F, Gil-Gregorio P, Campo P, Viano J

Dement Geriatr Cogn Disord, 2005;20(2-3):169-77

Whole-head magnetoencephalographic recordings were obtained from 10 patients with Alzheimer's disease (AD) and 10 healthy controls in a resting position. Spectroscopic examinations were performed by means of a 1.5-tesla whole-body scanner in the temporoparietal regions of both hemispheres. The relationship between (1)H-MRS-based and magnetoencephalography (MEG)-based measures and their conjoined capability to improve the diagnosis of AD were investigated in this study. Logistic regression analyses were performed. Three separated logistic models were calculated for (1)H-MRS-based metabolites, low-frequency magnetic activity, and the combination of both measures. A combined myoinositol/N-acetyl aspartate (mI/NAA)-delta dipole density (DD) model predicted the diagnosis with 90% sensitivity and 100% specificity. Additionally, the combination of temporoparietal mI/NAA and delta DD values explained the variability of individuals' cognitive status. The results support the notion that a multidisciplinary approach may improve the understanding and diagnosis of AD.

Alpha rhythms in mild dements during visual delayed choice reaction time tasks: a MEG study.

Babiloni C, Cassetta E, Chiovenda P, Del Percio C, Ercolani M, Moretti DV, Moffa F, Pasqualetti P, Pizzella V, Romani GL, Tecchio F, Zappasodi F, Rossini PM

Brain Res Bull, 2005;65(6):457-70

Can simple delayed response tasks affect latency and amplitude of magnetoencephalographic midline alpha rhythms (6-12 Hz) in early dementia? We recruited 15 mild Alzheimer's disease (AD) and 10 vascular dementia (VaD) patients (paired mini mental state exam of 17-24). The control groups comprised 18 young and 22 elderly normal subjects. In the first task, a simple "cue" stimulus (one bit) was memorized along a brief delay period (3.5-5.5s) up to a "go" stimulus triggering (right or left) button press. In the second task, the "cue" stimulus remained available along the delay period. Event-related reduction in power of the alpha rhythms indexed the cortical activation (event-related desynchronization, ERD) for the trials associated with correct behavioral responses. Behavioral performances to both tasks were lower in the AD and VaD patients than in the normal subjects. In particular, just four AD and five VaD patients executed a sufficient amount of correct responses for the alpha ERD analysis, so they were included in a unique group. In both tasks, the alpha ERD peak was later in latency in the demented and normal elderly subjects than in the normal young subjects. Furthermore, the alpha ERD peak was stronger in amplitude in the demented patients than in the normal subjects. These results suggest that simple delayed response tasks during physiological recordings are quite difficult for patients even at an early dementia stage. Such difficulty may induce the abnormal amount of the related cortical activation in dementia as revealed by the alpha ERD.

Profiles of brain magnetic activity during a memory task in patients with Alzheimer's disease and in non-demented elderly subjects, with or without depression.

Maestu F, Fernandez A, Simos PG, Lopez-Ibor MI, Campo P, Criado J, Rodriguez-Palancas A, Ferre F, Amo C, Ortiz T

J Neurol Neurosurg Psychiatry, 2004;75(8):1160-2

The presence of depression is common among the elderly and it often complicates the early diagnosis of Alzheimer's disease (AD). In this study, we searched for brain activity measures that characterise AD. We compared brain magnetic activity profiles during a memory task, obtained from patients with AD, elderly patients with late onset depression, and age matched volunteers without history of neurological or psychiatric disease. AD patients showed significantly reduced activity in left temporal lobe regions during late portions of the event related magnetic response (400 ms or later after stimulus onset), compared with both groups of patients who did not present with serious cognitive decline. This finding highlights the potential usefulness of MEG protocols supporting the differential diagnosis of AD and major depression related cognitive decline in the elderly.

Time-modulated enhancing of the fronto-parietal circuits in the very-old elders.

Maestu F, Campo P, Fernandez S, Capilla A, Gil-Gregorio P, Fernandez A, Amo C, Ortiz T

Brain Res Cogn Brain Res, 2004;21(1):69-76

Several studies have shown that memory circuits can be reorganised as a function of age. Brain magnetic activity evoked by a memory task was recorded in 19 healthy elderly subjects divided into two groups, a young-elder group (mean age of 62) and senior-elder group (mean age of 76). The young-elder group showed greater activity over the left medial temporal lobe in the late latency windows (between 400 and 800 ms) than the senior-elder group. The senior-elder group showed an initial increased activity (between 150 and 400 ms) over the complex of motor areas, followed by an increased activity in the left temporo-parietal cortex at the late latency window. These results revealed a reorganization of brain networks supporting memory in the eldest subjects. Furthermore, these circuits are reorganised in a time-dependent manner, meaning the rehearsal articulatory process active in the early time window followed by a phonological storage and recognition process in the late latency window.

A neural complexity measure applied to MEG data in Alzheimer's disease.

van Cappellen van Walsum AM, Pijnenburg YA, Berendse HW, van Dijk BW, Knol DL, Scheltens P, Stam CJ.

Clin Neurophysiol, 2003;114(6):1034-40

OBJECTIVE: A measure of neural complexity (C(N)) (Proc. Natl Acad. Sci. USA 91 (1994) 5033) was applied to magnetoencephalography (MEG) data to test the hypothesis that C(N) decreases when information processing in the brain is impaired, as is the case in patients with Alzheimer's Disease (AD). METHODS: One hundred and fifty-one channel MEGs were recorded in 20 AD patients and 20 healthy age-matched controls in a resting condition with eyes open (EO) and eyes closed (EC). Artifact-free epochs of 117 channels were selected for analysis. C(N) and D(2) were computed in different frequency bands, and correlated with the MMSE. RESULTS: The Group x Frequency band interaction was significant for both C(N) and D(2). C(N) was higher in AD, as compared with controls, in the 2-4 and 4-8Hz bands, and D(2) was higher in AD patients in the 14-20 and 20-30Hz bands. The C(N) was higher in the EC condition compared to the EO condition, whereas the D(2) was higher in the EO condition. CONCLUSIONS: The hypothesis of Tononi et al. (Proc. Natl Acad. Sci. USA 91 (1994) 5033) that the neural complexity decreases in AD patients has to be rejected. However, both neural complexity and the correlation dimension did show differences between controls and AD patients which depended on frequency band.

Magnetoencephalographic--features related to mild cognitive impairment

Puregger E, Walla P, Deecke L, Dal-Bianco P

Neuroimage, 2003;20(4):2235-44

We recorded changes of brain activity from 10 MCI patients and 10 controls related to shallow (nonsemantic) and deep (semantic) word encoding using a whole-head MEG. During the following recognition tasks, all participants had to recognize the previously encoded words, which were presented again together with new words. In both groups recognition performance significantly varied as a function of depth of processing. No significant differences were found between the groups. Reaction times related to correctly classified new words (correct rejections) and incorrectly classified repetitions (misses) of MCI patients showed a strong tendency toward prolongation compared to controls, although no statistically significant differences occurred. Strikingly, in patients the neurophysiological data associated with nonsemantic and semantic word encoding differed significantly between 250 and 450 ms after stimulus onset mainly over left frontal and left temporal sensors. They showed higher electrophysiological activation during shallow encoding as compared to deep encoding. No such significant differences were found in controls. The present results might reflect a dysfunction with respect to shallow encoding of visually presented verbal information. It is interpreted that additional neural activation is needed to compensate for neurodegeneration. This finding is suggested to be an additional tool for MCI diagnosis.

Do cognitive patterns of brain magnetic activity correlate with hippocampal atrophy in Alzheimer's disease?

Maestu F, Arrazola J, Fernandez A, Simos PG, Amo C, Gil-Gregorio P, Fernandez S, Papanicolaou A, Ortiz T

J Neurol Neurosurg, 2003;74(2):208-212

BACKGROUND: Many reports support the clinical validity of volumetric MRI measurements in Alzheimer's disease. OBJECTIVE: To integrate functional brain imaging data derived from magnetoencephalography (MEG) and volumetric data in patients with Alzheimer's disease and in age matched controls. METHODS: MEG data were obtained in the context of a probe-letter memory task. Volumetric measurements were obtained for lateral and mesial temporal lobe regions. RESULTS: As expected, Alzheimer's disease patients showed greater hippocampal atrophy than controls bilaterally. MEG derived indices of the degree of activation in left parietal and temporal lobe areas, occurring after 400 ms from stimulus onset, correlated significantly with the relative volume of lateral and mesial temporal regions. In addition, the size of the right hippocampus accounted for a significant portion of the variance in cognitive scores independently of brain activity measures. CONCLUSIONS: These data support the view that there is a relation between hippocampal atrophy and the degree of neurophysiological activity in the left temporal lobe

Correlations of hippocampal atrophy and focal low-frequency magnetic activity in Alzheimer disease: volumetric MR imaging-magnetoencephalographic study.

Fernandez A, Arrazola J, Maestu F, Amo C, Gil-Gregorio P, Wienbruch C, Ortiz T

AJNR Am J Neuroradiol, 2003;24(3):481-7

BACKGROUND AND PURPOSE: Patients with Alzheimer disease (AD) have more low-frequency activity on conventional EEG and increased focal magnetoencephalographic (MEG) dipole density (DD) in delta and theta bands. This activity concurs with atrophy and reduced metabolic and perfusion rates, particularly in temporoparietal structures. The relationship between functional and structural measures and their conjoined capability to improve the diagnosis of AD were assessed in this study. METHODS: Whole-head MEG recordings were obtained in 15 patients in whom the diagnosis of AD had been made and in 16 healthy control subjects during a resting condition. MR imaging volumetric data were also obtained; these included global cerebral, temporal lobe, and hippocampal volumes. RESULTS: DD in the delta and theta bands was enhanced in the AD group compared with the healthy control subjects. Slow-wave activity differed significantly between the groups in the temporoparietal regions of both hemispheres. Left hippocampal volume was correlated with left temporal and parietal delta DD and left temporal theta DD. A combination of left hippocampal volume and left temporal theta DD enabled correct classification in 87.1% of the patients with AD or control subjects. CONCLUSION: Results support the predominant role of temporoparietal hypofunction as defined by DD and hippocampal structural deficits shown on MR images in patients with AD. A multidisciplinary perspective of different techniques may improve our understanding of the disease and our diagnostic abilities.

Generalized Synchronization of MEG Recordings in Alzheimer's Disease: Evidence for Involvement of the Gamma Band.

Stam CJ, Van Cappellen, Van Walsum AM, Pijnenburg YA, Berendse HW, De Munck JC, Scheltens P, Van Dijk BW

J Clin Neurophysiol, 2002;19(6):562-74

SUMMARY The purpose of this study was to investigate interdependencies in whole-head magnetoencephalography (MEG) of Alzheimer patients and healthy control subjects. Magnetoencephalograms were recorded in 20 Alzheimer patients (11 men; mean age, 69.0 years [standard deviation, 8.2 years]); Mini-Mental State Examination score, 21.3 points; range, 15 to 27 points) and 20 healthy control subjects (9 men; mean age, 66.4 years [standard deviation, 9.0 years]) during a no-task eyes-closed condition with a 151 channel whole-head MEG system. Synchronization likelihood (a new measure for linear as well as nonlinear interdependencies between signals) and coherence were

computed for each channel in different frequency bands (2 to 6, 6 to 10, 10 to 14, 14 to 18, 18 to 22, 22 to 40 Hz). Synchronization was lower in Alzheimer patients in the upper alpha band (10 to 14 Hz), the upper beta band (18 to 22 Hz), and the gamma band (22 to 40 Hz). In contrast, coherence did not show significant group differences at the $p<0.05$ level. The synchronization likelihood showed a spatial pattern (high synchronization central, parietal and right frontal; low synchronization, occipital and temporal). This study confirms a widespread loss of functional interactions in the alpha and beta bands, and provides the first evidence for loss of gamma band synchronization in Alzheimer's disease. Synchronization likelihood may be more sensitive to detect such changes than the commonly used coherence analysis.

Focal temporoparietal slow activity in Alzheimer's disease revealed by magnetoencephalography.

Fernandez A, Maestu F, Amo C, Gil P, Fehr T, Wienbruch C, Rockstroh B, Elbert T, Ortiz T

Biol Psychiatry, 2002;52(7):764

BACKGROUND: Patients suffering from Alzheimer's disease exhibit more activity in the conventional electroencephalographic delta and theta bands. This activity concurs with atrophy and reduced metabolic and perfusion rates, particularly in temporoparietal structures.METHODS: Whole-head magnetoencephalographic recordings were obtained from 15 patients diagnosed with Alzheimer's disease and 19 healthy control subjects during a resting condition. The generators of focal magnetic slow waves were located employing a single moving dipole model.RESULTS: Dipole density in the delta and theta bands was enhanced in the Alzheimer's disease group compared with healthy control subjects. Slow-wave activity differed significantly between groups in temporoparietal regions of both hemispheres. Right temporoparietal slow-wave activity covaried with cognitive performance, whereas left temporal delta activity varied with a functional status scale.CONCLUSIONS: Our results support the predominant role of the temporoparietal areas in the diagnosis of Alzheimer's disease. Magnetoencephalography and the source analysis of focal slow activity in particular provide interesting and potentially clinically useful tools to assess functional modifications of patients' brain and to evaluate its relationship with the cognitive status.

Spatio-temporal patterns of brain magnetic activity during a memory task in Alzheimer's disease.

Maestu F, Fernandez A, Simos PG, Gil-Gregorio P, Amo C, Rodriguez R, Arrazola J, Ortiz T

Neuroreport, 2001;12(18):3917-22

The brain magnetic activity patterns in a high load probe-letter (targets and distractors) memory task were examined in patients with Alzheimers's disease (AD) and elderly controls. Control subjects showed a higher number of activity sources over the temporal and parietal cortex between 400 and 700 ms after stimulus onset. However, AD patients showed a higher number of sources over the frontal motor areas, including Broca's and the insula. The number of activity sources on the left parietal areas in response to the target stimuli predicted the AD score oncognitive (MMSE, CAMCOG) and functional staging (FAST) scales. These results suggest that a high information load reveals a deficient functioning of phonological store and reduced task-related activity in temporal and parietal areas, manifesting in a rapid information trace decay. The increased levels of activity in motor areas may reflect a compensatory strategy in an attempt to facilitate rehearsal speed.

Magnetoencephalographic analysis of cortical activity in Alzheimer's disease: a pilot study.

Berendse HW, Verbunt JP, Scheltens P, van Dijk BW, Jonkman EJ.

Clin Neurophysiol, 2000;111(4):604-12

OBJECTIVES: In the present study, MEG was used to analyze spectral power and reference-free coherence in patients with probable Alzheimer's disease (AD).METHODS: Sixty-one channel MEG was recorded in 5 AD patients and 5 age-matched controls at rest with eyes open and eyes closed, as well as during the performance of two different mental tasks. Artefact-free epochs were selected for the analysis of power and coherence values in each of 5 4-Hz wide frequency bands ranging from 2 to 22 Hz.RESULTS: In AD patients, the absolute low frequency magnetic power was significantly and rather diffusely increased relative to controls with a fronto-central maximum. High frequency power values were significantly decreased over the occipital and temporal areas. Reactivity to eye-opening and mental tasks was reduced in the patient group. Relative to controls, a general decrease of MEG coherence values, including all frequencies analyzed, was found in AD patients.CONCLUSIONS: These observations confirm the pattern of changes in spectral power and reactivity known from EEG studies and suggest that coherence decreases in AD patients are widespread and include frequencies outside the alpha band.

Impaired preconscious auditory processing and cognitive functions in Alzheimer's disease.

Pekkonen E, Jaaskelainen IP, Hietanen M, Huotilainen M, Naatanen R, Ilmoniemi RJ, Erkinjuntti T.

Clin Neurophysiol, 1999;110(11):1942-7

OBJECTIVE: To study whether preconscious auditory processing is deteriorated in patients with Alzheimer's disease (AD) having mild to moderate cognitive symptoms. To investigate whether auditory processing correlates with the impairment of the higher cortical functions. METHODS: P50m and N100m responses elicited by a sequence of repetitive tones were recorded with a whole-head magnetometer from 22 patients with probable AD and from 18 healthy age-matched controls. In addition, an extensive neuropsychological test battery assessing main cognitive domains was administered to all subjects. RESULTS: The patients with AD had significantly delayed N100m responses in the left hemisphere that correlated with the impairment of the language functions. CONCLUSIONS: N100m auditory responses measured with magnetoencephalography may be useful in evaluating the severity and progression of the cortical dysfunction in dementia.

Alzheimer's disease affects parallel processing between the auditory cortices.

Pekkonen E, Huotilainen M, Virtanen J, Naatanen R, Ilmoniemi RJ, Erkinjuntti T

Neuroreport, 1996;7(8):1365-8

Auditory evoked magnetic fields (AEFs) were recorded from 11 patients with Alzheimer's disease (AD) and 11 age-matched controls using the 122-channel whole-head magnetometer. Auditory stimuli were monaurally presented with interstimulus intervals (ISI) of 0.5 and 2.5 s in different blocks. The peak latencies of P50m and N100m responses were significantly longer in AD patients than in controls over the ipsilateral but not over the contralateral auditory cortex with respect to the ear stimulated. This finding suggests that parallel auditory processing is impaired between the auditory cortices in AD patients. The present MEG measurement might provide an objective index to evaluate auditory dysfunction in AD.

Magnetic field tomography of coherent thalamocortical 40-Hz oscillations in humans.

Ribary U, Ioannides AA, Singh KD, Hasson R, Bolton JP, Lado F, Mogilner A, Llinas R

Proc Natl Acad Sci U S A, 1991;88(24):11037-41

This paper introduces the use of magnetic field tomography (MFT), a noninvasive technique based on distributed source analysis of magnetoencephalography data, which makes possible the three-dimensional reconstruction of dynamic brain activity in humans. MFT has a temporal resolution better than 1 msec and a spatial accuracy of 2-5 mm at the cortical level, which deteriorates to 1-3 cm at depths of 6 cm or more. MFT is used here to visualize the origin of a spatiotemporally organized pattern of coherent 40-Hz electrical activity. This coherence, initially observed during auditory input, was proposed to be generated by recurrent corticothalamic oscillation. In support of this hypothesis, we illustrate well-defined 40-Hz coherence between cortical-subcortical sites with a time shift that is consistent with thalamocortical conduction times. Studies on Alzheimer patients indicate that, while a similar activity pattern is present, the cortical component is reduced in these subjects.