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- 1. A meta-analysis of the cortical silent period in epilepsies - F. Giovannelli, A. Borgheresi, L. Tramacere, S. Colon, E. Sirabella, M.P. Viggiano, G. Zaccara, M. Cincotta (Firenze)**

The cortical silent period (CSP) following transcranial magnetic stimulation reflects GABAB-mediated inhibition in the primary motor cortex (M1) and could contribute to understand the pathophysiological substrates of epilepsies. Increased CSP duration has been reported in idiopathic generalized epilepsy (IGE) and in partial epilepsy (PE) involving the M1, although other studies yielded discordant findings. We used meta-analysis to systematically assess the consistency of CSP changes in untreated epileptic patients. We searched for controlled studies evaluating the CSP in drug-naïve or drug-free patients with IGE or PE. The mean difference between CSP duration obtained in patients and controls was calculated. Fourteen studies (267 patients and 234 controls) were included. A significant mean difference was found, with longer CSP in patients than in controls. The difference was still greater if only IGE patients were analyzed. CSP modifications did not depend from differences in motor threshold between patients and controls. Meta-analysis confirms CSP modifications in epilepsies, with enhancement of this cortical inhibitory measure in most IGE patients. This provides rationale for further investigations aiming to verify the hypotheses that increased CSP reflects compensatory neural phenomena counteracting transition from the interictal to ictal state and that CSP variability reflects the pathophysiological heterogeneity of epileptic syndromes.

- 2. Follow-up of five cases with Rasmussen encephalitis with magnetoencephalography - D.S. Rossi, E. Visani, D. Duran, F. Rotondi, L. Canafoglia, E. Freri, F. Ragona, T. Granata, F. Panzica, S. Franceschetti (Milano)**

Magnetoencephalography (MEG) recordings of interictal and/or ictal discharges can provide valuable information about the location of the epileptogenic area in the brain. Rasmussen Encephalitis (RE) is characterized by intractable epilepsy, progressive hemiparesis, and unilateral hemispheric atrophy. The progression of the symptoms to significant neurological impairment usually occurs within months to a few years. Five patients (mean age at first observation $7,6 \pm 3,0$ yrs) fitting Bien's criteria for the diagnosis of RE were enrolled for the study and follow-up for at least 1,5 years (4-7 MEG measures per patient), in order to evaluate correlation between the evolution of clinical picture, neuroradiological and MEG findings. MEG data were visually inspected and interictal spikes were selected for the source localisation by means of equivalent current dipoles (ECDs). Cortical thickness was evaluated from Magnetic Resonance Imaging (MRI). All patients showed ictal/interictal multifocality, reduction of background cortical magnetic activity and progressive focal cortical atrophy on MRI of the affected hemisphere. Moreover, our preliminary data showed that dipole clusters were found mainly in the most atrophic cortical regions, suggesting a close relationship between MRI and MEG alterations maintained progressively in time.

- 3. Evaluation of long term cognitive risks associated with the presence of seizure during acute disseminated encephalomyelitis - L. Santangelo, E. Cainelli, M. Nosadini, S. Sartori, M. Sole, A. Suppiej (Padova)**

A small percentage of paediatric acute disseminated encephalomyelitis (ADEM) presents with seizures, the expression of neuronal involvement. The association of epileptic activity with demyelination could represent an increased risk for long lasting cognitive sequelae, this has not yet been well-explored in the literature. Objective of this study was to compare long term neuropsychological outcomes between children and adolescents with history of ADEM with or without seizures. A neuropsychological evaluation (explored areas: general intelligence, language, attention, memory, visuo-motor skills and executive functions) was administered to 20 children and adolescents with history of ADEM (12 boys; mean age at ADEM onset 6.5 years (DS 4.23), mean age at follow-up 13.8 years (DS 5.65) and mean length of follow-up 6.8 years (DS 3.7). Multichannel-EEG recordings during hospitalization for ADEM were evaluated by a neurophysiologist trained in the identification of epileptic activity. 4/20 patients had EEG confirmed seizures. Neuropsychological scores of patients with and without seizures were compared using Mann-Whitney test. No significant differences were found between children with and without seizures, in none of the cognitive domains explored. In conclusion, the presence of seizures during ADEM do not appear to represent a risk factor for developing long term cognitive impairment.

- 4. Neurophysiological Pattern related to recovery of responsiveness in patients with Disorders of Consciousness after Cardiac Arrest - A. Grippo, R. Carrai, T. Atzori, A. Vettori, B. Hakiki, E. Portaccio, AM. Romoli, M. Scarpino, C. Macchi, A. Amantini (Firenze)**

Most of the patients surviving a Cardiac Arrest (CA) recover responsiveness in the first 30-40 days, but further recover is possible also in the following months. We conducted a prospective study to correlate the recovery of responsiveness and consciousness and EEG and Somatosensory Evoked-Potentials (SEP) findings. Level of responsiveness were evaluated by means of Coma Recovery-Scale-Revised. 22 inpatients (12 VS, 6 low grade MCS, 4 high grade MCS) were followed for up for a mean of 200 days (range 112-300) since CA. EEG and SEPs have been recorded within one week after the admission and every four weeks. At the end of follow up 2 patients had died, 7 VS patients did not recover responsiveness, 4 VS patients become low grade MCS and 1 VS patient becomes high grade MCS; 5 MCS patients did not change clinical condition; 1 low grade MCS and 4 high grade MCS patients recovered consciousness. Concerning the Neurophysiological Tests, only patients with SEP present can regain responsiveness/consciousness. No EEG pattern is able to predict no recovery of responsiveness/consciousness, whereas reactive EEG correlated with a progression of clinical condition. In the presence of Epileptiform Discharges (even after 2 months after CA) a recovery of consciousness is still possible.

5. Psychophysiological responsivity and conscious appraisal of affective stimuli in non-organic syncope - D. Crivelli, G. Lecci, B. Nelli, P.L. Baldi, M. Balconi (Milano)

Transient losses of consciousness and muscular tone that characterize syncope are due to a sudden decrease of blood flow to the brain. Nevertheless, in part of patients reporting syncope episodes the classic diagnostic process do not lead to a proper organic etiology – e.g. neutrally mediated or cardiac. Psychological non-organic factors like emotional dysregulation or anxiety mechanisms might act as triggers for those clinical manifestations. Given the link between affective experience and sympathetic-parasympathetic autonomic system, this research aims at investigating the hypothesis of a psychogenic etiopathogenesis and at sketching a clearer picture of affective responses in syncope. Control (healthy volunteers) and clinical (syncope patients with no organic etiology) groups were presented with arousing affective visual stimuli and assessed by psychometric tests. In order to explore both automatic and conscious processing of affective information, we recorded participants' psychophysiological responses (autonomic and EEG) and subjective appraisal ratings (valence and arousal). The comparison of psychometric, electrophysiological and autonomic data across patients and control subjects showed anomalous response profiles, with partially incongruent autonomic automatic psychophysiological responses and conscious appraisal ratings. While the dysregulation of psychophysiological responsivity might characterize syncope profiles, the complexity of clinical pictures suggest that there may exist different non-organic syncope subtypes.

6. Sensory-motor networks' topology in multiple sclerosis fatigue – F. Miraglia, F. Vecchio, C. Porcaro, C. Cottone, A. Cancelli, P.M. Rossini, F. Tecchio (Roma)

The large majority (80%) of people with multiple sclerosis (MS) complain of fatigue, which is the most disabling symptom in half of them. While the few drugs used to treat MS fatigue are limitedly useful, it was recently observed the efficacy of a personalized neuromodulation treatment, supporting the concept that interventions modifying the sensorimotor network activity balances could be suitable non-pharmacological treatments for MS fatigue. Aim of the present study is to strengthen knowledge of the brain unbalances, which proper neuromodulations should target to compensate. We collected electroencephalographic (EEG) data in 18 people with mild MS, while they were in resting state with open eyes. To ensure a wide range of fatigue, we enrolled patients to have Higher- or Lower-Fatigue based on scores of the modified Fatigue Impact Scale (mFIS). We selected the graph theory small-world index, calculated on networks of cortical nodes estimated by eLORETA, to evaluate the characteristics of left and right frontal (Motor) and parieto-occipital-temporal (Sensory) brain networks separately. Fatigue symptoms increased together with the small-world index in the Sensory network of the left dominant hemisphere. This finding hones understanding of the targets of neuromodulation interventions indicating the sensory network of the dominant left hemisphere as a specific target.

7. EEG characteristics in “eyes open” vs “eyes closed” conditions: small world network

architecture in healthy aging and age-related brain degeneration – F. Miraglia, F. Vecchio, P.M. Rossini (Roma)

Applying graph theory, we investigated how cortical sources small worldness (SW) of resting EEG in eyes-closed/open (EC/EO) differs in mild cognitive impairment (MCI) and Alzheimer's disease (AD) subjects respect to normal elderly (Nold). EEG were recorded in 30 Nold, 30 MCI, 30 AD during EC and EO. Undirected and weighted cortical brain network was built to evaluate graph core measures. eLORETA lagged linear connectivity was used to weight the network. In Nold, EO condition presented more random network (higher SW) in alpha bands and more regular organization (lower SW) in beta2 and gamma bands. In MCI, SW trend was the same, except for delta and theta bands with more ordered organization. AD showed similar trend of Nold, but with less fluctuations between the conditions. Furthermore, in both conditions, MCI SW architecture presented midway properties between AD and Nold. In low frequencies, Nold showed more random network organization, while SW parameter displayed a more ordered architecture with disease progression. Small world properties had different patterns in pathological aging in open eyes, with different trends in EEG frequency bands. Graph theory provides an excellent tool to characterize neuronal network capacities from coupling parameters of time-varying signals.

8. Autonomic correlates of seeing one's own face in patients with disorders of consciousness – S. Bagnato, C. Boccagni, C. Prestandrea, G. Galardi (Cefalù)

The ability to recognize one's own face, or “self-face”, is a hallmark of self-awareness. In healthy subjects, the sympathetic skin response (SSR) evoked by self-face recognition has a greater area than responses evoked by other visual stimuli. We evaluated the SSRs evoked by self-face images and by six other visual stimuli (conditions) in 15 patients with severe disorders of consciousness and in 15 age-matched healthy subjects. Under all conditions, the evoked area of the SSR was smaller in patients with unresponsive wakefulness syndrome (UWS), intermediate in patients in a minimally conscious state (MCS), and greater in healthy subjects. In patients with UWS, no differences were found between the SSR area evoked by self-face images and those evoked by other conditions. In patients in an MCS, the area of the SSR evoked by self-face presentation was greater than those evoked by other conditions, but statistical significance was reached only in the comparison to other stimuli not involving a real face. This finding may be due to the inability of these patients to differentiate their own face from those of others. These results probably reflect a varying level of self-awareness and suggest some diagnostic implications in patients with severe disorders of consciousness.

9. “Validation of the new portable recording system BluNet for identifying patients with Respiratory Sleep Disorders” - I. Roma, T. Atzori, A. Vettori, F. Gigliotti, B. Binazzi, V. Roma, A. Grippo (Firenze)

This study was designed to evaluate the diagnostic and technical accuracy of the new portable recording device BluNet. BluNet has innovative features that introduce a new

generation of devices: modularity, communication with the iPad/iPhone world, ease in data exchange (European Data Format file), impressive small sizes and weight, use of wireless transmission (Bluetooth "Low Energy" 4.0). The validation is done by comparing N= 10 recordings in patients with clinical suspicion of Respiratory Sleep Disorders. We performed simultaneous polygraphic recordings with BluNet and with the main reference portable PSG device, Embletta GOLD. The PSG data acquired during the night have been: air flow through a nasal cannula, chest and abdomen movements via inductive belts, oxygen saturation and heart rate via saturimeter. The recordings were analysed manually by a blinded investigator. The AHI obtained by the BluNet device are closely correlated to that obtained by Embletta (Pearson correlation, $r= 0.988$); the correlation between oxygen desaturation index by BluNet and the one by Embletta was also strong ($r= 0.943$). Similar diagnostic sensitivity in detecting OSA was found with the two portable devices. We concluded that BluNet was found clinically applicable, technically reliable, and sensitive for the diagnostics of Respiratory Sleep Disorders.

10. Visual electrophysiology. A good friend can help you in need – MC. Tozzi, S. Silipo, S. Monaco, L. Bertolasi (Verona)

Scotopic and photopic full field-Electroretinogram (ERG), pattern electroretinogram (PERG) and visual evoked potential (VEP) are stimulating and recording methods to evaluate the functionality of the different layers of retina and visual pathway from retina to visual cortex of the brain. Visual electrophysiology is a useful diagnostic tool which aid in cases of unexplained visual loss if the clinician is well-versed in this techniques. Furthermore the new ocular imaging tests such as OCT give only morphological informations about retina and the head of optic nerve that need functional correlations with the symptoms of the patient. We review the diagnostic protocol for neurophysiological assessment of afferent visual system performed in our lab and describe normative data from 30 healthy subjects.

11. Visual electrophysiology revealed the diagnosis in an unusual case of bilateral blindness at the multiple sclerosis center. A case of bilateral chronic optic neuropathy related to inverted papilloma of paranasal sinuses - S. Silipo, M. Calabrese, I. Juergenson, Mc. Tozzi, S. Monaco, L. Bertolasi (Verona)

The afferent visual pathway can be evaluated by the neurophysiologist using full-field ERG, transient or stationary P-ERG and PEV pattern. We report a case of 65 years-old-man which was admitted to the Multiple Sclerosis Center because of chronic bilateral blindness where the visual electrophysiology gave important clues for an unexpected diagnosis. Recurrent episodes of subacute vision loss, without improvement after steroid therapy, led the patient to blindness in the right eye at age 45. Ten years later he developed a progressive loss of visual acuity on the contralateral eye. Ophthalmological examinations disclosed also recurrent episodes of left anterior uveitis lately complicated by cataract. However the visual acuity on the left eye didn't improve after phacoemulsification. Brain and spinal MRI were normal as well as CSF examination and anti NMO antibodies. Rheumatological screening

revealed only a positivity to HLA B27. The visual electrophysiology was consistent for bilateral chronic optic neuropathy without involvement of the retina or features of Leber disease or glaucoma. A tailored MRI of the orbits and CT scan of the face disclosed a butterfly-like inverted papilloma of paranasal sinuses which destroyed the wall of both optic canals. The patient went through a surgical treatment.

12. Sensitivity and predictive value of OCT and VEP in Multiple Sclerosis – G. Di Maggio, R. Santangelo, S. Guerrieri, L. Ferrari, F. Vitali, S. Medaglini, M. Rodegher, B. Colombo, L. Moiola, U. Del Carro, V. Martinelli, G. Comi, L. Leocani (Milano)

To evaluate the role of optical coherence tomography (OCT) and visual evoked potentials (VEPs) in patients with multiple sclerosis (MS). Study of 121 consecutive subjects with MS. Of 242 eyes, 166 had no previous history of optic neuritis (ON), 22 had a single recent ON episode (<3 months); 54 had chronic ON (at least 1 episode >3 months before). All patients underwent assessment of EDSS, OCT retinal nerve fiber layer (RNFL) thickness and VEP (checkerboard, size 15'). 77 subjects underwent to a second EDSS (EDSS2) evaluation after a mean time of 1, 94 (± 0.69) years (median EDSS 2, range 0-7). In eyes with recent ON, the sensitivity of OCT was 38.9% with a higher sensitivity of VEP (77.3%; McNemar $p < 0.02$). In eyes with chronic ON, no significant difference was found between OCT (68.5%) and VEP (81.5%) sensitivity. In asymptomatic eyes, VEPs had a higher sensitivity (31.7%) vs OCT (19.9%; $p=0.005$); VEP/OCT combined detected abnormalities in 39.2%. In follow up evaluation, OCT alterations were associated with development of disability after 2 years ($p=0.013$). VEP alterations did not predicted future disability development neither in patients without previous ON nor in those with previous ON. The present findings confirm a higher sensitivity of VEPs in the subacute phases of optic neuritis (less than 3 months) and in asymptomatic eyes. In eyes without previous optic neuritis, early asymptomatic OCT abnormalities are associated with short-term worsening of disability. Further longitudinal study are needed to confirm our findings.

13. Optical Coherence Tomography and Multifocal Visual Evoked Potential clinical usefulness in identifying visual pathway involvement - S. Guerrieri, G. Di Maggio, F. Vitali, R. Santangelo, S. Medaglini, L. Moiola, U. Del Carro, V. Martinelli, G. Comi, L. Leocani (Milano)

Full-field visual evoked potentials (ff-VEP) are fundamental in neurological practice, for defining the nature of visual disturbances. We explored whether, in case of normal ff-VEP and suspected organic visual pathway involvement, multifocal visual evoked potentials (mf-VEP) and optical coherence tomography (OCT) can be useful in the diagnostic workup. Observational case reports. Three patients arrived at our department for visual disturbances. Two had relapsing optic neuritis (ON) and visual acuity (VA) loss, with normal or non-significant ff-VEP outside acute clinical episodes. In both cases OCT showed a retinal nerve fiber layer (RNFL) thickness reduction, allowing visual pathway damage identification. The third, with

meningioma involving left optic nerve, complained of blurred vision in the nasal field of the left eye as confirmed by computerized perimetry (CP). While ff-VEP showed normal latency and non-significant amplitude reduction in the left eye, mf-VEP showed important amplitude reduction in the whole lower left eye field. OCT scan confirmed axonal damage showing left RNFL thinning. Sometimes ff-VEP fails in identifying abnormalities in patients with processes involving the visual pathway, particularly in cases with axonal or sectoral optic nerve involvement. We suggest the importance of a multimodal evaluation, including OCT and mf-VEP.

14. An abnormal transduction of the chromatic stimuli from the outer to the inner retinal layers may contribute to the mechanism of photophobia in migraine - G. Coppola, L. Corso, A. Di Renzo, A. Fadda, F. Martelli, C. Di Lorenzo, V. Parisi, J. Schoenen, B. Falsini, F. Pierelli (Rome, Latina, Liège BE)

Recent experimental evidences point out a possible involvement of retina in hypersensitivity of migraine patients to light stimuli. To investigate the short-wavelength-sensitive and the medium/long-wavelength-sensitive cone photoreceptors of the visual pathways in migraine without aura (MO) patients between attacks and in healthy volunteers (HV) by using yellow-blue (Y-B) or red-blue (R-B) visual flicker stimuli. Square-wave focal electroretinograms (FERGs) were recorded in 22 MO patients and 20 HV. Fourier analysis allowed extracting from the FERG data the fundamental (1F) and the second harmonic (2F) components (amplitude and phase) that are related respectively to outer and inner retinal activity. Usual headache severity and photophobia during migraine were scored on a 0 to 10 visual analogue scale. When compared to HV, MO patients had an advanced 1F phase but normal amplitude in all blocks of Y-B FERG. Self-rated intensity of ictal photophobia positively correlated with attack frequency, headache severity, 1F Y-B phase, 1F R-B phase, 2F Y-B amplitude, habituation slope, and 2F R-B phase. These results suggest that an abnormal signal transduction from the outer to the inner retinal layers could contribute to the mechanisms by which light causes pain or discomfort during the migraine headache.

15. Scalp Somatosensory Evoked Potentials recordings after human Subthalamic and Pedunculopontine Tegmental Nucleus stimulation - A. Insola, P. Mazzone, M. Valeriani (Roma)

The study aimed to investigate the pathways activated by deep brain stimulation (DBS). Four patients, suffering from parkinson disease (PD), underwent DBS electrode implant in the Pedunculopontine (PPTg) nucleus (2 patients) and in the Subthalamic (STN) nucleus (2 patients) for neuromodulation. Somatosensory evoked potentials (SEPs) were recorded from the scalp to either median nerve or DBS electrode stimulation. The PPTg stimulation evoked a parietal negative and a frontal positive response at a latency of 3 ms, corresponding to the N20 and P20 potentials to median nerve stimulation, respectively. The STN stimulation evoked a negative potential at a latency of 6 ms in both the parietal and frontal electrodes. Our findings show that the electrical stimulation of the PPTg electrode contacts

activate an oligosynaptic (probably lemniscal) pathway, while the scalp responses to STN stimulation are mediated by a polysynaptic pathway.

16. Vestibular Evoked Myogenic Potentials (C-Vemps And O-Vemps) in some otoneurological diseases - R. Del Colle, A. Lupato, S. Ricci, M. Turazzini, L. Bevacqua, A. Polo (Legnago)

c-VEMPs and o-VEMPs are a new diagnostic tool to detect diseases of the inner ear and the vestibular pathways. The aim of our study was to assess the reliability of c-VEMPs and o-VEMPs in some otoneurological diseases. We examined 27 patients, 15 F, 12 M, mean age 42,5. 20 Ménière disease (MD), 3 Benign Paroxysmal Positional Vertigo (BPPV) and 4 vestibular neuritis (VN). c-VEMPs were recorded from electrodes placed over the SCM, with reference over the clavicle. o-VEMPs from the same electrodes placed beneath the eye and reference 2 cm below. For both c-VEMPs and o-VEMPs we used acoustic stimuli (tone burst, 117 dB SPL). MD: both c-VEMPs and o-VEMPs were normal in 13 patients (65%); c-VEMPs were abnormal in 1 patient (5%); o-VEMPs in 4 patients (20%) and both c-VEMPs and o-VEMPs in 2 patients (10%). BPPV: normal in 2 pts.(67%) ; o-VEMPs abnormal in 1 pt. (33%) VN: c-VEMPs abnormal in 1 pt;(25%), o-VEMPs in 1pt. (25%) both c-VEMPs and o-VEMPs in 2 pts.(50%). c-VEMPs and o-VEMPs seem to be reliable tests to improve the diagnosis of otoneurological diseases. We point out that in some MD pts the only abnormal test was o-VEMPs.

17. Pain modulation in patients with Multiple Sclerosis, pain and spasticity after oromucosal cannabinoid spray (THC/CBD): A study with quantitative sensory testing and laser evoked potentials - M. Turri, F. Donato, F. Teatini, G. Zanette, V. Tugnoli, L. Deotto, G. Moretto, G. Squintani (Bolzano, Verona, Peschiera del Garda, Ferrara)

Oromucosal cannabinoid (THC/CBD) spray administration for the treatment of pain in patients affected by Multiple Sclerosis (MS) has been well documented and MS patients generally complain of different kind of pain, including spasticity-related and neuropathic pain. Our purpose was to examine pain modulation and thermal/pain threshold of MS patients before and after THC/CBD. 16 MS patients underwent clinical examination (including NRS scale), Quantitative Sensory Testing (QST) and Laser Evoked Potentials (LEPs) before and after one month of oromucosal spray. Psychophysiological and neurophysiological testing were compared to sex- and age-matched controls. Patients reported a significant reduction in pain (NRS 7,2 /4,7 before/after THC/CBD); QST thresholds were altered in patients and did not change after THC/CBD; there was a significant reduction of LEPs amplitude and increase of LEPs latency in MS patients compared to controls and no significant threshold or LEPs parameters change was noted after drug administration. Our results suggest that THC/CBD is effective on pain but LEPs and QST are not sensitive enough to detect pain modulation; the fact may be dependent on different factors, including the high disease burden as well as different kind of pains (nociceptive and neuropathic) affecting MS patients.

18. Laser evoked potentials and quantitative sensory testing in patients affected by multiple sclerosis: clinical, neurophysiological and psychophysiological correlates – M. Turri, F. Donato, G. Zanette, F. Teatini, V. Tugnoli, L. Deotto, G. Moretto, G. Squintani (Bolzano, Verona, Peschiera del Garda, Ferrara)

Pain is a common finding in patients affected by Multiple Sclerosis (MS). Many different types of pain can afflict MS patients, including neuropathic, nociceptive, or mixed pain. TSA-II-Thermotest (QST) and Laser evoked potentials (LEPs) are psychophysical and neurophysiological tests commonly used to explore pain. The study aims to determine psychophysical and neurophysiological correlates in MS patients. 16 MS patients (5 men, 11 women, mean age 59 years, mean EDSS 7) were clinically and neurophysiologically tested. 5 patients presented neuropathic central pain (according to NeuPSIG 2011 guidelines), 8 patients presented nociceptive or mixed pain, and 3 patients were pain-free. For QST, the dorsum of both hands and feet were examined; for LEPs, the dominant hand and both feet were tested. Results were collected and compared to age and sex matched controls. Pin-prick was altered in 37,5%, LEPs were abnormal in 57,8% and QST was pathological in 85,9% of examined sites. We detected a significant correlation between pain and clinical examination (0,022), pain and altered QST (0,042), while LEP abnormalities correlated well with the presence of neuropathic pain (0,012). Our results suggest that LEPs are more specific than QST to differentiate neuropathic from nociceptive pain.

19. Central motor conduction time along the phrenic nerve pathway in patients with cervical syringomyelia - P. Ciaramitaro, D. Renosio, E. Spagone, S. Giorgi, G. Faccani, D. Cocito (Torino)

The aim of this study was to investigate phrenic central motor conduction time (CMCT) in patients affected by Syringomyelia (Syr) and Chiari Malformation (CM) to point out subclinical phrenic pathway alterations. Forty-two patients (12 M, 30 F, age 18-71 years, mean $49,43 \pm 13,56$) without clinical signs of respiratory impairment were included and divided into subgroups according to different clinical phenotypes (cervical Syr, cervical-dorsal Syr, Syr with CM). TMS was bilaterally performed, recording by surface electrodes from hemidiaphragm; latency/amplitude of cortical and spinal motor-evoked potentials (Cx-MEP/Sp-MEP) and CMCT were measured in all patients. No adverse local or systemic reactions were reported. Neurophysiological data were analyzed and compared with 16 healthy subjects (T-test). CMCT was significantly prolonged ($p < 0,05$) in patients versus controls and in two subgroups: c-Syr with CM, Syr with CM and surgical indication; in all patients Sp-MEP amplitude was reduced ($p < 0,05$). This study seems to confirm CMCT along the phrenic nerve pathway is a sensitive measure to reveal diaphragmatic impairment and may be an efficacy and safe neurophysiological test in Syr and CM. In conclusion this technique could reveal phrenic pathway alterations involved in voluntary respiration pattern, that could be used to engrave eventually surgical option in the future.

20. Cortical brain connectivity evaluated by graph theory in dementia: a correlation study between functional and structural data - F. Vecchio, F. Miraglia, G. Curcio, R. Altavilla, F. Scrascia, F. Giambattistelli, C.C. Quattrocchi, F. Vernieri, P.M. Rossini (Roma, L'Aquila)

Functional connectivity, revealed by EEG, evaluates time synchronization in anatomically distinct but functionally collaborating brain regions. Structural connection, revealed by diffusion tensor imaging (DTI), detects fractional anisotropy (FA). FA decreases in pathological aging corpus callosum (CC) and could reflect functional disconnections. We investigated correlations between structural damage of CC (MRI-DTI) and functional abnormalities of brain integration (cortical Characteristic Path Length of EEG). Resting state EEG and MRI were evaluated in 9 healthy controls-Nold, 10 Mild Cognitive Impairment -MCI, 10 mild Alzheimer Disease -AD, 11 moderate AD. Undirected and weighted brain network was built to evaluate graph Path Length weighting network edges by eLORETA lagged connectivity. Callosal FA reduction was associated to a loss of brain interhemispheric functional connectivity characterized by increased delta and decreased alpha Path Length. Global (path length as index of how efficient is the information transfer inside network) functional measure can reflect the reduction of fibers connecting the hemispheres as revealed by DTI. Functional and structural disconnections do not share the same timing (functional coming first) in the prodromal stage of disease, but in disease evolution (from healthy to dementia) it is possible to obtain statistical correlations between connectivity's indexes.

21. Generators of oddball P300 to visual omitted stimuli: a simultaneous EEG-fMRI study - A. Di Rollo, M. Cosottini, I. Pesaresi, S. Fabbri, D. Barloscio, A. Ragazzoni, F. Sartucci (Pisa, Firenze)

The present study aimed at investigating the cerebral sources of the visual P300 event-related potential (ERP) by the simultaneous recording of EEG and functional magnetic resonance imaging (fMRI). In addition to a standard two-stimuli visual "oddball" paradigm we applied a similar paradigm, in which the rare (target) stimuli were omitted in a sequence of regularly presented visual stimuli. Both conditions were preceded by a trial in which the subject gave no attention to the stimuli (passive condition). The EEG showed a clear N1/P3 complex during the standard "oddball" paradigm, whereas during the "omitted stimulus oddball" only a P300 component, with reduced amplitude and increased latency (about 700 msec, compared to 400 msec in the standard paradigm) was observed. fMRI showed, during the standard "oddball", activations in lateral frontal, fronto-operculum, anterior insula regions, prevailing on the right. Minor activations were observed bilaterally in the parietal cortex near the infraparietal sulcus and in posterior temporal regions, also more evident on the right hemisphere. The "omitted stimuli" paradigm showed fMRI activations in the very same locations as those obtained in the standard "oddball". These results highlight the "real" cortical sources of the endogenous P300, not contaminated by sensory activations.

22. Auditory stimulation enhances thalamic somatosensory High-Frequency Oscillations in healthy humans: a neurophysiological marker of cross-sensory sensitisation? - D. Restuccia, G. Coppola (Roma)

Electrical stimulation of upper limb nerves evokes a train of high-frequency wavelets (high-frequency oscillations, HFOs) on the human scalp. These HFOs are related to the influence of arousal-promoting structures on somatosensory input processing, and are generated in the primary somatosensory cortex (post-synaptic HFOs) and the terminal tracts of thalamocortical radiations (pre-synaptic HFOs). We previously reported that HFOs do not undergo habituation to repeated stimulations; here, we verified whether HFOs could be modulated by external sensitising stimuli. We recorded somatosensory evoked potentials (SSEPs) in 15 healthy volunteers before and after sensitisation training with an auditory stimulus. Pre-synaptic HFO amplitudes, reflecting somatosensory thalamic/thalamocortical activity, significantly increased after the sensitising acoustic stimulation, whereas both the low-frequency N20 SSEP component and post-synaptic HFOs were unaffected. Cross-talk between subcortical arousal-related structures is a probable mechanism for the pre-synaptic HFO effect observed in this study. We propose that part of the ascending somatosensory input encoded in HFOs is specifically able to convey sensitised inputs. This preferential involvement in sensitisation mechanisms suggests that HFOs play a critical role in the detection of potentially relevant stimuli, and act at very early stages of somatosensory input processing.

23. Visuo-motor connectivity in photosensitive epilepsies - G. Strigaro, L. Falletta, E. Matino, G. Tondo, C. Lunardon, C. Pizzamiglio, C. Varrasi, R. Cantello (Novara)

Visual and motor cortex are involved in the origin/propagation of the photoparoxysmal response (PPR), a stronghold for the diagnosis of generalized photosensitive epilepsies. The study of the functional connection between these two distant cortical areas with transcranial magnetic stimulation (TMS), could help clarify the pathophysiology of photosensitivity. Eleven patients with idiopathic generalized epilepsy and photosensitivity were compared to 11 healthy subjects. We measured the resting motor threshold of the left hand motor area and the phosphene threshold. The paradigm consisted in a conditioning stimulus (CS) delivered over the phosphene hotspot of the visual cortex and followed at random interstimulus intervals (15-40 ms) by a test stimulus over the left motor cortex to evoke a motor evoked potential (MEP) of ~1mV from the right FDI. The conditioned-MEP was expressed as a percentage of the unconditioned-MEP amplitude. In healthy subjects the CS over the visual cortex produced significant inhibitory changes on the corticospinal excitability with a time course between 18-40 ms. Patients with IGE and photosensitivity showed a failure of the physiological inhibition. In photosensitive patients the alteration of the normal visuo-motor functional connectivity could be responsible for the origin/propagation of the PPR from the hyper-excitable visual cortex to the motor cortex.

24. Sensorimotor cortex excitability and connectivity in Alzheimer's disease: an EEG-

TMS co-registration study - A. Guerra, F. Ferreri, F. Vecchio, L. Vollero, S. Petrichella, D. Ponzio, S. Määttä, E. Mervaala, M. Könönen, F. Ursini, P. Pasqualetti, G. Iannello, P.M. Rossini, V. Di Lazzaro (Roma, Kuopio FI)

Several experimental studies have shown that, nevertheless motor symptoms are late events in the natural history of Alzheimer's disease (AD), neuropathological progression in the motor cortex parallels that in other brain cortices generally considered more specific targets of the aggression. In the last years we have clearly demonstrated that motor cortex excitability is enhanced in AD since the early stages of the disease and this is probably related to its severity and progression. To further investigate, for the first time without peripheral or attentional confounding effects, the neurophysiological hallmarks of motor cortex functionality in AD we used here transcranial magnetic stimulation (TMS) combined with electroencephalography (EEG). We then demonstrated that in mild AD, despite the lack of clinical manifestations, the sensorimotor system is strongly hyper-excitable and its connectivity is deeply rearranged with the recruitment of additional neural sources, the activation of reverberant circuits and their integration in the distributed excitatory network subtending sensorimotor functions.

25. Strategies to Reduce Intertrial Variability of motor responses to nerve root and transcranial stimulation: a condition for follow-up studies in the individual patient - W. Troni, A. Di Sapio, F. Melillo, S. Malucchi, A. Bertolotto (Orbassano)

We investigated the Intertrial Variability and Relative Intertrial Variation (RIV) of latency and area of motor responses to High Voltage Electric Stimulation (HVES) of lumbo-sacral roots and to Transcranial Magnetic Stimulation (TMS) recorded from several sites of lower limbs. The purpose was to obtain normative variability values to detect significant changes in the individual patient in follow up studies. Maximal CMAPs to HVES of lumbo-sacral roots were obtained from 10 proximal and distal muscle districts of lower limbs; MEPs to TMS using the double cone coil were recorded from the same sites. The procedure was repeated twice, 1-2 days apart, in 30 subjects, including healthy volunteers and clinically stable multiple sclerosis patients. The use of stable recording and stimulation sites with maximal root-CMAPs and adequately stabilized MEPs allowed a significant reduction of ITV for all latency and area parameters. Mean RIV values (5th-95th percentile) for Central Motor Conduction Time and Area Ratio (MEP/CMAP) did not exceeded -14.8 and + 16.0 msec and - 26.0 and +33.7 mVmsec respectively. The combined monitoring of latency and areas indexes allows assessment of both conduction slowing and conduction failure, i.e the variable association of axonal damage and conduction block, which directly correlates with motor impairment.

26. Rhythmic activity of leg muscles during standing in healthy subjects - L. Marinelli, W.N. Massaro, D. Romaggi, S. Leandri, M. Leandri (Genova)

Traditionally, the stretch and possibly polysynaptic reflexes are considered the mainstay of antigravity leg muscles. We found evidence of a different mechanism. In a

group of young normal subjects, surface EMG was recorded from tibialis anterior, soleus, vastus medialis and biceps femoris muscles in quiet upright stance without and with balance perturbation. In quiet stance, a modest amount of activity could be recorded from the soleus and the biceps femoris only, and none from tibialis anterior and vastus medialis. Such activity was organized in bursts whose duration ranged 50-100ms, and frequency of 8-12/s. Simultaneous recording of the centre of pressure via stabilometric platform, showed that when a forward shift occurred, frequency and amplitude of the soleus bursts increased, but all activity ceased in a backward shift. When balance was perturbed by a backward tilt, the very first ensuing activity was a brief response by the soleus (weak stretch reflex) followed by several bursts of the tibialis anterior. Little if any activity was recorded from the thigh muscles. We conclude that action of antigravity muscles of the leg seemed more linked to modulation of a rhythmic preordained activity rather than to a simple reflex response.

27. Mg-guided injection of Botulinum Toxin A in the treatment of Iliopsoas Spasticity - V. Rossi, S. Pistoni, D. Dall'Agata (Genova)

Ultrasound guided (US) botulinum toxin A (BT-A) intramuscular injection is an established treatment for the iliopsoas muscle (IM) spasticity, but it is not always possible to use it. To describe a technique with EMG guidance for the intramuscular injection of BT-A to treat spasticity of the IM and evaluate the efficacy of this technique. The EMG-guided technique for BT-A injection was used on 9 patients (aged 7-59 years) with unilateral or bilateral spasticity of the IM. The Techniques of IM EMG examination have already been described (Katsavrias et. al, 2005) but have not been described for the intramuscular injection of BT-A. BT-A dose range from 30U to 50U for IncobotulinumtoxinA and OnabotulinumtoxinA, 120U for AbobotulinumtoxinA. Outcome measures included muscle tone (using MAS) and range of motion (ROM), assessed before the treatment and after 3, 6 and 12 months. After one year from the first EMG-guided injection of BT-A, MAS score decreased from 3.8 to 1.8 and ROM score increased from -53.1 to -20.8 ($p < 0.0001$ for all; ANOVA). This EMG-guided technique allows accurate guidance for the injection of BT-A of the IM and it can be considered a viable alternative to the US-guided technique.

28. Treatment with onabotulinumtoxinA a pectoral spasm after expander-based breast reconstruction – L. Maderna, A. Doretto, B. Riccardi, F. Gregorini, S. Gerevini, V. Silani (Milano)

Breast reconstruction tissue Expander-based is the most common technique used for reconstruction after radical mastectomy for cancer. Breast reconstruction with fat grafting (FAT transfer) is a technique widely used in current practice. 62-year-old woman has been subjected to mastectomy and subsequent reconstructive surgery of the breast Expander based, retaining the expander for 10 months. After 3-4 weeks from placement of the breast implant, developed a sub-rhythmic spasm of chest muscles during standing. This spasm is persisted even after the removal of the prosthesis a year later and without any pain. She had never been subjected to chemotherapy or radiotherapy. Electromyography showed unintentional

electrical activity sub-rhythmic burst with 200-250 msec, frequency 2 Hz. We have also studied the brachial plexus nerve and breastplate with magnetic resonance imaging (DTI sequences) and ultrasound of the breast region. The patient was subjected to infiltration under electromyography and ultrasound guidance of pectoralis major muscle with onabotulinumtoxinA with cramp reduction/interruption. Chest cramps is not due to nerve compression trauma implants pectoral mammal, but it should be due to the irritative activity of the graft on the pectoral nerve. In fact the spasm started after the placement of the graft.

29. Can the neurophysiologic study help for the right diagnosis of narrow canal? - G. de Scisciolo, R. Caramelli, V. Schiavone, C. Martinelli, S. Troiano, A. Cassardo (Firenze)

Spinal stenosis is an abnormal narrowing of the spinal column that may occur in any of the regions of the spine. The most common clinical features are lumbar spinal stenosis (LSS). There are three major types of lumbar stenosis, and accurate identification is vital to stenosis treatment: lateral, central and foraminal. If the narrowing is substantial, it causes compression of the nerves, which causes the painful symptoms of LSS. In our laboratory were studied 136 patients (41-81 years), both asymptomatic and symptomatic Neurophysiological test were performed in all patients. EMG/ENG was abnormal in all symptomatic patients. In accordance with many studies there was no correlation between clinical symptoms and radiological findings; in fact, even if the neuroimaging investigation can distinguish mono- and multisegmental stenosis and its severity, often there is not correlation between the pain and functional symptoms. The electrophysiological recordings indicate a lumbar nerve involvement that is complementary to the history and neurological examination of the patient as well as the neuroimaging. Therefore we think that for a correct diagnosis of LSS only the combination of clinical, radiological and neurophysiological recordings could be useful and may be helpful for the planning and selection of appropriate and early therapeutic approaches.

30. Facial neuropathy as the initial manifestation of chronic inflammatory demyelinating polyradiculopathy – C. Tamborino, E. Gastaldo, R. De Gennaro, L. Caldana, E. Barensi, M. Polastri, A. Critelli, R. Quatralo (Venezia Mestre)

We report the clinical and electrophysiological features of a patient who presented unilateral facial weakness as the Initial manifestation of Chronic inflammatory demyelinating polyradiculopathy (CIDP). A 40-year-old man presented facial numbness and weakness. Examination demonstrated severe unilateral facial weakness with no other cranial or segmental clinical abnormalities. Blink and jaw-jerk reflex latencies were prolonged bilaterally, with a reduction of R1 amplitude recording by the symptomatic side. Somatic neurophysiological examination showed slowing of motor nerve conduction velocities, lengthening of distal motor latencies, prolonged minimal F wave latencies and partial conduction motor block, without any unusual sensory electroneurophysiological abnormalities. Cerebrospinal fluid demonstrated an elevated protein level. After 1 week of intravenous immunoglobulin treatment, the symptoms and electrophysiological findings improved. This

case could represent an unusual initial presentation of isolated cranial nerve involvement in asymptomatic CIDP. Blink reflexes may be a useful electrophysiological technique to assess for peripheral nerve demyelination in patients with suspected CIDP.

31. Sensory peripheral neuropathy in a novel mutation of FLVCR1 - S. Pro, M. De Luca, R. Miliucci, B. Alessandri, M. Di Capua (Roma)

Posterior Column Ataxia and Retinitis Pigmentosa (PCARP) is an autosomal-recessive neurodegenerative syndrome. Standard phenotype expected: areflexia and retinitis pigmentosa in infancy; night blindness and peripheral visual field loss in late childhood; evaluation to sensory ataxia secondary to degeneration of the posterior columns of the spinal cord. We reported a case of 3 yrs old children with PCARP secondary to FLVCR1 mutation and atypical phenotype. Our patient have a congenital and progressive acro-osteolysis of fingers and precocious ataxia with general hypohonia, and deep tendon reflex absent in the legs. No visual impairment was reported and the fundus oculi was normal. Nerve conduction study showed sensory peripheral neuropathy; ERG was normal. Median-nerve SEPs were not recordable for sensitive neuropathy. Brain and total spinal cord MRI was normal. Genetic study showed a truncated FLVCR1 protein by mother and new potentially pathogenetic mutation by father. Sensory peripheral neuropathy was reported in only few cases of PCARP. We presented a case of 3 yrs old children with PCARP secondary to FLVCR1 mutation and atypical phenotype.

32. Phrenic nerve study in infants: normative data and technical aspects in Verona experience - S. Romito, A. Segatti, L. Alessandrini, F. Donato, G. Squintani, G. Moretto (Verona)

The evaluation of phrenic nerve conduction is an important technique for assessing ventilatory function. Slightly different methods are described in literature for adults and children, and studies with normative data in infants are few. We present our study aimed at collecting normative data of phrenic nerve conduction in infants. Diaphragmatic action potentials (DAPs) were bilaterally recorded from 16 neurologically healthy babies aged 0-6 months. The active electrode was placed over the xiphoid process and the reference electrode over the chest margin, on the mid-clavicular line or 1 cm laterally, ipsilaterally to the stimulation side. Transcutaneous electrical stimulation of 0,1 ms duration was applied over the phrenic nerve between the clavicular and the sternal heads of sternocleidomastoideus (SCM) muscle. Peak-to-peak DAP amplitude, onset latency, DAP area and interside differences were analysed. M-wave amplitude mean value was 2,3 mV (DS 0,8 mV) and its latency mean value was 5,4 ms (DS 0,7 ms). Our technique is slightly different from those of previous reports in children and let us to obtain always clearly reproducible DAPs, with higher amplitudes than in other works. Moreover this method allows a precise pre/post-operative comparison in children undergoing surgery with a great risk of phrenic nerve damage.

33. A rare case of Guillain-Barre' Syndrome and Pseudotumor Cerebri, with normal

cerebrospinal fluid protein - G. Stipa, S. Caproni, E. Moschini, A. Sensidoni, D. Frondizi, C. Di Schino, F. Galletti, A. Di Chirico, V. Rossi, A. Mancini, N. Roscini, S. Carletti (Terni)

A 19 years old female patient was referred for assessment of head and cervical pain, upper limbs dysesthesias, diplopia, visual impairment (mainly in left eye) and postural instability. Initial examination revealed left ptosis, left abducent nerve palsy, diffuse hyporeflexia and limb ataxia. At admission lumbar puncture was performed with a normal cerebrospinal fluid analysis and a temporal dispersion of F waves and Skin Reflex was observed by electromyography. In suspected Guillain-Barré syndrome a IV immunoglobulin treatment was administered. In first days after admission a progression of signs and symptoms was observed; a left peripheral facial palsy was also noted. In particular, the visual acuity decreased in both eyes (5/10 at right, 1-2/10 at left), severe bilateral papilledema and increased optic nerves diameters (7.4 mm at left) were revealed. Brain and spine MRI was unremarkable. Thus, through a second lumbar puncture a cerebrospinal fluid pressure of 25 mmHg was measured. In light of this 10 cc of cerebrospinal fluid were subtracted and high dosage escalating diuretic treatment (mannitol, steroid, acetazolamide and topiramate) was administered. A further slow improvement of motor and visual signs and symptoms was observed. At discharge the patient referred a complete remission of headache and dysesthesias.

34. An unusual case of familiar conduction block neuropathy - M. Ceccanti, C. Cambieri, E. Onesti, V. Frasca, G. Tartaglia, M. Inghilleri (Rome)

Tangier disease is a rare autosomal recessive disorder, resulting from mutations in the ATP binding cassette transporter (ABCA1) gene. The deficiency of ABCA1 protein impairs high-density lipoprotein (HDL) synthesis and cholesterol esters trafficking. A 57 year-old female presenting with intrinsic hands muscles hypotrophy and distal paresthesias was visited in our laboratory in July 2014. The neurological examination showed weakness in orbicularis oculi and oris and in hypotrophic muscles. Moreover, a C3-D12 suspended sensory loss for pain was observed. Similar findings were observed in the two sisters and the brother. ENG-EMG examination detected a reduction in SAP amplitude registered from ulnar and median nerves, bilaterally. cMAPs from the same nerves showed a conduction block neuropathy. Screening laboratory exams were requested. Extremely low levels of total cholesterol (58 mg/dl) and triglycerides (96 mg/dl) were detected. Particularly, HDL levels were almost undetectable (1 mg/dl). We hypothesized a Tangier disease. Patient underwent to abdominal ultrasound detecting a liver echostructure more compact than usual. Cervical dorsal MRI excluded syringomyelic cavities. Reduction in global systolic function and corneal opacity were also observed. Muscle biopsy was normal. Finally, genetic analysis confirmed mutation in ABCA1 in the whole family.

35. Vestibular-coclear nerve involvement in Charcot-Marie-Tooth disease: a pilot-study - S. Silipo, GM. Fabrizi, T. Cavallaro, MC. Tozzi, S. Monaco, L. Bertolasi (Verona)

Some authors suggested a multifactorial genesis of imbalance in patient affected by Charcot-Marie –Tooth disease (CMT) caused not only by reduced proprioceptive input but also by a vestibular impairment. Nowadays no neurophysiological studies have been performed to support this hypothesis. Aim of our pilot case-control study is to determine the prevalence of vestibular coclear nerve involvement in patients affected by CMT. Second aim is to compare the severity of vestibular coclear neuropathy among the neurophysiological subtypes of CMT (nominated as demyelinating, axonal or intermediate) or lasting of the disease. 20 patients affected by CMT (10 demyelinated, 5 axonals and 5 intermediate forms) underwent to a neurological and neurootological examination, cVEMPs, oVEMPs, BAERS, and caloric stimulation by Fitzgerald-Hallpike standard protocol. The severity of disease was evaluate using CMT-neuropathy score 2. Preliminary data suggested an high prevalence of bilateral vestibulopathy even in the early stage of the disease.

36. Sensitivity of single fibre electromyography in ocular myasthenia – V. Donadio, M.P. Giannoccaro, V. Di Stasi, P. Avoni, R. Liguori (Bologna)

The diagnosis of ocular myasthenia (OM) can be challenging due to the mildness of symptoms and to the absence of a gold diagnostic standard test. In several studies single fibre electromyography (SFEMG) showed a sensitivity of 0.86-0.99 for the diagnosis of OM. However these studies presented some methodological limitations. Our aim is to determine the diagnostic sensitivity of SFEMG in OM. We studied 157 consecutive patients diagnosed with OM on the basis of the presence of at least one of the following criteria: 1) positive edrophonium test; 2) abnormal repetitive nerve stimulation; 3) positive antiacetylcholine receptor antibodies; 4) improvement with corticosteroid therapy. Other diseases presenting with ptosis/diplopia were excluded. Stimulation SFEMG was performed on orbicularis oculi (S-SFEMG) in all cases and on the frontalis during voluntary activation (V-SFEMG) in 120 patients. In the whole population S-SFEMG was positive in 71% of cases whereas V-SFEMG was positive in 62% of cases. In patients with isolated ptosis (45%) S-SFEMG and V-SFEMG were positive in 87% and 85% of cases, respectively. In patients with isolated diplopia (31%) S-SFEMG and V-SFEMG resulted abnormal in 27% and 3% of patients, respectively. In patients with ptosis and diplopia (24%) both S-SFEMG and V-SFEMG were positive in 100% of cases. SFEMG showed a lower sensitivity than previously reported. However, sensitivity appears to be highly variable in relation with the clinical phenotype, being particularly low in patients presenting with isolated diplopia. S-SFEMG on orbicularis oculi is more sensitive than V-SFEMG on frontalis.

37. Dysphagia in Myotonic Dystrophy type 1: preliminary results of an integrated neurophysiological and swallowing protocol - E. Raimondi, M. Zardoni, S. Bruno, C. Nascimbene, MB Pasanisi, L. Morandi, F. Gianelli, M. Colombo, A. Schindler, C. Mariani, M. Osio (Milano)

Dysphagia is common and under-diagnosed in Myotonic Dystrophy (DM1), leading to nutritional derangement and

ab-ingestis pneumonia. We tried to define the prevalence of dysphagia and to understand underlying mechanisms through an integrated swallowing evaluation on DM1 patients. Our protocol includes: laryngeal accelerometric sensor, submental and cricopharyngeal (CP) muscles EMG to evaluate Dysphagia Limit (DL) (volume at which a second swallow becomes necessary to swallow a water bolus) and swallowing jitter; needle EMG of genioglossus muscle (G-EMG); fiberoptic endoscopic swallowing evaluation (FEES), clinical swallowing scales. Our results in 10 DM1 patients (6M-4F, mean age 46±10), compared to 6 healthy subjects (3M-3F, mean age 30±3), showed myotonic discharges (9/10 patients) in G-EMG; reduction in DL in all DM1 patients; abnormal swallowing jitter in 6/10 patients, with 5 of them showing anomalies in temporal features of the swallowing reflex; myotonia in CP muscle in 3 patients. 2 patients did not show dysphagia at FEES; penetration signs were present in 4 and 5 patients respectively with liquids and semisolids. Our data confirm that swallowing problems are common in DM1. DL and swallowing jitter are the most sensitive altered parameters in these patients. We are extending this protocol to a larger cohort of patients.

38. Prolonged phone-call posture as risk factor for developing Ulnar Nerve Entrapment at elbow: a dynamic Neurophysiological Study – D. Coraci, L. Padua, C. Erra, P. Doneddu, G. Granata, P.M. Rossini (Roma, Milano, Sassari)

Ulnar neuropathy at elbow (UNE) is often related to postures and work-hobby activities. The use of mobile-phones has drastically increased in the last decades leading to prolonged phone posture (PPP) with flexed elbow. We aimed to assess the effect of PPP in patients with symptoms of UNE and in symptom-free subjects. Patients with pure sensory symptoms of UNE and negative neurophysiological tests (min-UNE) and symptoms-free subjects were enrolled. We evaluated ulnar motor nerve conduction velocity across elbow at baseline and after 6, 9, 12, 15, 18 minutes of PPP. Thirty-eight symptom-free subjects and thirty-eight patients were enrolled and 121 ulnar nerves were studied. Conduction velocity of ulnar nerve across the elbow significantly changed over PPP time both in control group and, at a greater extent, in patients with min-UNE. Conduction velocity during PPP showed different evolution between the two groups. The changes became significantly different after 6 minutes of PPP and progressively increased, with the greatest difference at 15 minutes. In conclusion, PPP causes a modification of nerve function, expressed by slowing of motor nerve conduction velocity, which is greater in patients with min-UNE although it also occurs in symptom-free subjects. Excessive PPP should be avoided in patients with UNE-symptoms.

39. CMAP area variability is a function of area size - A. Di Sapio, F. Melillo, A. Bertolotto, M. Matta, W. Troni (Orbassano)

We studied the relationship between CMAP area variability and CMAP area size in an experimental setting in which any other possible cause of variability was removed. In 10 normal volunteers we recorded from Abductor Digiti Minimi a CMAP of large area and one of small area simultaneously after maximal stimulation of the ulnar nerve at wrist. Ulnar nerve stimulation was repeated 5 times, 4-6

second apart, and two sets of 5 CMAPs were obtained: one of large area and one of small area. The same procedure was performed with stimulation of the ulnar nerve at the elbow. Non-polarizable, ring-shaped sintered Ag/AgCl Multitrode® surface electrodes were adopted. For each set of rectified responses (large and small) Coefficient of Variation (COV,%) was calculated. Areas and COVs from all subjects were expressed as mean±SD. Mean intrasession variability of small CMAPs elicited at wrist was significantly greater than that of large CMAPs elicited at the same site (paired t test: p<0.01). Variability was even slightly greater with stimulation at elbow. These results suggest the presence of component of variability unavoidable even under optimal recording conditions that partly varies as a function of the area, being significantly greater for smaller responses than for larger ones.

40. Immunofluorescent intraepidermal nerve fiber normal density at distal leg: a multicenter study - V. Provitera, CH Gibbons, G. Wendelchafer-Crabb, V. Donadio, DF. Vitale, A. Stancanelli, G. Caporaso, R. Liguori, N. Wang, L. Santoro, WR. Kennedy, M. Nolano (Telese Terme, Boston US, Minneapolis US, Bologna, Napoli)

We created an age and gender adjusted normative dataset for intraepidermal nerve fiber (IENF) density at distal leg in skin samples processed with immunofluorescence. We collected from four experienced laboratories worldwide IENF density data of 528 healthy individuals. Skin samples were collected, processed and analyzed according to standard procedures. We employed quantile regression analysis to tailor the fit of the 5° percentile as the normal cut-off value and to measure the effect of age, gender, body mass index (BMI), and race as possible influential variables. Age and sex showed an independent linear correlation with IENF density. For each decade, the 5° quantile cut-off showed a 0.54 fibers/mm decrease, while females exhibited a 1.0 fibers/mm cut-off greater than males. BMI didn't affect IENF counts and we did not find significant differences between Caucasian and non-Caucasian subjects although our cohort was not suitable to draw definitive conclusions on this issue. In conclusion, we presented for the first time an age and gender adjusted normative dataset for intraepidermal nerve fiber density at distal leg obtained with indirect immunofluorescence by sharing data from four experienced laboratories worldwide. This dataset can be used as reference for laboratories processing skin biopsies with this technique.

41. Early morphological abnormalities of Myelinated Fibers in a rat model of CMT 1A – M. Nolano, L. Nobbio, V. Provitera, C. Pisciotta, G. Caporaso, A. Stancanelli, D. Visigalli, G. Capodivento, F. Manganeli, A. Schenone, L. Santoro (Telese Terme, Genova, Napoli)

Abnormalities of internodal and nodal length associated with aspects of axonal degeneration have been described in skin samples of Charcot-Marie-Tooth type 1A (CMT1A) patients. It is not clear how early such abnormalities occur and if they change with aging. To elucidate these aspects we assessed myelinated fiber (MF) density and morphometry in skin samples and in the sciatic nerve of hemizygous CMT1A transgenic rats (Sereda et al, 1996) in an asymptomatic and in a late disease course (22 days and 1

year of age). Specimens were obtained from anterior and posterior foot pads, tail and sciatic nerve of CMT1A rats and wild-type littermates and processed with indirect immunofluorescence technique. Quantitative assessment of MF and measurements of caliber, G-ratio, internodal and nodal length were performed. We observed in both, skin and nerve of young and old CMT rats, in addition to nerve fiber loss, several and frequent morphological abnormalities of MF rarely observed in controls. Interestingly, the nerve fibers loss associated at severe aspects of dysmyelination was very marked in the homozygous rat. Measurements on dermal MF showed values of internode length and caliber with a large variability but significantly lower than in controls while nodal length values were significantly higher.

42. The effects of THC on Cutaneous Silent Period – L. Fionda, C. Cambieri, M. Ceccanti, G. Tartaglia, E. Onesti, A. Cicchinelli, M. Inghilleri (Roma)

The analgesic effects of cannabinoids are mediated through the activity on the endogenous cannabinoid system. (-)-trans- Δ^9 -tetrahydrocannabinol (THC) is the principal psychoactive constituent of cannabis and it shows a partial agonist activity on cannabinoid receptors, in particular CB1 receptor, mainly expressed by neurons of the central and peripheral nervous system. There are several studies that demonstrate the effects of THC on pain perception. Aim of this study is to evaluate the effects of THC in 13 healthy volunteers (HV) through the analysis of Cutaneous Silent Period (CSP), a nociceptive spinal inhibitory reflex, considered a defense response, specific for the human upper limbs. CSP parameters have been recorded from the abductor digiti minimi (ADM) before and after an hour the administration of a cannabis-based preparation. We recorded the same parameters before and after the administration of placebo in the same volunteers. The results show that the CSP latency and amplitude left unchanged in HV after the drug administration at the dose commonly used to suppress nociceptive reflexes in humans. These differential effects of a narcotic-analgesic drug provide evidence that the cutaneous silent period is not a THC-sensitive nociceptive reflex.

43. Pain-related cortex function in patients with Alzheimer's disease. Preliminary results – A. Pepe, G. Di Stefano, S. La Cesa, C. Leone, F. D'Antonio, Trebbastoni, C. De Lena, G. Cruccu, A. Truini (Roma)

Previous studies found that patients with Alzheimer's disease (AD) have increased pain threshold and pain tolerance. Nevertheless it is still unclear whether these findings are explained by communication problems, or rather they are associated with degenerative processes affecting pain-related cortex. In this neurophysiological study we aimed at assessing pain-related cortex function, by recording laser evoked potentials (LEPs) after hand stimulation in patients with AD. We enrolled 10 patients with a diagnosis of probable mild-to-moderate AD, recruited from the Alzheimer Evaluation Unit of "Sapienza" University of Rome. In all patients we recorded the SII-generated N1-LEP, and the N2-P2 complex of LEPs, generated in the insula and cingulate cortex. All patients also underwent the recording of A fibre mediated somatosensory evoked potentials (SEP), after median nerve

stimulation. LEP and SEP variables were compared with normative reference ranges, matched for age and gender. Whereas SEP variables, and the N1-LEP component came within reference values in all patients, the N2-P2 complex of LEP was dampened or absent in 7 patients. Our findings suggest that in patients with AD the degenerative processes affects pain-related cortex. This damage predominantly involves the insular cortex and the anterior cingulate cortex.

44. Onabotulinumtoxin-a treatment in Chronic Migraine: a long-term prospective open label study - C. Butera, F. Bianchi, S. Amadio, R. Guerriero, M. Cursi, O. Vimercati, G. Comi, U. Del Carro (Milano)

A large multicentre clinical trial (PREEMPT) demonstrated efficacy and safety of onabotulinumtoxin A for prophylactic treatment of chronic migraine (CM), in prophylactic drug-free patients. This study aimed to verify the efficacy of repetitive injections of onabotulinumtoxin A in CM patients with ineffective chronic poly-therapy. Patients and methods: we studied 45 CM patients (36 females and 9 males) taking multiple prophylactic/symptomatic medications treated with onabotulinumtoxin-A for a follow up period of 9 months. The overall dose ranged between 155 and 180 U administered in 31-36 sites following PREEMPT protocol, repeated at 12 weeks intervals. Main efficacy variables included number of headache/migraine days and episodes, total cumulative headache hours, MIDAS and HIT-6 scores; all items had assessed at baseline and at the 12th-24th-36th week follow-up. Results: all variables showed statistically significant changes at 36th-week time-point. We observed a responder rate (partially responder plus completely responder patients) of about 40% after first treatment; the rate reached the 90% after the third treatment. Adverse events were uncommon and did not require treatment discontinuation. Conclusions: repeated treatments with onabotulinumtoxin A in CM patients with unsatisfactory prophylactic drug treatments, is very effective in improving all variables examined, determining a measurable positive impact on quality of life.

45. Diabetic distal sensorimotor and autonomic polyneuropathy in adults with type 1 and 2 diabetes - C.M. Ministeri, S. Maccora, A.A. Modica, M.S. Aliquò, S.Giordano, F. Cardella, R. Roppolo, I. Maccora (Palermo)

Emerging evidence suggests that distal symmetric sensorimotor polyneuropathy (DSPN) and diabetic autonomic neuropathy (DAN) derive from nerve dysfunction in early stage of diabetes. Neurophysiological assessment can provide an early diagnosis of such complications and should be carried out at diagnosis and during disease progression. We studied 44 patients, 24 type 2 diabetes (mean age 61 years, duration 14 years, mean HBA₁C 8,2%) and 20 type 1 (mean age 19 years, duration 11 years, mean HBA₁C 8,4%). All subjects complained of symptoms proper to peripheral neuropathy. Neurophysiological evaluation included Nerve Conduction Studies/Electromiography, Heart Rate Variability including time domains (mean RR-interval and RR-standard deviation), Sympatic Skin Response (SSR). Peripheral neuropathies due to any other cause were excluded. The prevalence of DSPN, DAN and the association between

DSPN and DAN was significantly higher in patients with type 2 compared with those with type 1 diabetes ($P < 0.001$), being the duration of disease and age significantly higher ($P=0,01$) in type 2 diabetes patients. Poor glycemic control and the disease duration are some of the concurrent factors in diabetic polyneuropathy and CAN pathogenesis. Since DSPN and DAN probably share the same pathogenesis, neurophysiological follow-up should be considered as a useful tool for early diagnosis of such complications. In our opinion, however, mean duration of diabetes and the age could be an important etiologic factor of PNS.

46. Abnormal sympathetic and cardiovascular reactivity during mental stress in patients with Narcolepsy and Cataplexy – V. Donadio, G. Plazzi, F. Pizza, R. Liguori (Bologna)

To ascertain abnormalities of sympathetic and cardiovascular reactivity during mental stress in patients with narcolepsy and cataplexy (NC). We studied 10 untreated patients with established criteria for NC and hypocretin deficiency, and 15 sex and age matched healthy subjects. Subjects underwent sitting microneurographic recording of muscle sympathetic activity (MSNA) from peroneal nerve, heart rate (HR) and blood pressure (BP) during resting state and mental stress (3-min of paced auditory serial arithmetic test -PASAT) and a cold test (two minutes immersion of a hand in ice water). The awake state was continuously monitored by an ambulatory polygraphic recorder. NC patients disclosed a tendency to show decreased MSNA and BP during resting state compared to controls although the difference was not significant. However during mental stress NC patients showed decreased MSNA, BP and HR compared to controls but no difference were found during cold test. Our data demonstrated a decreased sympathetic and cardiovascular reactivity during mental stress in NC patients suggesting a possible regulation of hypocretin on autonomic reaction during mental activation as reported in animal models.

47. Autonomic dysfunction in ALS patients: an early phase study – preliminary data – F. Barbieri, L.G. Bongiovanni, G.M. Fabrizi, L. Fondrieschi, S. Monaco (Verona)

Amyotrophic Lateral Sclerosis (ALS) is a fatal degenerative motoneuron disease. Since 40 years, study investigating a possible Autonomic Nervous System (ANS) involvement are reported. Though results are contradictory and studies difficult to compare, ALS appears not to be a single disease entity, but a spectrum of disorders involving mainly, but not only, motor neurons. The aim of the study is to investigate cardiovascular ANS function in ALS patients with low disability and normal respiratory function. We have included patients diagnosed with ALS according to El Escorial criteria, able to walk unaided. We excluded patients with swallowing difficulties, affected by autonomic dysfunction of other origin and taking ANS influencing drugs. We also excluded patients with respiratory insufficiency. Patients underwent cholinergic and adrenergic evaluation: SSR and standard autonomic tests during continuous monitoring of heart rate and blood pressure. We evaluated HRV, BRS and spectral analysis of HF and LF of RRI and BP. We compared patients with matched normal controls. We haven't noted any significant difference between groups, indicating a tendency toward a normal

function of ANS in early phase of disease. We will expand our sample and possibly try a genotypic-phenotypic correlation, given the heterogeneity of ALS spectrum.

48. PoTS: long term follow-up of an Italian cohort – F. Barbieri, L.G. Bongiovanni, L. Fondrieschi, S. Monaco (Verona)

Postural Tachycardia Syndrome (PoTS) is an intermittent autonomic dysfunction characterized by orthostatic intolerance and a heart rate (HR) increase of at least 30 bpm, or a HR \geq 120 bpm during standing. We reviewed clinical and neurophysiological characteristics and outcome after a long term follow-up of our cohort. Patients underwent clinical assessment, standardized autonomic testing and validated questionnaires to determine the severity of autonomic symptoms. The majority of our patients are young female, without either neuropathic features or a hyperadrenergic subtype. We found normal responses to Ewing tests and an increase of LF in the power spectrum of R-R interval and diastolic BP, during head-up tilt. In the same way total peripheral resistances (TPR) were maintained, even with differences among subjects. This indicates intact, though enhanced, baroreflex function. A coexisting tendency to autonomic mediated syncope was found in some patients. Orthostatic symptoms improved in most patients and half of them are now free of therapy and asymptomatic. The treatment consisted in different combinations of beta-blockers, exercise training and increased water intake. Our data are in keeping with a generally favorable prognosis in patients with POTS, if correctly diagnosed and treated, supported by absence of structural damage of ANS.

49. Disrupted autonomic control in spinal cord injury – L.G. Bongiovanni, F. Barbieri, F. Rossini, F. Brigo, F. Paluani, L. Fondrieschi, S. De Marchi, S. Monaco (Verona)

To investigate residual cholinergic and adrenergic responses to orthostatic stimulus in spinal cord injury, we evaluated 10 subjects with different outcome of traumatic (5) and inflammatory (5) spinal cord involvement, with lesions between C6 and T10. The power spectra analysis of blood pressure and heart rate variability was performed during resting condition and during head up tilt test. The difference between the two conditions was tested using Wilcoxon signed rank test and the results were compared with control subjects. The typical decrease of HF power of R-R interval at changing posture was obtained only in control subjects and in patients with paraplegia and incomplete lesions. In such conditions the SSR was always present at the plantar side. In complete lesions, the reduced decrease of HF, is probably due to vagal activity down-regulation. In the same patients the absence of LF peak, in the spectra of both heart rate and blood pressure variability, are associated with the presence of some LF power of SBP. This seems to indicate the possibility of a LF generation either at a spinal level, without supraspinal control, or by other mechanisms, like the myogenic vasoconstrictor reflexes.

50. Decreased heart rate variability in Rem Sleep Behavior Disorder - C.M. Ministeri,

A.A. Modica, D. Lo Coco, S. Maccora, I. Maccora (Palermo)

Aim of our study was to evaluate the role of decreased heart rate variability (HRV) in patients with REM sleep behavior disorder (RBD) as a marker of autonomic dysfunction. We studied HRV in 9 RBD patients (7 men and 2 women; mean age, 71.3 ± 7.3 years) by means of 5-minute segments of single channel electrocardiogram recorded during wakefulness. Subjects with other causes of reduced HRV were excluded. Measures of beat-to-beat RR variability including time domains (mean RR-interval and RR-standard deviation) were assessed. Basal RR interval and RR-DS were within normal range of values in all patients. On the contrary, HRV was decreased after deep breathing and standing-up procedures in all patients. HR-increase to standing up (max HR after 15" from standing-up – mean basal HR) was impaired in 90% of patients. Moreover, after standing-up, RR-DS and RR-ratio were both decreased in 80% of patients. HRV during wakefulness is frequently decreased in RBD patients, suggesting abnormalities of both sympathetic and parasympathetic function. Since RBD patients may later develop synucleopathies, such as Parkinson's Disease, and cardiac autonomic dysfunction is also impaired in these neurodegenerative disorders, our findings suggest that decreased HRV measured by routine electrocardiograms may be an early sign of neurodegeneration.

51. Hand somatosensory Functional Source Separation (FSS) analysis reveals hypoactive sub-cortical source signals in migraine interictally - C. Porcaro, G. Di Lorenzo, S. Seri, F. Pierelli, F. Tecchio, G. Coppola (Roma, Birmingham UK, Latina)

Recent morpho-functional evidences pointed out that abnormalities in the thalamus could play a major role in the expression of migraine neurophysiological and clinical correlates. To this aim, we used Functional Source Separation algorithm to extract, from EEG signals, the activity of different neuronal pools recruited at different latencies along the somatosensory pathway in interictal migraine without aura (MO) patients. Twenty MO patients and twenty healthy volunteers (HV) underwent EEG recording. Four functional sources, two sub-cortical (FS14 at brainstem and FS16 at thalamic level) and two cortical (FS20 radial and FS22 tangential parietal), were extracted along the somatosensory pathway in response to the median nerve stimulation. High-frequency oscillatory (HFO) was extracted using band-pass digital filter (450-750Hz) from the broadband EEG signal. Significant HFO reduction in the sub-cortical FS14 and FS16 were observed for the MO patients respect to the HV. No significant differences were reached, instead, for the cortical ones. Reduced sub-cortical brainstem and thalamic HFO activations plays an important role in MO patients. Present results are the first neurophysiological evidence supporting the hypothesis that a functional disconnection of the thalamus from the subcortical monoaminergic system may underline the interictal cortical abnormal information processing in migraine.

52. Impaired visual inhibition in migraine with aura - G. Tondo, G. Strigaro, A. Cerino, L. Falletta, E. Matino, C. Varrasi, R. Cantello (Novara)

The pathophysiology of migraine with or without aura (MA, MO) is still a matter of debate. We thus studied patients with MA and MO by means of paired-pulse flash-visual evoked potentials (paired F-VEPs). This technique analyses the overall excitability of visual system as detected from the cortical occipital signal. We enrolled 13 adult patients with MO and 13 with MA. Twenty-two normal subjects acted as controls. Stimuli were single flashes, intermingled at random to flash pairs at critical interstimulus intervals (ISIs, 16.5–125 ms) with closed and open eyes. The “single”(unconditioned) F-VEP was split into a “main complex” (50–200 ms after the flash) and a “late response” (200–400 ms). As for paired stimulation, the “test” F-VEP emerged from electronic subtraction of the “single” F-VEP to the “paired” F-VEP. In the MA group, the “main complex” of the “test” F-VEP did not show the size reduction (at ISIs 50–62.5 ms) which was typical among the control and MO groups in the “eyes-closed” state. Paired F-VEPs document a defective neural inhibition in the visual system of patients with MA and may warrant inclusion in future clinical studies, to evaluate its potential role in the pathophysiology and management of MA.

53. OnabotulinumtoxinA in the treatment for Chronic Migraine: four years of follow-up in the experience of Careggi Hospital – C. Cesaretti, E. Molesti, F. Lolli, A. Amantini, S. Lori (Firenze)

The purpose of this study was to evaluate the efficacy, safety and tolerability of onabotulinumtoxinA as prophylactic therapy in patients with “refractory” chronic migraine (CM). We analyzed 76 patients (12M, 64F), mean age 52 years (23–82 yr) with CM resistant to conventional symptomatic and/or prophylactic polytherapy, afferent to the Regional Reference Center of Chemical denervation (RRCCd) of Careggi Hospital, between 2011–2014. Each patient was treated (after informed consent) with onabotulinumtoxin A (dose-range 155–195U) every 3 months, according to Blumenfeld’s protocol. We considered the following parameters: frequency (F) and intensity (I) of migraine attacks and drug’s amount (D). We employed an ANOVA for repeated measures to test for changes with time. All 76 patients received the toxin treatment at least four times: 44/76 responded to treatment (38F–6M). The parameters F, I, D showed a progressive and gradual decline with time (p < 0.001 for each variable), reaching the maximum effect from the IV treatment. Only one patient (1.3%) dropped out for neck pain. In our study a high percentage of patients (58%) showed an improvement of the quality of life with a reduction of frequency/intensity of migraine attack and a reduction in the consumption of drugs. OnabotulinumtoxinA represents a safe, tolerated and effective prophylactic treatment in “refractory” chronic migraine

54. Dronabinol inhibits nociceptive transmission in humans. A double blind randomized controlled study – C. Leone, G. Di Stefano, A. Biasiotta, S. La Cesa, S. Piroso, A. Pepe, G. Tartaglia, M.C. Gori, M. Onesti, M. Inghilleri, G. Cruccu, A. Truini (Roma)

Cannabinoids proved to be effective in several experimental neuropathic pain models, and there is increasing evidence for their use in human neuropathic

pain conditions. In this study we aimed at testing whether dronabinol inhibits nociceptive transmission in humans. To do so we verified whether dronabinol modulates the nociceptive-mediated laser evoked potentials (LEPS). We conducted a double blind randomized controlled trial in fourteen healthy volunteers. All subjects underwent two separate sessions: one with 5 mg of dronabinol and the other with 1.5 mg of bromazepam as control drug. The two sessions were randomly alternated among subjects. In each session LEPs were recorded from 32 scalp electrodes after hand stimulation. Each session consisted of two recording blocks: before oral administration of dronabinol or bromazepam and 60 min after dronabinol or bromazepam. Both the dronabinol and the bromazepam left the LEP latency unchanged. While the dronabinol reduced the N1-, N2-, P2-LEP components (P < 0.01), bromazepam did not produce any significant changes. Our findings show that dronabinol inhibits nociceptive transmission, thus suggesting that it might play an important role in the treatment of neuropathic pain.

55. Selective stimulation of A delta fibres by micropatterned interdigitated surface electrodes – L. Marinelli, L. Pellegrino, A. Siri, M. Leandri (Genova)

Electrophysiological assessment of the nociceptive pathway is a difficult task, just recently accomplished using laser stimulators, which only activate pain endings. Unfortunately, there are several drawbacks to this type of stimulus, for its costly generator, for the possible skin lesions and difficult handling. Electric stimuli are far more easy to generate and deliver, but they lack the necessary selectivity. We demonstrate here that by using a bipolar comb like electrode where multiple rails of opposite polarity are only distant 50µm (Pat. No. I0158846), selective activation of a sufficient number of nociceptors pertaining to the A delta range is possible. In 5 healthy volunteers, the radial nerve innervation territory was stimulated with 1ms pulses delivered through the electrode; recordings were performed from the radial nerve above the wrist, with near nerve needles. Sensory nerve potentials could be recorded with conduction velocity ranging 12–20m/s, compatible with A delta fibres. Increasing the electrode inter rail distance up to 200µm and stimulating the same site brought an increase of conduction velocity up to 42m/s, in the range of A beta fibres. □ 0.001 for each variable), reaching the

56. A new method for sham-controlled acupuncture in experimental visceral pain – M. Valeriani, J. Juel, S. Liguori, C. Graversen, S.S. Olesen, A.M. Drewes (Aalborg DK)

This study aimed to investigate the validity of a new method for sham acupuncture in experimental visceral pain. Fifteen subjects underwent a sequence of either sham stimulation or acupuncture followed by visceral experimental pain stimulation. Experimental pain was induced by rectal stimulation with an inflatable balloon. The balloon was distended until the pain threshold was reached. Before and after intervention, an electroencephalogram (EEG) was recorded for 2.5 minutes to explore central effects of acupuncture. Only 5 participants (36%) were able to indicate the correct sequence of sham and acupuncture (P=0.4; compared to chance level). A significant increase in balloon volume was observed after sham acupuncture

($P=0.049$) and acupuncture ($P=0.046$). However, the change in rectal balloon volume was not different between groups ($P=0.6$). No differences in EEG spectral power distributions between sham stimulation and acupuncture were seen (all $P>0.6$). The presented sham procedure provides a valid method for blinding of "sham acupuncture" and may be used in future blinded controlled trials of acupuncture for visceral pain.

57. Cerebellar DC stimulation does not interfere with motor cortex excitability and transcallosal communication in humans – P. Tocco, E.P. Casula, L. Rocchi, R. Chieffo, S. Monaco, L. Bertolasi, R. Hannah, J.C. Rothwell (Londra UK, Verona, Roma, Padova, Milano)

The cerebellum is involved in motor execution. It controls the primary motor cortex activity (M1), and ensures the correct amount of inhibition to produce the right motor output. Besides, it plays an important role in the error monitoring mechanisms during bimanual coordination of the in-parallel motion. We investigated the role of the cerebellum in the modulation of the M1 excitability and M1-M1 interhemispheric inhibition (IHI) using transcranial direct current stimulation (tDCS). Thirteen healthy volunteers received cerebellar tDCS at 2 mA for 20 minutes among three randomized sessions (anodal right, anodal left, sham). M1 excitability (PA direction, single-pulse, 1 mV MEP) and short-latency IHI (PA direction, paired-pulse, conditioning stimulus 110% RMT, ISI 8 and 10 msec) were determined before (pre-), after 5 minutes from the onset (on), and after 30 minutes from the end of stimulation (post). All measures were taken bilaterally. The M1 excitability compared before, during and after cerebellar tDCS did not change among sessions (ANOVA, $p > 0.05$). The short-latency M1-M1 IHI was always determined, but did not change among sessions (ANOVA, $p > 0.05$). The cerebellar anodal tDCS does not interfere neither with the motor cortex excitability nor with the transcallosal inhibition at rest.

58. Repetitive transcranial magnetic stimulation induces neuroprotection via activating CaMKII α -CREB-Bcl-2 pathway in rat brain - C. Terranova, V. Rizzo, T.S. Rajan, A. Naro, A. Ahmad, M.F. Ghilardi, D. Bruschetta, P. Girlanda, S. Cuzzocrea, H.Y. Wang, A. Quartarone (Messina, New York US, Manchester UK)

Repetitive transcranial magnetic stimulation (rTMS) affects neuronal plasticity in humans and in animals, however, molecular mechanisms underlying rTMS effects remain not clear. In this study we examined whether low and high frequency rTMS may be neuroprotective. To this end, we determined Bcl-2/Bax expression in the prefrontal cortex of rats treated with 1Hz or 5Hz rTMS for five consecutive days. In addition, we examined brain plasticity related proteins, CaMKII α and CREB and their role in regulating Bcl-2/Bax. We found that both 1Hz and 5Hz rTMS increase Bcl-2, CaMKII α and CREB expressions. Our results suggest that both 1 and 5 Hz rTMS treatment for 5 days may have produce neuroprotective effects by increasing expression of neuroprotective Bcl-2. This rTMS-induced Bcl-2 synthesis is likely mediated by the heightened activation and expression of CaMKII α - and CREB.

59. Variability in response to 1 Hz repetitive TMS - G. Strigaro, M. Hamada, R. Cantello, J.C. Rothwell (Novara, Tokyo JP, Londra UK)

Responses to different plasticity-inducing brain stimulation protocols are highly variable. However there is little data available on the variability of response to 1 Hz repetitive transcranial magnetic stimulation (1Hz rTMS). We tested the effects of 1Hz rTMS over the motor cortex on corticospinal excitability. We examined whether an individual's response could be predicted from measurements of onset latency of motor evoked potential (MEP) following stimulation with different orientations of TMS. Thirty-two healthy subjects participated in a crossover-design. Baseline latency measurements with different coil orientations and MEPs were recorded from the FDI muscle prior to the application of 900 pulses of 1Hz rTMS with different stimulus intensities. Thirty MEPs were measured every 5 min for half an hour after the intervention. At the group level, there were no significant aftereffects of 1Hz rTMS: about 50% individuals had only a minor or no response to 1Hz rTMS whereas the remainders had a facilitatory effect. There was no significant correlation between the latency difference of MEPs (anterior-posterior stimulation minus latero-medial stimulation) and the response to 1Hz rTMS. This large variability is in line with similar studies using other forms of non-invasive brain stimulation. Individual factors may influence the responsiveness to these protocols.

60. The effect of cerebellar degeneration on Human Sensori-Motor Plasticity - R. Dubbioso, G. Pellegrino, A. Antenora, G. De Michele, A. Filla, L. Santoro, F. Manganeli (Napoli, Montreal CA)

We investigated how cerebellar degeneration influences the plasticity of the M1 by using PAS (paired associative plasticity) technique. PAS involves repeated pairs of electrical stimuli to the median nerve and transcranial magnetic stimulation (TMS) of the motor cortex. If the interval between peripheral and TMS stimulation is around 21–25 ms, corticospinal excitability is increased via a long term potentiation (LTP)-like effect within M1. Our aims were: (i) to explore the presence of a time-specific influence of cerebellar degeneration on human associative plasticity; (ii) to evaluate the role of somatosensory pathway on cerebellar modulation of sensory-motor plasticity. We studied 10 patients with pure cerebellar atrophy and 10 age-matched healthy subjects. Motor-evoked-potentials amplitudes, short-afferent inhibition, motor thresholds, I/O curves, somatosensory-evoked-potentials (SEPs) were measured before, just after and 30 min after PAS at interstimulus intervals of 21.5 and 25 ms. In cerebellar patients, LTP-like effect induced by PAS was abolished at 25 ms but not at 21.5 ms. SEPs showed the amplitude of P25 wave was markedly reduced in patients with a more severe clinical and radiological impairment of cerebellum. Cerebellar patients have an altered capability of cerebellar filtering or processing of time-specific incoming sensory volleys, influencing the plasticity of M1.

61. Progressive Supranuclear Palsy patients show abnormal response to conditioned and unconditioned TMS stimuli compared to Parkinson's disease and healthy subjects - M. Fichera, E. Houdayer, F. Avantaggiato,

R. Chieffo, G. Comi, M.A. Volonté, L. Leocani (Milano)

Progressive Supranuclear Palsy-PSP is the second most common parkinsonian syndrome after Parkinson's disease-PD, with some overlapping clinical features in the early phases. Non-invasive neurophysiological techniques, such as transcranial magnetic stimulation-TMS, could prove useful to gain insight into these pathologies and as widely available methods for differential diagnosis. Seventeen PD, 13 PSP and 11 healthy controls-HC subjects were included in this study. TMS evaluation included resting motor threshold-RMT, motor evoked potentials-MEP amplitude and latency, response to inhibitory-SICI and facilitating-ICF conditioned stimuli, cortical silent period-CSP and ipsilateral silent period-iSP. Statistical analysis was performed using either parametric or non-parametric ANOVA and post-hoc tests according to data distribution. For paired-pulse a repeated measures ANOVA was adopted, using interstimulus interval-ISI and group as factors. PSP and PD groups did not significantly differ in UPDRS. TMS assessment showed different distribution of RMT across groups (p.008), with PSP patients showing highest values and PD lowest (PSP vs PD p.002). Group also affected iSP duration (p.016), being longest in PSP and lowest in HC (PSP vs HC p.005). On paired-pulse inhibition and facilitation, a significant effect of ISI (p<.001) and GROUP (p.035) but not interaction was found, with lower SICI and higher ICF in PSP vs both PD (p.017) and HC (p.032) and no significant difference between the latter two groups. This study suggests that TMS can help differentiate PD and PSP. PSP patients displayed different response to the perturbation induced by conditioning stimuli and iSP elongation, probably due to impairment of GABA-mediated neurotransmission.

62. Sensory Tricks in Cervical Dystonia: a neurophysiological study with Short Latency Afferent Inhibition – F. Bianchi, S. Amadio, M. Cursi, I.P. Urban, C. Butera, R. Guerriero, G. Comi, U. Del Carro (Milano)

A classic hallmark of cervical dystonia (CD) is the improvement of dystonic symptoms during a specific maneuver, defined 'sensory trick' (ST). Even if the mechanism by which ST improve dystonia is not well understood, it seems probable that cortical sensorimotor integration processes are involved. On this basis, we previously performed a preliminary study by means short latency afferent inhibition (SAI) in a group of CD patients, in order to evaluate whether the inhibitory effect of somatosensory afferent volley on motor output is preserved in this group of patients and to assess if ST change SAI profile. To date we have increased our sample including 28 patients with primary CD (18 with ST, CD+, and 10 without ST, CD-) and 11 controls. The analysis of variance showed no significant differences between CD- and controls. Contrary, a remarkable trend of reduced SAI was observed in CD+ when they did not perform ST and, interestingly, SAI was further reduced, reaching a strong statistical relevance, when they performed ST. Our results show the presence of an abnormal sensorimotor integration in CD patients owing ST. Furthermore they prove that ST act by modulating the abnormal link between sensory input and motor output.

63. A study of cortical and spinal excitability in patients affected by Multiple Sclerosis and Spasticity after oromucosal cannabinoid spray (THC/CBD) – F. Donato, M. Turri, G. Zanette, V. Tugnoli, L. Deotto, F. Teatini, S. Romito, G. Moretto, G. Squintani (Verona, Bolzano, Peschiera del Garda, Ferrara)

The therapeutic efficacy of oromucosal cannabinoid spray (THC/CBD) for the treatment of spasticity is well documented by clinical trials, while in Italy THC/CBD has been approved for the treatment of spasticity in Multiple Sclerosis (MS) for not long time. Our study aims to assess neurophysiological correlates of the effect of THC/CBD on spasticity modulation in MS. We enrolled 16 MS patients who underwent a neurological examination (together with modified Ashworth scale) and neurophysiological testing. For the assessment of the cortical and spinal excitability, we performed TMS with double stimulation and detected LICI, SICI and ICF; we studied also CSP, H/M ratio and H reflex recovery cycle. Clinical and neurophysiological results were tested before and after one month of THC/CBD spray treatment and compared with 10 controls' data. Patients referred a subjective decrease of spasticity after THC/CBD, confirmed by modified Ashworth scale, and showed a significant difference of the H recovery cycle (at ISI 500 msec) and LICI compared to controls, that normalized after THC/CBD. CSP was not different from healthy subjects. Our data showed that THC/CBD oromucosal spray is effective in spasticity and probably act at spinal and subcortical level modulating the GABA-ergic inhibitory circuitry.

64. Differences in intracortical inhibition of tongue motor representations between persistent adult developmental stutterers and normal speakers – P. Busan, G. Del Ben, F. Monti, P.P. Battaglini (Trieste)

The causes of developmental stuttering are not known, but increasing evidence shows differences in the motor system of persistent adult developmental stutterers (PADS) in comparison to normal speakers (NS). Right handed males PADS and matched NS (considering age, sex, handedness, smoking habits and musical expertise) were evaluated by using transcranial magnetic stimulation on their tongue primary motor cortex, in both hemispheres, measuring variables such as resting and active motor thresholds, silent period thresholds (SPT), and silent period durations (SPD, stimulating at 130% of SPT). Preliminary results suggest the presence of higher SPT for the PADS group with respect to NS. Moreover, SPD were increased in the left hemisphere of PADS with respect to NS. This suggests a particular intracortical balance in the tongue motor cortex of PADS with respect to NS. More specifically, while the higher SPT in PADS could suggest lower intracortical inhibition, the presence of longer silent period duration in the left hemisphere of PADS is pointing toward a greater inhibition in these brain regions, thus compensated by the presence of lower inhibition in the right one of the same group. This evidence, in line with previous evidence in stuttering research, could be useful for rehabilitative purposes.

65. Transcranial Magnetic Stimulation in refractory NCSE: personal experience and future studies - F. Monti, L. Stragapede, G. Furlanis, L. Mantovan, G. Romano (Trieste)

The use of repetitive TMS for epilepsy is a potential therapy. In literature several case reports were published with different results. We describe two cases of refractory focal NCSE treated with rTMS with different stimulus parameters. We monitored in all two cases, in all stimulation period, the electrical activity with standard EEG, according with our previously experiences in EEG/TMS co-registration. The stimulus was applied over the epileptic focus, according with EEG registration. We used a train stimulus of 0.5 or 1 Hz at 70 or 100 % of motor threshold, for 20 minutes. In the first case TMS decreased suddenly the electrical paroxysm. In the second case TMS reduced but not abolished the ictal activity. We think that the use of repetitive TMS in selected refractory cases, bot convulsive than non convulsive status epilepticus, can be useful when conventional therapies have failed. In addition in these cases the coregistration is mandatory. Future studies should investigate various rTMS parameters in different patients with refractory focal status epilepticus.

66. Cannabinoids may influence motor cortical excitability: a double-blind neurophysiological study – C. Cambieri, M. Ceccanti, L. Fionda, G. Tartaglia, A. Cicchinelli, V. Frasca, E. Onesti, M.C. Gori, M. Inghilleri (Roma)

Endogenously released cannabinoids (CBD) are involved in several neuronal processes; those compounds act via two receptors subtypes: Cannabinoid receptor type 1 (CB1) – expressed in central nervous system neurons – and cannabinoid receptor type 2 (CB2) – expressed in immune system cells, microglia and neuronal progenitor cells. Δ^9 -tetrahydrocannabinol (THC), the most important active metabolite of cannabidiol, shows a partial agonist activity on cannabinoid receptors. The aim of this study was to evaluate, in 13 healthy subjects, the effect of the dronabinol on the Resting Motor Threshold (RMT) registered at the first dorsal interosseous (FDI), on the motor evoked potential (MEP) amplitude and on the latency and duration of the Cortical Silent Period (CoSP). All subjects underwent two separate sessions: one with dronabinol (5 mg) and the other with bromazepam (1.5 mg) used as control-drug. Healthy subjects were tested immediately before and one hour after the drug administration. No significant differences were found on MEP amplitude and CoSP values between the two groups. RMT significantly reduced in subjects treated with dronabinol compared to those treated with bromazepam ($p < 0,05$). Previous studies indicate that - even after a single exposure to THC - prolonged cortical hyperexcitability occurs, with an increased susceptibility to convulsions. Recent studies show that chronic cannabis use is associated with a reduction in cortical inhibition potentially related to activity at the GABA-A receptors. Our preliminary data suggest that further research is needed to delucidate the effects of CBD on cortical excitability and to better understand the mechanisms underlying CBD's involvement in epilepsy.

67. Neural response to Transcranial Magnetic Stimulation in adult Thyroid Hormone Resistance – C. Allegra, C. Terranova, V. Rizzo, S. Benvenga, L. Bartolone, F. Morgante, P. Girlanda, A. Quartarone (Messina)

Thyroid hormone resistance describes a rare syndrome where the thyroid hormone levels are elevated but the

thyroid stimulating hormone level is not suppressed. The importance of thyroid hormones for the normal function of the adult brain is corroborated by the frequent association of thyroid dysfunctions with the presence of neurological and psychiatric symptoms. In this study we investigated whether adult thyroid hormone resistance affects cortical excitability and modulates inhibitory and excitatory intracortical circuitries by using transcranial magnetic stimulation. Cortical excitability was probed with transcranial magnetic stimulation in 6 patients with thyroid hormone resistance, 10 patients affected by hypothyroidism and 10 age-matched healthy controls. We tested motor thresholds, motor evoked potential recruitment curve, cortical silent period, intracortical inhibition and intracortical facilitation. Patients with thyroid hormone resistance showed decreased steepness of the motor evoked potential recruitment curves. These changes were paralleled by shorter cortical silent period and increased intracortical inhibition. Thyroid hormones may influence cortical excitability and cortical inhibitory circuits in adults.

68. The effect of a neuromodulation protocol on executive functions in healthy elderly: psychometric and EEG evidences - D. Crivelli, F. Pala, R. Finocchiaro, E. Grippa, G. Lecci, M. Balconi (Milano)

Executive functions tend to decrease their efficiency during the physiological aging process. Nevertheless, cognitive and brain reserves are thought to act as protective factors against cognitive decline and the re-activation of cognitive and neural networks by means of non-invasive brain stimulation (NIBS) may help in maintaining those reserves and improving functional profiles. The present research thus investigates the effect of prefrontal NIBS in empowering executive functions and electrophysiological attention responses in healthy elderly people. Twenty-two volunteers have been assigned to a control or NIBS group. The NIBS protocol (anodal transcranial Direct Current Stimulation) lasted eight weeks (three sessions per week), with twice-weekly administration of tasks tapping on executive functions. Participants' cognitive and electrophysiological profiles have been assessed at the beginning, after the treatment period, and after six months. Data analyses showed interesting positive modulations in post-intervention performances for the NIBS group – specifically in tests tapping on executive functions and automatic electrophysiological attention responses. Besides, participants' subjective reports of improvement in everyday functioning, behavioral and electrophysiological evidences suggest that a moderately intensive NIBS protocol might help in empowering specific cognitive functions even in healthy aging and hint at interesting implication for prevention and early intervention.

69. Prolonged inhibitory effect of 1 Hz rTMS of the motor cortex on the nociceptive evoked potentials to contralateral hand stimulation – E. Testani, G. Granata, C. Pazzaglia, L. Padua, M. Valeriani (Roma)

There are only few data about the effect of the low frequency motor cortex rTMS (LF-rTMS) on both clinical and experimental pain. Since LF-rTMS should have an inhibitory effect on motor cortex, whose activation is known to reduce experimental pain (Le Pera et al., 2007), one could

expect that 1 Hz motor cortex rTMS increases an objective pain measure, such as laser evoked potentials (LEPs). In 8 healthy subjects, we investigated the effect of 1 Hz rTMS of the left motor cortex on LEPs to stimulation of both right and left hand dorsum. LEPs were recorded at 4 different times: baseline, T0 (immediately after 20 minutes of 1 Hz rTMS), T+20 (20 minutes after 1 Hz rTMS), and T+40 (40 minutes after 1 Hz rTMS). We found that rTMS modified the amplitude of the N2/P2 LEP component only to right hand stimulation ($F=12.06$, $p<0.001$), while there was no effect on left hand LEPs ($F=0.7$, $p=0.56$). Post-hoc analysis showed that the N2/P2 amplitude was reduced at T0, T+20, and T+40, as compared to baseline ($p<0.01$). Instead of the expected facilitatory action of LF-rTMS on pain, our results show that LF-rTMS of the motor cortex inhibits contralateral pain; this effects last up to 40 minutes after the cortical stimulation.

70. Rehabilitation of verbal and visuospatial memory by oscillatory tDCS and sleep consolidation – A. Del Felice, A. Magalini, S. Masiero, P. Manganotti (Padova, Verona, Venezia Lido, Trieste)

Temporal lobe epilepsy (TLE) is often associated with memory deficits. Given the putative role for sleep spindles in learning and encoding, the distribution of spindle generators skewed toward the affected lobe in TLE subjects may be a neurophysiological marker of defective memory. Slow-oscillatory transcranial direct current stimulation (sotDCS) has been shown to improve memory possibly by increasing slow-wave sleep and modulating sleep spindles. To test if excitatory anodal sotDCS over the affected temporal lobe affects sleep spindles, thus improving memory performance. In this randomized controlled cross-over study 12 people with TLE underwent either sotDCS (0.75Hz; 0-250 μ V, 30 minutes) or a sham procedure before a daytime nap. Declarative verbal and visuospatial learning were tested. Fast and slow spindle signals were recorded by 256-channel EEG during sleep. In both study arms, we used electrical source imaging (ESI) to localize cortical generators. Neuropsychological data were analyzed with general linear model statistics or the Kruskal-Wallis test (p or $Z<0.05$), and neurophysiological data were tested with the Mann-Whitney t test and a binomial distribution test (p or $Z<0.05$). An improvement in declarative ($p=0.05$) and visuospatial memory performance ($p=0.048$) was noted after sotDCS. SotDCS increased the current density of slow spindle generators ($Z=0.001$), with a shift to the anterior cortical areas. Anodal sotDCS delivered over the affected temporal lobe can improve declarative and, to a lesser extent, visuospatial memory performance by modulating cortical source generators of slow sleep spindles. SotDCS appears to be a promising tool for memory rehabilitation in people with TLE.

71. Repetitive Transcranial Magnetic Stimulation (rTMS) applied with h-coil in alzheimer's disease: a placebo-controlled, double-blind, pilot study - E. Coppi, L. Ferrari, A. Nuara, R. Chieffo, E. Houdayer, A. Ambrosi, M.P. Bernasconi, M. Falautano, A. Zangen, G. Comi, G. Magnani, L. Leocani (Milano, Beer-Sheva IL)

Focal rTMS in Alzheimer's disease (AD) revealed cognitive benefits. H-coil can depolarize deeper and wider structures compared with focal coils, thus targeting widespread networks involved in neurodegenerative disorders. We aimed to evaluate H-coil rTMS safety and efficacy in AD. Thirty AD subjects (70.21 ± 8.66 y.o.), randomized in real or sham groups, underwent 16 rTMS sessions (3 weekly for 4 weeks, 1 weekly for other 4 weeks), over fronto-parieto-temporal lobes at 10Hz. Neuropsychological assessment was performed at baseline, after 4 weeks (4w), at the end of treatment (8w). Primary outcome was an improvement in Alzheimer's disease Scale-cognitive (ADAS-cog). No serious side effects were reported. Four subjects were excluded (1 acute myocardial infarction in the sham group, 1 misdiagnosis, 2 missing data), thus statistical analysis included 26 subjects. At 4w, percent ADAS-cog improvement from baseline (4w%) was greater in the real compared with the sham group ($p=0.042$). The relationship between baseline ADAS-cog and 4w% differed between the two groups ($p=0.009$), with higher improvement for less cognitively impaired subjects at baseline only in the real. These findings suggest that H-coil may be safe and effective in AD and that deep rTMS may better impact the course of the disease when administered at earlier stages.

72. Electrophysiological differences between Early Onset and Late Onset Alzheimer Disease Patients – F. Di Lorenzo, A. Martorana, S. Bonni, C. Caltagirone, G. Koch (Roma)

Early Onset Alzheimer Disease (EOAD) and Late Onset Alzheimer disease (LOAD) share the same pathological features and are considered the same disorder affecting people at different ages, under 65 years for EOAD, over 65 years for LOAD. Whether the different pathological burden could influence also synaptic plasticity mechanisms has never been addressed yet. The aim of our study is to investigate the neurophysiological characteristics of these patients through transcranial magnetic stimulation protocols, comparing with two control groups, respectively old healthy and young healthy age-matched subjects. To verify this hypothesis we evaluated a group of 22 sporadic EOAD and 33 LOAD for plasticity induction of LTP/LTD-like effects using respectively intermittent TBS (iTBS) or continuous TBS (cTBS). Central cholinergic activity was evaluated by means of short afferent inhibition (SAI) protocol. Patients, both EOAD and LOAD, showed an impairment of LTP mechanisms while healthy controls, showed a normal profile of cortical plasticity. SAI protocol results show a positive correlation between SAI dysfunction and aging, reflecting acetylcholine role in aging. The central cholinergic pathway seems to be affected more by age than by the disease process itself. LTP mechanisms are altered in AD patients despite the age, thus representing a reliable marker of disease.

73. Neurophysiological features of motor cortex excitability and plasticity in Subcortical Ischemic Vascular Dementia: a TMS mapping study – A. Guerra, S. Petrichella, L. Vollero, D. Ponzio, P. Pasqualetti, S. Maatta, E. Mervaala, M. Kononen, F. Bressi, G. Iannello, P.M. Rossini, F. Ferreri (Roma, Kuopio FI)

The aim of this study was to evaluate neurophysiological features of M1 excitability and plasticity in Subcortical Ischemic Vascular Dementia (SIVD), by means of TMS mapping technique. Seven SIVD and nine AD patients, along with nine control subjects were tested. The M1 excitability was studied by resting thresholds, area and volume of active cortical sites for forearm and hand's examined muscles. For M1 plasticity, coordinates of the hot-spot and the center of gravity (CoG) were evaluated. The correlation between the degree of hyperexcitability and the amount of M1 plastic rearrangement was also calculated. Multivariate analysis of excitability measures demonstrated similarly enhanced cortical excitability in AD and SIVD patients with respect to controls. SIVD patients showed a medial and frontal shift of CoG from the hot-spot, not statistically different from that observed in AD. A significant direct correlation was seen between parameters related to cortical excitability and those related to cortical plasticity. The results suggest the existence of common compensatory mechanisms in different kind of dementing diseases supporting the idea that cortical hyperexcitability can promote cortical plasticity. This study characterizes neurophysiological features of motor cortex excitability and plasticity in SIVD, providing new insights on the correlation between cortical excitability and plasticity.

74. Cerebellum and pain: a transcranial Direct Current Stimulation (tDCS) study - T. Bocci, G. Carli, E. Santarcangelo, M. Hesgens, A. Di Rollo, D. Barloscio, L. Parenti, A. Priori, M. Valeriani, F. Sartucci (Pisa, Siena, Milano, Roma, Aalborg DK)

The cerebellum is involved in a wide number of integrative functions, but its role in pain experience is poorly understood. We evaluated the effects of transcranial cerebellar direct current stimulation (tcDCS) by studying the changes in the perceptive threshold, pain intensity (VAS:0-10) and laser evoked potentials (LEPs) variables. Twenty-five subjects were studied before and after anodal, cathodal and sham tcDCS. LEPs were obtained using a Nd:YAP laser and recorded from the dorsum of the left hand. VAS was evaluated by delivering laser pulses at different intensities, respectively two and three times the perceptive threshold. Cathodal polarization dampened significantly the perceptive threshold and increased the VAS score, while the anodal one had opposite effects ($p < 0.001$, two-way repeated measures ANOVA, "time" x "stimulation"). Cathodal tcDCS increased the N1 and N2/P2 amplitudes and decreased their latencies, whereas anodal tcDCS elicited opposite effects ($p < 0.0001$). tcDCS modulates pain perception and its cortical correlates. As it influences both N1 and N2/P2 components, we speculate that the cerebellum modulates the activity of both somatosensory and cingulate cortices. Present findings prompt investigation of the cerebellar direct current polarization as a novel and safe therapeutic tool in chronic pain patients.

75. Intraoperative Monitoring in Minimally Invasive Lateral Transpoas Approach: our experience - G. Stipa, D. Frondizi, C. Fanelli, D. Gobbi, P. Mazzetelli, A. Ciampini, S. Carletti (Terni)

The minimally invasive lateral transpoas approach to the lumbar and spine has become an increasingly popular

approach for achieving interbody fusion. The reported advantages include minimally invasive access to the spine, absent manipulation of aorta and vena cava, less blood loss compared to open procedures, decreased operative times, shorter hospital stays, less postoperative pain. The patient is placed in the lateral decubitus position. A lateral X-ray confirms that the patient is in a truly lateral position. A series of tubes and dilators are used to identify the mid-position of the disk to be incised. The dilator is introduced through a small incision and the surgeon's index finger directs the dilator through the retroperitoneal space to the psoas muscle. Due to the location of the lumbar nerve root contribution to the lumbosacral plexus within the psoas muscle, the risk of motor and sensory nerve injury is present when traversing the lumbosacral plexus with the dilator or during retractor positioning over the disc space. Neural monitoring (Free-Run EMG L2-S1 and intraoperative monopolar electrical stimulation, PEM and PES) is believed to be critical in localizing the lumbosacral plexus during positioning of the retractor system. We monitored 15 patients with no complications.

76. Intraoperative Recording of Saphenous Nerve Somatosensory Evoked Potentials during Spine Deformity Surgery - V. Simioni, F. Pastorelli, R. Plasmati, E. Granieri, M. Di Silvestre, V. Tugnoli, T. Greggi (Ferrara, Bologna)

Intraoperative SEPs from lower-extremity are typically elicited by stimulating the posterior tibial nerve. Recently, Silverstein et al described the novel technique of monitoring saphenous nerve SEP (snSEP) during transpoas approaches to the spine in order to detect femoral nerve injury at the L2-L3-L4 levels. The aim of this study was to record snSEP during spine deformity surgery in order to monitor dorsal column and L2-L3-L4 roots at risk during spinal instrumentation procedures. Twenty consecutive patients were involved. Multimodal-IOM, with MEPs, SEPs (stimulating saphenous and posterior tibial nerves), EMG and pedicle screw stimulation, was employed in the patients. Saphenous nerve was stimulated through needle electrodes placed in between the vastus medialis and sartorius muscles, using a repetition rate of 2.7 Hz and a stimulus intensity of 30-45 mA. The cortical response, recorded at the CPz and Fz location, was a positive downward deflection with reproducible latencies at 30 ms. Saphenous nerve stable SEP was recorded in 18/20 patients. Changes were noted in one patient who presented a bilateral transient reduction of lower limbs MEPs and snSEPs during deformity correction. SnSEP monitoring may be a complementary technique in preserving dorsal columns and upper lumbar roots function during spine surgery.

77. "Correlations between electrophysiological and clinical changes in spinal surgery" - M.L. Giobbe, A. Borio, S. Marmolino, G. Faccani, P. Costa (Torino)

Changes in somato-sensory evoked potentials (SSEP) or motor evoked potentials (MEPs) are variably associated with clinical modifications. This study aimed to investigate if neurophysiological changes during IOM are related with clinical modifications in patients underwent spinal surgery. 71 patients that presented neurophysiological changes in somato-sensory evoked potentials (SEPs) or motor evoked potentials (MEPs) during spinal surgery were considered.

The pathologies included in the study were: cervical/thoracic myelopathy (27 pts., 38%), spinal cord tumors (31 pts., 44%), scoliosis correction (3 pts, 4%), trauma (7 pts, 10%) and spinal vascular malformations (3 pts, 4%). Clinical outcome, estimated with McKormick scale, was evaluated in the immediate postoperative period and at one month follow-up. Neurophysiological changes were associated to clinical modifications at one month follow-up in 36 patients (51 %). When a clinical improvement was observed (19 pts), the percentage of SEPs or MEPs reappearance from basal absence was 42% (8 pts). Contrariwise, evoked potentials disappeared in 65% (11 pts) of observed clinical worsening (17 pts). Neurophysiological modifications in SEPs or MEPS seem to be associated clinical changes in patients submitted spinal surgery.

78. Diagnostic Accuracy of Neurophysiological Tests (EEG and SEP) in comatose patients after cardiac arrest: protocol presentation of Italian Multicentric Study (ProNeCA) – A. Amantini, D. Audenino, C. Callegarini, R. Carrai, M.G. Celani, M. Di Capua, F. Donato, C. Foresti, P. Lanteri, M. Lombardi, L. Madera, A. Marelli, S. Megarelli, C. Minardi, F. Minicucci, C. Monetti, E. Montalenti, Motti, M. Osio, O. Piazza, L. Politini, F. Ricci, E. Rota, M. Scarpino, M. Spalletti, F. Valzania, E. Vitelli, P. Costa, A. Grippo (Firenze, Genova, Ravenna, Perugia, Roma, Verona, Bergamo, Empoli, Milano, L'Aquila, Cesena, Ferrara, Torino, Reggio Emilia, Salerno, Legnano, Piacenza, Modena, Lodi)

The prediction of neurologic outcome in comatose patients after cardiac arrest(CA) has been investigated and the findings were summarized in a practice parameter of the American Academy of Neurology(1). This guidelines did not included the EEG as a reliable outcome indicator but recent studies on continuous EEG recorded during TH have re-evaluated the role of EEG(2-4). These studies underline the utility of a simplified classification system of EEG patterns and point to which pattern attains reliable predictive value both for good and bad outcomes. These reports are of high clinical relevance because, until today, the possibility of identifying early prognostic indicators of good outcome in patients surviving to CA has not been investigated. At the best of our knowledge, only few multicentric prospective studies (4-6) analysed the prognostic value of EEG and SEP recorded in the same patient after CA as single predictor but none analysed the diagnostic accuracy of the association of these two tests. We present the study protocol of Italian Multicentric Study about prognostic value of EEG and SEP in comatose patients after CA (ProNeCA) proposed by study group of “Intraoperative and Intensive Care Clinical Neurophysiology” of the Italian Society of Clinical Neurophysiology.

79. Status epilepticus and myoclonus in comatose patients after cardiac arrest: to treat or not to treat - R. Carrai, A. Grippo, M. Spalletti, M. Scarpino, C. Cossu, G. Lanzo, A. Peris, S. Valente, A. Amantini (Firenze)

Status epilepticus and myoclonus are common in comatose patients after cardiac arrest (Krumholz et al.,1988; Young et al.,1990). There is no consensus on when and for

how long to treat this condition. This point became more relevant after introduction of therapeutic hypothermia(TH) because of some patients with MS treated with TH recovered consciousness (Rossetti et al.,2009). We propose a treatment protocol based on clinical-EEG features and somatosensory evoked potentials (SEPs) as prognostic indicator. In patients with absent SEPs we do not treat aggressively with AED considering the poor outcome. In patients with preserved SEPs we treat myoclonus if associated with GPEDs, convulsive status epilepticus and non convulsive status epilepticus (Beniczky et al., 2013). We use a combination of AED (valproate, levetiracetam) with sedation (propofol or midazolam). We present two representative cases in which we describe in more detail our therapeutic approach.

80. EEG is a time-dependent reliable indicator of good or poor outcome in comatose patients after cardiac arrest - M. Spalletti, R. Carrai, A. Grippo, M. Scarpino, A. Ammannati, A. Cassardo, A. Peris, S. Valente, A. Amantini (Firenze)

The prognostic role of EEG during early phase after cardiac arrest (CA) has been recently emphasized, but different classifications and definitions have been employed among studies. A standardised terminology for ICU patients has been recently proposed by American Clinical Neurophysiology Society (ACNS). We retrospectively evaluated the prognostic value of EEG according to different times of recording in postanoxic comatose patients, classifying EEGs according to the ACNS terminology with a main focus on background continuity. The study included EEG of 211 patients, recorded at 12, 24, 48 and 72hs. At each timing we observed at least one EEG pattern with specificity of 100% for poor or good outcome. At 12hs “continuous” and “nearly continuous” EEGs were always associated to good outcome, whereas isoelectric EEG and “burst-suppression with highly epileptiform discharges” were always associated to poor outcome. At 24hs isoelectric and all “burst-suppression” EEGs were always associated to poor outcome. At 48hs and 72hs isoelectric, “burst-suppression” and “suppressed” (<10 μ V) EEGs were always associated to poor outcome. Using a standardised classification, EEG provides time-dependent reliable indicators of good or poor outcome.

81. Clinical and electrophysiological findings in critically ill paediatric patients – D.P. Rossi, S. Fornarino, M. Pallavidino, S. Buratti, A. Moscatelli, P. Lanteri (Genova)

To describe clinical and electrophysiological features in critically ill paediatric patients. Acquired neuromuscular weakness due to critical illness polyneuropathy (CIP)- which could develop during a severe illness requiring intensive care- has been rarely described in childhood, but it's likely to occur more often than previously thought. A case series of critically ill neonates and children admitted and hospitalized for more than 1 week into Paediatric Intensive Care Unit (PICU) was observed prospectively. Selected clinical and laboratory parameters were evaluated. Conduction velocities studies were performed during the first week, and then repeated during the second, third and fourth week in order to detect sign of CIP. Clinically muscle weakness could not be easily evaluated in critical ill

neonates and sensory loss is often difficult to assess in children and especially in those sedated or intubated. CIP is less common in children than in adult, but early electrophysiological investigations could help to detect this condition or to discover rare neuromuscular diseases, as very early onset hereditary polyneuropathy. We propose electrophysiological examination as an available method to detect CIP in childhood -in order to avoid unnecessary diagnostic procedures- and a screening tool in studies of critically ill children with implications for the diagnosis and management of paediatric intensive care survivors.

82. EEG epileptiform abnormalities in patients with severe disorders of consciousness – C. Boccagni, S. Bagnato, A. Sant'Angelo, C. Prestandrea, G. Galardi (Cefalù)

Although epileptiform abnormalities are a common electroencephalographic finding after a brain injury, not much is known about their prevalence and prognostic value in patients with severe disorders of consciousness. In this study, we evaluated the occurrence of epileptiform abnormalities in the electroencephalograms recorded at admission in 106 consecutive patients with unresponsive wakefulness syndrome (UWS, 59 patients), or in a minimally conscious state (MCS, 47 patients). Using the Coma Recovery Scale Revised (CRS-R), we compared the three-months outcome of patients with and without epileptiform abnormalities. Epileptiform abnormalities were found in 34 patients (32.1%), with a similar occurrence in patients with UWS (33.9%) or in a MCS (29.8%). The CRS-R score at admission was 7.5 ± 4.6 in patients with epileptiform abnormalities, and 7.4 ± 4.3 in patients without epileptiform abnormalities. After three months, the CRS-R score was 13.6 ± 8 in patients with epileptiform abnormalities, and 15.1 ± 7.7 in patients without epileptiform abnormalities. ANOVA showed no significant differences between groups in the three-months changes of the CRS-R score ($F_{1,104}=1.59$; $p=0.2$). In conclusion, epileptiform abnormalities are common in patients with UWS or MCS after a severe brain injury; yet, their occurrence does not seem to correlate with short term outcome.

83. Isoelectric electroencephalogram as early marker of poor prognosis: a case report – B. Frigeni, F. Ferri, C. Foresti, S. Quadri, E. Venturelli (Bergamo)

Isoelectric electroencephalogram (EEG) in conformant with clinical findings is one of the criteria of brain death. In clinical practice, isoelectric EEG in not brain-dead patients is rarely seen. We present a case of a 66-year-old woman with headache and acute confusional state. Brain TC showed aneurysmal subarachnoid hemorrhage for the rupture of anterior communicating artery aneurysm. During anesthesia and intubation patient presented acute anisocoria. Brain CT showed rebleeding with subarachnoid blood in anterior interemispheric cistern and intraventricular. Serial EEG were flat and somatosensory evoked potentials demonstrated absent waves at the cortical level but there was evidence of preserved cerebral blood flow on computed tomography angiography. Her neurological examination continued to show evidence of residual brainstem function (cranial nerve reflexes and coughing). He survived this condition for 5 days and afterward every criteria for brain death could be

applied. EEG records activity from only the cortical layers immediately beneath the scalp; it does not record from subcortical structures but EEG can be a very early marker of diffuse cortical damage. This case demonstrates that isoelectric EEG can not be equated with brain death but can be a very early marker of poor prognosis.

84. A proposal of Early Neonatal Sep Classification as prognostic predictor in Hypoxic Ischemic Encephalopathy – E. Molesti, M. Bastianelli, S. Gabbanini, G. Bertini, I. Corsini, S. Lori (Firenze)

Aim of this studio is evaluate the relationships between a new classification of somatosensory-evoked-potentials in cascade (SEP-c) with simultaneous video-electroencephalogram (VEEG) obtained by 1-hour integrated neurophysiological monitoring (1h-IMNA) and clinical assessment by Sarnat-Sarnat (SS), Resistance-Index (RI) in the cerebral arteries using pulsed-Doppler and magnetic resonance imaging (MRI) as early predictors of a 1-year outcome in Hypoxic-ischemic-encephalopathy (HIE). 1h-IMNA of EEG and SEP-c were doubly assessed in 8(4M-4F) asphyxiated term-infants within 1 and 4 weeks from birth. In all infants SS, RI and MRI were early performed. 1h-IMNA and RI were also assessed in 20 healthy term-infants, as control-group. SEPs' trend was evaluated in relation to behavioural-states during the v-EEG-recording (wakefulness, quiet/active sleep). In control-group SEPs were present and modulated. In the 8 asphyxiated infants were identified 4 SEPs' patterns: bilateral absence/pathological-alteration (A-A), monolateral absence/pathological alteration (A-n), hypovoltated/non-modulated (h/nm), normal (nn) in agreement with RI and MRI. The recognize of SEPc-pattern during 1h-IMNA, considering hypovoltage and/or modulation in relation to behavioural-state, especially if concurring with RI and MRI's patterns, could implement the early prognostic-value to identify the moderate asphyxiated newborns. This proposal of neonatal SEPs' classification and its relations with IR and RMI call for further studies as early predictors of HIE, especially if mild.

85. EEG automated analysis compared to direct vision in ION setting: an overall impression - C. Foresti, B. Frigeni, A. Furnari, A. Salmaggi, L. Stanzani, E. Venturelli, M.R. Rottoli (Bergamo, Lecco)

The automated analysis is an alternate representation of the raw EEG traces to deliver a more compacted form of information to clinicians, in order to quickly understand a large amount of data for the diagnostic purposes. Also ION instruments have the possibility to perform similar automatic analysis to provide visual or audible warning messages during surgical procedures. Anyway clinician's primary concern is whether false alarms or true positives might create a useful and reliable tool for detection and diagnosis. We compared automatic EEG analysis to expert physician visual direct examination in some different condition (carotid endo-arterectomy; MAV surgery; exclusion of intracranial aneurism; carotid-media artery bypass). The automated analysis was performed through an algorithm based on Fourier spectral transform. Compared to early and accurate expert physician surveillance, this framework showed a good but delayed sensitivity in

detecting significant neural activity modifications. Our overall impression is that direct visual EEG evaluation still represents the most consistent monitoring system. Although creating an algorithm that produces correct results in all instances is nearly impossible, the EEG automated analysis pitfall is yet a lack of a prompt processing of data trending, so as to fit the aim of ION procedure about timely warning messages.

86. Diagnostic value of standard EEG in prolonged disorders of consciousness - A. Estraneo, V. Loreto, P. Moretta, I. Guarino, V. Boemia, G. Paone, A. Pascarella, L. Trojano (Telese Terme, Caserta)

Assessment of responsiveness is critical for definition of treatment and prognosis of Disorders of Consciousness (DOC), but is very challenging. In the present cross-sectional study we analyzed the background predominant EEG activity (in terms of frequency and voltage) and reactivity to eye closing and to tactile, acoustic, noxious stimuli and Intermittent Photoc Stimulation (IPS) in 63 prolonged traumatic, vascular and anoxic DOC patients (30 F; mean age 55.4 yrs.), with a clinical diagnosis of vegetative state (VS, n=33) or minimally conscious state (MCS, n=30). The distribution of specific patterns of background EEG activity was significantly different between the two diagnosis ($p=.001$) and across the three etiologies ($p=.003$). Reactivity to several stimuli was significantly more frequent in MCS than in VS: such difference was significant for IPS ($p=.004$), whereas it only approached the significance level for eye closing ($p=.06$) and acoustic stimuli ($p=.06$). Presence of at least one reactivity, including or excluding IPS reactivity, was significantly more frequent in MCS than in VS ($p<.006$), and had good sensibility but low specificity for diagnosis of MCS. Presence of at least 3 kinds of reactivity had the highest specificity (.83). Qualitative analysis of standard EEG can provide additional elements for diagnosis of DOC.

87. Median nerve SEPs predict motor outcome in neonatal hypoxic-ischemic encephalopathy treated with hypothermia - M. Agatiello, E. Cainelli, E. Fava, E. Toffoli, L. Tessari, F. Scarabel, A. Cappellari, M. Sole, M. Di Capua, A. Suppiej (Roma)

The role of SEPs in motor prognosis of hypoxic-ischemic neonatal encephalopathy has been evaluated in pre-hypothermia era (Suppiej 2010) but their role in babies treated with hypothermia has not been studied yet. We investigated motor outcome at 12 months of age in 38 children who suffered from hypoxic-ischemic neonatal encephalopathy and were treated with hypothermia at the NICU of the Paediatric University Hospital of Padua. All performed median nerve SEPs in the neonatal period, traces were scored as bilaterally present (group1) or as bilaterally/unilaterally absent (group2) cortical N20 response. At follow up 4/38 children had the diagnosis of cerebral palsy (all of them had bilaterally absent cortical SEP). Of the remaining 34, 7 had abnormal ($< 15^\circ$) scores at the motor subscales of the Griffith's Scale. A significant difference was found between motor scores of group 1 (mean 97 DS 13) and group2 (mean 82 SD 14) ($p=.023$ Mann-Whitney test). Data seem to suggest a prognostic value of SEPs to predict neuromotor outcome as evaluated

with Griffiths Scale at one year of age. However, these results need to be confirmed at 24 months of age when clinical prognosis is known to be more reliable.

88. Intraoperative motor evoked potentials monitoring: assessment of corticospinal tract development in very young children - P. Lanteri, G. Prato, G. Piatelli, S. Martelli, M. Tumolo, A. Andaloro, E. Veneselli, A. Cama (Genova)

The most frequent method of intraoperative motor tract monitoring now in widespread use is referred to as transcranial electric stimulation (TES) applied to the motor cortex recordings of reliable muscle motor evoked responses (MEPs). While monitoring of MEPs is well established in adults, its use and reliability in the pediatric population are debated. Overall, TES is considered a safe method. Between November 2013, and February 2015, at G. Gaslini Institute we performed 100 procedures (80 neurosurgical and 20 scoliosis procedures) (age range, 1 month and 20 days -20 yr) with intraoperative motor tract monitoring. 14 of the surgeries were performed in children who were younger than 1 year of age. TES was performed to record MEP from abductor brevis pollicis, tibialis anterior (TA) and/or abductor hallucis muscles. The standard anesthesia regimen consisted of propofol, and remifentanyl. There were no complications related to this technique. There was an exponential, systematic reduction in the latency of MEP with age, especially for lower limb within 3 months of age, less noticeable until one year of age. The adult-type response was present by 2 years. The most significant maturation of corticospinal tract responses to TES takes place during the first 3 months of life.

89. Recovery of evoked potentials in spine surgery - P. Costa, M.L. Giobbe, A. Borio, D. Milani, S. Marmolino, G. Faccani (Torino)

The role of intraoperative neurophysiologic monitoring (IOM) in detection and prevention of an iatrogenic injury has been well documented. Only few studies, however, has been focused on recovery of evoked potentials. Aim of this study is to describe the rate of reappearance of basally unexcitable muscle-motor evoked potentials (m-MEPs) and somatosensory evoked potentials (SEPs) in a large cohort of spinal surgeries. Data on 720 spinal surgeries are shown. Transcranially elicited lower limbs m-MEPs and tibial nerve SEPs were intraoperative recorded according to standard protocols. Reasons for surgery included cervical/thoracic myelopathy (300 pts., 41.7%), spinal cord tumors (190 - 26.4% -), lumbar stabilization (109 pts, 15.1%), scoliosis correction (83 -11.5% -), trauma (32- 4.4% -) and spinal vascular malformations (6 pts, 0.8%). Overall no intraoperative changes were observed in 648 surgeries (90%), 54 (7.5%) transient or persistent deterioration of evoked potentials and 18 (2.5%) recovery of basally unexcitable SEPs or MEPs (9 myelopathies, 4 spinal cord tumors, 2 metastasis, 3 trauma). The large majority of these "positive" modifications (17/18 - 94.4%) consisted in reappearance of MEPs. Surgical decompression of spinal cord may lead to an acute improving of spinal motoneuron functionality. IOM can provide useful information even in patient with basally absent m-MEPs.

90. Cost-Benefit analysis of multimodal intraoperative monitoring during spine surgery - C. Martinelli, A. Ammannati, S. Gabbanini, A. Cassardo, R. Caramelli, A. Grippo, A. Amantini, G. de Scisciolo (Firenze)

Multimodal intraoperative neurophysiological monitoring (IOM) during spine surgery was introduced in clinical practice to reduce the risk of permanent neurological deficit post-surgery. The early detection of changes in neurophysiological parameters during surgical procedure, makes it possible to reverse the damage before it becomes permanent. The economic impact of the IOM, a rather difficult topic, was estimated with sufficient accuracy. We have done a review of the costs, in our department, ranging into a minimum of 220 euro for the peripheral nervous system and a maximum of 630 euro for spine surgery. Even if the rate of complications during IOM remains very low (about 1%), the costs of performing IOM surely do not exceed those of health care for the injured patients, so that the economic burden of neurological damage justifies widely the cost of the procedure. Moreover, indirect costs are often underestimated: loss of job, career setbacks of the patient or a family member close to him. One aspect that can not be measured is the impact of a possible psychological and social permanent deficit, especially when the affection of a specific function limits the chances of social relationship.

91. Impaired Interhemispheric Processing In Early Huntington's Disease: A Transcranial Magnetic Stimulation Study - T. Bocci, M. Hespens, A. Di Rollo, D. Barloscio, L. Parenti, A. Priori, F. Sartucci (Pisa, Milano)

A growing number of papers have recently investigated changes in interhemispheric connectivity in HD, although little is known about their temporal relation with clinical features and electrophysiological parameters. Here, we studied, for the first time, interhemispheric connectivity in Huntington's Disease (HD) by using a Transcranial Magnetic Stimulation (TMS) protocol. We evaluated ipsilateral Silent Period (onset latency, iSPOL, and duration, iSPD) and Transcallosal Conduction Time (TCT) in early manifest HD patients compared with sex and age-matched healthy volunteers; then, in HD group, we correlated TMS data with cognitive (MMSE), genetic (CAG-length) and clinical (UHDRS-I) scores. Compared with healthy volunteers, patients showed a marked decrease of iSPD, paralleled by a significant lengthening of iSPOL and TCT ($p < 0.01$). The impaired interhemispheric processing in HD significantly correlated with clinical (Mini-Mental Examination score and UHDRS-I) and genetic (CAG-length) data ($p < 0.05$). Callosal processing is impaired in early manifest HD; the interhemispheric disruption may have, at least in part, implications for the impaired sensorimotor integration and motor control, in addition to the defective gating of peripheral afferent input. Our results prompt further research in the whole field of hyperkinetic movement disorders, where data about TMS and interhemispheric excitability changes are still lacking.

92. Brainstem reflexes: new tools for differential diagnosis between idiopathic and psychogenic cervical dystonia? - L. Briscese, M.C. Carboncini, D. Barloscio, A. Crecchi,

L. Parenti, S. Mazzucchi, B. Rossi, F. Sartucci, T. Bocci (Pisa)

Cervical idiopathic dystonia (CID) is the most common kind of primary dystonia, but its pathogenesis remains still unclear. As in other movement disorders, the major challenge is to recognize the organic from the psychogenic phenotype. Our objective was to evaluate reliability of blink reflex test (BRT) in detecting powerful differences in patients with diagnosis of CID or (clinically presumed) psychogenic dystonia (PD). Twelve subjects were enrolled (6 CID, 6 PD) and BRT was assessed in term of R1 and R2 latencies and habituation phenomenon (trains of 10 stimulus, 1 Hz of frequency, 200 ms of duration). Electrodes were placed over the orbicular inferior muscle (recording electrode) and lateral canthus (reference). CID patients showed both an enhanced latency of polysynaptic R2 responses and a lack of habituation compared with subjects diagnosed as PD (t-test: $p < 0.001$). Our results support the hypothesis of a dysfunction of brainstem reflex circuits on the basis of CID. As in Parkinson Disease, one could speculate that this phenomenon relies on changes in the inhibitory drive from basal ganglia output structures, via tecto-reticular projections, to the superior colliculus.

93. Phosphorylated α -synuclein biomarker in skin nerves is differently expressed in pure autonomic failure and idiopathic Parkinson disease - V. Donadio, A. Incensi, C. Piccinini, P. Cortelli, M.P. Giannoccaro, A. Baruzzi, R. Liguori (Bologna)

To characterize the expression in skin nerves of native (n-syn) and misfolded or phosphorylated (p-syn) α -synucleins in pure autonomic failure (PAF) and idiopathic Parkinson disease (IPD). We studied 30 patients including 16 well-characterized IPD and 14 patients fulfilling PAF diagnostic criteria and 15 age-matched controls. Subjects underwent skin biopsy from cervical, thigh and leg sites to study small nerve fiber and intraneural n-syn and p-syn. PAF and IPD both showed a skin denervation, more severely expressed in patients with higher p-syn load. N-syn was similarly expressed in both groups of patients and controls. By contrast, p-syn was not found in controls but was disclosed in all PAF and IPD patients with different skin innervation. In addition, abnormal α -syn deposits were found in all analysed skin samples in PAF but in only 49% of samples with higher positivity rate in the cervical site in IPD. 1) intraneural p-syn was a reliable in vivo marker of PAF and IPD; 2) neuritic p-syn inclusions differed in PAF and IPD suggesting a different underlying pathogenesis; 3) searching for abnormal p-syn deposits in skin nerves, the site of analysis is irrelevant in PAF but it is critical in IPD.

94. Electromyographic correlates of paratonia - L. Marinelli, L. Mori, M. Pardini, G. Abbruzzese, C. Trompetto (Genova)

Paratonia can be defined as the inability of relaxing limb muscles during passive mobilization. It is divided into facilitatory paratonia, when the subject facilitates the examiner's movements, and oppositional paratonia, when the subject resists to the examiner's movements. Both types of paratonia may coexist and have been related to cognitive impairment and frontal lobe dysfunction. Even if paratonia is frequently encountered in clinical practice, very few studies have been published and its pathogenesis is still

unknown. Measuring this phenomenon is difficult and only semi-quantitative clinical scales are available. We propose an innovative method to measure both facilitatory and oppositional paratonia: the examiner performs metronome-synchronized continuous or discontinuous movements with the patient's elbow joint while angle and flexors/extensors EMG activity is recorded. EMG activity during passive movements could be recorded in a group of patients with paratonia assessed by clinical examination. Such EMG activity is prevalent in elbow flexors and appears both during flexion and extension movements. Continuous alternating elbow movements increase the EMG bursts amplitude and duration compared to discontinuous movements. Such EMG activity is probably the neurophysiologic equivalent of paratonia and allows a quantitative measure and distinction between facilitatory and oppositional paratonia.

95. A computerized static posturography protocol in the assessment of balance impairment of Multiple Sclerosis patients - F. Melillo, A. Di Sapio, M. Malentacchi, S. Malucchi, M. Capobianco, W. Troni, A. Bertolotto (Orbassano)

Balance impairment is common in Multiple Sclerosis (MS) patients. We administered the modified Clinical Test of Sensory Interaction on Balance (mCTSIB) to 73 MS patients and 57 healthy controls, to collect normative data and compare sensitivity of mCTSIB and clinical examination in detecting balance impairment. Subjects were asked to stand quietly upright for 10 seconds with eyes opened and then eyes closed (EC) (3 times per condition) on a firm surface on a fixed dual forceplate. The centre of gravity (COG) sway was expressed as velocity (deg/sec) and path length (mm); MS patients were examined with the Romberg Test (RT), scored according to Neurostatus. mCTSIB-EC clearly allowed to differentiate patients with positive RT (0.38 deg/sec, CI 0.32-0.43) from those with negative RT (0.19 deg/sec, 95% CI 0.17-0.21, $p < 0.001$). ROC analysis identified a cut-off value of 0.5 deg/sec to define "positivity" to the mCTSIB (sensitivity 100%, specificity 95%, PPV 82%, NPV 100%). mCTSIB detected balance impairment in 19 MS patients (10 with negative RT). Compared to RT, the computerized posturographic test is more sensitive in detecting balance impairment in MS patients. It is easy to perform, fast to administer, not operator-dependent and provides objective data on postural control.

96. Corticospinal reserve measured with the H-coil predicts walking impairment in progressive multiple sclerosis - A. Nuara, R. Chieffo, F. Esposito, F. Martinelli Boneschi, A. Zangen, M. Comola, G. Comi, L. Leocani (Milano, Beer-sheva IL)

Walking impairment affects multiple sclerosis (MS) patients, impacting their quality of life. Despite a known relationship between objective and subjective walking measures, gait and neurophysiological motor parameters relationships remains to be explored. 50 progressive MS people underwent functional and neurophysiological assessments: 10-meters-walking-test (10mWT), 2 and 6 minutes-walking-test (2mWT, 6mWT), Modified-Ashworth-Scale (MAS), Spasticity and pain Numerical-Rating-Scale

(NRS), Fatigue-Severity-Scale (FSS), expanded-disability-status-scale (EDSS), 12-items-MS-walking-scale (MSWS-12). A Walking-Fatigability-Index (WFi, performance decay from 2 to 6 minutes during 6mWT) was calculated according to the formula: $[(2mWT * 3 - 6mWT) / 2mWT * 3]$. Resting-motor-threshold (RMT, the lowest intensity for evoking an electromyographic or visually-evident muscle activation) was obtained using a H-Coil. Correlations were explored using the Spearman-rho coefficient (significance set at $p = 0.05$). RMT was correlated positively with the 10mWT ($p = 0.012$) and with MSWS-12 ($p = 0.005$), and negatively with the 2mWT ($p = 0.016$), but not with 6mWT, nor with fatigue (FSS) or fatigability (WFi). WFi was significantly correlated with disability (EDSS; $p < 0.0001$) and spasticity (MAS; $p = 0.007$). Resting motor threshold, as measure of pyramidal reserve, is correlated with subjective impact of MS on walking, predicting walking speed rather than endurance or fatigability, the latter being associated with disability and spasticity. The lack of association between subjective fatigue and objective fatigability suggests different mechanisms underlying the two phenomena.

97. Event Related Potentials recorded by intracerebral electrodes - S. Pro, N. Specchio, L. De Palma, C.E. Marras, L. Fusco, F. Vigevaro, M. Valeriani (Roma)

Preoperative evaluation, by means of intracerebral electrodes, provides an opportunity to explore neural generators of ERPs and also N140 (a long latency SEP that is modulated by attention manipulations). We studied 5 pediatric patients with drug resistant epilepsy. ERPs and SEPs (to median and tibial nerve stimulation) were recorded from the intracerebral electrode contacts referred to the earlobe ipsilateral to the stimulation. The analysis was addressed to the electrode contacts where an inversion of neurophysiological component polarity was observed or where the EP amplitude was higher. P300 was recorded by electrodes located in hippocampus; MMN was also well recorded by electrodes placed in opercular-insular cortex; N140, increased in amplitude during attention condition, showed the maximum amplitude in the frontal electrode contacts and in the opercular-insular traces. Numerous investigations revealed that generators of Event Related Potentials are independent and also with a cortical-subcortical distribution. In this short case series, we could show some brain areas clearly involved in the generation of P300, MMN and N140 components.

98. Correlations between P300, MRI parameters and neuropsychological tests in multiple sclerosis patients - M.C. Mantovan, E. Gastaldo, R. De Gennaro, F. Cagnin, E. Mosconi, M. Polastri, E. Cagliari, R. Quatrala (Venezia Mestre)

To evaluate the correlations between event-related evoked potentials (ERPs), neuropsychological and neuroradiological parameters in multiple sclerosis (MS) patients. We studied 10 patients with definite MS (6 males, 4 females, average age 43.6, SD=11.3), moderate disability (EDSS 2.85, SD=1.45; range: 1.0-6.0). All patients underwent standardized neuropsychological tests, P300 evoked potentials study and MRI. Registration of ERPs (P300) was performed by random double auditory

discrimination task paradigm and recorded through scalp electrodes placed at Fz, Cz and Pz and linked to the referred ears. Pearson bivariate correlation test was used to evaluate correlation between latency and amplitude of P300, neuropsychological tests, clinical (age, EDSS, illness length, relapses) and MRI (cortical atrophy, Apparent Diffusion Coefficient –ADC- maps) parameters. In our little series, latency of P300 was related to ADC of corticospinal tracts ($p=0.001$) and illness length ($p= 0.001$), no clear correlation between P300 and neuropsychological or other clinical parameters was found. We suggest that P300 and MRI ADC maps could be combined to give a numerical indirect parameter of disease progression.

99. Auditory event-related potentials (ERPs) evoked by human syllables, musical notes/chords and animal sounds in pre-school children with specific expressive language disorders (SELDs) for assessing the selectiveness of auditory processing - V. Scaioli, E. Granocchio, S. Curzi, S. Alverà, G. Airaghi, G. Musso, S. Magazù, I. Pesce, D. Sarti, S. Giacomelli, B. Molteni (Milano)

Auditory ERP recordings are a useful neurophysiological means of assessing the temporal domain of the pre-linguistic and linguistic sensory deficits involved in expressive specific language impairment (SLI). We recorded auditory ERPs in 32 pre-school children aged 3-5 years with SLI before they underwent a rehabilitation programme. The ERPs were evoked using syllables (SyERPs), music (MuERPs) and animal sounds (AnERP) chosen from among those used in the trials carried out before, during and after an intensive rehabilitation programme in order to assess: a) the quality of ERP abnormalities; b) the selectiveness of the ERP changes associated with the three types of stimuli; and c) the changes induced by the rehabilitation programme. The SyERPs and MuERPs gave rise to four components (in P1, N1, N2 and P2) classified on the basis of their latency and polarity; the AnERPs only gave rise to P1 and N1 components. The ERPs had both common and distinctive features in terms of their waveforms and topographical distribution: the SyERPs were more left lateralised, and the MuERP more right lateralised. Later negative components were also recorded depending on the type of stimulus. In comparison with controls, P1 and P2 SyERPs were the most abnormal. As the rehabilitation led to selective SyERP changes, these may be useful for diagnosis and monitoring SLI.

100. Laterality Indices determined by Magnetoencephalography (MEG) in three different temporal span may reflect better than one the complex reality of the language dominance - D. Rossi Sebastiano, D. Duran, E. Visani, F. Rotondi, L. Canafoglia, F. Panzica, S. Franceschetti (Milano)

The determination of language lateralization is an important goal for patients with medically intractable epilepsy or a brain tumor near the language areas to limit the risk of post-surgical language deficits. Our aim was to identify the hemispheric dominance and to localize the cortical activation during language tasks using MEG. We applied a novel method for the language dominance testing 10 patients candidate to neurosurgery, using three well

known tasks: Verb Generation, Word Recognition and Picture Naming. Source localization was performed using a MNE-based inverse model and the laterality index (LI) was calculated for each task using three different range intervals: 150-600ms, 150-300ms (prevalent Wernicke's activation) and 400-600ms (prevalent Broca's activation). Data showed that there was a good consistence between the LIs and both fMRI and Edinburgh Handedness Inventory (80%). In particular the Wernicke activation showed to be more appropriate for the LI calculation. Our results showed that MEG can be considered a reliable and non-invasive alternative to the Wada test.

101. Functional changes of cortical motor circuits after piano training in adults: TMS and EEG evidence – E. Houdayer, M. Corsi, A. Nuara, S. Zanini, R. Gatti, G. Comi, L. Leocani (Milano)

We aimed to study short-term effects of keyboard training in music-naive subjects on motor cortex activity and interhemispheric interactions, using electroencephalography and transcranial magnetic stimulation (TMS). Twelve subjects underwent, before and after a two week-piano training: (1) hand-motor function tests: Jamar, grip and nine-hole peg tests (NHPT); (2) electroencephalography, evaluating the mu rhythm task-related desynchronization (TRD) during keyboard performance, and (3) TMS, targeting bilateral abductor pollicis brevis (APB) and abductor digiti minimi (ADM), to obtain duration and area of ipsilateral silent periods (ISP). We included ten controls who also underwent these measurements twice, without training. Trained subjects improved keyboard performance and left-hand NHPT scores. Pre-training, ISP durations were asymmetrical (left ISP > right ISP). Post-training, right ISP_{APB} increased, leading to symmetrical ISP_{APB}. Mu TRD during bimanual performance also became symmetric, more focal and of lower amplitude than in pre-training, owing to decreased activity over ventral premotor cortices. These bilateral modifications correlated with keyboard performance and NHPT scores. No performance or neurophysiological changes were evidenced in controls. A 10-day piano-training was associated with rebalanced interhemispheric interactions both at rest and during motor activation. Piano training, in a short timeframe, may reshape local and inter-hemispheric motor cortical circuits.

102. Enhanced cognitive control in healthy aging revealed by increased prefrontal bioelectrical activity to the Stroop task – N. Amato, A. Nossa, G. Magnani, A. Martins-Silva, V. Martinelli, G. Comi, L. Leocani (Milano)

Healthy aging is associated with processing slowing, reduced executive functions and reduced efficiency of inhibitory mechanisms. Aim of this study was to investigate the effects of aging on bioelectrical activity and processing speed to Stroop test, assessing frontal function. 23 younger and 19 older healthy subjects were included. Event-related potentials-ERPs were recorded with 29-channels during covert Stroop task performance, consisting in mental discrimination between congruent and incongruent colour names written in different colours. Manual reaction times (RTs) to the same stimuli were recorded separately. Group effects on RTs and ERPs latency were analysed using statistical multivariate analysis and ERPs source analysis

was performed using low resolution brain electromagnetic tomography (LORETA). Compared with the younger group, older subjects had significantly slower RTs, but not decreased accuracy; significantly delayed ERP late processing components with increased prefrontal source activation, but normal early afferent components. In conclusion, healthy aging mainly impacts higher order processing rather than generalized visuomotor speed. Increased prefrontal activity suggests enhanced compensatory cognitive control or impaired intracortical inhibitory mechanisms.

103. Reward Sensitivity and “unbalance” cortical effect as a biomarker of new addictions. A multi-method study - R. Finocchiaro, A. Pecoraro, M. Balconi (Milano)

The present study explored the effect of cortical lateralisation activity during the decisional process in a gambling context. It is assumed that increasing of the left DLPFC activity and personality trait make subjects' strategies more disadvantageous and “gambling” during an online game. Twenty-one subjects were tested using the IGT and GO/noGo task while the EEG was registered and alpha-band modulation was considered. Secondly, the Behavioral Activation System (BAS)/Behavioral Inhibition System (BIS) scale was used to test the effect of reward sensitivity. Moreover, metacognitive questionnaire was applied. It was found that high-BAS subjects increased their tendency to opt in favour of the immediate reward rather than the long-term option, while a significant increasing of the left-hemisphere activation was found in response to immediate reward choices compared to low-BAS subjects. Finally, they tended to have difficulties to inhibit the automatic response, and they showed dysfunction of metacognitive abilities. A reward bias effect was supposed to explain both the bad strategy and the unbalanced hemispheric activation for high-BAS subjects. These findings could have important repercussions in the social context for the prevention of dysfunctional behaviours that affect compulsive disorders like new forms of addiction.

104. Resting lateralized activity (fNIRS) predicts the cortical response and appraisal of emotions – M.E. Vanutelli, E. Grippa (Milano)

The present study explored the effect of lateralized left-right resting brain activity on prefrontal cortical responsiveness to emotional cues and on the explicit appraisal of emotions based on their valence. Indeed subjective response to different emotional stimulus should be predicted by brain resting activity and should be lateralized and valence-related (positive vs. negative valence). Hemodynamic measure was considered (functional Near-Infrared Spectroscopy, fNIRS). NIRS resting activity and brain response to emotional cues were registered when subjects viewed emotional positive vs. negative stimuli (IAPS). LIR (lateralized Index Response) during resting state, LI (Lateralized Index) during emotional processing and SAM rating were considered. Regression analysis showed the significant predictive effect of resting activity (more left or right lateralized) on both brain response and appraisal of emotional cues based on stimulus valence. Moreover, significant effects were found as a function of valence (more right response to negative stimuli; more left response to positive stimuli) during emotion processing.

Therefore resting state may be considered a predictive marker of the successive cortical responsiveness and appraisal of emotions.

105. Hemodynamic (fNIRS), electrophysiological (EEG) and autonomic responses to affective pictures: a multi-method approach to the study of emotions - M.E. Vanutelli, E. Grippa, M. Balconi (Milano)

The activation of the prefrontal cortex during affective picture processing has been extensively studied in its temporal (by EEG), spatial (by neuroimaging studies) and peripheral (by autonomic system measures) features, even if little is known about the relation between neural measures, and between cortical and psychophysiological ones. Nonetheless emotions and their multilevel processing need to be explored by means of a multi-method approach. The aim of the present study was to examine emotional processing in healthy adults, instructed to look at affective (positive and negative) IAPS pictures during simultaneous hemodynamic (near-infrared spectroscopy, fNIRS), EEG and autonomic activity recording. Twenty subjects participated at the experiment. Stimuli were presented for 6 s in a randomized order, with 12 s inter-stimulus interval. Our main results indicated a differential involvement of prefrontal areas (dorsolateral prefrontal cortex, DLPFC) according to the valence of the stimulus and a relevant lateralization effect, with negative pictures inducing increased oxygenated hemoglobin (O₂Hb) and increased theta and delta activity (frequency band analysis) in the right hemisphere. Also, an increased systemic skin conductance response (SCR) emerged. Finally, an intrinsic relation was found and discussed between these three different levels.

106. Parietal cortex involvement in visual perceptual learning: a rTMS investigation - F. Giovannelli, M. Bartolucci, A. Borgheresi, D. Battista, E. Del Sordo, G. Zaccara, M.P. Viggiano, M. Cincotta (Firenze)

Practice-induced visual perceptual learning is thought to reflect the plasticity of sensory brain regions. The hypothesis that changes in early visual areas may depend on top-down modulation from higher level brain regions by attentional mechanisms is still debated. We used a causal approach by repetitive transcranial magnetic stimulation (rTMS) to evaluate the role of primary visual cortex (V1) and posterior parietal cortex (PPC) in visual perceptual learning. Twelve healthy volunteers performed a forced-choice orientation discrimination task of gabor patches (consisting of 500 trials in five blocks) without any intervention or immediately after a conditioning inhibitory 1-Hz rTMS protocol delivered over the V1, the right PPC, and the vertex (control area), in four different days. Conditioning inhibition by 1-Hz rTMS over the V1 produced an overall worsening of the performance accuracy but no effect in the learning rate, as measured by the slope of the learning curve. The learning rate was lower after right PPC inhibition compared to the other conditions when evaluated during the first two blocks (200 trials) where occurred most of the learning. These preliminary findings suggest that higher level brain regions may be involved in the mechanisms underlying perceptual learning.

107. Intraoperative Neurophysiologic Monitoring in 145 Surgical Treatments for Scoliosis - A. Borio,

**D. Milani, S. Marmolino, M. Mogno,
D. Serpella, P. Costa, A. Thiery (Torino)**

Post-operative sensory-motor outcome is related to intraoperative surgical or vascular complications. Intraoperative Neurophysiologic Monitoring (IONM) identifies changes to allow quick correction of the causes before neurological damages. The aim of the study is to assess the significance of IONM during scoliosis surgery, in particular for evaluating the relevance of motor evoked potential. 145 patients in TIVA/TCI anaesthesia were monitored through motor evoked potentials derived by upper and lower limbs' muscles (mMEPs) and Somatosensory Evoked Potentials derived from Erb-point and scalp by Median and Posterior Tibial nerve stimulation (SEPs). 94,5% of patients were recordable, while 5,5% presented no basal mMEPs and/or SEPs for previous pathologies and were non-elected. 2% had abortion of mMEPs for anaesthetic plane. 5,5% presented fleeting alteration of peripheral responses from Erb-point during surgery. 6% suffered of transitory modification of neurophysiological parameters: 100% of the alterations hit the mMEPs and just 22,2% the SEPs but anyone had only SEPs modifications in preserved mMEPs. Intraoperative combined SEPs and mMEPs monitoring is a safe, reliable and sensitive method to detect and reduce intraoperative injury to the spinal cord during scoliosis surgery, in particular, mMEPs are elective for early intraoperative detection of anterior medullar ischemia.

108. Reliability of phase reversal of somatosensory evoked potentials and their utility in the localisation of the sensorimotor cortex during surgery for central brain tumours – L. Caldana, E. Barensi, C. Tamborino, M. Polastri, R. De Gennaro, E. Gastaldo, R. Quatralo (Venezia Mestre)

To determine the reliability of intraoperative monitoring in neurosurgical operations using phase reversal of somatosensory evoked potentials (SEPs) and to examine the effect of tumour masses in the rolandic area on the waveform characteristics and feasibility of SEP. In the last 2 years, in 26 patients with tumours of the sensori-motor region, SEP phase reversal of N20-P20 were recorded from the exposed cortex, using a strip electrode. The intraoperative phase reversal of SEP was successful in 65,3% of patients with various morphologic characteristics results. In 11,5% of the patients N20 wasn't recorded, plus in 3,9% the typical phase inversion was questionable or missing, 30,8% of the cases. In those patients with clear localization of the central sulcus, it was possible to obtain motor evoked potentials in 89% of the cases, with maximal signal amplitude from arm and hand; on the other side, in patients where recording of a cortical potential inversion failed, only 50% showed clearly monitorable motor responses. The SEP phase reversal of N20-P20 is a simple, feasible and reliable technique, but it is not always clearly recognizable, in these latter cases the motor monitoring is frequently not easy through the strip electrodes.

109. Laser Evoked potentials and skin biopsy to evaluate small nerve fiber dysfunction in Fabry disease: a preliminary study - E. Pagliarani, A. Incensi, V.A. Donadio, V. Di Stasi, R. Liguori (Bologna)

Fabry's disease (FD) is caused by an X-linked mutation, and a characteristic feature is a severe loss of small myelinated fibers (AA) and small unmyelinated fibers (C) shown by skin biopsy. However, the pathophysiological mechanisms underlying the disease are still largely unknown. We recruited 3 patients with previously diagnosed Fabry's disease. The specific aim of this study is to verify a possible correlation between laser evoked potentials and skin biopsy to diagnose small nerve fiber involvement in these patients. Two patients showed abnormal skin biopsy which disclosed a somatic and autonomic small fiber neuropathy and altered LEPs with increased latencies of N2-P2 and N1 cortical responses (or absence), involving both AA fibers' responses (hand, foot and trigeminal nerve) and C-fiber responses. The third patient showed LEPs and skin biopsy normal findings. Our data demonstrated a good concordance between LEP and skin biopsy in evaluating small nerve fiber loss in FD. However these data should be considered preliminary and a larger number of patients must be recruited before to draw any definite conclusion.

110. Tongue's motor evoked potentials in the diagnosis of Primary Lateral Sclerosis (PLS): Preliminary report - L. Parenti, T. Bocci, D. Barlosci, B. Vannini, E. Giorli, A. Di Rollo, S. Mazzucchi, F. Sartucci (Pisa)

Primary Lateral Sclerosis (PLS) is an adult-onset neurodegenerative disorder due to a selective loss of precentral pyramidal neurons. Our purpose was to evaluate preferential impairment of pyramidal tract to bulbar muscles in patients with PLS and identify a valuable electrophysiological method to help clinicians in the differential diagnosis from Amyotrophic Lateral Sclerosis (ALS). We recorded Motor Evoked Potentials (MEPs) from tongue and anterior tibialis muscles in six patients with PLS and compared the results, in terms of Central Motor Conduction Time (CMCT), amplitude of MEPs and duration of controlateral silent period (cSP), with those obtained both from ten age-matched healthy volunteers and ten patients affected by ALS. For lower limbs, CMCT resulted significantly increased in PLS and ALS samples compared with healthy subjects ($p < 0.01$); we did not disclose any difference between ALS and PLS groups ($p = 0.417$). Instead for tongue's recordings, CMCT, absolute amplitude of MEPs and cSP were significantly altered in PLS patients towards both ALS patients and healthy volunteers. Altogether tongue's MEPs are selectively impaired in PLS. This technique could be helpful for the diagnosis of PLS and to differentiate patients with PLS from those affected by upper motor neuron-predominant variants of ALS.

111. Intraoperative Neurophysiological Monitoring of Corticobulbar Muscle Motor Evoked Potentials in Children Younger than 2 Years - V. Tramontano, C. Arcaro, F. Basaldella, B. Masotto, A. Bricolo, G. Squintani, F. Sala (Verona)

Corticobulbar muscle motor evoked potentials (CBT-mMEPs) monitoring is usually reported for the VII cranial nerve (CN) but rarely for the IX/X and XII CN, and its application is anecdotal in young children. We present three cases of children younger than 2 years operated on for brainstem tumour, with continuous monitoring of lower CN CBT-mMEPs. CBT-mMEPs were elicited by transcranial

electrical stimulation at C3/Cz and C4/Cz using a train of 4 stimuli (ISI 2 ms, duration 0.5ms each, at 1 Hz and intensity up to 200 mA). Recording hook-wire electrodes were placed in pharyngeal and hypoglossal muscles for the IX/X and XII CN respectively. In all patients CBT-mMEPs were stable throughout the entire surgical procedure with no changes in threshold intensity. Post-operatively, none of the children experienced significant tongue palsy or dysphagia/dysphonia. Therefore three true negative cases were observed. CBT-mMEPs of the lower CN is not of widespread use; in particular, there is virtually no report on the use of this technique in very young children where the incomplete myelination of motor pathways may impair a successful monitoring under general anaesthesia. CBT-mMEPs for the IX/X and XII CN is feasible and reliable even in children younger than 2 years.

112.Hmax/Mmax ratio and H-reflex recovery curve in patients affected by Multiple Sclerosis and Spasticity – L. Alessandrini, F. Donato, M. Turri, S. Romito, G. Moretto, G. Squintani (Verona, Bolzano)

Spasticity is classically defined as an increase of the velocity dependent stretch reflex and the H-reflex (HR) is commonly used to study the excitability of spinal motor circuitry. Some features of upper neuron syndrome like spasticity are associated with H-reflex alterations and different patterns of HR abnormalities have been reported. However, the simple evaluation of the soleus HR amplitude and Hmax/Mmax ratio may lack clinical and physiological relevance when approaching spasticity. We studied HR stimulating tibial nerve at popliteal fossa and recording at soleus muscle bilaterally in 16 subjects with Multiple Sclerosis (MS) and spasticity. Hmax/Mmax, recovery cycle (HRC) of HR with ISI ranging from 5 to 1000 ms were detected and results were compared with age-sex- matched controls. HRS was increased significantly in MS subjects at ISI 500 ms compared to healthy subjects. No difference was detected regarding H/M ratio. Our data demonstrated that HRC is more sensitive than Hmax/Mmax ratio in MS patients affected by spasticity and may represent the neurophysiological correlate of spinal inhibitory interneurons and descending pathways impairment in MS patients with spasticity. These findings could serve as electrophysiological tool to assess spasticity and monitor efficacy of therapeutic interventions.

113.Spinal Direct Current Stimulation modulates short intracortical inhibition - D. Barloscio, T. Bocci, M. Bartolotta, L. Parenti, B. Vannini, A. Di Rollo, F. Sartucci (Pisa)

Transcutaneous spinal Direct Current Stimulation (tsDCS) is a new and safe technique for modulating spinal cord excitability. We evaluated healthy subjects before (T0) and at different intervals (T1 and T2) after anodal, cathodal and sham tsDCS (20', 2.0 mA) applied over the thoracic spinal cord (T10-T12). We assessed changes in cortical Silent Period (cSP), paired-pulse short intracortical inhibition (SICI, interstimulus interval, ISI = 3 ms) and intracortical facilitation (ICF, ISI =10 ms). Motor Evoked Potentials (MEPs) were recorded from first digital interosseus (FDI) and tibialis anterior (TA) muscles. Cathodal tsDCS increased MEP amplitudes at ISI of 3 ms, while anodal one elicited opposite effects (FDI: $p = 0.0023$;

TA: $p = 0.0004$); conversely, tsDCS left MEP amplitudes unchanged at ISI of 10 ms (FDI: $p = 0.39$; TA: $p = 0.45$). No significant change in cSP duration was found from upper ($p = 0.81$) and lower limb ($p = 0.33$). tsDCS modulates inhibitory GABA(A)ergic drive, as assessed by SICI, without interfering with cSP and ICF. tsDCS may be helpful to modulate spinal drive through non spinal mechanisms. tsDCS could represent an early rehabilitation strategy in patients with acute brain lesions and in the treatment of spinal diseases or pain syndromes.

114.An unexpected target of Spinal Direct Current Stimulation: interhemispheric connectivity in humans - B. Vannini, T. Bocci, M. Caleo, M. Vergari, S. Rossi, A. Priori, M.J.M. Hensgens, F. Sartucci (Pisa, Milano, Siena)

Transcutaneous spinal Direct Current Stimulation (tsDCS) is a noninvasive technique based on the application of weak currents over spinal cord. We studied the effects of tsDCS on interhemispheric connectivity and visual processing by evaluating changes in ipsilateral Silent Period (iSP), Transcallosal Conduction Time (TCT) and hemifield Visual Evoked Potentials (hVEPs), before and at different intervals following sham, anodal and cathodal tsDCS (T10-T12 level, 2.0 mA, 20'). Motor Evoked Potentials (MEPs) were recorded from abductor pollicis brevis (APB), abductor hallucis (AH) and deltoid muscles. hVEPs were recorded bilaterally by reversal of a horizontal square wave grating. Anodal tsDCS increased TCT ($p < 0.001$) and the interhemispheric delay for both the main VEP components (N1: $p=0.0003$; P1: $p < 0.0001$), dampening iSP duration (APB: $p < 0.0001$; AH: $p = 0.0005$; deltoid: $p < 0.0001$), while cathodal stimulation elicited opposite effects ($p < 0.0001$). tsDCS would be a promising therapeutic tool in managing a number of human diseases characterized by an impaired interhemispheric processing, with anodal stimulation leading to a functional disconnection between hemispheres. It could also be helpful as an early rehabilitation strategy in patients with acute brain lesions, when other non-invasive brain stimulation techniques are not indicated due to safety concerns.

115.Cathodal transcutaneous spinal direct current stimulation (tsDCS) improves motor unit recruitment in healthy subjects - B. Vannini, T. Bocci, A. di Rollo, L. Parenti, D. Barloscio, M. Vergari, A. Priori, F. Sartucci (Pisa, Milano)

Transcutaneous spinal direct current stimulation (tsDCS) is a new promising technique for modulating spinal cord function in humans. However, its effects on corticospinal pathways and lower motorneuron excitability are poorly understood. We studied the effects of tsDCS on motor unit recruitment by evaluating changes in motor unit number (MUNE) and peripheral silent period (PSP) after sham (s-tsDCS), anodal (a-tsDCS) and cathodal (c-tsDCS) tsDCS applied either over the cervical or the lower thoracic spinal cord in healthy subjects. We used the multipoint incremental technique recording from either the ulnar nerve innervated abductor digiti minimi (ADM) or the median nerve innervated abductor pollicis brevis (APB) muscle. c-tsDCS dramatically increases MUNE values, while sham and anodal polarization have no significant effects (APB: $F_{(4,99)} = 26.4$, $p < 0.001$; ADM: $F_{(4,99)} = 22.1$, $p < 0.0001$). At the

same time, c-tsDCS dampened PSP respect to sham and anodal conditions ($p < 0.0001$). Interestingly, also thoracic c-tsDCS significantly improved motor unit recruitment compared with both s-tsDCS and a-tsDCS (APB: $F_{(4,99)} = 20.1$, $p < 0.0001$; ADM: $F_{(4,99)} = 16.6$, $p < 0.0001$). Our data in healthy subjects suggest that tsDCS, possibly also through supraspinal effects, could provide a novel therapeutic tool in managing pathologies characterized by reduced motor unit recruitment.

116. Atypical AIDP with predominantly sensory involvement and increased duration of SAPs - F. Basaldella, F. Donato, C. Zuco, G. Moretto, S. Ottaviani, T. Bovi, S. Romito, G.M. Squintani (Verona)

The diagnosis of AIDP is based on clinical, electrophysiologic, and CSF data. Increased duration of cMAPs has been recently considered in the diagnosis of CIDP. However, the contribute of sensory neurography has not been well characterized. We describe a case of a 26 years old woman who came to our attention for oral and upper limb tingling which occurred ten days after flu-like symptoms and progressively extended to lower limbs. A first EMG revealed an increased distal latency of motor nerves and interestingly, a significantly increased duration (total and negative) of SAPs of median and ulnar nerves bilaterally. At admission, neurological examination revealed diffuse hypopallesthesia in the extremities and absence of OT reflexes in lower limbs. CSF examination revealed a mild hyperproteinorrachia (0,74 g/l, normal value $< 0,45$). The patient was treated with iv-IgG with clinical benefit. The increased duration of SAPs is dependent on distal temporal dispersion and may be considered a sign of focal distal demyelination in sensory nerves. In conclusion, the duration of the distal SAPs may be considered an early and specific electrophysiologic feature of distal demyelination in sensory nerves, and may be relevant in patients with acute/chronic disimmune neuropathies with prevailing sensory deficits.

117. Phrenic nerve palsy in pediatric heart surgery: the neurophysiological contribution in follow up and decision making - A. Segatti, L. Alessandrini, S. Zanelli, P.A. Santuz, P. Biban, G.B. Luciani, G. Squintani, F. Donato, S. Romito (Verona)

Phrenic nerve palsy after cardiac surgery in infants is a known adverse event. The resulting diaphragmatic dysfunction can lead to ventilatory support weaning failure and other respiratory complications. Diaphragmatic palsy can be resolved with plication, but the timing of the procedure is still debated. The aims of this study were to demonstrate the possibility of a temporary phrenic nerve paralysis, longer than reported in other works, and to compare ultrasounds and electroneurographic findings. 28 infants under one year of age, with different heart malformations, were studied both by phrenic nerve conduction study (pnNCV) and by diaphragmatic ultrasonography, before heart surgery and periodically in the first 4 postoperative months. 11 subjects showed postsurgical phrenic nerve palsy, 5 of which were permanent, with electrophysiological demonstration of prolongation of diaphragmatic action potential (DAP) latency and/or fall in DAP amplitude. A consensual

diaphragmatic hypomotility or immobility was found echographically. A correlation seemed to be found between the amplitude of the DAP and both muscular motility at ultrasound and ventilatory dysfunction. We found that both neurophysiology and echography represent important tools in the respiratory follow-up after heart surgery in children, and considerations regarding the timing of the possible recovery of a phrenic neuropathy are discussed.

118. Appearance of Muscle Motor Evoked Potentials After Untethering of the Spinal Cord - A. Nuti, C. Arcaro, V. Tramontano, F. Basaldella, G. Squintani, F. Sala (Verona)

To describe the intraoperative appearance or improvement of lower extremity muscle motor evoked potentials (mMEPs) during tethered cord surgery for spinal dysraphisms. A 3-year old male child with dermal sinus and dorsal lipoma, and a 30-year old male with a sacral lipoma were operated on for untethering the cord under Intraoperative neurophysiological monitoring (IONM) surveillance. The IONM protocol included: Transcranially elicited mMEPs, Posterior Tibial Nerve Somatosensory Evoked Potentials (TPN-SSEPs), recording of the bulbo-cavernous reflex (BCR), and mapping of the cauda equina. Recording electrodes were inserted bilaterally in the Anterior Tibialis (AT), Gastrocnemius (GR), Abductor Hallucis Brevis (AHB), and the anal sphincter muscles (ASM). In the child, at baseline only the right AHB mMEP was elicitable at 200 mA. Following cord untethering a progressive reappearance of the left GR, AT and AHB mMEP was observed starting about 10 min. after the cord was completely untethered. In the adult case, all mMEPs were present at baselines but, in spite of unchanged stimulation intensity, after untethering the cord mMEP amplitude increased significantly in the left AHB and GR muscles. The anesthesiological regimen was stable throughout the procedures. IONM may detect acute improvement of mMEPs during cord untethering, possibly due to better oxidative metabolism in the conus.

119. Multiple Sclerosis presenting in a patient affected by peripheral Multifocal Motor Neuropathy - L. Gallicchio, V.R. Recchia, E. D'Errico, M. Gatto, A. Petruzzellis, F. Tamma (Acquaviva delle Fonti)

Few cases of Multiple Sclerosis (MS) and Multifocal Motor Neuropathy (MMN) occurring in the same patient are described. We report a 43 year old woman who presented on April 2010 with progressive upper limbs weakness and paresthesia; furthermore few months later she showed lower limbs involvement. Brain and cervical spinal cord Magnetic Resonance (MRI) were no indicative of central nervous system damage; ENG revealed peripheral multifocal demyelinating neuropathy; CSF examination detected albumin/citologic dissociation. She underwent several cycles of intravenous immunoglobulin treatments, with symptomatological improvement. On May 2014 she presented transitory diplopia for twenty days; three months later she presented optic neuritis in right eye. The MRI control revealed right optical nerve neuritis and left frontal cortex lesion indicative of central demyelinating disease. We suggest that the central and the peripheral lesions may be two different aspects of the same demyelinating process.