

**VI CONGRESS OF THE ITALIAN SOCIETY OF PSYCHOPHYSIOLOGY (SIPF)**  
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**ABSTRACTS**

**Oral Presentations**

**Event-Related Potentials: Principles and Applications**

*Fattapposta, F., Cordischi, M.V., Traversa, G., Pierelli, F., & Amabile, G.*

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The authors reviewed the most recent psychophysiological methods that investigate particular associative functions. P3 component of the ERPs can be considered as an index of working memory and its latency proportional to stimulus classification time, so that its prolongation is thought to demonstrate a slowing of the information processing speed. The use of single or multiple stimuli should be considered in the application of P3 in clinical testing; for instance, Parkinsonian Patients (PP) experience excessive cognitive slowing with advancing age. Mismatch Negativity, which is not dependent on attention, is the temporally first discriminative response to stimulus deviation; so, it indirectly provides a measure of the accuracy of the neural representation of the repetitive stimulus (in audition). It appears to be suitable for testing aphasic patients, in aging, in patients with unilateral frontal lobe lesions, in learning and in schizophrenia. Interesting psychophysiological suggestions come from the application of the Skilled Motor Perceptual Task in PP. Contingent Negative Variation represents until today the most prominent electrocortical sign of sensory-motor association in man. These potentials show different aspects and stages of our behaviour and of its possible modifications; now, we wish to obtain a lot of further information from new advanced techniques of analyzing the bioelectrical signals, single trial analysis and functional MRI.

**Sustained Attention and Attentive Tone**

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Attentive processes represent a keystone in the interpretation of consciousness, which may be considered the result of an adaptive integration of the subject with the external world, that come about by means of an attentive serial mechanism, based on short term memory. The elementary serial attentive mechanism which allows the continuous integrative process of refocalization of the consciousness contents can be revealed by the concomitant spontaneous eye blink. This integrative mechanism takes place together with different processes and mind contents, amongst these the most relevant to the consciousness, appear to be the transition of the attentive orienting between the external and the internal world and vice versa. The blinking phenomena scan such transitions. Also the modulation of the polysynaptic components of the blink reflex provoked by sustained attention after the presentation of a non reflexogenic warning stimulus may be a suitable method to study sustained attention modulation. In fact with this non-task paradigm, using an appropriate interstimulus interval, a sharp inhibition of the polysynaptic R3 component of the blink reflex may be observed. In Parkinson disease, where a dopaminergic disruption is well documented, such sustained attentional modulation is impaired. A similar pattern have been demonstrated also after head injury.

## **Attention and Consciousness in Hypnosis: Psychophysiological Aspects**

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A review of psychophysiological research we have previously undertaken was performed in order to identify possible physiological and cognitive indicators of hypnotic responses and hypnotic susceptibility. The hypothesis is examined that hypnosis is a condition of focused arousal in which perceptual monitoring processes and consciousness are dissociated. Evidence that differences in levels of attention may account for hypnosis and individual differences in hypnotizability has been found in studies of traditional EEG rhythms, event-related potentials and 40-Hz EEG activity. The alteration of stimulus perception may be a secondary effect with respect to allocation of attention resources. In both waking and hypnotic conditions high hypnotizables appeared to show greater task-related EEG hemispheric shifts than did low hypnotizables. Data concerning cognitive and physiological correlates of hypnotic analgesia may be explained in terms of dissociated control and consequent imagination as the basis of hypnotic responding.

## **Nonlinear Analysis of the EEG**

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Recent advances in the understanding of the dynamics of nonlinear systems provided tools for the analysis of time series recorded from such systems. In particular, with such tools it is possible to have insights about the structural complexity of the generator mechanisms by means of the calculation of the correlation dimension. This corresponds to an estimate of the minimum number of variables needed to describe the system. Moreover, if a noninteger value of correlation dimension is found, then the system can be assumed to be generated by complex nonlinear interactions between a limited number of variables. This kind of analysis has been applied to a variety of normal and pathologic EEG in different clinical conditions (i.e. Alzheimer disease, epilepsy, depression, schizophrenia, etc.). However, there is a lack of standardization and many still unclear points need to be clarified: the EEG is the result of a very large number of different neuronal processes and it is unclear how the estimation of the correlation dimension yields quite low values, there exists a marked structural and functional variety in different brain areas and this should be reflected by this kind of analysis, the EEG contains a number of nonstationarities which can not be described by this type of approach, etc. In a recent work, we showed that it is possible to evaluate the correlation dimension also of different features extracted from the EEG. In fact, we performed the calculation of the correlation dimension of the profiles of EEG slow-wave activity during sleep, in young subjects, and this allowed us to conclude that sleep regulation might be considered as a deterministic non-linear process with an average dimension above 3. Subsequently, we have also shown that the correlation dimension of the EEG slow-wave activity during sleep does not show significant changes across consecutive nights, in the same subject, and does not seem to change significantly with age in children and young adults. Thus, we think that, while there still remain many problems concerning the nonlinear analysis of the EEG, the evaluation of the complexity of some features extracted from it can be reliably performed by means of the tools of the nonlinear systems theory.

## **EEG Coherence Analysis**

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Coherence is a function of spectral analysis giving information about the correlation of couples of signals and can be considered an indirect measure of the functionality of cortico-cortical connections. In the use of this parameter, some important methodological aspects have to be taken in consideration as the choice of the model for spectral parameters extraction, the reference and the statistical approach to the large amount of data that are generated. As regard reference choice, common reference as linked-ears is widely used, but its use is accepted only with low signal content. Laplacian reference could be more "reference-free" and should have the advantage to reduce the contribution of volume conducted coherence, but some studies suggest that they can inflate artifactual coherence. We studied different type of dementias, as Alzheimer's disease, Multi-infarct dementia, Multiple Sclerosis (MS) and AIDS. The most frequent abnormality was alpha coherence decrease, more relevant in subcortical dementias. Different patterns of EEG coherence changes were present according to the different clinical pictures and in all cases were correlated to the degree of cognitive impairment. In MS patients alpha coherence decrease was significantly correlated to lesional load of subcortical structures that is known to be related to the degree of cognitive deterioration.

## **High Resolution EEG**

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In this study the performance of two new high resolution electroencephalography (EEG) technologies was tested on movement-related and somatosensory-evoked potentials recorded from 128 scalp electrodes in two normal subjects. These two technologies computed the surface Laplacian (SL) and the linear inverse estimation or spatial deconvolution (SD) of the EEG potential on realistic magnetic resonance-constructed subject's head models. Matching between SL and SD potential distributions was performed with the computation of root mean square error (RMSE). It was observed that these distributions showed similar patterns of task-related cortical responses (RMSE range: 0.65-0.81). This result would indicate that the new technologies provided nearly equal enhancement of the spatial information content of the EEG potential distributions.

## **Psychophysiology and Psychiatry: Acquisitions and Perspectives**

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The psychophysiological research, that went to an explosive growth in the last 30 years, has provided valuable tools to assess the cognitive processes of human behaviour, by means of the analysis of physiological variables under the experimental situations employed in cognitive psychology. The study of the changes of brain activity during the execution of specific tasks testing cognitive function, started in the early 60s with discovery of ERPs by Grey Walter, Sutton and Kornhuber. This kind of psychophysiological approach proved soon a valuable method to assess brain reactivity not only in normal subjects, but also in psychiatric patients, that revealed impairment of cognitive functions, as shown by abnormal ERPs findings. The most important results have been detected in schizophrenic patients, that show a global impairment involving working memory and categorization (lower P300 and mismatch negativity), as well as cognitive

attention (low CNV amplitude and PINV) and motor preparation (abnormal BP). Nowadays, EPRs investigation remains of main importance despite the introduction of new psychophysiological techniques, as PET and functional MRI, that can provide localization of some neural generators of cognitive processes, yet with the limit of their poor time resolution. On the other hand, the integration between the electrophysiological and neuroimaging techniques may be useful for a better comprehension of the abnormalities of cognitive processes in psychiatric diseases.

### **Electrophysiological Indexes of Attentional Control of Visual Perception**

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Due to the amount of visual information received by a human observer, it is necessary a selection of the latter to improve the computational activity primed in the sensory and perceptual neural systems. When individuals selectively attend to visual stimuli, in fact, they are facilitated in perceiving those stimuli and to respond appropriately to them. Recent advances in neurosciences have indicated that the mechanisms of visual information selection include relative increases in information flow in the visual pathways via a "gating" or "gain control" process. Moreover, they have indicated that the selection may be carried out on both spatial (i.e., location) and non-spatial features (i.e., spatial frequency, colour, etc.) basis, thus revealing the differential activity of the dorsal visual stream ("where" system) versus the ventral visual stream ("what" system). Classic electrophysiological studies had suggested that the gating or gain control process for spatial location operated already at the early sensory processing level (i.e., in the range of 60-140 msec post-stimulus), as reflected by the modulation of the scalp-recorded P1 component of the event-related brain potentials (ERPs). Recently, however, a number of studies by us and other groups have indicated that, with the exception of colour attribute, an early modulation of sensory-evoked P1 can be specific of both types of stimulus features. These findings are consistent with recent neurophysiological findings in monkeys.

### **Event-Related Desynchronization (ERD): Methodology and Applications**

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Event-related desynchronization (ERD) of the electroencephalogram (EEG) is introduced by Pfurtscheller (1977), which refers to the transitory depression of an EEG rhythm in relation to an event. Pfurtscheller (1977) also introduced a method for the quantification ERD for selected frequency bands. The methodology for ERD calculation, together with an overview of applications in the literature are presented. Particular emphasis is given to the evaluation of motor activity in normals (motor learning, motor imagery) and in different pathologies (Parkinson's disease, vascular lesions) of the central nervous system.

### **Objective and Subjective Investigation of Cognitive Deficits in Young Schizophrenic Patients**

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Relationship between subjective and objective deficits in schizophrenia triggered off a great scientific interest in recent years. We investigated this issue by taking in account evoked cognitive potential (P300), neuropsychological deficits and subjective cognitive disturbances in schizophrenic

subjects. Twenty-one schizophrenic paranoid outpatients (DSM IV), mean age 26.6 (s.d. 6.8), mean length of illness 3.3 years (s.d. 3.1) were considered. Evoked related auditory potentials, assessment of clinical symptoms (SAPS, SANS), neuropsychological deficits (Luria-Nebraska battery, LNNB) and cognitive subjective disturbances (Frankfurt questionnaire for basic-symptoms, FBF) were performed. Twenty-one healthy subjects, age and sex matched, community recruited, were considered as comparison group. Schizophrenics showed significant reduction of amplitude ( $F: 10.6; p = 0.004$ ) and prolongation of latency ( $F = 15.6; p = 0.001$ ) compared to comparison group. Schizophrenic subjects who showed P300 performances out of normal range, presented higher rate of subjective cognitive symptoms ( $F: 5.3; p < 0.05$ ), and a LNNB profile exceeding the critical level for many subscales (particularly: intellective processes and memory). The LNNB profile of patients with normal P300 appeared similar to that of healthy subjects. The two subgroups did not differ in clinical symptoms. Data indicate a relationship between objective and subjective cognitive deficits, and hypothesize the presence of a cluster of schizophrenic patients characterized by neuropsychological, neurophysiological and subjective higher cognitive impairments.

### **Vision during Saccadic Eye Movements**

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Saccadic eye movements create two related but distinct problems for the visual system: they cause image motion on the retina, and a displacement of the retinal image. We will present data relating to both of these problems. Measurements of contrast sensitivity show that sensitivity for low spatial frequency gratings modulated in luminance are strongly suppressed during saccades, while sensitivity for high-spatial frequencies, and gratings modulated in chromaticity remain unchanged. These and supplementary experiments suggest that we do not notice the motion during saccades because of selective suppression of the magnocellular pathway, the major input for motion analysis. We further investigate the problem of retinal displacement by measuring perceived visual direction during saccades, and present a novel theory for visual stability across saccades.

### **Event-Related Potentials, Cognitive Functions and Psychopathology**

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Event-related potentials (ERPs) were recorded in 22 obsessive-compulsive (OC) and 13 panic disorder (PD) patients, and in two groups of matched healthy controls. The ERP Late Positive Complex (LPC) and the two positive components preceding it were measured for stimuli presented to the centre of the visual field (central condition) as well as to the right and the left hemifield (lateral condition). Correlations of ERP component amplitude with psychopathological and cognitive indices were evaluated in each patient group. The positive components preceding the LPC were larger in patients than in controls. Their amplitude was associated with a poor performance on tests exploring the executive functions. The LPC amplitude did not show significant differences between OC patients and controls; its amplitude was associated with a better performance on tests investigating the executive functions. In PD patients, the LPC was smaller than in controls and its amplitude was associated with a more accurate performance on executive tasks and with the phobia total score. The results indicate that ERP characteristics might be associated with cognitive dysfunctions but not with symptomatology. The LPC and the positive components preceding it seem to have different functional roles.

## **Psychophysiology, Psychiatry and Neuroscience**

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Increasing evidence is available on the functional correlation between cell properties and (electro)physiological events generated by large neuronal pools of neurons in concomitance with higher brain processes in animals and man. This physiological know-how is: (1) preliminary to successful heuristic approaches; (2) an instrumental compensation for the "communication" limitations imposed on psychophysiology by concepts/definitions borrowed from conventional psychology; (3) a basic pre-requisite to the development of a "scientific" psychophysiology; and (4) a promising approach to the investigation of the biodiversity of elementary mechanisms subserving higher brain function. The specificity of physiological measures with respect to the phenomena to be studied also depends on the progressive approximation to the definition of models intrinsic to the field (e.g. psychiatry) and to the independent categorization of the conditions to be studied.

## **Methodological Aspects of Psychiatric Neurophysiology**

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Three major problems of neurophysiology in psychiatry are discussed at the light of recent own investigations: (1) Lehmann (1987) has developed reference-independent methods to quantify the brain electrical fields. These parameters have been shown to be valid and robust for the assessment of brain potentials related to cognitive processes (Fallgatter et al, 1997) and to subgroups of psychiatric patients (Strik et al, 1994; 1996). Compared to traditional assessments, the parameters were free from interactions between map amplitudes and topography (Strik et al, 1994), and unique for latency assessments. (2) The neuroanatomical and neuropsychological interpretation of the fields related to cognitive activity must prevalently rely on indirect validations. Three dimensional electrical source localisation of ERPs allowed a mutual integration and validation of the insights from metabolic brain imaging studies (Strik et al, 1998). Correlations with regional specific neuropsychological tests provided indications as to the affected brain functions and regions (Heidrich and Strik, 1997). (3) The current psychiatric diagnoses are considered to be etiologically heterogeneous. The subclassification based on a largely independent classification system grounded in Wernicke's work (Leonhard, 1979) was neurophysiologically more homogeneous and indicated different neurophysiological mechanisms at the basis of schizophrenic subgroups, cycloid psychoses and mania (Strik et al, 1993; 1994; 1996).

## **Chromatic Visual Evoked Potentials in Multiple Sclerosis**

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It has been recently shown that VEPs to pure equiluminant chromatic contrast stimuli represent an useful tool for earlier diagnosis of Multiple Sclerosis (MS) (Brain 1996, 119: 723-740). We developed a set of stimuli parameters yielding robust and reliable visual evoked responses, and we assessed their sensitivity compared with that of classical common luminance VEPs. In 30 patients with different forms of MS (22 definite, 2 probable, 6 suspected; age range 10-56 yrs) we recorded VEPs in response to full-field equiluminant red-green (R/G) or blue-yellow (B/Y) gratings, 2 cpd, presented in Onset-Offset mode (300 msec On-, 700msec Off) at two contrast (K) levels (90% and

25%); these responses were compared with those obtained using conventional black/white luminance 50%K checkerboard stimuli. R/G gratings detected abnormalities in 53.3% of the eyes at 90%K, in 58.3% at 25%K; B/Y in 56.6% and 48%, respectively; luminance 50%K checkerboard in 46.6%. Therefore, chromatic VEPs were, on average, more altered in amplitude and latency than luminance VEPs. Moreover, in some cases, the impairment of chromatic responses exhibited a separate vulnerability for R/G or B/Y stimuli. In conclusion, chromatic VEPs appear to reveal earlier and more subtle losses in MS than luminance VEPs. Moreover, the two different streams of the parvocellular visual pathway were involved, on the whole, in a comparable extent, although in some cases a different involvement of R/G and B/Y chromatic VEPs was found.

### **Quantitative EEG Analyzed with Artificial Neural Networks Predicts Relapse in Patients with Chronic Alcoholism and Points to a Frontally Pronounced Cortical Hyperactivation**

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The capability of predicting relapse in chronic alcoholism using Quantitative EEG was investigated. For this purpose, 78 in-patients with alcoholism underwent EEG-recordings (eyes closed) seven days after the beginning of detoxification. Additionally, other clinical evaluations were carried out. After discharge from hospital, patients were regularly re-evaluated for the duration of three months in order to determine whether they relapsed or abstained from alcohol during this time. For classification of the two diagnostic subgroups (relapsers versus abstainers) multivariate discriminant analysis as well as artificial neural network technology has been applied. Correct classification of patients' EEG's was achieved in 83-85%. Furthermore, artificial neural networks improved classification results when compared with discriminant analysis (correct classification: 75%). It was found that, in comparison to abstainers, EEG's of relapsers are more desynchronized over frontal areas, which was interpreted as a functional disturbance of the prefrontal cortex indicating increased cortical activation.

### **MEG: Technical Topics and Clinical Applications**

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Magnetoencephalography (MEG), namely the study of magnetic fields generated by brain electrical activity, has been given in the last years a strong impulse by the availability of total head covering instruments. Mapping the magnetic field over the head allows the localisation of small regions of electrical activity as well as extended current distributions. The high temporal resolution (in the millisecond range), and its complete non-invasiveness, make MEG an ideal tool for functional studies of the brain. Some of the fields of application of MEG are: topographic brain studies, preoperative mapping, and brain plasticity. The integration of MEG with other imaging techniques like PET and fMRI is an area of research of growing interest.

## Poster Presentations

### **Use of Cutaneous Conductance for the Evaluation of the Level of Attention during the Performance of the Raven Matrix (P.M. 38) in Patients Suffering from Alzheimer Disease and in non Demented Controls**

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Introduction and aims of the study: attention represents an important function as it is closely correlated with the mnemonic function. The evaluation of the level of attention during the course of a test by means of the cutaneous conductance, may represent a simple clinical aid for evaluating the level of attention paid by the patient, and the fatiguability of this parameter over the entire duration of the test. Cutaneous conductance will be evaluated using a software able to provide us the levels of tonic and phasic activity. In addition to the following parameters after every stimulus: latency; amplitude; duration; recovery time. The computerized test of the Raven matrix P.M. 38 of the duration of ten minutes will be used. Twelve patients with Alzheimer's disease will be selected according to the NINCDS-ADRDA and the DSM-IV criteria. The value of MMSE will range from 20-24. Twelve elderly non demented subjects will make up the controls group. None of the patients will be taking drugs for Alzheimer's disease at the time of evaluation.

### **Reaction Time in Head Injury Patients: Test-Retest Performance**

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Attentional deficits are common in mild head injury patients. In order to evaluate the spontaneous evolution of such deficits during the first month after a head injury, neuropsychological tests (Digit Symbol Substitution test, Stroop test, Number Barrage test, Reaction Time test) were administered to 12 patients; their age ranged from 15 to 65 years, their education from 4 to 19 years; in their clinical history psychiatric illness, neuropsychological disturbances or alcohol or substance abuse were not reported. The C.T. scan revealed the absence of cerebral focal lesions. To evaluate the incidence of a possible test-retest effect, the same tests were administered to a control group of 12 subjects comparable for age and schooling. The performance of head injury subjects in the attentional tests was worse than the controls'; it improved at the end of the first month post onset; but the performance of the control group subjects improved as well, an effect of test-retest learning. Thus the performance of head injury subjects was worse than the controls' even after one month post onset.

### **Exposure to Weak Oscillating Magnetic Fields Enhances Habituation in Humans**

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It's known that exposure to weak oscillating magnetic fields (MFs) can influence pain perception in humans. Aim of this study was to obtain an objective confirmation of this phenomenon by recording pain-related somatosensory evoked potentials (PrSEPs). Eleven healthy volunteers took part in the experiment. Pain perception thresholds (Pt) significantly increased after sham treatment (Off), whereas, after real magnetic exposure (On), an opposite, not significant, trend was detected. PrSEP amplitudes resulted surprisingly in contrast to our expectations, i.e. they showed a clear-cut

decrease after On treatment, just when subjects experienced increased pain feelings. The first hypothesis we may put forward is that MFs could have independently influenced both nociceptive processes and cerebral bioelectrical activities, causing a disruption of the correlation between PrSEP amplitude and pain subjective ratings. Nevertheless, one could also consider the possible role of habituation of neural responses to repetitive stimulation. If the slight PrSEP amplitude decrease occurred after Off treatment can be partially attributed to habituation, then, the significant decrease obtained after magnetic treatment could consequently be interpreted as an enhancement of habituation itself. Therefore, MFs could have affected habituation, either directly or influencing some associated phenomena, such as sensory filtration and/or passive attentional processes.

### **EEG Spatially Adapted Segmentation Global Descriptors as "Markers" of an Evolutionary Process from Physiological Ageing to Early Alzheimer's Dementia (AD)?**

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In recent studies significant differences in microstate duration and topography between mild and moderate AD patients and elderly healthy controls have been disclosed. On this basis we compared the resting EEG microstates of 39 mild or moderate AD ( $69.1 \pm 6.8$  years), 19 Age-Associated Mnesic-Impairment (AAMI) ( $67.8 \pm 8.2$  years), and 39 normal elderly ( $67 \pm 9.8$  years), our hypothesis being that EEG spatially adaptive segmentation global descriptors can be an useful tool for differentiating very closed clinical groups from elderly normals. As a matter of fact, a significant "classification" in microstate spatial configuration at the posterior centroid position (sagittal direction,  $p < 0.001$ ) has been disclosed: AD patients are anterior, AAMI posterior, and elderly controls very posterior. Moreover, as elderly subjects, AAMI and AD patients differ essentially at the posterior centroids, in accordance with the neuropathological findings in AD (structural precocious damage of posterior temporo-parietal, and, later, of frontal areas), one could argue that the above mentioned global descriptors are "markers" of an evolutionary process from physiologic ageing to early degenerative dementia.

### **Mismatch Negativity in Autistic Low-Functioning Patients**

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Autism is a biologically based developmental disorder characterized by severe abnormality of reciprocal social relatedness and of development of communication, and by rigid and restricted behavioral repertoire and imaginative skills. It has been postulated that one of the most important deficits in autism is represented by abnormalities in stimuli processing. A considerable number of literature has been produced on event-related potentials (ERPs) in autism; however, because of the need of cooperation, only high-functioning non mentally retarded patients were included in such studies. In this respect, it should be taken into account that up to 88% of these patients are also affected by mental retardation; thus, it seems important to be able to study stimuli processing also in this majority of subjects who are unable to cooperate, by studying those ERPs for which no particular collaboration is needed, such as mismatch negativity (MMN). To our knowledge, there exists only one previous study on MMN in autism and, also in such a case, high-functioning subjects were analyzed who did not show particular abnormalities, as compared to normal controls. In the present study we have recorded binaural auditory MMN in response to deviant tones (1,300

Hz) as compared to standard tones (1,000 Hz) in a group of 6 mentally retarded autistic subjects (diagnosis based on the DSM-IV criteria), aged 8-20 years and in a group of 5 age-matched normal controls. The most important result of this study is that MMN showed significantly higher amplitudes in the autistic group than in normal controls, while there were no significant latency or topographic differences. This finding can be explained on the basis of some peculiar behavioral and cognitive features of autistic subjects and might be considered as a biological correlate of their intolerance to changes in environment.

### **Reaction Time and g-band Movement-Related Synchronization Response**

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In this study we employed a Go-NoGo paradigm with a same-different discrimination task and examined gamma event-related synchronization (ERS) activity with the onset of motoric response (button press). A time-frequency analysis of averaged and single-trial data recorded from 21 right handed subjects was performed to characterize ERS in the gamma band (30-44 Hz). We found an increased peak power with the onset of motoric response across frontal, parietal and occipital recording sites. The largest peak was at a frequency of 32 Hz, and this peak was maximal at the F3, P3 and O2 recording sites. Single trial analysis revealed a highly significant ( $p < 0.0001$ ) relationship between reaction time and peak power at the F3 and O2 sites, for 30 Hz, 36 Hz and 38 Hz frequencies.

### **ERPs and Cognition: Reliability and Control**

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Functional inferences from ERP studies on cognitive processes are based on assumptions that cannot be always fulfilled. Two problems are relevant. The first one regards the reliability of ERP modulation within each subject which can lead to uncorrect ERP estimates. The second one regards the generalizability of the modulation effects to the universe of subjects or experimental conditions which cannot be always evaluated since the small number of subjects and the lack of replication studies which characterize ERP research. A solution to these problems may come from the bootstrap technique and the Generalizability Theory. The bootstrap technique may be used to test, within each subject, the null hypothesis that the ERP modulation is due to chance. The Generalizability Theory may be used to estimate the generalizability of each factor (subjects, conditions etc.) to the correspondent universe. We applied these techniques to ERPs from odd-ball (P300) and cued-recall (old/new effect) experiments. In both cases classic ANOVAs showed highly significant differences between target and standard stimuli (P300) and between old and new stimuli, but the bootstrap analysis showed that a reliable P300 was present in 10 subjects out of 12 (Cz), while a reliable old/new effect was present only in 7 subjects out of 15 (Cz). The Generalizability Theory showed that the difference between target and standard stimuli was highly generalizable across subjects, while the old/new difference was generalizable only for the subjects which showed a reliable effect. Results from these two experiments confirm the usefulness of these techniques to draw more accurate inferences from ERP experiments.

## **Abnormal Visual Event-Related Potentials in Obsessive-Compulsive Disorder**

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Visual event-related potentials and spline map topography during a simple (SRT) and a discriminative (DRT) response task were studied in 12 obsessive-compulsive (OC) patients and 12 age-matched healthy subjects. In SRT the subject had to press a button whenever a stimulus appeared on the screen. In DRT the subject had to press a button only to target stimuli (vertical bars intermixed with an equal probability of horizontals). OC patients have N1 amplitude and latency greater than controls. Moreover, in the discriminative task patient's P3 amplitude was larger than controls for the target stimuli, but not for non-target stimuli. In patients group, NA amplitude, deriving from the difference waves (non-target minus SRT), was larger than controls only in the frontal sites. In normals, non-target stimuli (No-Go task) produce a larger activation than target stimuli (Go task). In OC patient the target stimuli produce the same large activation of the non-target. Treatment with clorpromine reduces the ERP abnormalities except for the N1 alteration. These findings were consistent with theories that considerate the OCD like an attentional disorder derived from a misallocating of cognitive resources. Moreover, was confirmed (with spline map topography) that P3 hyperactivation is localized principally on the frontal lobes.

## **Peak Evoked Gamma Latency and Reaction Time**

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Increasing attention is being directed towards activity in the gamma frequency range as the functional importance of these rhythms is recognized. In this study the relationship of peak evoked gamma activity was examined in relation to reaction times in target auditory oddball data in 40 normal subjects. A moving Welch window and short time FFT were employed to elucidate the time course of gamma (29 to 45 Hz) activity for each single-trial. Following this the time point with maximum total gamma amplitude (across all sites) in each post-stimulus response was identified automatically. The amplitude, power and latency of this peak evoked gamma activity was determined for each target stimulus presentation. No relationship between peak gamma amplitude or power and reaction time was found, but a highly significant and robust correlation between peak gamma latency and reaction time was found by two different methods ( $p = 0.006$ ;  $p = 0.0007$ ). Further frequency analysis revealed that the 37 to 41 Hz was primarily involved. Exclusion of possibly EMG contaminated epochs increased the significance ( $p = 0.00002$ ) and strength of the correlation. Peak evoked gamma latency is correlated with reaction time and therefore this gamma activity is likely to have functional significance in relation to stimulus processing.

### **N100, Reaction Time and a-synchronicity at Stimulus Onset**

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The influence of the level of alpha synchronicity at stimulus onset on the N100 component and reaction time (RT) was examined, in target auditory oddball data from 25 normal subjects. A new measure of alpha synchronicity was employed, consisting of the angular or circular variance (phase coherence) of the alpha phase at stimulus onset across the parieto-occipital sites. The lower the angular variance, the higher the synchronicity (the more closely in phase the alpha activity across these sites) and vice versa. Sub-averaged ERPs were formed for high and low pre-stimulus alpha synchronicity. N100 amplitude was significantly greater in the high than the low synchronicity sub-averages ( $p = 0.002$ ). In addition, RT was significantly reduced in the high pre-stimulus alpha synchronicity cases ( $p = 0.04$ ). Alpha synchronicity reflects an aspect of brain state which influences subsequent stimulus processing.

### **Neuropsychophysiology and Rehabilitation**

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Neuropsychomotricity bases its rehabilitative intervention on the specific stimulation of the two cerebral hemispheres. In fact, psychomotor deficits always present a characteristic picture of cerebral cortical activity that may be either of primitive or secondary origin. The neuronal plastic response, if monitored and strengthened by precise differentiated stimulations according to the hemispheres' characteristics, will always aim to not randomly bypass the damaged area, by means of often compensatory modifications of either the area itself or the surrounding areas. Up to recent times, little attention has been paid to the cerebral asymmetries which are present both in physiological and in pathological conditions, associated or not to a deficit. It is extremely useful to monitor the neuropsychomotor rehabilitative intervention through brain mapping techniques as well as adequate psychometric tests, for the purpose of restoring a synergetic activity of the two cerebral hemispheres and a consequent full or partial recovery of the deficit. Clinical case: We will discuss the characteristics of the rehabilitative intervention on a one-year old child stroked by cortical and sub-cortical atrophy as a consequence of cerebral oedema, 1st degree coma, and we will present the type of cerebral stimulation utilised and the fundamental role of EEG monitoring.

### **Visual Event-Related Potentials (P300) in Migraine Patients**

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Neuropsychologic impairment has been reported in migraine patients between attacks. In many studies event-related potentials were evaluated to verify the involvement of cognitive processing in headache. CNV showed an increased amplitude and a loss of habituation in pain-free period. P300 evoked by visual or by auditory stimuli is considered an easier test but of small diagnostic value because of conflicting results. To verify the relationship between P300 and migraine we studied 13 patients pain-free before treatment. ERPs were evoked by a visual oddball paradigm. 11 patients showed a significantly longer latency if compared to controls. 10 patients were treated with 2 drugs

with opposite actions on DA systems, flunarizine and dihydroergocriptina. 3 patients showed a marked decrease in P300 latency after treatment with flunarizine (1 patient) or dihydroergocriptina (2 patients). Latency was unmodified in 7 patients. In this study the relationship between P300 and migraine seems confirmed. This test may be useful in monitoring the action of prophylactic drugs. More significant results could be found with evaluation of cognitive habituation of P300.

### **Cognitive Impairment in Multiple Sclerosis: A 8-Year Follow-Up Neuropsychological Study**

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Neuropsychological investigations have shown that cognitive impairment occurs in 43 to 65% of patients with Multiple Sclerosis (MS) even in absence of severe physical disability. The pattern of cognitive deficit in MS is not uniform and a great individual variability in neuropsychological performances has been observed. Patients usually show specific deficits in memory, sustained attention, executive function, conceptual reasoning with a quite good preservation of language and high level visuo-perceptual functions. In our study we followed the evolution of cognitive impairment in a sample of 15 "cognitively mildly deteriorated" MS patients. The follow-up assessment was performed 8 years after the first evaluation. Besides, Event-Related Potentials (ERPs) to the oddball task have been recorded. No patient was in exacerbation for baseline or follow-up control. Physical disability was rated according to the Kurtzke EDSS. The score at baseline and at follow-up was 4 or less. On initial testing patients showed impaired performances on verbal and visual-spatial memory, attention, conceptual reasoning, executive functions. At follow-up assessment a progressive decline was observed on memory tests and learning, attention, visuo-motor and visuo-constructive skills, reasoning and executive functions. Correlations between cognitive impairment, brain MRI lesion volume, disability, visual and auditory P300 latency and amplitude are discussed.

### **Neurophysiological Correlates of Edge Detection and Surface Filling-in**

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Texture visual evoked potentials have been recorded in 11 volunteers with a special paradigm that was aimed to disentangle perceptual processes related to edge detection and surface filling-in. The paradigm consisted in 4 stimuli that cyclically alternated. The first stimulus (U1) was a uniform texture of either vertical or horizontal line segments; the second one (U2) was also a uniform stimulus with texture elements orthogonal to U1; the third one was a segmented checkerboard (S1) in which the elements in adjacent squares were orthogonal; the fourth one was also a segmented checkerboard (S2) with line elements orthogonal to S1. The two segmented stimuli differed in that in S1 segregation appeared, while in S2 segregation was maintained in the same position. Segregation-related components were obtained by subtracting U1 from S1 or U2 from S2. In both cases a single negative segregation-related component appeared with peak latency of about 150 ms. However the segregation-appearance component (Sa) showed an earlier onset than the segregation-maintenance component (Sm), but both had the same offset latency. By computing the difference Sa-Sm a negative component with peak latency of about 100 ms (Sd) appeared that was attributed to edge detection, while Sm might reflect filling-in-related processes.

## **Genetic Association Study of Promoter Region Polymorphisms in Tryptophan Hydroxylase and Serotonin Transporter Genes with Obsessive Compulsive Disorder**

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Dysfunction of serotonin (5-HT) metabolism has been hypothesized in obsessive compulsive disorder (OCD). Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in 5-HT synthesis, while serotonin transporter (5-HTT)-mediated 5-HT reuptake into the presynaptic neuron is a key step in 5-HT catabolism to 5-hydroxy-indolacetic acid. Genetic variants of the promoter regions of TPH and/or 5-HTT could alter gene transcription and account for the alterations in 5-HT metabolism observed in OCD. Forty-three unrelated patients fulfilling DSM-IV criteria for OCD and 45 healthy controls were included in the study. The TPH promoter was screened for sequence variation by SSCP. An insertion/deletion polymorphism of the 5-HTT promoter (5-HTTLPR), associated with reduced expression of the 5-HTT gene in lymphoblasts carrying the short allele, was genotyped. We identified four polymorphisms of the TPH promoter region exhibiting complete linkage disequilibrium and each had allele frequency 0.54. Patients and controls did not differ in allele or genotype frequencies. No polymorphisms were detected in the region of the TPH promoter +1 to -252 bp which includes several putative cis-regulatory elements with significant effects on transcriptional activity. The frequencies of the 5-HTTLPR short and long alleles were 0.53 and 0.47. No statistically significant differences in allele or genotype frequencies were observed between controls and patients. We conclude that genetic variation of neither the TPH nor the 5-HTT promoters is likely to account for a large part of the genetic predisposition to OCD.

## **Evaluation of Attentional Processes in Patients with Stroke**

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The psychophysiological approach to the study of the attentional processes has a fundamental role for the evaluation of cognitive functions. Fourteen patients with cerebrovascular accident have been compared with 11 healthy subjects, to connect the functional deficit to the anatomic damage. The components of the Blink Reflex modulation, has been evaluated according to the unwarned and warned conditions; event related potentials (P300), and the short (BAEPs) and long (CERA) latency acoustic stimulus related potentials. These data confirm the effect of the attentional modulation on the amplitude of the Blink Reflex components and show the no inhibition of the R3 in the stroke patients if compared to the healthy ones and more particularly in the left stroke ones, where the attentive effort didn't reduce the amplitude of the R3 component, which is inhibited in the right stroke patients. The latency of the P2, N2, and P3 components was significantly more in the patients with stroke compared with healthy ones. The P3 latency didn't show differences in right stroke patients compared to the healthy ones. By these data we suppose both hemispheres are needed to elaborate event related potentials, and involved in the checking of the attentive function, but the left hemisphere has a prevailing role. The BAEPs and CERA have no utility for the study of this function.

## **Endocrine and Psycho Physiological Effects in Postmenopausal Women in a Double Blind Study with a Novel Drug: Pivagabine**

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Pivagabine (4-[2,2-(dimethyl-1-oxopropylamino)butanoic acid] CAS 69542-93-4, Toner) is a hydrophobic compound involved in the modulation of the adaptive response to stress and an anticonvulsant effect. In particular, at the neuroendocrine level this drug (200 mg/kg) is able to antagonize the alteration of corticotropin-releasing factor (CRF) immunoreactivity concentration induced by acute stress in rats hypothalamus and cortex and prevents the functional decrease of cortical and hippocampal GABA<sub>A</sub> receptors produced by stressful stimuli. The aim of this study was to evaluate the neuroendocrine and psychophysiological effects of the administration of pivagabine in postmenopausal women in a double blind study. Postmenopausal women (n = 20) (age range 45-55 years) were randomly divided in two groups. The first group was treated for 7 days with pivagabine (PVG; 900 mg /twice daily) and the second group received placebo. All subjects underwent: Symptom Questionnaire (SQ) Crown & Crisp Experiential Index (CCEI), Pisa Stress Questionnaire (PSQ). SQ & CCEI were administered before and after 7 days PVG treatment, PSQ before only. Furthermore, before and after the treatment, all patients underwent a Psychophysiological profile (PPP) with simultaneous registration of: frontal EMG, SCL/SCR, Temp, HR, and RR. PPP was carried out according to 3 different sessions: 6 min baseline, 6 min stress (with the administration of a computerised MST), and 6 min recovery. Salivary samples were collected during the baseline and recovery session of the PPP; two more samples (one at 7 AM and the other at 11 PM) were collected, by the patients themselves, in order to evaluate the daily cortisol excursion. After an overnight fasting plasma samples were collected before and after therapy every 15 minutes for 4 hours. In each sample were evaluated plasma luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL), cortisol, growth hormone (GH), insulin-like growth factor-1 (IGF-1) and b-endorphin (b-EP) levels. Results: The t paired statistical test, in the comparison before - after treatment (placebo Vs treated), have shown the following significant differences: menopausal women, treated group: CCEI: phobic anxiety  $t = 4.65$ ,  $p = 0.002$ ; depression  $t = 2.92$ ,  $p = 0.04$ , hysteria  $t = 2.81$ ,  $p = 0.04$ , total score  $t = 2.64$ ,  $p = 0.05$ ; SQ: depression  $t = 2.75$ ,  $p = 0.03$ , somatic disorders  $t = 2.46$ ,  $p = 0.04$ , total score  $t = 2.64$ ,  $p = 0.034$ . Menopausal women placebo group: CCEI: Free floating anxiety  $t = 3.21$ ,  $p = 0.011$ , somatic compliance  $t = 2.44$ ,  $p = 0.034$ , total score  $t = 3.02$ ,  $p = 0.01$ . No significant statistical differences were found in the physiological recorded indexes, in the salivary cortisol levels and in plasma LH, FSH, GH, PRL, IGF-1 cortisol, b-EP and salivary cortisol levels. Discussion: Despite the very short period of treatment the PVG seems to be able to significantly reduce some of the principal stress-related symptoms-behaviours although physiological and endocrinological indexes didn't show any appreciable variation. The continuation of the study with a larger group of patients and a longer therapy time is now in progress.

## **Cerebral Activation during Lexical Recall of Proper and Common Names: An Electrophysiological Study**

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Neuropsychological and functional neuroimaging data suggest that memory recall of proper and common names is subserved by different neuro-functional systems. The present study investigated

the spatio-temporal dynamics of brain activation during retrieval of proper Vs. common names by means of a high-resolution electrode recording in healthy young volunteers. Event-related potentials (ERPs) of the brain were recorded to probes and syllables in a phonological decision task involving names retrieval upon written definition. The task consisted in silently retrieving the target names, and to decide whether a syllable was part of the defined target. ERPs to the probe were characterized by a series of negativities asymmetrically distributed over the left hemisphere. N200 component was much larger to common than proper names and had a posterior temporal distribution which spread over secondary visual areas in the case of common names. This involvement of visual areas might be related to the greater imagery value of nouns compared to proper names. This negativity was followed by a large positivity which had multiple generators. There was a right parietal focus which did not differ in amplitude as a function of name category, and a P315 selectively elicited by proper names over the left dorsolateral prefrontal area.

### **Asymmetric Visuomotor Integration in Callosal Agenesis**

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In an acallosal boy, without other detectable neural defects, we measured visuomotor responses following the Poffenberger paradigm. In this task crossed and uncrossed RT reflect the time of inter- and intrahemispheric integration and the difference (CUD) estimates the interhemispheric transfer time. In the agenetic subject we found that the CUDs in the two hemifields are largely asymmetric suggesting that interhemispheric integration is slow when the contralateral stimuli are responded by the right hand and fast when the crossed motor responses are executed by the left hand. We believe that lengthened interhemispheric transfer due to the callosal lack can well account for the slow visuomotor integration, while involvement of ipsilateral motor routes from the left hemisphere (LH) is the most conceivable explanation for the fast integration. In agreement with earlier neurological reports, recent MRI studies performed in normal subjects have documented that, unlike the right hemisphere (RH), the LH is substantially activated during ipsilateral finger movements. The functional superiority of the LH in controlling the ipsilateral motor output may be shielded, in normals, by the interhemispheric callosal transfer that, although asymmetric, is very fast in both directions. In the acallosal brains the direct access of the LH to the left hand becomes the most efficient mechanism for mastering fast visuomotor integration because it spares the long interhemispheric transfer that is needed when the right hand responds to stimuli detected by the RH.

### **A Case Report on P300 Evolution in Creutzfeldt-Jakob Disease**

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Serial EEG and P300 recordings were carried out in a 52 year old woman affected by Creutzfeldt-Jakob disease. The diagnosis was assessed by clinical, EEG, MRI, bioptic and immunoistochemical data. To obtain the P300 both the active and passive classical odd-ball paradigm were used. The EEG was recorded using the routine method. The evolution of EEG, P300 and clinical data, simultaneously collected, was then studied. Two months after the clinical start of the disease, when the patient was still conscious and aware, although with some ideomotor slowness, we were not

able to record P300 using the active paradigm. On the contrary, using the passive paradigm, P300s were found at various checks starting from this time until the apallic syndrome, that appeared in the following weeks, worsened (marked reduction of spontaneous eye movements and apparent environmental contact, reduction of involuntary movements). The use of a odd-ball conditioning technique was also unsuccessful in obtaining the P300 at this time. We were able to elicit P300 when the EEG was characterised both by persistent background activity and by the continuous occurrence of periodic triphasic complexes, while its disappearance was associated with amplitude reduction of the EEG triphasic complexes under 80-40 mV, prolongation of their interval over 1.2 sec and their restriction to the frontal scalp areas.

### **A Comparison between EEG Reactivity and Somatosensory Evoked Potentials for Outcome Prediction following Traumatic and Anoxic Coma**

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A retrospective analysis of 40 patients, mean age 37 (range 10-73), in severe post-traumatic (33 patients) and post-anoxic (7 patients) coma was undertaken. On the basis of clinical criteria the prognoses was uncertain after the first week. The mean duration of coma was 14 days (range 6-56). The patients were evaluated by means of Glasgow Coma Scale (GCS), EEG reactivity and short-latency somatosensory evoked potentials (SEPs) to establish the ability of the different diagnostic measures to predict outcome at two years. GCS was performed at the entry in intensive care unit. EEG and SEPs were recorded at 3 and 13 days from the entry. The results were correlated with outcome using discriminant analyses (SPSS/PC+). Mean GCS was 4.5, range 4-7; its predictive value was of 62%. EEG reactivity was present in 19 patients, doubt in 4 and absent in 17, with a predictive value of 67.5%. SEPs were normal or altered on one side in 21 patients; in 8 patients SEPs were abnormal on both sides or absent on one side; in 11 patients SEPs were absent on both sides or absent on one side and abnormal on the other. Their predictive value was 92.5%. The present data show that the accuracy of EEG reactivity to predict prognosis is consistently lower than predictive value of SEPs. Bilaterally normal SEPs in post-traumatic coma are always predictive for good outcome, while they don't exclude poor outcome in post-anoxic coma. Otherwise, bilaterally absent SEPs predict poor outcome. EEG reactivity is not predictive for the presence of cortical SEPs. A convincing physiopathological interpretation of this finding is not available.

### **Movement Related Potentials in Dyslexic Subjects: Individual Comparison with Normative Data Age Related**

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The essential feature of Reading Disorder is reading achievement that falls substantially below that expected given the individual's chronological age, measured intelligence, and age-appropriate education (DSM-IV). In a previous study (Chiarenza, 1990) 8 dyslexic males aged 10 were submitted to a Skilled Motor-Perceptual Task (SMPT). Both Motor Performances (PM) and Movement Related Brain Potentials (MRP) showed relevant alteration compared to the control group. PM and MRP are significantly dependent on the chronological age of subjects. In this work 10 dyslexic subjects (8M/2F, aged 8-31) have been tested; their PM and MRP were individually compared with normative values of 119 normal subjects. Most of them displayed marked alterations both of PM and MRP; the latter were altered in all subjects in different brain areas. In particular,

they were less accurate during the execution of the SMPT, significantly performing a small number of target responses and lower performance time. BP was decreased in onset and amplitude, MCP and N100 were delayed in latency and of smaller amplitude. Most of subjects displayed also relevant alteration of SPP and PAN; PAN was not recorded in more than half of dyslexic subjects. Dyslexia should be considered not only a disturbance of visual and/or auditory perception, but a more generalized defect of temporal integration that involves different processes in various cerebral areas.

### **Biofeedback Evaluation in Parents of Children with Autism**

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Background. Previous studies have shown that a significant proportion of parents of autistic children showed impaired executive function. Methods. Psychophysiological diagrams of 20 couples of parents of autistic children without organic disease (PA1) and of 20 couples of parents of autistic children with organic disease (PA2) have been recorded by a Biolab system. Results. (1) The diagrams of the PA1 show significant differences in comparison to the PA2; (2) the diagrams of PA1 show, starting from baseline, absence of regular correlation without modification during the entire section; (3) in the PA1 group we did not evidence psychotic symptoms but during the biolab performance we noticed increasing anxiety and confusion. Conclusions. We can hypothesize that the irregularity in the diagram of the PA1 can cause problem in the reciprocity with the children before the birth and since the beginning of the attachment relationship.