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57° Congresso Nazionale Società di Neurofisiologia Clinica **Riassunti**

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57° CONGRESSO NAZIONALE

Società Italiana Neurofisiologia Clinica SINC

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57° CONGRESSO NAZIONALE

SOCIETA' ITALIANA DI NEUROFISIOLOGIA CLINICA

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RIASSUNTI

EEG

COMUNICAZIONI ORALI

ABNORMAL HYPOTHALAMIC OSCILLATIONS IN HUMAN PATHOLOGICAL AGGRESSIVENESS

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Aim of the study

The neurophysiological basis of aggressiveness are still largely unknown in humans. Despite ample evidence confirming the hypothalamus as a pivotal structure in human aggressiveness, no research has investigated intrinsic pathophysiological abnormalities at hypothalamic level in the neural network circuit mediating aggressiveness.

Methods

To assess whether a specific neural activity pattern underlies pathological human aggressiveness, we compared hypothalamic local field potentials (LFP) recorded in two patients undergoing deep brain stimulation (DBS) surgery: in one patient to treat pathological aggressiveness and in the other, a behaviourally normal person considered as a control, to treat cluster headache. After stereotactic macroelectrode implant in the posterior hypothalamus (pHyp), LFPs were bipolarly recorded intra-operatively.

Results

Power spectral density for pHyp LFP recorded in the aggressive patient showed increased low-frequency power (2-7 Hz) and decreased alpha power (8-12 Hz) compared to control patient (mean±standard deviation: 39.60±9.07% vs 11.78 ±4.11% $p<0.005$; 26.16±8.98% vs 80.35±4.89%; $p<0.005$; one way ANOVA). Postoperative follow-up at 3 months showed that after DBS one patient manifested less aggressive behaviour and the other experienced fewer cluster headaches.

Conclusions

The abnormal hypothalamic activity in the aggressive patient reflects a neural network disinhibition in the brain circuit mediating aggressiveness. If so, then our findings suggest that hypothalamic DBS improves drug-resistant aggressive behaviour by controlling the abnormal oscillations in the hypothalamus.

RESTING STATE CORTICAL ELECTROENCEPHALOGRAPHIC RHYTHMS ARE RELATED TO GRAY MATTER VOLUME IN SUBJECTS WITH MILD COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE

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Cortical gray matter volume and electroencephalographic rhythms are typically abnormal in subjects with amnesic mild cognitive impairment (MCI) and Alzheimer's disease (AD). Here we tested the hypothesis that in the continuum of MCI and AD subjects, abnormalities of the EEG rhythms are a functional reflection of cortical atrophy across the disease. Eyes-closed resting state EEG data were recorded (10-20montage system) in 57 healthy elderly (Nold), 102 amnesic MCI, and 108 AD patients. Cortical gray matter volume was indexed by magnetic resonance imaging recorded in the MCI and AD subjects according to Alzheimer's disease neuroimaging initiative project (http://www.adni-info.org/). EEG rhythms of interest were delta (2-4Hz), theta (4-8Hz), alpha1 (8-10.5Hz), alpha2 (10.5-13Hz), beta1 (13-20Hz), beta2 (20-30Hz) and gamma (30-40Hz). EEG rhythms sources were evaluated by LORETA. Compared with Nold, MCI showed a decrease in amplitude of alpha1 sources. With respect to Nold and MCI, the AD showed an amplitude increase of delta sources, along with a strong amplitude reduction of alpha1 sources. In MCI and AD subjects as a whole group, the lower the cortical gray matter volume, the higher the delta sources, the lower the alpha1 sources. In general, the better the score to cognitive tests (i.e. memory, executive functions, verbal fluidity), the higher the gray matter volume, the lower the pathological delta sources, and the higher the alpha sources. These results suggest that in amnesic MCI and AD subjects, abnormalities of EEG rhythms are not epiphenomena but are strictly related to neurodegeneration (i.e. atrophy of cortical gray matter) and cognition.

ACTION-RELATED SEMANTIC CONTENT AND NEGATION POLARITY MODULATE MOTOR AREAS DURING SENTENCE READING: A MU EVENT-RELATED DESYNCHRONIZATION STUDY

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Objective

Our study evaluated motor cortex involvement in reading sentences referring to hand-actions. We aimed at defining whether sentential negation polarity would modulate motor cortex activation using the event-related desynchronization (ERD) analysis of the mu rhythm.

Methods

Eleven healthy volunteers performed a reading task involving 160 sentences (80 affirmative: 40 hand-related, 40 abstract; 80 negative: 40 hand-related, 40 abstract). After reading each sentence, subjects had to decide whether the verb was high or low frequency in Italian. Electroencephalographic (EEG) activity was recorded with 32 surface electrodes and mu ERD analyses were performed for each subject.

Results

Hand-action related sentences induced a greater mu ERD over the left premotor and motor hand areas compared to abstract sentences. Mu ERD was greater and temporally delayed when the hand-related verbs were presented at the negative vs. affirmative form.

Conclusions

Motor areas were activated during sentences referring to hand actions, according to the “embodied semantic” theory of language understanding. Motor cortex activation was larger for negative than affirmative motor sentences. The latter finding is compatible with the hypothesis that comprehension might be more demanding for negation understanding.

QEEG CORRELATES OF CLINICAL PARAMETERS IN PARKINSON DISEASE

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Objective

To search for quantitative EEG (qEEG) correlates of clinical features in Parkinson disease (PD).

Methods

Twenty- seven PD patients (males:22; age 62±7 years), free of antiparkinson medication at least for 12 hours, underwent 5 min eye-closed, resting 30-channel EEG recording. Clinical assessment was performed using Hohen & Yahr (H&Y) and the motor Unified Parkinson's Disease Rating Scale (UPDRSIII). UPDRS-partial scores were obtained considering axial involvement (AS), tremor (TS) and rigidity (RS). Artifacts-free epochs were selected and subjected to sLORETA analysis for measuring CSD in selected Regions of interests. The chosen ROIs included: PCC(BA31), Prefrontal cortex(BA9), Premotor cortex (BA6), motor cortex(BA4). For BA4 and BA6 only the values of more affected hemispheres were used. Then, CSD values in ROIs were correlated with clinical values using Spearman's correlation test. Subsequently, partial correlation with factor age was applied and only correlations remaining significant are reported below.

Results

H&Y and AS positively correlated with theta CSD in BA4 and BA6, delta and theta CSD in BA31(BL), BA9(BL). Further subdivision of group (according to laterality of disease) revealed that alpha2 CSD in BA4 correlated negatively with Rigidity Subscore.

Conclusions

PD-cardinal features share different EEG-correlates, probably reflecting different pathophysiological substrates. Theta and delta correlations might reflect thalamo-cortical functioning, while correlation between alpha and rigidity might be based on cerebello-thalamo-cortical functioning. These results may suggest that qEEG might be used for objective assessment in PD and may be worth validation as markers of treatment response or disease monitoring.

PROGNOSTIC POTENTIAL OF CONTRALESIONAL EEG POWER INCREASE IS MEDIATED BY INTERHEMISPHERIC DISCONNECTION IN ACUTE STROKE

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Background and purpose

Despite similar clinical onset, recovery from stroke can be largely variable. We searched for electrophysiological prognostic indices, believing that they can guide future neuromodulation treatments boosting clinical recovery.

Methods

19-channels resting electroencephalogram was collected in 42 patients after 4-10 days (t0) from a unilateral ischemic stroke and 20 controls. National Health Institute Stroke Scale(NIHSS) was collected at t0 and 6 months later (t1). Standard spectral band powers and interhemispheric coherences between homologous regions were calculated in both hemispheres.

Results

Total spectral, delta and theta band powers were higher in patients than in controls and directly correlated with NIHSSt0 in both hemispheres. A linear regression model including each electroencephalogram patient's variable differing from those of controls and correlating with effective recovery [ER=(NIHSSt0–NIHSSt1)/(NIHSSt0–NIHSS in healthy conditions)] showed contralesional delta power as the only valid predictor of ER. A further regression model including also NIHSSt0 confirmed that contralesional delta power can add prognostic information to acute clinical impairment. Contralesional delta activity was best explained by interhemispheric functional coupling reduction in addition to the increasing ipsilesional delta activity.

Conclusions

Contralesional electroencephalographic delta activity retains relevant prognostic information as marker of interhemispheric functional uncoupling. Present results point to the interhemispheric interplay as a decisive target in setting up enriched rehabilitation.

ARTIFACTS EEG DURING DENSE ARRAY EEG (256 CHANNELS) ACQUISITIONS: A COMPARISON WITH THE 10-20 STANDARD SYSTEM

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Purpose

In order to better differentiate between what is genuine neuronal activity and what is not, we deploye a method to better understand the topographic field distribution of EEG artifacts i.e.the 256 channel EEG. Because of the profuse number of zygomatic, sovraorbitary, upper cervical and upper margin jaw electrodes, we can better distinguish the artifacts' sources. We focus on a Topo Plot Map montage i.e. a projection of each electrode's activity on a scalp model.

Methods

We measured first the head circumference finding the vertex (Cz, 10-20 system).

The applied net arranges the electrodes across the surface of head and face, with an interelectrode distance in the range of 20 to 25 mm. Electrodes were located in a plastic pedestal with an Ag/Cl basis covered by little sponges, soaked in a physiological-potassium-shampoo solution for about 5 minutes.

The sampling rate was 250 Hz, interelectrode impedance below 100 Kohms, acquisition reference was at vertex, band pass filter 0.03-70 Hz, 7,5 MicronVolts sensitivity,50 Hz Notch filter avoiding noise interferences.

Results

Physiological artefacts were eye movements (horizontal and vertical blinking) with antero posterior topography, ballistogram with temporal topography, mouth movements and chewing with maximal activity over the zygomatic electrodes, occipital or temporal EMG activity. Non physiological artefacts were the electrolyte bridges, the digital filters artefacts, the 50 hz current artefact .Visual comparison for each of these artefacts was performed between bipolar 10-20 standard system montage and 256 Topo Plot Map, in order to define the recognition of field potential sources and topographic distribution.

NEUROGRAFIA - EMG

COMUNICAZIONI ORALI

EVALUATION OF CLINICAL AND NEUROPHYSIOLOGICAL CRITERIA IN THE DIAGNOSIS OF AMYOTROPHIC LATERAL SCLEROSIS

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Introduction

The Awaji Commission recently proposed a modification of the electrodiagnostic criteria for Amyotrophic Lateral Sclerosis (ALS), where neurophysiological evidence of lower motor neuron (LMN) involvement was considered equivalent to clinical.

Objective

To assess whether the Awaji recommendations could increase the diagnostic yield in ALS.

Methods

51 patients with ALS diagnosis according to the El Escorial criteria were investigated. Needle EMG studies were performed, following a standardized protocol, in at least two muscles of different root or spinal nerves, both in cervical and lumbosacral region, and in at least one muscle in the cranial region. Motor and sensory nerve conduction studies were performed in at least three nerves.

Results

On the basis of the Airlie House criteria, 21% of patients were categorized as definite ALS, 51% as probable, 10% as probable laboratory-supported (LS), 4% as possible and 14%, who had a pathogenic mutation, as clinically definite familial ALS-LS. On the basis of the Awaji recommendations, 43% patients were categorized as definite, 45% as probable and 12% as possible. When the Awaji criteria were used, among the 7 patients categorized definite familial ALS-LS, 4 were classified as probable, 1 as possible and 2 as definite. Using the Awaji criteria in combination with the Airlie House criteria, 57% of patients were categorized as definite.

Conclusion

The Awaji criteria increased the possibility to detect LMN dysfunction in patients with suspected ALS. The highest diagnostic yield was obtained by using the neurophysiological Awaji criteria in combination with those of Airlie House.

MONITORING AND PREDICTIVE ROLE OF COMPOUND MOTOR ACTION POTENTIAL (CMAP) IN AMYOTROPHIC LATERAL SCLEROSIS

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Amyotrophic lateral sclerosis is a degenerative disease involving upper and lower motor neurons, thus leading to progressive spasticity and weakness. Motor elettroneurography is a non invasive test to evaluate muscular action potential generated by supramaximal nerve stimulation (cMAP).

Purpose of this study is to relate reduction in cMAP amplitude to functional impairment in ALS patients.

We recruited 104 patients, 29 with bulbar, 75 with spinal onset. Patients were periodically visited every 3 months for one year; medial plantar, ulnar and frenic nerves were examined in each patient. ALSFRS-R scale was submitted and forced vital capacity was measured in each visit.

Statistical analysis showed a significant correlation between ALSFRS-R score reduction and cMAP reduction (visit2 vs visit1) measured in ulnar (p=0,02), plantar medial (p=0,035) and frenic (p=0,039) nerves. Correlation between ALSFRS-R and ulnar cMAP reduction was highly significant (p=0,001) in spinal group.

Moreover, frenic cMAP measured in the first visit was related to FVC measured three months later, following a logarithmic function (p=0,004; R=0,472).

All these data are demonstrating a key-role of cMAP examination in monitoring desease progression in ALS patients; frenic nerve cMAP assessment could be used as a 3 months FVC predictive factor.

A REAPPRAISAL OF F WAVE BY MEANS OF A COMPUTATIONAL MODEL OF SPINAL ALPHA-MOTONEURON

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Background

The F wave recording, a widely utilized neurophysiological test for gaining information on proximal nerve segments and excitability of spinal motoneurons, results from backfiring of antidromically activated anterior horn cells. Antidromically travelling action potentials following distal stimulation of motor fibres are seldom able to invade the soma of α-motoneurons in spinal cord, due to their passing through regions of high non-uniformity. When soma invasion occurs, a further smaller number of cells exhibit an efferent (orthodromic) backfiring, also known as recurrent discharge. Details of the electrophysiological interplay between adiacent regions of elevated non-uniformity (axon-soma junction), which are the basis of the recurrent discharge, are lacking. A computational neuron model of spinal α-motoneuron is developed aimed at elucidating these otherwise hardly testable phenomena.

Method

Conductance-based compartmental models of single cat spinal α-motoneurons were instantiated, according to morphological and biophysic data from previous in vivo and in silico studies. Both reduced and morphologically detailed neuron models were developed, along with the ability to modify different geom etric parameters across realistic ranges of values.

Results

Antidromic action potential invasion of the soma always implies a junctional delay at axon-soma transition. When the delay is long enough to go across the refractory period of the most proximal axonal regions a resurgent activation at initial segment/first nodes is able to start an efferent orthodromic action potential. Somatic sub-threshold depolarizations does not always have permissive effects on recurrent discharge.

Conclusions

The F wave test does not convey univocal information on α-motoneuron excitability.

ELECTROMYOGRAPHIC AND ULTRASONOGRAPHIC EVALUATION OF THE DIAPHRAGM IN PATIENTS WITH MYOTONIC DYSTROPHY: A NEW APPROACH IN THE ASSESSMENT OF DISORDER VENTILATORS IN THESE TWO DISEASES

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Introduction

Myotonic Dystrophy (DM) is the second most common form of adult muscular dystrophy. In DM muscle atrophy is combined with action myotonia and respiratory disorders such as dyspnea. Sleep apnea are particularly frequent in DM patients. To date there is only one report in the literature about the diaphragm muscle EMG activity in subjects with DM.

Method

We evaluated 7 patients with genetic diagnosis of DM (DM1). All patients were assessed by spirometry, hemogasanalysis, pulmonary assessment, polysomnography, phrenic nerve conduction study, EMG evaluation of diaphragmatic muscle with ultrasound approach (US) used to localize the point of needle insertion. Being an electrical phenomenon, myotonia has been well demonstrated by EMG examination.

Results

Comparing the EMG and polysomnographic data with US, we found that the patient with "central" type apnea had also myotonic disorders on EMG and US, while other patients who tested positive to the latter two tests did not have apnoic episodes of central type. The correlation with spirometry was rather different: of the six patients with abnormalities, four patients were positive both for EMG and US, while of the remaining two patients one was positive only for EMG and the other negative for both EMG and US.

Conclusion

We conclude that these two methods, EMG and US M-mode of the diaphragm, especially when combined, seem to be able to confirm the early diagnosis of possible onset of apnea, even before they occur in a significant way by polisomnography. in DM patients.

PROPOSAL OF ELECTRONEUROMYOGRAPHY AND MUSCLES ULTRASOUND COMBINED STUDY IN PRETERM NEWBORN: RELATIONSHIP BETWEEN TECHNIQUES TO EVALUATE THE MATURATION OF PERIPHERAL NERVOUS SYSTEM

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Background

it's a recent feature the combined use of electromyography and ultrasound to study Peripheral Nervous System (PNS). There's only one report about electroneurographic (ENG) and muscle-ultrasound (mUS) correlation in diabetic adults. No ENG-mUS correlated in newborn exists up-to-date.

Rational

To verify the feasibility of a combined-protocol to obtain information about neuro-muscular morphology and functionality and collect normative data to evaluate PNS development in preterm and term babies.

Materials-Methods

We propose to study combined ENG-mUS parameters in 15preterm babies with gestational age≥28weeks (study-group) with acquisitions in series from birth until term and in 15healthy term babies at birth (control-group) with just an acquisition. ENG:small-dimension disposable skin electrodes (0,7x1cm) located by Tibialis Anterior (TA) muscle, with belly-tendon montage, stimulation with a small-sized bipolar stimulator (anode-cathode 2mm tick with 10mm interelectrodic-distance), tailored to newborn. The electrical stimulus is delivered by caput fibulae (0,2ms duration; 20-25mA intensity). mUS:small-sized ultrasound probe (Frequency 11,3MHz, Gain 55, Compression 65, Depth 3cm) used to acquire two digital images positioning the probe above TA belly, with extended limb and 90° flexus foot.

Preliminary-Results

Up-to-date only 4term babies examined. Mean ENG parameters: 1,73ms Latency, 7,87mV Amplitude (p-p), 36,67µV/s Area (tot), 14,7ms Duration. Mean mUS parameters: 787,7mm higher TA diameter, 541,5mm diameter at higher Compound Muscular Action Potential. Every parameters will be statistically analyzed.

Conclusion

This ENG-mUS combined-study could be useful to evaluate PNS development in preterm babies during extra-uterine growth and the existence of prospective further information based on the association between muscular morphological (mUS) and functional (ENG) results.

"Cogito-ergo-mUS"

INTRAOPERATIVE BLINK REFLEX DURING CEREBELLOPONTINE ANGLE (CPA) SURGERIES: THE EXPERIENCE OF FERRARA

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Introduction

Facial nerve paresis is a frequently complication in the surgical approach of cerebellopontine angle tumors. For this reason, intraoperative neurophysiological monitoring of Facial nerve (FN) has become an integral part of CPA surgeries. In addition to direct electrical stimulation of the nerve, free-run electromyographic signal and facial motor evoked potential (FMEP), recently some authors (Deletis et al 2009) described a technique to elicit the blink reflex (BR) during anesthesia.

Objective

To investigate the feasibility of BR during IOM for CPA, its reliability and usefulness in predicting FN outcome.

Materials and Methods

15 pts (5 man, 10 women; mean age 60 y), affected by APC tumours were included. FN cMAP, BR and EMG were performed pre (preIOM), intra (IOM) and postoperatively (postIOM). During anesthesia we recorded EMG and BR continuously (BR in agreement with Deletis technique), CMAP before and after tumor removal, by stimulating the proximal portion of FN.

Results

BR was abnormal in 9/15 pts at preIOM. R1 component of BR was elicitable in 14/15 pts during IOM and remained stable in 9/14 pts; in one patient disappeared in spite of stimulation increase; different EMG patterns (A-train, bursts and other train-type activities) were recorded in 13/15 pts with various frequency. The patient who showed IOM BR disappereance and two of those with BR instabilty had a severe FN deficit at post IOM evaluation, despite mild EMG abnormal activity during IOM. The 9 pts with stable BR didn't show any FN deficit even if 4/9 had continuous EMG activities during IOM.

Conclusions

BR during anesthesia is an easy and reliable tecnique to monitoring facial nerve integrity. Stable IOM BR in our experience proved to be a good predictor of a postoperative outcome of FN function also in presence of preIOM reflex abnormalities or repetitive EMG discharges during IOM.

POTENZIALI EVOCATI

COMUNICAZIONI ORALI

CEREBRAL CORTICAL EXCITABILITY IS INCREASED IN PATIENTS WITH PAINFUL CHRONIC PANCREATITIS

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Abdominal pain is a key symptom in chronic pancreatitis (CP), but its underlying mechanisms are not yet completely understood. In many patients there is no pathology suitable for endoscopic or surgical interventions and increasing evidence indicates that central nervous system pain processing is abnormal in many of these patients.

The aim of the study was to compare changes in contact heat evoked potentials (CHEPs) following repetitive painful stimuli (habituation) between CP patients and healthy subjects. Fifteen patients with a diagnosis of CP and 15 healthy subjects were included. CHEPs were recorded from 64 scalp electrodes. Three consecutive sequences of 31 stimuli with interstimulus intervals varying randomly from 8 to 12 seconds were delivered to the epigastric area and to the right forearm. In all subjects, a vertex biphasic (negative–positive) complex (N2/P2) was recorded. In addition, a negative N1 potential in the temporal region and, at approximately the same latency, a positive P1 potential in the frontal region contralateral to the stimulation site were identifiable in all subjects. As compared to healthy subjects, CP patients showed a decreased CHEP amplitude habituation. This was most prominent after stimulation of the epigastric area, which shares spinal innervation with the pancreatic gland.

Our results suggest a segmental amplification of pain from the pancreatic gland, where increased neuronal excitability or impaired damping of pain signals results in an exaggerated cortical response.

LASER EVOKED POTENTIAL: ANALYSIS OF THE METHODOLOGY IN POST HERPETIC NEURALGIA

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Background

Selective activation and the contemporary recording of A delta and C fibres from Yap laser on the scalp is a new neurophysiological assessment, allowing the selective activation of the nociceptive system.

Objectives

To evaluate, in a sample of 26 patients affected by Herpes zooster (HZ), if the damage of the nociceptive system was related to post herptic nevralgia (PHN) development; secondly, to assess if the impairment of thermal pathway and PHN development are related as well.

Methods

Thirty-two patients were selected for the study, 26 were included in the study; 6 were excluded because of cognitive impairment. All 26 were submitted to LEP analysis at T0 (baseline) and T1 (after six months); we also monitored the clinical index between clinical thermal disease and the development of PHN.

Results

For patients with acute infection, the essential element concerning pain duration is evidenced by the presence or absence of an instrumental signal. There is total concordance between the absence of signal and pain duration. We have also noted a clinical concordance between the clinical thermal disease and the duration of pain, but without statistical significance (57 %).

Conclusions

Our results suggested a possible role of LEP for PHN prognosis estimation; indeed, most patients affected by acute HZ, with absence of instrumental LEP signal, had pain > 6 months. We also noted a discrete clinical concordance between the thermal pathway damage, the absence of instrumental signal and PHN development, but it lacks of statistical significance (57 % of the cases).

Further studies are needed to address this issue.

ANAL VERSUS PENILE OR CLITORAL PUDENDAL SOMATOSENSORY EVOKED POTENTIALS IN HEALTHY SUBJECTS

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Aims

Somatosensory evoked potentials (SEPs) of pudendal nerve represent an important tool for the evaluation of pelvic floor disorders affecting genitourinary or anal sensory innervations. The gender influence on response latencies has not been established yet. The aim of our study was to define normative data of penile/clitoral and anal pudendal SEPs.

Methods

The anal and penile/clitoral SEPs were recorded in a group of 72 male and female healthy subjects.

Pudendal SEPs were evoked through a bipolar surface electrode stimulating the clitoris or the base of the penis and the anal orifice. Cortical responses were recorded through cup electrodes fixed to the scalp. Latency of the first positive component (P1) was measured for statistical analysis.

Results

Cortical P1 responses were found, in female subjects, at mean latency of 36.48 msec (SD 3.21) and 37.03 (SD 2.64 msec) for clitoral and anal stimulation, respectively. In male subjects mean latency was of 40.41 msec (SD 3.63 msec) and 38.13 (SD 2.90 msec) for penile and anal stimulation. Two way mixed ANOVA showed a statistically significant main effect of stimulation site and gender and a significant interaction between these two variables.

Conclusions

Penile/clitoral and anal pudendal SEPs represent a simple and reproducible method to assess the functional integrity of the sensory pathways, that may provide valuable information in diagnosing disorders of urinary, bowel and sexual function. Gender-specific reference data must be obtained in each electrophysiological laboratory because of latency difference in anterior and posterior SEPs between males and females.

NEUROPHYSIOLOGICAL STUDY OF PELVIC FLOOR: NORMATIVE DATA OF SOMATOSENSORY EVOKED POTENTIALS AND SYMPATHETIC SKIN RESPONSE

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In the last few years we observed a progressive increase of sacral neurophysiological examination, due to greater ask of evaluation both in pelvic floor dysfunctions and in sacral neuromodulation implants.

In our laboratory the neurophysiological evaluation consist in Sacral Reflex (SR), pudendal somatosensory evoked potential (SEPs), sympathetic skin response (SSR), perineal muscles Electromyography (EMG); in some case motor evoked potential (MEP) can be evaluated. In each case we choose the combination of single tests in function of the clinical picture.

Since 2007 we have studied 124 non consecutive patients admitted to our department with normal clinical evaluation: 60 males and 64 females with age between 22-87 years (mean age 52).

To optimize our instrumental examination, we collected normal values of cortical P40 SEPs recorded by stimulation of different branches of pudendal nerve: penis/clitoris dorsal nerve (NDP-NDC), anal canal (AC) and urethral sphincter (US); furthermore we recorded SSR from right and left, perineal and perianal areas.

In order to detect any difference of latency's values of SEPs, we divided patients in two groups, by height and age, using, as cut off, 1.70 mt. and 60 y. Amplitude and latency of SSR were divided only according to age.

To define normal ranges we chose mean value ± 2 Standard Deviation both for SEPs and SSR.

Considering our results, we can affirm that there are no significant variations between values of several groups, for height and age, in SEPs and SSR.

SOMATOSENSORY EVOKED POTENTIALS RECORDED FROM THE HUMAN PEDUNCULOPONTINE TEGMENTAL NUCLEUS AREA: THEIR FEATURES AND THEIR GENERATORS

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Our aim was to categorize the various somatosensory evoked potential (SEP) components recorded from deep brain stimulation (DBS) leads implanted in the human Peduncolopontine Tegmental nucleus (PPTg).

Twenty-one patients suffering from parkinson disease underwent electrode implantation in the PPTg. After median nerve stimulation, SEPs were recorded in all the patients from the DBS electrode contacts and from 2 scalp leads, placed in the frontal and parietal regions contralateral to stimulation. The DBS quadrupolar electrode recorded three SEP configurations: biphasic, triphasic and mixed (biphasic and triphasic in different contacts). The biphasic potential (P1-N1) showed a predominant positive peak with an average latency of 16.3 ± 0.9 ms (P16). The P16 potential shifted in latency of 0.2 ± 0.1 ms from contact 0 (lower) to contact 3 (upper) of the intracerebral electrode. The triphasic potential (P1-N1-P2) showed a predominant negaitive peak, while the P1 average latency of 15.3 ± 0.7 ms (P15). The last mixed SEP configuration showed a bilobed P1 positive peak (P15 and P16) with average latencies of 15.3 ± 0.7 ms and 16.3 ± 0.9 ms, respectively.

Our data suggest that: a) the different SEP configurations recorded by the PPTg electrode are related to the distance between the four electrode contacts from the generators, b) the traces recorded in the PPTg area include a potential travelling along the medial lemniscus fibers at ponto-mesencephalic level (P16) or both a stationary (P15) and travelling potential (P16) simultaneously recorded from the cuneo-thalamic volley.

SSEP AS PREDICTORS OF AWAKENING IN PROLONGED ANOXIC VEGETATIVE STATE. A TWO-YEAR PROSPECTIVE STUDY

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Background

The number of patients in prolonged post-anoxic vegetative state (VS) is increasing. However, besides data obtained in the acute phase, scarce information is available about prognostic markers of long-term outcome in patients who remain in VS more than one month post-onset.

Objectives

The present two-year prospective clinical study aimed to identify prognostic markers, recorded in the chronic phase, useful to predict awakening in prolonged post-anoxic VS patients.

Methods

Subjects: Forty-three inpatients with prolonged (1 to 6 months) anoxic VS (23 females; age range: 12-83 years).

Variables definition: Anamnestic information, clinical variables, and neurophysiological examination (SSEP classified as present when N20 cortical response was recorded on at least one side, or absent and standard EEG graded according to Synek prognostic classification) at study entry.

Outcome definition. At 24 months post-onset patients were classified as responsive or unresponsive on the basis of CRS-R score.

Results

Nine patients recovered responsiveness with severe disability, whereas 12 patients remained in VS and 22 died in VS. Responsive patients were significantly younger, showed higher CRS-R total score and lower DRS score at study entry; all of them had spared pupillary light reflex and nociceptive response, and parossistic sympathetic activity. Logistic regression analysis showed that presence of SEP and CRS-R total score≥ 6 were significant predictors of recovery of responsiveness.

Conclusions

Presence of SEP is a significant independent predictor of awakening in prolonged post anoxic VS patients. SEP recording in chronic phase is as important and informative as in acute phase.

TMS - TdCS

COMUNICAZIONI ORALI

EVIDENCE FOR HOMEOSTATIC PLASTICITY IN HUMAN PRIMARY VISUAL CORTEX: PRE-CONDITIONING OF VISUAL EVOKED POTENTIALS (VEPS) BY A COMBINED TDCS-RTMS PROTOCOL

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Introduction

The ability of cortical networks to regulate neuronal activity within a useful dynamic range, called homeostatic plasticity, has recently received growing attention. The threshold and direction of excitability changes primed by low- and high-frequency rTMS in the primary motor cortex (M1) can be effectively reverted by a preceding session of tDCS. Whether there is a similar mechanism in human visual pathways is still a matter of debate.

Materials and Methods

In 10 healthy subjects we evaluated changes in visual evoked potentials (VEPs) amplitude at two different contrasts (K90% and K20%) by applying anodal or cathodal tDCS (20', 1.5 mÅ) to occipital cortex, followed by low- or high-frequency rTMS (0.5 for 20' and 5 Hz for 60", respectively, 85% of RMT), to assess whether a mechanism resembling homeostatic plasticity is operating in the intact human primary visual cortex.

Results

Anodal tDCS improved the amplitude of VEPs and this effect was reverted by applying either low- or high-frequency rTMS ($p<0.005$). Similarly, cathodal tDCS led to a decrease in VEPs amplitude, which is reverted in its turn by a subsequent application of 0.5 or 5 Hz rTMS ($p<0.01$). There are no significant changes in RMT values over time ($p>0.5$), confirming the spatial selectivity of our protocol.

Discussion

Our data show that preconditioning excitability with tDCS over the V1 can modulate the direction of plasticity induced by subsequent application of 1 or 5 Hz rTMS. This pattern was observed for both N1 and P1 components; since they appear to be generated in striate and extrastriate cortex, respectively, these findings indicate that homeostatic mechanisms could operate in both primary and higher-order visual areas.

MEASURES OF CORTICAL PLASTICITY AFTER TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS)

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Surface potentials recorded using EEG in response to single TMS pulses may be used as neurophysiological markers of the cortical excitability state. In the early studies, they have been shown to provide a direct measure of the cortical plasticity modulations induced by neuromodulatory protocols, such as transcranial paired associative stimulation.

In the present study we investigated the TMS-evoked cortical responses as a probe of the cortical effects induced by tDCS during the application of a standard protocol proved to be effective in modulating corticospinal excitability. tDCS is a non invasive technique used to manipulate cortical excitability through weak electric currents applied transcranially. The effects induced by tDCS are dependent on the current polarity: anodal stimulation increases excitability, while cathodal polarization decreases it.

Anodal and cathodal tDCS (1 mA; 25 cm^2;13 min) was delivered to sixteen young healthy subjects above the motor cortex. TMS-evoked cortical potentials were recorded from 10 scalp electrodes and motor evoked potentials were recorded from the first dorsal interosseous before and after tDCS application. Motor evoked potentials increased after anodal tDCS and decreased after cathodal tDCS, confirming the efficacy of the stimulation protocol in the present experiment. Consistently with the expectations, also TMS-evoked cortical potentials amplitude increased after anodal tDCS over the stimulated area, while it decreased after cathodal tDCS. This study provides direct evidence that TMS-evoked cortical responses are a reliable neurophysiological marker of the plasticity changes induced also by a tDCS protocol.

WALKING IMPROVEMENT AFTER DEEP RTMS WITH H-COIL ASSOCIATED WITH REHABILITATION IN PATIENTS WITH PROGRESSIVE MULTIPLE SCLEROSIS: A RANDOMIZED, CONTROLLED, DOUBLE BLIND STUDY

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Objective

To investigate whether repeated sessions of transcranial repetitive magnetic stimulation (rTMS) with H-coil could enhance the benefit of rehabilitation on walking abilities in patients with spasticity associated with multiple sclerosis (MS).

Background

Impaired walking has a strong impact on disability associated with MS and its treatments options are limited. Preliminary findings showed that repeated sessions of focal repetitive transcranial stimulation improved spasticity associated with MS but no data are available on the impact on walking ability. Recently, the development of H-coils has been proved to allow reaching deeper brain regions as compared with focal stimulation.

Design/Methods

Twenty-three progressive MS patients with lower limb spasticity, undergoing inpatients rehabilitation, were randomized to receive real (11 pts) or sham (11 pts; one patient refused to participate after randomization) 10-min sessions of high-frequency rTMS for 3 weeks following their rehabilitation sessions. Primary outcome was percent change at the 10-meter walk test. Secondary outcomes were: walking-endurance (6-min walking test), Modified Ashworth Scale (MAS) and Visual Analogue Scale (VAS) for spasticity, Fatigue Severity Scale (FSS), EDSS, PASAT and Nine-Hole Peg Test (9HPT).

Results

At the end of treatment, both groups showed improvement in all outcome parameters, although significant improvement in walking tests (10-mt-WT and 6-min-WT) was significant in the real rTMS group only. The latter group, when compared with the sham group, had significantly better improvement of the primary outcome (10-mt-WT; $p<0.05$) and of 6-min-WT ($p=0.002$) and MAS score ($p=0.037$). No serious adverse effects were reported and no patient discontinued the study due to adverse effects.

Conclusions

These findings demonstrate that deep brain stimulation with H-Coil increases the effects of rehabilitation in improving walking ability, in terms of both speed and endurance. The treatment is safe and feasible. These encouraging results need to be validated with phase-3 studies.

SAFETY AND EFFICACY OF EXCITATORY REPETITIVE DEEP TRANSCRANIAL MAGNETIC STIMULATION WITH H-COIL: AN OPEN STUDY IN 24 PATIENTS WITH PARKINSON'S DISEASE

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Objectives

To evaluate the safety and efficacy of repetitive Deep Transcranial Magnetic Stimulation (DTMS) in Parkinson's Disease (PD), using the novel H-coil.

Patients and Methods

24 PD-patients (aged 60 ± 6.7; PD-duration: 6.6 ±3; motor Unified Parkinson's Disease Rating Scale-UPDRSIII: 38.8 ± 10.5) underwent in 4-weeks-time 12 DTMS-sessions, performed over primary motor (M1) and prefrontal(PF) cortices. An excitatory 10Hz-frequency was used for both targets. Clinical assessment included total UPDRSIII and partial scores, for the worse (WS) or less affected (LS) PD-side, for axial involvement (AS), tremor (TS) and rigidity (RS). Four timed tests (arm tapping-AT; Nine Hole Peg Test- NHPT; foot tapping- FT; walking- W) were also performed. Patients were evaluated OFF therapy at baseline (T0), after the first (T1) and the last (T2) DTMS-session. Both clinicians and patients were not blind to the stimulation. An analysis for repetitive measures was performed.

Results

DTMS is a safe and effective PD-treatment, showing a significant improvement in UPDRSIII at every time-point, with a reduction of 16% and 23% at T1 ($p<0.001$) and T2 ($p<0.001$) respectively. Similar results were also obtained comparing subscores for WS, LS, AS, TS and RS. An improved performance in timed tests was also observed, except for W, which did not reach significance.

Conclusions

Despite the lack of blindness, DTMS is a safe and promising new therapeutic perspective in PD.

ALTERED MECHANISMS OF LONG-TERM CORTICAL PLASTICITY IN MIGRAINE WITHOUT AURA PATIENTS ARE CAUSED BY A REDUCED THALAMOCORTICAL ACTIVATION

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Background

Migraine between attacks is characterized by a paradoxical responses to repetitive transcranial magnetic stimulation. Abnormal long-term cortical functional plasticity may play a role and it can be assessed experimentally by paired associative stimulation (PAS), in which peripheral nerve stimuli are followed by TMS of the motor cortex.

Method

Changes in motor evoked potential (MEP) amplitudes were recorded in 16 migraine without aura (MO) patients and 15 healthy volunteers (HV) before and after PAS, which consisted of 90 peripheral electrical right ulnar nerve stimulation and subsequent TMS pulse over the FDI muscle site activation with a delay of 10ms (excitability depressing) or 25ms (excitability enhancing). As a control experiment of the 31 subjects studied, 8 (4 MO and 4 HV) also underwent before PAS10 the recording of somatosensory high-frequency oscillations (HFOs) reflecting and thalamo-cortical activation (early HFOs).

Results

While PAS10 reduced MEP amplitudes in HV (-17.7%) it significantly increased amplitudes in MO (+35.9%). While in HV after PAS25 MEP amplitudes significantly potentiated (+55.1), only a slight not significant increase was observed in MO (+18.8%). In the control experiment, performed in 8 subjects pooled together, Person's correlation showed an inverse relationship between percentage of MEP amplitude changes after PAS10 and early HFOs amplitudes (r= -0.81; p=0.01).

Conclusion

Since we observed that more deficient is the long-term PAS-induced change more decreased is the thalamo-cortical activation we postulate that the abnormalities in long-lasting cortical plasticity observed in migraine interictally could be due to an altered thalamic control.

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) IN THE TREATMENT OF CHRONIC MIGRAINE: A SAFE APPROACH WITH A PROMISING EFFECT

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Introduction

Chronic migraine (CM) is a disabling condition and a challenging therapeutic problem since prophylactic drugs often have inadequate response or unacceptable side effects. A few pilot studies have explored the possibility of applying repetitive transcranial magnetic stimulation (rTMS) in migraine for acute or chronic treatment with controversial results.

Objectives

To evaluate rTMS safety and efficacy in CM.

Methods

Twenty-two patients (median age 34 years, 70% female), affected by CM resistant to preventive pharmacological therapies and in a 3 months stable condition participated to the study. rTMS was applied to prefrontal areas at 110% motor threshold intensity and 20 Hz frequency. Three rTMS sessions per week were performed for six weeks with a follow-up visit at 4, 8, 12, 24 weeks, after end of treatment. Patients underwent headache diary assessment, MIDAS, BDI

Results

No side effects were evident during the study. Ten patients presented with a significative reduction (50%) in headache days ($p<0.0001$) and attacks ($p=0.02$), and pain intensity ($p=0.005$); a parallel decrease in the number of acute medications ($p<0.01$)- was evident, together with improvement in quality of life items ($p<0.01$). A partial response to treatment (20% - 40% attacks reduction) occurred in 7 other patients. 5 patients reported no modification in their headache.

Conclusion

The use of rTMS could be a major step forward in CM treatment, particularly in patients where available drugs are ineffective, poorly tolerated or contraindicated rTMS may be able in modulating the activity of cortico-subcortical and cortico-cortical pathways involved in pain control.

MISCELLANEA

COMUNICAZIONI ORALI

CUTANEOUS SENSORY AND AUTONOMIC DENERVATION IN AMYOTROPHIC LATERAL SCLEROSIS

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Although motor impairment dominates the clinical picture of amyotrophic lateral sclerosis (ALS), sensory disturbances may occur along the course of the disease. Sensory symptoms and electrophysiological abnormalities have been reported in about 30 percent of ALS patients while sural nerve biopsy had revealed nerve abnormalities, in 91 percent of them (Hammad et al. Neurology, 2008). These findings suggest that sensory involvement in ALS may be more than an occasional problem.

To evaluate the involvement of peripheral sensory nerves in ALS, we extensively studied cutaneous innervation in 40 patients (20 male and 20 female age 64.3±11.6 years) and 20 age and sex matched controls. Skin biopsies were taken from distal leg, thigh and fingertip using a 3 mm punch, after local injection of lidocaine. Samples were processed using indirect immunofluorescence techniques and an extensive panel of primary antibodies to mark both myelinated and unmyelinated somatic and autonomic nerve fibers. Quantification of epidermal nerve fibers (ENFs), Meissner corpuscles (MCs) and intrapapillary myelinated endings (IMEs) was performed using confocal images and dedicated software.

Compared with controls, ALS patients showed a loss of ENF in thigh ($p<0.01$), leg ($p<0.01$) and fingertip ($p<0.01$) and a loss ($p<0.01$) of Meissner corpuscles in glabrous skin. Epidermal denervation showed a length dependent pattern. In addition, a severe involvement of autonomic nerve fibers was present.

Our findings suggest that the involvement of last endings of sensory and autonomic nerve fibers is part of the neuropatological picture of ALS that should be considered a multisystemic degenerative disorder.

NEUROPHYSIOLOGICAL ASSESSEMENT IN TWO UNREPORTED ITALIAN FAMILIES WITH AUTOSOMAL DOMINANT CORTICAL TREMOR, MYOCLONUS, AND EPILEPSY

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On a clinical basis “autosomal dominant cortical tremor, myoclonus and epilepsy” (ADCME) is mainly characterized by distal action tremor and myoclonus. Neurophysiological findings often show a giant somatosensory evoked potential , enhanced C reflex and a postural high frequency irregular tremor [1]. Here we describe the neurophysiological assessment of few members belonging to two Italian previously unreported families with ADCME.

Methods

3 members family 1(2F, 1M) and 2 (2M) members from family 2 were studied. All patients were under antiepileptic drugs (AED) and have been seizure free since several years. They all showed hyperkinetic involuntary movements of the upper limbs against gravity and during voluntary movement. Somatosensory evoked potentials (SEP) , C-reflex and a multichannel EMG recording were performed.

Results

A giant SEP and an enhanced C-reflex were both recorded in two patients . The EMG multichannel recording showed cortical Jerks mainly against gravity and during movements but there was no definite tremor activity in 3 out 5 the patients. Only for two patients an irregular postural tremor could be recorded. Spectral analysis of the tremor showed a mean frequency around 8 Hz but signal was highly dispersed.

Discussion

Our findings are coherent with neurophysological features previously described in ADCME [2]. The EMG multichannel recording showed that these patients present with very frequent cortical jerks not producing a proper tremor. This finding and the lack of detection of giant SEP and C reflex in every patient could be ascribed to long term treatment with AED.

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THERMAL SENSITIVE PROFILE IN BURNING FEET SYNDROME

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Burning feet syndrome (BFS) is a disorder characterized by isolated burning symptom (BS) or more complex sensitive features. BS are diffusely considered in the screening tools for neuropathic pain (NP) descriptors. Axonal damage and C-nociceptors sensitization are possible pathogenetic factors, also if there is no general agreement about the specific underlying mechanisms. The aim of the present study was to define the thermal sensory profile in BFS.

We evaluated Thermal Quantitative Sensory Testing in 48 patients affected by chronic BFS. They were divided in idiopathic (IBFS, n:28) and symptomatic (SBFS, n:20). All pts complained burning pain in the feet that extends proximally. QST was performed on the proximal leg and the dorsal foot areas.

Different profiles of thermal abnormalities were observed: 21% of pts in IBFS and in SBFS showed cold hypoesthesia and warm allodynia; 11% of pts in IBFS and 10% in SBFS showed warm hypoesthesia and cold allodynia; 48% of pts in IBFS and in SBFS showed cold and warm hypoesthesia without any allodynia.

Conclusions

Burning pain is not the simple consequence of only C fibres damage. Important functional aspects of A-delta fibres emerge as key role in BS. Our data seem to outline the presence of a sort of physiological balance between A-delta and C fibres. The loss of this condition should explain the association between hypofunction of one thermal modality and allodynia for the second one. When the fibres damage spread out over the entire small fibres spectrum, the deficitary symptoms are prevalent.

MUSCLE SYMPATHETIC RESPONSE TO AROUSAL PREDICTS NEUROVASCULAR REACTIVITY DURING MENTAL STRESS

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Introduction

Mental stress often begins with a sudden sensory stimulus causing a brief arousal reaction followed by a more long lasting stress phase. Both arousal and stress regularly induce blood pressure (BP) increases whereas effects on muscle sympathetic nerve activity (MSNA) are variable.

Objective

To search for a link between MSNA responses induced by arousal and by mental stress.

Methods. We recorded 30 healthy males. Firstly we studied the effect of a simple arousal (electrical) stimulus on MSNA. Subsequently we have compared responses of MSNA and BP during arousal and mental stress evoked by a 3-min paced auditory serial arithmetic test (PASAT) in 30 healthy males aged 33 ± 10 years. We also monitored corresponding effects of a cold test (two minutes immersion of a hand in ice water).

Results

The arousal stimulus evoked significant inhibition of one or two MSNA bursts in 16 subjects, i.e. responders; the remaining 14 subjects were non responders. During mental stress responders showed a significant decrease of MSNA and a lesser BP increase compared to non responders. During the cold test MSNA and BP increased equally much in responders and non responders. In the whole group of subjects there was a significant correlation ($r = 0.80$, $p<0.001$) between MSNA responses induced by arousal and by mental stress but not between responses evoked by arousal and the cold test ($r < 0.1$, $p>0.6$).

Conclusion

We conclude that in males the MSNA response to arousal predicts the MSNA and BP responses to mental stress.

SOMATOSENSORY TEMPORAL DISCRIMINATION THRESHOLD IS INCREASED IN CEREBELLAR ATAXIA

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Introduction

Several brain areas are involved in the temporal processing of somatosensory events and in particular processing of time in the millisecond range seems to depend on cerebellar function. Processing of time in the millisecond range can be assessed by using the somatosensory temporal discrimination threshold (STDT) testing that measures the ability to discriminate two stimuli as separated in time. STDT abnormalities have been reported in Parkinson disease and dystonia, highlighting the role of the basal ganglia in determining STDT, while the influence of cerebellum on STDT testing has not yet clearly established.

Objective

To investigate STDT in a group of ataxic patients with cerebellar atrophy.

Patients and Methods

Fifteen patients (6 women, mean age 47.1 $\pm$ 13.9 years; disease duration 13.5 $\pm$ 9.9 years) with ataxia and cerebellar atrophy at brain magnetic resonance imaging, involving both vermis and hemispheres, underwent STDT evaluation. The test was performed by delivering paired stimuli starting with an interstimulus interval (ISI) of 0 ms followed by progressively increasing ISI (in 10 ms steps) applied in three different cutaneous areas (hand, neck and eye) on the left side. The ISI at which the patients were able to discriminate the pair of stimuli as separate in time was considered the STD threshold. STDT mean values of cerebellar patients were compared with those of eleven age-matched healthy subjects (mean age 51.9 $\pm$ 15.5 years).

We excluded patients who had dementia, extrapyramidal clinical features and neuropathy. The International Cooperative Ataxia Rating Scale (ICARS) was used to measure the degree of cerebellar dysfunction.

Results

STDT of the patients was significantly higher than controls (hand: 135.3 $\pm$ 21.6 vs 78.6 $\pm$ 22.5, $p<0.0001$; neck: 119.6 $\pm$ 22.8 vs 72.0 $\pm$ 19.4, $p=0.0006$; eye: 126.6 $\pm$ 7.5 vs 71.6 $\pm$ 18.8, $p=0.0001$). STDT values did not correlate with ICARS total score and subscores.

Discussion

We demonstrated that STDT is abnormal in patients with cerebellar atrophy. Our findings focus on the cerebellum other than basal ganglia as another neural structure playing a role in STDT and confirm the role of cerebellum in somatosensory temporal discrimination in the millisecond range.

PREFRONTAL HYPOMETABOLISM IN PATIENTS AFFECTED BY MYOTONIC DYSTROPHY 1

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Objective

Myotonic dystrophy type 1 (DM1) is a multisystemic diseases with impairment of the frontal cognitive functions. However, no correlation data is available on the relationship between neuropsychological tests results and the prefrontal functional impairment. We evaluated prefrontal cortex (PFC) function trough a 2-channel functional near-infrared (fNIRS) during a phonological word fluency task.

Methods

Eighteen patients and 22 healthy subjects were studied. We used a fNIRS system to investigate the changes in oxygenated ([O2Hb]t) and deoxygenated ([HHb]t) hemoglobin concentrations on the PFC during the word fluency task. [O2Hb] baseline-corrected activation values ([O2Hb]c) were calculated by the difference between [O2Hb]t and [O2Hb] before the task initiation ([O2Hb]b).

Results

No difference was found between DM1 sample and healthy subjects in the score of the word fluency task. [O2Hb]t of the PFC was bilaterally decreased in DM1 patients compared to the control group (respectively p= 0.02 and p= 0.03 for right and left PFC). The number of subjects with bilateral activation of PFC was lower in the DM1 sample than in the control group (respectively 28% and 64%, chi-square 0.02). In DM1 patients a positive correlation was found between [O2Hb]t of the left PFC and the score at the phonological word fluency task. No correlation was found for the right PFC.

Conclusions

DM1 patients show bilateral hypometabolism of PFC. Hypometabolism of the left PFC correlates with the score at the word fluency task which however, does not differ in DM1 and healthy subjects. The hypometabolism is a subclinical parameter in our DM1 group.

SPASTICITA’

COMUNICAZIONI ORALI

TREATMENT OF SHOULDER PAIN WITH BOTULINUM TOXIN TYPE A IN SPASTIC HEMIPLEGIA

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Objective

The purpose of this study was to assess the beneficial effect of Botulinum toxin in the treatment of hemiplegic shoulder pain in chronic phase.

Materials and Methods

23 consecutive hemiplegic patients with hypertonus of the muscles of the shoulder (Modified Ashworth Scale (MAS) ≥ 1) and painful shoulder, referred to 5 Rehabilitation Centers,underwent to neuromuscular blockade with pure Botulinum toxin type A (150 Kd). The rating scales were: the Franchay Arm Test (FAT), the MAS, the pROM, the Medical Research Council (MRC) and the Visual Analogic Scale (VAS) at rest and during nursing. Evaluations were performed at enrollment (T0), after one month (T1) and after three months (T3).

Results

The MAS ($p = 0.04$) and passive ROM ($p < 0.0001$) at the shoulder level decreased significantly at T1 without further changes at T3. At T1 there was a statistically significant reduction in VAS at rest and during nursing (ANOVA $F(2,28) = 39.5$, $p < 0.0001$). The results were maintained at T3. The degree of pain reduction was similar in both groups of patients with different degrees of spasticity. There were no significant changes obtained with regard to the MRC and FAT.

Discussion

The rationale for the use of botulinum toxin in painful shoulder is based on two different mechanisms of action: reduction of muscle tone and antinociception action. Our data suggest a role of botulinum toxin in reducing shoulder pain through an antinociceptive mechanism independent from the level of spasticity. This finding is supported by recent laboratory and clinical observations.

DOES THE TREATMENT OF SPASTIC LOWER-LIMB MUSCLES WITH BOTULINUM NEUROTOXIN (BONT/A) INCREASE GAIT SPEED? A PRELIMINARY STUDY

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Objective

To investigate if BoNT/A injected to treat lower-limb focal spasticity ameliorates ambulatory capacity, as measured by a change in gait speed.

Methods

Twenty-three spastic (10 post-stroke, 13 MS) patients received a single treatment of BoNT/A in the hip adductors, triceps surae and tibialis posterior muscles. The muscle tone of the hip, knee and ankle joint was assessed using the modified Ashworth Scale (MAS) at baseline and at weeks 4 and 12 after BoNT/A. A cumulative Ashworth score was calculated for each joint, bilaterally. Gait speed was calculated using a timed walk test (WT) over a fixed distance of 10 m at baseline and at weeks 4 and 12. Patients were divided into 3 classes according to gait speed: <0.4 m/sec, 0.4-0.8 m/sec and >8 m/sec. Patients enrolled in a physical therapy protocol after treatment. Significant changes from baseline in the cumulative MAS score and WT at each time point were determined by ANOVA for repeated measures.

Results

After BoNT/A, a decrease from baseline was noted at weeks 4 and 8 for the cumulative MAS score at each joint ($p<0.01$). Six out of 23 patients had a gait speed greater than 8 m/sec at baseline. These were excluded from further analysis. The remaining 17 patients showed a decrease at week 8 for the WT ($p<0.016$). Five of these patients (29%) were able to improve their gait speed, as assessed by a class change.

Conclusions

After BoNT-A for lower-limb spasticity there was a small, but statistically significant increase in walking speed.

CASI CLINICI SNP - SNV

POSTER

ELECTROPHYSIOLOGICAL STUDY IN SMARD1 WITHOUT SEVERE SIGNS OF RESPIRATORY INVOLVEMENT: A NOVEL GENE MUTATION

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Spinal muscular atrophy with respiratory distress (SMARD 1) is a very rare autosomal recessive motor neuron disorder that affects infants; the mutations (>40 different mutations has been described) have been identified in the gene encoding immunoglobulin m-binding protein 2 (IGHMBP2), located on chromosome 11q13.

SMARD 1 is characterized by degeneration of anterior horn alpha-motoneurons with distinctive clinical features in contrast to SMA: diaphragmatic palsy, symmetrical distal muscular weakness, peripheral sensory and autonomic neuropathy.

We present a Female child with genetically confirmed a novel mutation of SMARD 1 displaying a mild phenotype and no severe respiratory signs.

This Italian child was born at term from not consanguineous parents, by a labour induced because of polyhydramnios. No decrease in fetal movement. At birth she weighed 2400 gr showing hypotonia with difficult of feeding.

At 6 months of age appeared Pes equinus, distal limb muscle atrophy with contracture and weakness ; the deep tendon reflexes were absent.

Electromyography revealed sensory motor axonal neurophathy included the bilateral phrenic nerves (chest x Ray not revealed diaphragmatic palsy) and a high threshold to painful stimulus; the SSR was normal. The genetic investigation revealed a new mutation in c.G1915A.pat in IGHMBP2.

The child showed an atypical clinical evolution: she achieved ability to stend with support and no severe signs of respiratory involvement up to 20 months despite a widespread neuropathy.These clinical observations suggest that respiratory function could be preserved in this SMARD form with novel mutation.

RHABDOMYOLISIS AND GUILLAN-BARRE' SYNDROME: A DANGEROUS ASSOCIATION

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GBS is an acute demyelinating symmetrical polyneuropathy with a clinical manifestation of flaccid paralysis with areflexia, which usually follows viral or bacterial illness.

We report a case of a 81-year-old man with GBS (subtype AMSAN, Acute Motor Axonal Neuropathy), secondary to a previous M. Pneumoniae infection, who presented with elevation of creatin kinase serum levels, and worsened by a co-administration of simvastatin (S) and clarithromycin (C). The patient suffered from hypertension, BPCO, diabetes type 2, gout, mild renal failure, coronary heart disease and had been admitted to the hospital with signs of rhabdomyolysis and moderate tetraparesis. Electroneurography displayed a motor-sensitive predominantly axonal poliradicoloneuropathy, needle electromiography (EMG) did not reveal a typical myopathic pattern and during the routine F-wave evaluation we recorded the presence of A-wave.

Cerebrospinal fluid showed a moderate damage of emato-encephalic barrier with an albumin-citologic dissociation and systemic production of 6 oligoclonal immunoglobulins. Electromiographic pattern, even through presence of rhabdomyolysis, was consistent with an axonal poliradicoloneuropathy. The EMG showed a nerve damage with a widespread denervation activity in progress on both left and right tibial anterior muscle, on the right side of diaphragm and on the first dorsal interosseous, suggestive of AMSAN.

This case shows how is important to evaluate the use of statins in association with others CYP3A4-inhibiting drugs, particularly in patients with prior infective conditions, renal insufficiency or other risks factors, in order to have awareness of the interaction's risk associated with these conditions because early diagnosis and aggressive therapy may reduce the comorbidity and mortality.

GUILLAIN-BARRÉ SYNDROME AFTER ICU ADMISSION: REPORT OF THREE CASES

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Guillain-Barré syndrome (GBS), an acute immunologic attack of the peripheral nerves causing rapidly ascending weakness and areflexia, can lead to severe weakness with respiratory failure and consequently to intensive care unit (ICU) admission. Only in few cases GBS has been reported in patients already admitted to the ICU for other diseases. In these cases it can be difficult to distinguish GBS from critical illness polineuropathy, even with a neurophysiological evaluation given the possible overlap between demyelinating and axonal features. We describe three cases in which the weakness developed after the admission in ICU.

A 56 years old Chinese woman with massive cerebellar ischemic stroke and a ventricular derivation for the consequent cranial hypertension, and a young women that four months after a surgery for cerebellar medulloblastoma developed abrupt epilepsy and coma for a HSV encephalitis, during a good but slow recovery, showed a relatively sudden reduction in motor responses. In both cases this feature was initially interpreted with a worsening of the brain functions, however, the presence of flaccidity and areflexia gave the suspect of a possible peripheral defect. The subsequent neurophysiological evaluation showed elements compatible with a demyelinating acute polyneuropathy both in cranial and in segmental nerves and cerebral fluid analyses showed a mild increase in proteins. In the first case the neurophysiological evaluation was conducted 2 days after the worsening of the motor performances, for the second patient after 15 days. In both the plasmapheresis gave a good recovery, in 24 hours in the first and in 10 days in the second case. The neurophysiological evaluation confirmed the recovery in both patients.

The third case differ from the others: a 73 years old man with a post-traumatic coma showed a relatively progressive improvement of cerebral function from the EEG, but without any recovery of motor function. A late neurophysiological examination showed a marked assonopathy with demyelinating features in cranial and arms nerves. In this case the IvIG gave only a partial but evident motor recovery.

Incidental Guillain-Barré syndrome in ICU patients is rare and is limited to case reports following head trauma, cerebral vein thrombosis, neurosurgery. These cases also highlight the importance of considering this diagnosis even in ICU settings, and the convenience of empiric course of plasmapheresis or intravenous immunoglobulin in these selected cases.

DAVID LACOMIS, MD,1,2* J. TERRY PETRELLA, MD,2 and MICHAEL J. GIULIANI. CAUSES OF NEUROMUSCULAR WEAKNESS IN THE INTENSIVE CARE UNIT: A STUDY OF NINETY-TWO PATIENTS Muscle Nerve 21: 610–617, 1998:

Most of the patients with demyelinating PN had typical clinical features of GBS,38 with ventilatory fail- ure, significant bulbar weakness, or both. Of the pa- tients with an axonal sensorimotor PN, only 1 was weak prior to ICU treatment. This patient had axo- nal GBS. The others developed weakness while in the ICU. The weakness was usually generalized; deep tendon reflexes were attenuated. Clinically, these pa- tients were similar to those diagnosed with critical illness myopathy. Twelve of 13 required mechanical ventilation. Only 5 received IVCS (0.1–3 g methyl- prednisolone), and 8 received NMBAs. In 4 of these 8 patients, NMBA doses were low (<30 mg vecuro- nium). All had sepsis or systemic inflammatory re- sponse syndrome (SIRS),2 multiorgan dysfunction (MOD), or a combination. Two had elevated CK; of these, 1 had a surgical procedure, and the other had trauma-related injuries.

PALATAL TREMOR AFTER BRACHIAL PLEXUS ANESTHESIA

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Palatal tremor, also called palatal myoclonus, is defined by short, rhythmic contractions of the palatal musculature and may be associated with synchronous movements of adjacent structures. In the essential form ear click can be present, involuntary contraction stops during sleep and brain MRI does not detect anomalies. Pathologic studies outlined an important role of lesions affecting the dentate-rubral-olivary pathway, or Guillain-Mollaret triangle.

We describe a 49 year-old woman with acute onset essential palatal tremor following brachial plexus anesthesia with levobupivacaine 0,5% due to surgery of ulnar collateral ligament. She also presented bilateral, involontary, and rhythmic activity of chin muscles evoked by the opening of the mouth. Physical examination showed intermittent bilateral rhythmic activity of the palatal musculature at rest, and bilateral higher rhythmic contraction of the chin muscles after voluntary activation. The palatal contraction could not be inhibited by external sensory stimuli, whereas chin contraction could be suppressed by selective tactile stimuli of the trigeminal area. The patient also complained bilateral ear click. The remainder of the neurological and otorhinolarygologic examinations were normal. Symptoms appeared immediately after surgery and did not improve after clonazepam and carbamazepine intake. Brain MRI was unremarkable, and we conducted a broad electrophysiologic evaluation in order to investigate troncoencephalic functions: blink-reflex, BAEPs, lower and upper limbs SEPs and MEPs were normal bilaterally.

As previously descibed, intratecal anestethics could induce myoclonus. This case suggests possible pharmacological toxic effect on the dentate-rubral-olivary pathway (Guillain-Mollaret triangle) even after local administration of levobupivacaine.

ULTRASOUND ABNORMALITIES OF SPINAL ACCESSORY NERVE DUE TO VIOLENT CONTUSION.

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Ultrasound (US) permits to depict smaller and smaller nerves and is acquiring an important role in the diagnosis of peripheral nerve injury. We report the case of a 20-year-old professional skier who presented to our EMG lab referring a 6 months history of right shoulder motor deficit.

Six months earlier he had suffered from violent contusion in the right cervical region after hitting a giant slalom gate with his neck during a race. After the trauma he noticed a hematoma in the same region.

On examination the patient had hypotrophy of upper trapezius muscle bundles and abduction deficit of the right arm. A winged scapula was evident during abduction and elevation of the scapula. Needle EMG of deltoid, biceps brachii, supraspinatus, infraspinatus, pectoralis major and serratus anterior showed normal findings while the evaluation of trapezius muscle showed fibrillation potentials and neurogenic recruitment. Motor nerve conduction studies of right spinal accessory nerve (SAN) showed decreased amplitude compared to the left SAN.

We sonographically evaluated the SAN along its course between the lateroposterior border of the sternocleidomastoid muscle and the anterior border of the trapezius muscle (posterior cervical triangle), where the nerve runs subcutaneously. On the right SAN was enlarged and hypoechoic, and remained enlarged up to the tract underneath the trapezius muscle. Clinical-electrophysiological and US findings suggested an axonal peripheral involvement of SAN.

To our knowledge this is the first case of SAN lesion demonstrated through US and it further encourages the use of US in evaluating SAN.

A CASE OF THYROTOXIC PERIODIC PARALYSIS IN A CAUCASIAN MALE

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Hypokaliemic Periodic Paralysis is a rare group of disorders which can cause sudden onset weakness. Thyrotoxic periodic paralysis is an endocrine disorder described predominantely in men of Asian origin. Thyrotoxic clinical features are often masked or absent. Life may be threatened because of severity of hypokalaemia and therefore a prompt diagnosis is essential.

We describe the case of a 32 year old Caucasian male who presented with sudden onset flaccid tetraparesis, hypokalaemia (1.2 mEq/l) and hyperthyroidism (TSH <0.01microUI/ml, FT_4 2.6 ng/dl). He reported episodes of transient mild weakness of the lower limbs in the previous 6 months. His family history was negative for periodic paralysis.

The neurophysiologic examination during the attack revealed a diffuse reduction of cMAPs amplitude. We performed the exercise test following Fournier protocol (Fournier et al. 04), which revealed a progressive decrease of cMAP amplitude that reached the maximal peak of 47% after 25 min. We performed the test after the normalization of potassium level and we didn't found significant modifications of cMAP amplitude, although the euthyroid state was not already achieved. Kir 2.6 genetic analysis is underway.

VAGAL FUNCTION AND ESOPHAGEAL MOTILITYG IN PATIENTS WITH OCULOPHARYNGEAL MUSCULAR DYSTROPHY

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Objective

Dysphagia is the most invalidating symptom in Oculopharyngeal Muscular Dystrophy (OPMD) and determines the prognosis of the disease. Previous reports focused on the involvement of the proximal part of the esophagus, without detailed studies about the overall motility. We tried to analyse the whole striated and smooth muscle activity and the autonomic function, in order to separate the possible involvement of the extrinsic parasympathetic vagal function from the intramural myenteric plexus innervation.

Materials and Methods

Three male subjects affected by sporadic OPMD with different degree of dysphagia were studied. The common myopathic EMG pattern was associated in two patients with rimmed vacuoles and in one patient with ragged red and cytochrome C oxydase negative fibers at the muscular biopsy. Both the adrenergic and cholinergic functions of autonomic system were investigated. High resolution oesophageal manometry with 22 perfused channels, 1.5 cm a part, was used to determine pharyngeal and oesophageal dysfunctions

Results and Conclusion

The common finding was the complete absence of post – deglutitive activity of the striated, proximal part of esophagus (S1 segment). The distal part showed in one patient synchronous contractions of normal amplitude, suggesting an impairment of neural control. In the second patient there was a complete aperistalsis with only synchronous contractions of low amplitude. In the third patient there were esophageal peristaltic contractions of low amplitude. Since autonomic tests were normal in all the patients, progressive reduction of peristalsis in the esophageal distal part could be related to the myenteric plexus derangement..

SKIN SYMPATHETIC FUNCTION IN PATIENTS WITH SPINAL CORD INJURIES

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Objective

Vasodilatation of the skin can be elicited by different stimuli. In spinal cord injury the reduced flare response was attributed to the increase of the sympathetic tone below the level of the lesion , even if the function of other sympathetic fibers innervating the skin seems to be decreased. To better understand the sympathetic residual function in such patients, we tried to investigate the role of sympathetic activity in maintaining the skin vasomotor and sudomotor control.

Materials and Methods

We evaluated eight subjects with different outcome of traumatic (3) and (5) inflammatory spinal cord involvement, with lesion between T10 and C6. Both the adrenergic and cholinergic function of autonomic system were investigated. Skin axon – reflex vasodilatation (SkARV) was elicited using a simple mechanical stimulation of the trunk. Postural vasoconstriction arteriolar reflex was tested on the big toe on the lowering. Sympathetic skin response (RSC) was recorded in the palm and sole. The Wilcoxon signed rank test was applied for amplitude analysis of the last two tests.

Results and Conclusion

In patients with complete ASIA A lesion, the correspondence between somatic level of the lesion and reduced SkARV was associated with the complete absence of the plantar RSC, whereas in patients with incomplete lesion the flare response was always associated with the presence of plantar RSC. No dysreflexia was present in such patients. These findings seem to suggest a relation between reduced vasodilatation and C fibers impairment.

POSTGANGLIONIC AUTONOMIC INVOLVEMENT IN MULTIPLE SYSTEM ATROPHY: A MORPHOFUNCTIONAL STUDY OF SUDOMOTOR FUNCTION

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Autonomic failure is one of the main manifestations of Multiple system atrophy (MSA). Solid evidences point toward the impairment of preganglionic structures as its causative moment, however, an involvement of postganglionic fibers has been also suggested.

We evaluated postganglionic involvement in MSA, quantifying sudomotor nerves in 3-mm punch skin biopsies from fingertip, thigh and leg of 17 patients (11 male and 6 female; age 59.1±8.5) with a diagnosis of probable MSA. A group of 16 healthy subjects (7 male and 9 female; age 56.9±7.4) was analyzed as control group. Skin samples were processed by indirect immunofluorescence to visualize sudomotor fibers using pan neuronal (PGP) and specific cholinergic (VIP) markers. Morphological data were compared, in a group of patients, with sudomotor function as evaluated by the dynamic sweat test (DST).

Total length of cholinergic sudomotor innervation per volume of glandular tissue (µm/ µm 3) was reduced in patients in all the examined sites (0.104 µm / µm 3 vs. 0.191 µm / µm 3, $p<0.01$, in fingertip; 0.074 µm / µm 3 vs. 0.172 µm / µm 3, $p<0.01$, in thigh; 0.071 µm / µm 3 vs. 0.169 µm / µm 3, $p<0.01$, in leg). The density of activated sweat glands after pilocarpine stimulation correlated with the density of sudomotor nerves.

We observed, in patients affected by MSA, a sudomotor impairment that correlated with sweat gland denervation. Our data support the hypothesis that a postganglionic impairment occurs in MSA.

CMT2B: HEREDITARY SENSORY-MOTOR NEUROPATHY OR HEREDITARY SENSORY-AUTONOMIC NEUROPATHY?

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Objective

To describe clinical and skin biopsy findings of the first Charcot-Marie-Tooth type 2B (CMT2B) Italian family and to discuss the possibility to include it within hereditary sensory autonomic neuropathy (HSAN) family.

Methods

Three healthy and four affected members from a large Italian family, after clinical and electrophysiological evaluation, underwent molecular analysis. Skin biopsy was performed at fingertip, thigh and leg in all the affected subjects. Skin samples were processed using indirect fluorescence technique to mark sensory and autonomic nerve fibers. The autonomic functions were assessed by means of dynamic sweat test (DST) and cardiovascular reflex tests in two patients (one male and one female).

Results

The clinical picture showed a wide intra-familial phenotypic variability. The CMT phenotype was mild in females and worsened by poorly healing ulcers in males, complicated by recurrent infections and/or leg amputation. Electrophysiological findings were consistent with a distal axonal sensory-motor neuropathy. Molecular analysis identified a Val162Met substitution in the *RAB7* gene which co-segregated with the disease within the pedigree. Skin biopsy showed a length dependent loss of myelinated and unmyelinated sensory nerve fibres and a widespread autonomic nerve fiber involvement, more severe in males. Consistently with morphological data, autonomic functional studies confirmed that sudomotor and cardiovascular systems were more severely affected in male patient.

Conclusions

Our findings show a length-dependent degeneration of peripheral motor, sensory and autonomic nerve fibers in CMT2B and point out a more severe clinical picture in males. The demonstration of autonomic nerve fiber involvement, never reported so far, expands the phenotypic spectrum of CMT2B and suggests a continuum between hereditary motor-sensory neuropathy and HSAN phenotype.

THE TREATMENT OF WEAK RESPONSIVE BLEPHAROSPASM TO BOTULINUM TOXIN A

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Introduction

Blepharospasm (BS) is a focal dystonia involving involuntary and sustained contractions of muscles around the eyes. BS can show a typical presentation with an activation of the orbicularis oculi (O.Oc) muscles resulting in eye closure, or it can present the levator palpebrae inhibition phenomenon. Typical BS benefits from botulinum toxin (BTX) injection in the O.Oc muscle in the orbital part (orbital injection) while in BS presenting the levator palpebrae inhibition phenomenon BTX injection is indicated in the pretarsal part of the O.Oc muscle.

Aim of the study

To assess the efficacy of BTX injection in both orbital and pretarsal part of O.Oc muscle (combined injection) compared to the orbital one in weak responsive typical BS using clinical and disability scales (Jankovich rating scale, JRS ; Blepharospasm Disability Index ,BSDI) [1,2,3].

Methods

We enrolled 19 patients with primary BS and typical presentation , treated at least three times with BTX type A (BTXA) injections in the orbital part of O.Oc and not having a satisfactory response . After three months from the last orbital injection patients were treated with the combined injection.

Results

Statistical analysis showed a significant difference ($p<0.05$) in the mean score of JRS and BSDI scales resulting from the orbital and combined injection.

Discussion

This study shows that the response from BTX treatment in weak responsive BS is improved using the combined scheme of injection.

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NEUROPHYSIOLOGICAL EVALUTATION IN YOUNG PATIENTS SUFFERING FROM TYPE 1 DIABETES

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Neuropathy is a common complication of diabetes. It can be somatic or autonomic, syntomatic or asyntomatic. It can present as symmetric sensory-motor polineuropathy, symmetrical motor proximal neuropathy, focal or multifocal neuropathy. Autonomic neuropathy can be associated to the above-mentioned neuropathies or come before them and increases cardiovascular risk and mortality. The most important risk factors are the duration of diabetes, the age of the patient, the metabolic control and the oxidative stress.

We examined 28 young patients with type 1 diabetes to evaluate the presence of somatic or autonomic neuropathy. Diabetes was related to autoimmune thyroiditis in 5 patients and to celiac disease (CD) in 2 of them.

The mean duration of diabetes was 10 years in our 28 patients (17 F and 11 M), we studied the motor Nerve Conduction Velocity (NCV) of medianus, ulnar, internal and external popliteal sciatic (EPS) nerves, the sensory NCV of sural and ulnar nerve, the F wave of EPS nerve.

We also checked the four limbs SSR and R-R interval in basal conditions and at the standing-up.

Our patients had both negative anamnesis and neurological examination but we found a moderate dysautonomia in 15/28 patients and moderate polineuropathy in 5/28; in 3 of them, peripheral and autonomic alterations coincide.

Parasymphatetic nervous system was significantly compromised. These alterations showed a relationship with the autoimmune comorbidities (Hashimoto thyroiditis), with the blood levels of HbA1c and a reverse relationship with the insulin requirement Kg/day and with the age of start of diabetes.

POTENZIALI EVOCATI E DOLORE

POSTER

WARMTH AND NOCICEPTIVE EVOKED POTENTIALS IN CRISPONI SYNDROME

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Crisponi syndrome (CS) is a rare severe infantile autosomal recessive disorder caused by mutations in the cytokine receptor-like factor 1 gene. It is characterized by dysmorphic features, feeding difficulties and hyperthermia. Hyperthermia frequently leads to death within the first months of life, whereas surviving patients develop scoliosis, psychomotor retardation and cold inducing sweating. Cold induced sweating is the most disabling symptom in adulthood. With environmental temperatures of 22°C or less, individuals sweat profusely on their face or upper body, with intense shivering and dermal vasoconstriction. Electromyography, motor and sensory nerve conduction velocities are usually normal, however, up to now, there are no studies evaluating thermal and pain sensations in patients with cold induced sweating syndrome.

The aim of the present study was to assess the function of A-delta and C fibers my means of CO_2 laser-evoked potentials (LEPs) in CS patietns. Four patients were studied, laser pulses were delivered on the skin of the hand and perioral region at painful intensity to record LEPs related to A delta-fiber inputs and at non-painful intensity to obtain LEPs related to C-fiber inputs. In all four subjects the latencies of N1/P1 and N2/P2 potentials were normal from both stimulation sites and for both A-delta and C fiber stimulation.

The results of this study demonstrate that cutaneous nociceptive and warmth pathway function in CS patients are normal, indicating that cold induced swallowing is not associated with any involvement of warmth and nociceptive fiber inputs.

UNDERSTANDING THE UNDERLYING MECHANISMS OF "NON CONVENTIONAL MEDICINE" IN THE THERAPY OF PAIN: A LASER EVOKED POTENTIAL STUDY

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Pain represents a behavioral response to a noxious stimulus that alerts us to the presence of an actual or a potential tissue damage. From this point of view, pain plays an essential protective biological function. Conversely, persistent pain offers no biological advantage and causes suffering and distress.

Concerning the therapy, there is no single therapeutic approach to pain and, more often than not, successful treatment comprises a combination of several. A different concept of what pain is and how to treat it is present in the Eastern tradition where pain is thought to result from blockage or stagnation of the normal movement of energy (qi) in the area that hurts and acupuncture is thought to restore the normal flow of qi.

In modern scientific study, acupuncture has been shown to have multiple effects on the central and peripheral nervous systems. These effects are presumed to change pain perception, although the exact mechanism is unknow, some studies have shown that the cortical areas involved in pain processing (also called the pain matrix) substantially overlaps with the areas activated by the acupuncture.Concerning the peripherical activation produced by acupuncture some studies report the effect of it on the somato-sensory reflexes or interoceptive-autonomic reflexes through stimulation of the afferent A-delta and fibers, or afferent group III and IV fibers beneath the acupuncture points.

Most of the presented studies have been conducted in a rigorous scientific setting but mostly relied on elettroacupunture, or presenting some methodological limitations. No studies have been conducted on the abdominal acupuncture, that is very effective in reducing acute pain and that permits a standardized treatment. In order to evaluate if the abdominal acupuncture is able to modify pain perception, we studied 10 healthy volunteer by recording the laser evoked potentials before, during and after a real and sham abdominal acupuncture protocol.We found a significative reduction of N2/P2 complex after the real abdominal acupuncture protocol and a reduction, non significant, in the placebo protocol.

The results of our study showed that abdominal acupuncture is able to reduce pain perception, following studies will be developed in order to study its efficacy on patients suffering from pain.

A IPSILATERAL SILENT PERIOD STUDY IN RELAPSING REMITTING MULTIPLE SCLEROSIS PATIENTS DURING AND AFTER MOTOR RELAPSE

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Objective

To investigate early changes in the ipsilateral silent period (iSP) after a motor relapse in Relapsing Remitting Multiple Sclerosis patients (RRMS).

Methods

Twelve RRMS non-disabled patients presenting first upper limb weaknessunderwent neurophysiological examination at study entry (T1) and end of the 12th week (T2) after a first single attack involving upper arm motor function. iSP measurements (onset, duration, and depth) were obtained in the abductor pollicis brevis. We used Nine Hole Peg Test (NHPT) to test dexterity. Data were compared with 18 healthy volunteers.

Results

NHPT performance was slower in the affected arm (AA) compared with the unaffected arm (UA) and with controls ($p<0.05$) at T1, not at T2, when it was significantly improved ($p<0.05$). Latency onset of iSP in both examinations, for both arms, was longer vs controls ($p<0.05$). The amount of iSP for both arms in T1 was smaller vs controls and vs T2 ($p<0.05$), without significant interhemispheric differences. In AA iSP duration was greater vs UA and controls in T1 ($p<0.05$) but not in T2. At T1, iSP in AA inversely correlated to NHPT improvement in T2 ($r=-0.54$, $p=0.05$) and not to baseline performance.

Conclusions

The finding of increased latency of iSP even in the unaffected arm is consistent with corpus callosum demyelination and suggests the possible usefulness of the technique for exploring transcallosal connections in addition to the corticospinal pathways. During relapse, iSP duration over the affected side can be a marker of corticospinal involvement and may deserve validation as predictor of subsequent clinical recovery.

MOTOR EVOKED POTENTIALS MONITORING FOR THE EVALUATION OF REVERSAL OF PROFOUND AND DEEP RESIDUAL ROCURONIUM-INDUCED NEUROMUSCULAR BLOCKADE BY SUGAMMADEX

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Sugammadex is the first of a new class of selective relaxant binding drugs developed for the rapid and complete reversal of neuromuscular blockade (NMB) induced by the aminosteroid neuromuscular blocking drugs rocuronium and vecuronium. Neuromuscular blocking drugs block the transmission from the peripheral nerve to the muscle units, with reduction and disappearance of the electromyographic activity. Usually neuromuscular monitoring for the investigational reversal drug is performed by calibrated acceleromyography. The aim of this study is to determine the time and the efficacy of sugammadex in reversing rocuronium induced neuromuscular blockade using motor evoked potentials (MEPs) monitoring.

30 consenting patients undergoing propofol and remifentanyl anesthesia for spine surgery were enrolled and divede into groups: Group 1, reversal of profound NMB (sugammadex 16 mg/Kg, 3 minutes after rocuronium 1.2 mg/Kg) and Group 2, reversal of “deep” residual NMB (sugammadex 4 mg, 15 minutes after rocuronium 0.6 mg/Kg). MEPs registrations of upper and lower limbs and the diaphragm were performed, as well as TOF monitoring.

After injection of 4 mg/Kg of sugammadex, the means of recovery time of the basal MEPs amplitudes (diaphragm, lower and upper limbs) were 124+/- 9.6, 143+/-163, 151+/-207 sec, respectively whereas after 16 mg/Kg of sugammadex the times were 109+/- 13.8, 124+/-0.6 and 135+/-14.1 sec. Times to TOF ratio 0.9 were 114+/-75 and 186 +/-105 sec in Group 1 and 2, respectively.

Neurophysiological monitoring using MEPs confirmed that sugammadex provided a complete recovery from profound and “deep” residual rocuronium- induced neuromuscular blockade.

PROPOSAL OF AN OBSERVATIONAL EVALUATION MODEL TO DESCRIBE VIDEO-SURFACE ELECTROMYOGRAPHIC MUSCLE PATTERNS IN AN INDIVIDUALIZED REHABILITATION TREATMENT OF PATIENTS WITH SEVERE ACQUIRED BRAIN INJURY

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Objective

The aim of this observational perspective study was to describe video-surface electromyographic muscle patterns in an individualized rehabilitation treatment protocol of patients with severe acquired brain injury.

Material and Methods

8 patients (5 females, 3 males; mean age 54 ± 19,7yy), affected by severe acquired brain injury and recovered in our Neurological Rehabilitation Section during june 2010, were recruited in our study. In accordance with our inclusion criteria (GCS ≤ 12, LCF ≤ 3, DRS ≥ 17 and ≤ 21), patients underwent at time TO (before rehabilitation treatment) and at time T1-T2-T3-T4-T5 (1 hour, 15 days, 30 days, 45 days and 60 days after rehabilitation treatment), to a clinical examination (proximal and distal pROM of upper and lower limbs; grade of muscle spasticity using MAS scale, muscle strenght evaluation using MRC scale), to a functional impairment evaluation (using the GCS, LCF and DRS scales) and to a video surface EMG evaluation of agonist/antagonist muscle activity in four observational conditions (resting bed position, passive and active mobilization of upper and lower limbs, during Babinski reflex evocation). Patients had been undergoing physiotherapy during the observational period, 6 days a week, in 2-hour session, consisting in individualized passive limb kinesis, neurodynamic limb exercises and postural control exercises.

Results

Clinical examination performed before (TO) and after rehabilitative treatment (T1,T2,T3,T4,T5) demostrated an increase of pROM on the upper limbs and a decrease on the lower limbs, an irregular state of muscle spasticity in each body district evaluated and an increased muscle recruitment (MRC) on the right upper and lower limbs. Video surface EMG recordings showed an abnormal and continous phasic co-activation, with a related frequent overpowering muscle signal, of agonist/antagonist limb muscles in all patients invastigated during the resting bed position proceeding from time T0 to time T5, a co-contraction muscle pattern of proximal and distal agonist/antagonists during the active mobilization of the upper and lower limbs proceeding from time TO to time T5 in 4 of our patient evaluated, the absence of EMG signal of agonist/antagonist upper and lower limb muscles during active limb mobilization in the other patients recruited, an irregular tonic co-activation of agonist/antagonist muscles during passive limb mobilization proceeding from time TO to time T5 in all patients recruited and an insignificant EMG muscle pattern during Babinski reflex evocation.

Conclusions

We demonstrated that our rehabilitation protocol lead to a non-linear clinical response in term to efficacy in all patients treated. Using video surface EMG we can identify a pathological range of electromyographic agonist/antagonist muscle patterns in a selected group of patients affected by severe acquired brain injury and treated with an individualized rehabilitative approach. Dynamic surface EMG analysis can assist clinicians in the description of abnormal muscle activity but can not be used as an outcome measure after a rehabilitative treatment in patients affected by SBI.

INTER-HEMISPHERIC COUPLING CHANGES ASSOCIATE WITH MOTOR IMPROVEMENTS AFTER ROBOTIC STROKE REHABILITATION

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Background

In the chronic phase of stroke brain plasticity plays a crucial role for further motor control improvements.

Objective

To assess the brain plastic reorganizations and their association with clinical progresses induced by a robot-aided rehabilitation program in chronic stroke patients.

Methods

7 stroke patients with an upper limb motor impairment in chronic phase underwent a multi-modal evaluation before starting and at the end of a 12-week upper-limb neurorehabilitation program. Fugl-Meyer Assessment (FMA) Scale scores and performance indices of hand movement performance (isometric pinch monitored through a visual feedback) were collected. Cerebral reorganizations were characterized on ipsilesional and contralesional hemisphere resting state properties of both 32-channel EEG bipolar derivations overlying the middle cerebral artery territory sensorimotor districts and primary somatosensory sources (FS_S1) obtained through the Functional Source Separation (FSS) method. Power Spectral Density (PSD) and interhemispheric coherence (IHCoh) at rest were measured and correlated with clinical and hand control robot-induced improvements.

Results

After the robotic rehabilitation we found an improvement of FMAS scores and motor performance paired with significant changes of brain connectivity. In particular, the improvement of motor performance correlated with modulation of the interhemispheric FS_S1 coherence in high frequency band rhythms.

Conclusions

Recently it has been shown that an upper limb robot-based rehabilitation improves motor performance in stroke patients. We confirm this potential and demonstrate that a robot-aided rehabilitation program induces brain reorganizations. Specifically, interhemispheric connectivity between primary somatosensory areas got closer to a 'physiological level' in parallel with the acquisition of more accurate hand control.

DIFFERENT BALANCE BETWEEN EXCITATION AND INHIBITION IN THE PRIMARY SOMATOSENSORY CORTEX OF MIGRAINE CHILDREN WITH IMPLODING OR EXPLODING PAIN

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Different physiopathological mechanisms are supposed to work in migraineurs with either imploding (IP) or exploding (EP) pain.

The aim of the study was to record the short-latency scalp somatosensory evoked potentials (SEPs) in migraine children and to investigate whether the inhibitory and excitatory tone of the primary somatosensory (SI) area depend on pain direction.

We studied 4 migraineurs with IP (3 girls and 1 boy; mean age 13±2 years) and 5 migraine children with EP (5 girls; mean age 12.3±3.9 years). SEPs to both right and left median nerve stimulation were recorded from 31 scalp electrodes. The parietal P24 amplitude was significantly higher (P=0.005) in EP (3.6±1.8 μV) than in IP patients (1.3±0.9 μV). In order to have a measure of the balance between excitation and inhibition in the SI area, we calculated also a $SI_{e/i}$ index ($\frac{N20-P24}{N20+P24}$).

This index was significantly higher (P=0.0008) in IP (0.37±0.34) than in EP (-0.34±0.23) migraineurs, meaning that the N20 amplitude was higher than the P24 amplitude in IP patients, while the opposite occurred in EP children. Since the parietal N20 and P24 SEP amplitudes represent respectively the excitatory and inhibitory phase of the somatosensory primary response, our results suggest that inhibitory mechanisms are dominant in the SI area of EP children, while in IP patients the excitatory tone is prevailing.

ELECTROENCEPHALOGRAPHYC AND BEHAVIORAL EFFECTS OF CHRONIC RAPAMYCIN TREATMENT IN TSC1 MICE

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Objective

Tuberous Sclerosis Complex (TSC), related to enhanced mTOR pathway, a key protein for synaptic plasticity and memory, is characterized by benign tumors, epilepsy and cognitive/psychiatric disorders. Rapamycine has been recently proposed as a treatment of benign tumours in TSC.

Methods

We analyzed background EEG, anxiety- and depression-like behavior at postnatal day 40 after administration of rapamycin from day 8 in wild type-Wt mice and in a mouse model where Tsc1 has been deleted since E9.5 Untreated Tsc1 mice died before day 20 and a clear epileptic behavior was observed and video-EEG recorded.

Results

Mean dominant frequency (MDF) in Tsc1 mice was lower with respect to Wt mice, treated or not with rapamycin. Moreover, a decrease in MDF was found in treated vs untreated Wt mice. In the elevated plus-maze test (EPM), Tsc1 spent more time in the open arm with respect to all controls. In the forced-swim test (FST), Tsc1 showed a decreased immobility time. Wt treated mice, with respect to controls, had a decreased immobility time in FST and an increased time in the centre in the EPM.

Conclusions

Rapamycin has positive effects on EEG, behaviour and life span in this animal model of TSC. The evidence of EEG and behavioural changes also in Wt animals after rapamycin administration suggest the need of further studies to test its potential cognitive effects.

BOTULINUM TOXIN IN THE TREATMENT OF CHRONIC PELVIC PAIN

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Chronic pelvic pain CPP) is a common disorder, much more frequent in women, causing significant morbidity. Often the etiology is not clear, resulting from a complex interaction between neurologic, muscoloskeletal, endocrine systems, etc which is also influenced by behavioural and psychological factors.

CPP very often do not respond to conservative physical therapy.

In the last years it has been showed botulinum toxin type A (BTX-A) is effective in treating pain, above all if it is associated to muscular spasm. Some studies suggest in fact that BTX-A blocks peripheral sensitization and, indirectly, reduces central sensitization.

We studied 17 patients, aged 35-87 years, who had more than 2 jears of CPP, mono/bilateral, who differed from one another in pain area and intensity. All patients were previously studied with radiological investigations of lumbosacral and pelvic region so that with neurophysiological examination of legs and pudendal nerve: the exams were normal in all cases.

Toxin type A 50-100 U was injected into two-four sites of sacral region, in relation with the area of diffusion of pain.

In 7 patients we had a very good resolution of pain, even if never complete, but enough to have a good quality of life as result also by VAS score. In 7 the improvement was good but the patient needed to continue the therapy. In 3 patients we don't have any improving.

In 4 patients was necessary two infiltration before having a good improvement.

TRANSCRANIAL MAGNETIC STIMULATION IN THE TREATMENT OF MEDICATION OVERUSE HEADACHE: PRELIMINARY RESULTS

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Background

Repetitive TMS (rTMS) may have a role as migraine prophylaxis.

Purpose

To investigate the efficacy of high-frequency rTMS over left dorsolateral prefrontal cortex (DLPFC) in the treatment of medication overuse headache (MOH).

Methods

A randomized, controlled, double-blind trial on patients suffering from MOH consecutively presenting in a six-month period in the Headache Centre of Trieste was performed. Patients were randomized into the rTMS or the sham-TMS group. Treatment consisted of 10 consecutively TMS session delivered on left DLPFC, each session being 10 trains of 2-s duration, separated by 30-s pause, 20 Hz frequency, 100% motor threshold intensity. Demographic and clinical information, headache days (HD), hours of headache (HH), and symptomatic drugs (SD) in the 3 months before (t1), and in the first (t2) and second month (t3) after stimulation were analysed using SPSS 14.0.

Results

We enrolled 8 patients (7 F, 1 M; mean age 44±11), four patients undewent rTMS and four sham-TMS. All patients were migraineurs without aura as initial primary headache. We found, in both rTMS and sham-TMS group, no significant difference between the 3 months before and the 2 months after stimulation (rTMS: HD=22±6t1 *vs* 22±11t2 *vs* 19±14t3, HH=223±205t1 *vs* 219±198t2 *vs* 205±196t3, SD 22±10t1 *vs* 18±7t2 *vs* 16±8t3; sham-TMS: HD=22±5t1 *vs* 12±6t2 *vs* 13±8t3, HH=180±117t1 *vs* 99±73t2 *vs* 97±28t3, SD 22±10t1 *vs* 16±3t2 *vs* 17±4t3).

Conclusions

Our preliminary data suggest that high-frequency rTMS over left DLPFC is not useful to treat MOH; however the small sample doesn't allow to draw safe conclusions.

MAGNETIC STIMULATION OF THE CERVICAL SPINE: EFFECT OF INTENSITY AND DISTRIBUTION OF THE MAGNETIC FIELD ON THE MEPS

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Magnetic stimulation over the cervical spinal cord is an available method to excitate proximal nerve at the exit of the roots close to intervertebral foramina.

We attempt to correlate both amplitude and latency variations of the cervical Motor Evoked Potential (MEP) by changing either intensity and position of the coil over the spine.

We examined 9 normal subjects. A round coil was placed, according to a grid painted on the cervical spine, corresponding to the spinous process of C6-C7-T1, laterally of 2cm and 4cm on the right and left side (Rgt2-Lft2 and Rgt4-Lft4 respectively). MEPs were recorded from the opponens pollicis by side A and B output of 40%-50%-60% .

MEP amplitude progressively increases as the coil is shifted from central to lateral positions. The difference is not significant with an output of 40%, while it is with an output of 60%: using side A on Rgt4, mean value was 7,7 mV sd 3,7; using side B on Lft4 (7 individuals) or Lft2 (2 individuals) the mean value was 6,1 mV sd 3,9.

Latency of MEP. Left MEP by sideB of the coil is shorter than righ MEP by side A: C7 (p=0.04) T1 (p=0.02) with an output of 60% only.

The induced current under the winding up of the coil is able to stimulate cervical roots, at low intensities, but it is useful to shift to an outer position , about 4 cm, to enhance the MEP amplitude.

The latency of the response is constant, regardless the position of the coil and the direction of the current flow within it; the threshold and the amplitude of the responses depends on the aforementioned elements.

TMS

POSTER

PLASTICITY OF MOTOR CORTEX AFTER MUSICAL TRAINING: A NEUROPHYSIOLOGICAL STUDY

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Objectives

To further understand the mechanisms of musical training-induced plasticity, we used electroencephalography (EEG) and transcranial magnetic stimulation (TMS) to investigate the effects of piano keyboard training on interhemispheric interactions and brain activity.

Methods

12 right-handed, music-naïve subjects underwent a motor training (ten 35-minute sessions; 2 weeks), playing an electronic piano keyboard. Before and after training, subjects underwent hand motor function (finger tapping, pinch, Jamar grip, and nine hole peg-9HPT) tests, EEG and TMS assessments. The 32 channel-EEG aimed at evaluating task-related desynchronization (TRD) of mu rhythm during keyboard performance. TMS, targeting *abductor pollicis brevis* (APB) and *abductor digiti minimi* (ADM) bilaterally, was performed to obtain resting motor threshold (RMT), amplitude of motor evoked potentials at 120 % RMT, and ipsilateral silent period (ISP) duration during voluntary APB-ADM co-contraction.

Results

Subjects' keyboard performance dramatically improved for both hands. Left hand 9HPT score significantly improved after training. Pre-training, left ISP durations were longer than right ISPs. Post-training, right ISP_{APB} significantly increased, leading to symmetrical ISP_{APB}. Mu TRD related to unimanual keyboard playing became more symmetrical, decreasing contralaterally and increasing ipsilaterally to the movement's side.

Conclusion

Bimanual motor-training was associated with hand dexterity improvement, more pronounced for the left hand, together with a reduced and more symmetrical cortical activation during motor performance. Interhemispheric inhibition from the right to the left hemisphere increased, rebalancing the pre-training asymmetry. These results suggest that 10 days of skilled motor training is sufficient to induce cortical plastic changes, sharing similarities with findings reported on professional musicians.

SIMULTANEOUS RTMS AND PIANO PLAYING IMPROVE HAND DEXTERITY AND INDUCE CHANGES IN CORTICAL EXCITABILITY IN A PROFESSIONAL PIANIST AFFECTED BY MULTIPLE SCLEROSIS: A CASE REPORT

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Introduction

Motor learning is a fundamental process of neurorehabilitation. One of its neurophysiological substrates -modulation cortex excitability- provides the rationale for non invasive brain stimulation techniques, such as repetitive transcranial stimulation (rTMS). Therefore, association of neuromotor rehabilitation and rTMS may be more effective than their use alone.

Methods

A 39 y.o. pianist affected by multiple sclerosis with a bimanual (L>R) sensory-motor impairment due to 3 cervical relapses in the previous 3-12 months (the last at C4 level) underwent 3-weeks neurorehabilitation sessions (twice a day, 5 days a week) together with treatment sessions of H-coil rTMS (10 Hz, bilateral fronto-parietal cortex, 90%MT) simultaneously to piano exercises. Before (T0) and at the end (T1) of the study, functional (Nine-Hole-Peg-Test, Pinch, Jamar, piano MIDI sequencing) and neurophysiological tests (focal cortical mapping at 115% MT) were performed. Nine hole peg test-NHPT and MIDI sequencing were also collected before and after each rTMS-piano session.

Results

At T1, the patient improved at NHPT in both hands (Right: 27.1'' vs 15.45'' ; Left 49.5'' vs 36.4'') and in piano performance. We found a decrease of MT and of cortical map motor area in both hemispheres. Improvement of these parameters occurring within single sessions was more evident in the first week of treatment, due to progressive improvement of baseline values.

Conclusion

Neurorehabilitation combined with simultaneous association of complex hand motor training and rTMS could improve hand motor performance and modulate motor cortical excitability. Placebo-controlled studies are needed to quantify the hypothetical synergic effect of rTMS and motor training.

THE ORGANIZATION OF THE NEURAL CIRCUITRY INVOLVED IN THE PREPARATION OF REACHING MOVEMENTS: NETWORKS, DYNAMICS AND CONNECTIONS INVESTIGATED BY MEANS OF TMS AND TMS/EEG

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Introduction

Our previous findings showed the involvement of dorso-medial parieto-frontal networks in reaching movements. Thus, new TMS and TMS/EEG experiments were performed to better investigate the networks functionality.

Material and Methods

Left lateral parieto-occipital, parietal and premotor cortices were stimulated, when subjects reached targets in peripersonal space, keeping straight-forward foveal view. TMS was applied at 25%, 50%, 75% of reaction time (RT). RTs were measured and compared to no-TMS. During TMS/EEG, left superior parietal lobule was stimulated, while subjects were at rest. Differences in cortical activity were investigated comparing real-TMS versus sham.

Results

TMS showed no effects on RTs. TMS/EEG showed activations in discrete time-ranges (35-300 msec after TMS) suggesting connections ranging from frontal to posterior brain regions. Considering the mean of neural activity, links with ventral stream were observed (time-range 130-245 msec), and wider connectivity with frontal and posterior areas in remaining time-windows.

Discussion

The present investigation, relatively to our previous findings, better defines the regions involved in reaching preparation. They are mainly segregated in the parieto-occipital, parietal and premotor dorso-medial regions of left, contralateral hemisphere with lower involvement of more lateral regions. Cortico-cortical connectivity shows articulated connections with parietal cortex. Thus, this system is not totally isolated, but involves structures that are not recruited in present behavioural reaching studies.

Conclusions

Data suggest that the system involved in preparing reaching is mainly located in dorso-medial parieto-frontal networks. Further studies are needed to investigate tasks and time involvement of brain regions in reaching, considering that networks could be more articulated.

UNILATERAL CORTICAL HYPEREXCITABILITY IN CONGENITAL HYDROCEPHALUS : A CASE REPORT

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Introduction

Cortical hyperexcitability is considered to play an important role in promoting brain plasticity both in healthy people and in neurological diseases. Hydrocephalus is a brain development disorder related to excessive accumulation of cerebro-spinal fluid in the ventricular system. The functional relevance of cortical structural changes described in this disease is largely unexplored in human. We investigated cortical excitability using multimodal transcranial magnetic stimulation in a case of congenital hydrocephalus with almost no neurological signs.

Methods

A French forty-years-old, ambidextrous and multilingual woman affected by occult spina bifida and congenital symmetrical hydrocephalous underwent a TMS study. The intracortical and interhemispheric paired pulse paradigms were used.

Results

No significant differences were found in the resting motor thresholds between the two hemispheres. On the other hand the intracortical excitability curve was statistically different in the two hemispheres (with SICI being strongly reduced and ICF enhanced in the right one) and the inter-hemispheric curves showed a clear decrease of transcallosal inhibition from left-to-right motor cortex, as compared to that from right-to-left motor cortex.

Conclusion

We hypothesize that in this ambidextrous subject the observed right hemisphere hyperexcitability could represent a mechanism of plasticity to preserve functionality of specific brain areas possibly devoted to some special skills, such as multilingualism.

A TRANSCRANIAL MAGNETIC STIMULATION STUDY OF CORTICAL EXITABILITY IN AMYOTROPHIC LATERAL SCLEROSIS PATIENTS

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Introduction

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease mainly affecting both the upper and lower motor neurons. The Silent Period (SP), determined by Transcranial Magnetic Stimulation (TMS) is a useful parameter for the evaluation of cortical excitability.

Objective

To evaluate the SP duration in a large sample of ALS patients and to correlate the change in SP with duration and progression of the disease.

Method

93 patients (59 males, 34 females; Age 63.32 ± 10.7) satisfying the El Escorial clinical and neurophysiological criteria for ALS were enrolled from September 2009 to March 2012. A monophasic stimulator (Magstim 200) attached to a circular stimulating coil of 9 cm diameter was used. The MEP was recorded from the opponens pollicis muscle.

Result

The SP duration of the patients in milliseconds (ms) resulted (mean ± SD) 102.01±63.28, recording from right opponens pollicis and 117.3 ± 80.61, recording from the left site. Further analysis of the data obtained form males and females yielded a statistically significant difference in SP duration: male 105,55 ± 73,06 ms vs female 75,46 ± 47,04 ms..

Conclusion

The SP duration is reduced in ALS patients in accordance with literature data. The interesting result of this study is the gender specificity, with lower SP duration in female compared with male patients.

HUMAN BRAIN CONNECTIVITY DURING SINGLE AND PAIRED PULSE TRANSCRANIAL MAGNETIC STIMULATION

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Objective

Intracortical inhibition (SICI) and facilitation (ICF) in the human motor cortex can be measured using a paired-pulse transcranial magnetic stimulation (ppTMS) protocol. Recently, a technical device has been introduced, which allows recording electroencephalographic (EEG) responses to TMS of a given scalp site. The latency, amplitude and scalp topography of such responses are considered a reflection of cortico-cortical connectivity and functional state. The aim of the present study is to better characterize the neuronal circuits underlying motor cortex connectivity as well as the mechanisms regulating its balance between inhibition and facilitation by means of EEG navigated-ppTMS coregistration.

Methods

Sub-threshold and supra-threshold single and ppTMS of the left primary motor cortex were carried out during a multi-channel EEG recording on 8 healthy volunteers; the between-pulse intervals used in the paired-pulse trials were 3 (for SICI) and 11 ms (for ICF). Motor Evoked potentials (MEPs) from the opposite hand were simultaneously recorded.

Results

Single and ppTMS induced EEG responses characterized by a sequence of negative deflections peaking at approximately 7, 18, 44, 100, 280 ms alternated with positive peaks at approximately 13, 30, 60 and 190 ms post-TMS. Moreover, ppTMS modulated both EEG evoked activity and MEPs. Amplitude variability of EEG responses was correlated with – and therefore might partially explain – amplitude variability of MEPs.

Interpretation

EEG-ppTMS is a promising tool to better characterize the neuronal circuits underlying cortical effective connectivity as well as the mechanisms regulating the balance between inhibition and facilitation within the human cortices and the corticospinal pathway.

Keywords
- Motor cortex; Cortical effective connectivity; EEG; Navigated Transcranial Magnetic Stimulation; SICI/ICF;

CEREBRAL CONNECTIVITY MODULATES MOTOR PATHWAY ACTIVATION: AN EEGTMS STUDY

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Brain functional connectivity of primary motor area (M1) can be tracked by cerebral recruitments evoked by transcranial magnetic stimulation, as measured by simultaneous electroencephalographic recordings (EEGTMS). This opens the opportunity to pursuit the aim of our study, answering the question whether the brain functional connectivity modulates the level of excitation effected by left M1 TMS, parameterized by the corticospinal motor pathway (CSMP) excitation level measured by MEP amplitude.

After averaging two subgroups of EEG evoked responses corresponding to high and low MEP amplitudes, we calculated the individual difference between them. The grandaverage across subjects of such differences was submitted to sLORETA algorithm; on individual basis the statistical significance of such dependence was estimated comparing current density in each RoI for the high and low CSMP excitation at latencies consistent with the activation of the corresponding grandaverage RoI.

A trend for lower recruitment at 6-10 ms of homotopic sensorimotor areas of the non-stimulated hemisphere (right BA 3, 4, 5) and lower recruitment at 18-25 ms of left parietal regions (left BA 2, 3, 40) for higher CSMP activation indicated that a robust output along the cortico-spinal tract corresponds to a weaker central-parietal projection efficacy at earliest post-stimulus latencies. Stronger bilateral at 26-32 ms and left at 44-47 ms frontal motor areas (BA 6, 8) recruitments for higher CSMP activations suggested to be originated by rebound and feedback mechanisms.

The proposed method sensitive to such brain connectivity patterns might be useful in studies of neurological diseases in which circuits relevant for motor control are impaired.

BRAIN AREAS INVOLVED IN TEMPORAL DISCRIMINATION TASK: A STUDY WITH ERPS AND TMS

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Objective

Time processing in the millisecond-to-minute range is reflected by Event-Related Potentials (ERPs), but the neural circuits of timing remains controversial. In the present study we investigated the role of different cortical areas in the processing of basic temporal information using an interference approach with rTMS and ERPs as indices of timing mechanisms.

Methods

Nine healthy volunteers performed a temporal discrimination task in which they had to decide whether the time interval between two tones was shorter (800 ms), equal to, or longer (1200 ms) than a previously listened standard interval (1000 ms) and press different buttons accordingly. The task was performed at the baseline and immediately after a 15-min-long train of focal 1-Hz rTMS delivered to supplementary motor area, right posterior parietal cortex, right superior temporal gyrus, or Oz (control area). Accuracy and reaction times and ERPs during (contingent negative variation, CNV) and after the end of the comparison interval were analyzed. Results

At the baseline, CNV was modulated by the interval duration and the analysis of the ERP evoked after the end of the comparison interval showed that the amplitude of the positive peak emerging approximately after 200 ms was higher for 'Long' compared to 'Short' intervals, whereas amplitude for 'Equal' was intermediate. RTMS interference had no significant effect on behavioural performance or ERP components.

Conclusion

These data may suggest that these cortical areas are less crucially involved than other brain regions (e.g. sub-cortical or cerebellar areas) in the neural mechanisms processing basic temporal information like interval duration.

HUMAN BRAIN CORTICAL CORRELATES OF SHORT-LATENCY AFFERENT INHIBITION (SAI): A COMBINED EEG-TMS STUDY

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Introduction

Linking in time electrical stimulation of peripheral nerve with TMS, the motor cortex excitability can be modulated to evoke clear inhibition as reflected by the amplitude decrement in the MEPs. This property, named short latency afferent inhibition (SAI), occurs when the nerve-TMS interstimulus interval is around 25 ms and is considered to be a cortico-thalamic phenomenon. The aim of the present study was to use EEG responses to navigated-TMS co-registration to better characterize the neuronal circuits underlying SAI.

Methods

The experimental set included MRI-navigated TMS and 60-channel TMS-compatible EEG devices. TMS-evoked EEG responses and MEPs were analyzed in 8 healthy volunteers; ISIs between median nerve and cortical stimulation were determined relative to the latency of the individual N20 component of SEPs obtained after stimulation of the median nerve. ISIs from the latency of the N20 plus 3 ms and N20 plus 10 ms were investigated.

Results

In all experimental conditions, TMS-evoked EEG responses were characterized by a sequence of negative deflections peaking at approximately 7,44,100 ms alternating with positive peaks at approximately 30,60 and 180 ms post-TMS. Moreover, ISI N20+3 ms modulated both EEG evoked activity and MEPs. Particularly it inhibited MEPs amplitude, attenuated P60 and N100 responses and induced motor cortex beta rhythm selective decrement of phase locking.

Conclusion

The findings of the present experiment suggest cortical origin of SAI that could result from the cortico-cortical activation of GABAergic mediated inhibition onto the corticospinal neurons modulated by cholinergic activation able to reducing intra-laminar inhibition and promoting intra-columnar inhibition.

QUANTITATIVE ANALYSIS OF BLOOD-BRAIN BARRIER PERMEABILITY IN THE HUMAN BRAIN

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Background

The delivery of toxins and drugs into the brain is restricted by the complex blood-brain-barrier (BBB), which maintains a constant extracellular environment within the central nervous system. Quantitative evaluation of BBB permeability in human is thus required for diagnostic and therapeutic reasons. Here we present a novel method for the quantitative evaluation of BBB permeability using human MRI and its potential use for diagnosis and treatment evaluation in patients with brain tumors.

Methods and results

The method is based on Dynamic contrast enhanced (DCE) MRI. 7-10 Spin echo T1-weighted scans (TE\TR = 8\660 ms, approximately 3.5 minutes scan time) were acquired after injection of Gadolinium-DTPA . The time between injection and scanning was about 5-10 minutes so that bolus effect was not visible. Additional pre-contrast high-resolution anatomical and T1-weighted scans were performed as well. Image processing was carried out using SPM 8 and included co-registration, segmentation and normalization. Following normalization to the signal intensity in the superior sagittal sinus, intensity at each voxel was fitted to a linear model. Normalization to vessel intensity significantly improved the linear fit and allowed intra and inter-subject comparison. Analysis of brain scans from 13 individuals showed the slope of the linear curve as the most representative parameter for BBB permeability, showing negative (close to zero) values in intact brain and positive values in extra-brain tissue as well as in abnormal brain regions (tumors and surrounding region).

In a preliminary study, the protocol was performed in 11 patients > 1y after surgical resection for malignant brain tumors following deep transcranial magnetic stimulation (TMS). Sham stimulation was used as control. Two patients were excluded due to lack of enhancement; 7 of the remaining 9 (78%) showed enhancing brain region around the tumor area and a significant increase in permeability following TMS.

Conclusions

The proposed imaging approach reliably detects pathological increase in vessels permeability. Our preliminary results suggest that TMS may be efficient as the first non-invasive method for a transient increase in BBB permeability.

DYSFUNCTION OF CENTRAL CHOLINERGIC CIRCUITS CORRELATES WITH DIFFERENT BEHAVIORAL DISORDERS IN ALZHEIMER'S DISEASE AND DEMENTIA WITH LEWY BODIES

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Background

The activity of central cholinergic circuits can be tested in vivo by the short latency afferent inhibition (SAI), a paired-pulse stimulation protocol coupling peripheral nerve stimulation with cortical magnetic stimulation. SAI is specifically reduced in cholinergic forms of dementia, such as Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). Cholinergic deficits have been largely correlated to behavioral disorders in dementia, but the involvement of cholinergic pathways is not homogeneous among different forms of dementia, suggesting different behavioral patterns.

Objective

To correlate the deficit of cholinergic activity, evaluated by SAI meaurement, with behavioral symptoms in patients affected by AD and DLB.

Methods

Behavioral and neuropsychologic tests, including Neuropsychiatric Inventory (NPI), Mini-Mental State Examination, and extensive neuropsychologic investigation were administered to 18 AD and 18 DLB patients. SAI values were compared with those from a control group of age-matched healthy individuals and the level of SAI in patients was correlated with behavioral measures.

Results

AD patients tended to be more impaired than DLB on long-term memory, whereas DLB patients were more impaired on constructional praxis tasks. NPI total score was similar, but with different behavioural pattern: delusions and hallucinations prevailed in DLB, whereas affective disturbances prevailed in AD. SAI was significantly reduced both in AD and DLB patients when compared with controls. SAI correlated with hallucinations in DLB patients and with euphoric manic state and disinhibition in AD patients.

Conclusions

Reduction of cholinergic activity as evaluated by SAI measurement correlates with different behavioral disorders in AD and DLB.

TMS + TdCS

POSTER

NEUROPROTECTIVE EFFECT OF TDCS IN THE RAT MODEL OF STROKE

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Ischemia generates electrical instability in the penumbra manifesting with spontaneous recurrent peri-infarction depolarizations (PIDs) which contribute to the expansion of ischemic lesion. Transcranial direct current stimulation (tDCS) is a form of brain excitability modulation. The direction of the excitability shifts is determined by current polarity (cathodal tDCS induces brain hyperpolarization, inhibition).

We studied whether cathodal tDCS might reduce in the rat stroke model the size of ischemia by reducing the number/duration of PIDs.

Permanent occlusion of distal middle cerebral artery was induced and cathodal tDCS delivered (200 μA for 4 or 6 hours) through an electrode glued to the skull. Ischemic lesions were evaluated by histology. PIDs were registered with an epidural gold screw placed medially to the infarct core.

The rats treated with cathodal tDCS for 4 and 6 hours soon after stroke induction had respectively an infarct volume (mean ±SE: 62.3 ± 1.6 mm3; 39 ± 3.3 mm3) lower than the untreated rats (± 75.2 ± 4.8 mm3; 57 ± 7.2 mm3) ($p = 0.011$; $p = 0.04$). The reduction in size was greater in the rats treated for 6 hours (31%) than 4 hours (20%). The rats treated by tDCS had about 1/3 of PIDS than untreated rats and the difference was more evident 3-4 hours after stroke induction.

Neuromodulation of cortical excitability with a non pharmacological treatment, already employed in humans, has a neuroprotective effect in the stroke model and could be applied into clinical trials to test efficacy in humans.

EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE ELECTRICAL ACTIVITY OF THE MOTOR CORTICAL NETWORK AT REST AND DURING MOVEMENT

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This study aims at systematically investigating the effects of cathodal and anodal tDCS on the electric activity of primary motor cortex during a motor task.

High density EEG was used to map changes on the entire brain and define the real spatial diffusion of tDCS effects. Ten healthy subjects performed a finger tapping task before and after three separate sessions of 20 minutes of sham, anodal or cathodal tDCS over left primary motor cortex.

During movement, we found an increment in alpha band ERD in contralateral central, bilateral parietal and frontal areas after anodal stimulation compared to sham and cathodal tDCS. In the rest pre-movement period, after sham as well as anodal conditions, we documented an increment of alpha band power over the course of pre- and post-stimulation recording sessions, localized in the sensorimotor, premotor and parieto-occipital regions. On the contrary, after cathodal stimulation no increment of alpha power was found across time. Finally beta band coherence among C3 and activity of bilateral parietal and right frontal regions was higher after anodal stimulation compared with sham condition. We hypothesize that the local modulation of membrane polarization as well as long-lasting synaptic modification induced by tDCS over M1 could result in changes of both local band power and functional architecture of motor network. These significant changes of intensity and reactivity both during rest and movement, probably allow to better address upcoming motor demands and could explain the improvement in motor performance previously described after anodal tDCS on the motor cortex.

BI-DIRECTIONAL ENDURING CHANGES OF CORTICAL PLASTICITY INDUCED BY A NOVEL PAIRED STIMULATION PROTOCOL

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Objective

In the present study we combined two different neurophysiological techniques each of which is capable of inducing a lasting change of cortical excitability, independently: median nerve repetitive electrical stimulation (rEPNS) and transcranial direct current stimulation (tDCS).

Material and Methods

Ten normal young volunteers were enrolled in the present study. All subjects underwent five different protocols of stimulation: (1,2) tDCS only (anodal or cathodal); (3) Sham tDCS plus rEPNS; (4,5) anodal or cathodal tDCS plus rEPNS. The baseline MEP amplitude from abductor pollicis brevis (APB) and flexor carpi radialis (FCR) muscle, the FCR H-reflex were compared with that obtained immediately after and 10, 20, 30, 60 min after the stimulation protocol.

Results

Anodal tDCS alone induced a significant transient increase of MEP amplitude immediately after the end of stimulation while Anodal tDCS + rEPNS determined MEP changes which persisted for up 30. Cathodal tDCS alone induced a significant reduction of MEP amplitude immediately after the end of stimulation while Cathodal tDCS + rEPNS prolonged the effects for up to 30 minutes. Sham tDCS + rEPNS did not induce significant changes in corticospinal excitability. Anodal or Cathodal tDCS + rEPNS and sham tDCS + rEPNS caused a lasting facilitation of H-reflex.

Conclusion

These findings suggest that by providing afferent input to the motor cortex while its excitability level is increased or decreased by tDCS may be a highly effective means for inducing an enduring bi-directional plasticity. The mechanism of this protocol may be complex, involving either cortical and spinal after effects.

LONG TERM DEPRESSION: A STUDY WITH RAPID-RATE PAS

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Objective

In a previous paper we showed that sub-motor threshold 5Hz rENS of the right median nerve when synchronized with sub-motor threshold 5Hz rTMS of the left M1 at a constant interval of 25 ms for 2 minutes caused a somatotopically specific increase in cortical excitability (5Hz PASLTP) In this study we used a similar protocol with a different interstimulus interval (ISI) to evaluate if an asynchronous paired stimulation could cause a reduction of motor cortical excitability (5Hz PASLTD). We also study the effect of 5Hz 5Hz PASLTD on intracortical paired-pulse excitability and sensorimotor intracortical inhibition.

Material and Methods

5Hz rPAS consisted of 600 pairs of stimuli which were continuously delivered to the left M1 at a rate of 5 Hz for 2 min in 20 healthy volunteers. . Each pair of stimuli consisted of an electrical conditioning stimulus given to the right median nerve followed by a biphasic transcranial magnetic stimulus given to the left M1 controlling APB at 15 ms interval. Before and after rPAS (T0-T30-T60), we measured the amplitude of MEP, intracortical inhibition (ICI) and facilitation (ICF), short (SAI 20) and long latency (LAI 200 ms) afferent inhibition.

Results

The 5Hz 5Hz PASLTD protocol caused a significant decrease in mean MEP amplitudes in the APB muscle that lasted for at least 1 h which was paralleled by a reduction of SAI.

Conclusions

These findings show that 2 min of 5Hz rPAS at 15 ms can induce a long-lasting specific reduction in the excitability of the corticospinal output from the stimulated M1 for 60 min.

THE INTERFERENCE OF TDCS ON P300: AN ELUSIVE EFFECT

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Objective

Little is known about the basic effects of transcranial Direct Current Stimulation (tDCS) on the electrophysiological correlates (Event-Related Potentials: ERPs) of cognitive functions. The aim of the present study was to evaluate the effect of tDCS on auditory ERP components.

Methods

Auditory ERPs were recorded in eight healthy volunteers using a two-tones oddball paradigm. EEG was recorded from three (Fz, Cz, Pz) scalp locations at the baseline and immediately after a conditioning tDCS protocol (2 mA intensity for 10 min). Subjects underwent anodal, cathodal, and sham stimulation on three different days, following a random order. A monopolar tDCS montage was used with the active electrode over Pz and the reference electrode over the right shoulder. Parietal cortex is a recognized source of the P300 ERP component. Latencies and amplitudes of two ERP components, N100 and P300, were measured for individual averages. Reaction times (RTs) to rare (target) stimuli were recorded from the right ABP muscle.

Results

In all subjects, the rare tones evoked the N100 and P300 components, with normal latencies and amplitudes. The measures did not show any significant tDCS effect either on ERP latencies/amplitudes or on RTs. However, P300 latency was delayed over all electrodes following anodal tDCS, but this effect did not attain statistical significance.

Conclusions

Anodal tDCS applied over the parietal cortex has a slight effect on auditory P300, whose latency is slowed down. This effect is not statistically significant and is not associated with modifications of the motor response (RT).

NON-INVASIVE BRAIN STIMULATION PROVOKE MODULATORY EFFECTS ON HEAT INDUCED PERCEPTION AND PAIN THRESHOLD

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Transcranial stimulation (magnetic and direct current) is able to change cortical excitability of the motor cortex. In case of chronic pain, modulatory effects have been demonstrated by using brain stimulation, and the mechanism is speculated to be due to plasticity changes.

Objective

The aim of this study was to demonstrate the effect of transcranial direct current stimulation (tDCS) to modulate pain and perception thresholds to heat stimuli.

Methods

In ten healthy controls anodal or sham tDCS was applied to the right primary motor cortex (M1) of the hand. We tested the threshold of heat induced perception and pain when applying heat to the cutaneous area of the superficial radial nerve of the contralateral and ipsilateral (control) hand. Furthermore, we tested cortical excitability using transcranial magnetic stimulation (TMS).

Results

We found a significant threshold increase of heat induced perception (15%) and pain (5%) on the contralateral hand. There were no significant effects on the ipsilateral hand, nor for sham stimulation. The effect of tDCS applied for 10 min lasted for about 1 hour. By using TMS applied to the right M1, before and after 10 min of anodal tDCS, we found a significant increase of the motor evoked potentials (MEP) amplitude on the contralateral hand. When TMS was applied to the left M1, no significant changes were observed.

Conclusions

The tDCS stimulator was able to modulate perception and pain thresholds, and might be a useful instrument for pain therapy. The effect of tDCS causes transitory brain plasticity and might be due to different mechanisms, such as increased cortical excitability, increased firing rate of neurons, physiological effect on the membrane resting potential, decreased muscle pain related to fatigue, or changes of the brain-derived neurotrophic factor (BDNF). However, more studies must be done to understand the mechanisms of effect on chronic pain.

EFFECTS OF ASSOCIATION OF SPINAL AND CORTICAL DC STIMULATION ON CENTRAL NOCICEPTIVE SIGNAL TRASMISSION IN HUMANS

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Objective

To evaluate the effects of direct current stimulation (DCs) applied on three different electrode positions on reflex pathways .

Methods

Three different montages were used: A) anode over thoracic spinal cord and cathode over sensory-motor cortex, B) anode over thoracic spinal cord and cathode over right shoulder, C) anode over thoracic spinal cord and cathode anterior over the abdomen. 12 subjects were studied and DCs was delivered at 2,5 mA for 20 minutes. To investigate the effects of the three different montages we evaluated the modification of lower limb flexion reflex (LL-RF) and H-reflex from soleus muscle after tibial nerve stimulation.

Results

Montage A reduced LL-RF total area by 24% (p=0,001) and RIII (nociceptive component) area by 27% (p=0,0005). Montage B reduced the total LL-RF area by 14% (p=0,021) and RIII area by 16% (p=0,016). Montage C did not induce any modification in all the tested flexion reflex. All montages left unchanged H-reflex parameters.

Discussion

The correct DCs application over the spinal cord is achieved by using the reference electrode on the right shoulder and not over the abdomen. The association of anodal spinal DCs to cathodal DCs over sensory-motor cortex elicited greater after-effects than other montages.

Conclusion

Anodal spinal DCs could modulate the excitability of mono-oligosynaptic segmental reflex and its effects can be further amplified by concomitant DCs over the scalp. By matching spinal and cortical stimulation we have an additive after-effects on reflex pathways and could be more effective for pain management.

CENTRAL FATIGUE IN MULTIPLE SCLEROSIS (MS): FROM MOTOR PREPARATION TO MOTOR EXECUTION

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Objective

In a previous study with TMS we have demonstrated that MS patients with fatigue have a lack of pre-movement facilitation. The neural circuits involved in this pre-movement facilitation are within the fronto-striatal loop. Aim of this study is to further explore the putative mechanisms of "central fatigue" extending our previous findings at a premovement level by studying corticospinal and behavioural changes induced by the sustained exercise.

Material and Methods

Ten MS patients with fatigue and ten without fatigue were recruited from Genoa and Messina. Focal TMS has been applied over the left motor cortex (M1) of the right APB muscle. Resting motor threshold (RMT), mean amplitude of the motor evoked potential (MEP) and premovement facilitation were recorded before and after a motor task (T0-T15-T30). During motor task the subjects, wearing a sensor-engineered glove (right hand), executed a simple sequence of finger opposition (thumb to index, medium, ring and little) for 5 minutes.

Results

After 5 minutes of exercise all patients showed a significant decrease of MEP that recovered after 15 minutes of rest. In the "no fatigue" group the premovement paradigm induced a significant increase of MEP that was greatest when TMS was delivered closer to the movement onset (50 ms before the movement). After 30 minutes of rest it was still present. In the "fatigue" group at baseline no premovement facilitation was recorded and the exercise did not induce any change.

Conclusions

Our results suggest an involvment of the fronto-striatal loop in the pathophysiology of central fatigue in MS.

PRELIMINARY DATA ON DEEP REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (DR-TMS) IN ALCOHOLICS: A NEW HOPE IN ALCOHOL ADDICTION?

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Several neuropsychological hypothesis have been formulated to explain transition from alcohol social use to addiction, characterized by compulsion to drug-seeking, loss of intake control and emergence of negative emotional state (dysphoria, anxiety, irritability).
Transition from social use to dependence is mediated by positive to negative reinforcement shift, in a continuous neuroadaptation process involving reward and other systems managing emotional stress.[1]
Transcranial magnetic stimulation is a non-invasive technique for brain stimulation based on creation of predetermined magnetic fields, inducing action potentials in brain cells. Magnetic stimulation is generated by a coil positioned on patient's scalp. Previously available circular and 8-shaped coils could not stimulate regions deeper than 1 cm below the skull; the new H-coil we employed can reach 4-5 cm under skull regions. Recent studies highlighted brain stimulation potential in studying and treating addiction.[2]
Excitatory dorsal medial prefrontal cortex (dm-PFC) stimulation may reduce HPA axis activation during withdrawal, by activating the pre-limbic CRF-inhibiting nucleus.[1] In this pilot randomized trial we applied Dr-TMS on the dm-PFC in alcohol-addicted patients to elevate the "hypofrontality" reported in alcoholics.[3]
Thirteen alcoholics were divided in two homogeneous groups in terms of age and drinks/drinking day: seven patients were included in the real group, six in the sham one. Excitatory stimulation was provided to the dm-PFC, ten days after last alcohol intake, three days after last benzodiazepines intake. Real stimulus was applied in ten sessions (five per week) at 20 Hz frequency, 120% of resting motor threshold, on dm-PFC. An olfactory-visual provoking stimulus was dispensed to patients just before each stimulation.[4]
Clinical and biochemical examinations were performed before and after Dr-TMS. Twelve of thirteen patients ended the trial, without side effects.

Results

Cortisol reduction (p=0·048) in the only real group:
pre-stimulation: m=13·4µg/100ml SEM=1·63
post-stimulation: m=9·65µg/100ml SEM=1·21
Reduction of drinks/drinking-days (pre-stimulation 95% IC 9·87-30·99; post-stimulation: 0; p=0·0048) and drinks/heavy drinking-days (pre-stimulation 95% IC 12·61-45·11; post-stimulation: 0; p=0·0057) in the only real group. Positive correlation (p=0·033; R=0·59) between pre-stimulation prolactin and drinks/day; pre-stimulation prolactin inversely correlates (p=0·009; R=0·513) with post-stimulation cortisol decrease.
Dr-TMS seems to be effective in reducing cortisol levels, particularly in patients with lower alcohol intake (functional damage), probably by activating prelimbic CRF-inhibiting nucleus. CRF decrease in central amygdale can also be hypothesized, thus leading to withdrawal stress reduction; indeed CRF-antagonist injection in animal's central amygdale is effective in reducing alcohol intake.[5]
Dr-TMS could represent a new treatment for reducing relapse in alcoholics.

EFFECTS OF THE TRANSCRANIAL DIRECT CURRENT STIMULATION TREATMENT ON CORTICAL EXCITABILITY IN ALZHEIMER'S DISEASE

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Transcranial direct current stimulation (tDCS) has been shown to induce specific effects on cortical excitability and behavior in a polarity-dependent way. Currently, there is a growing interest in applying this methodology in neurorehabilitation to reduce cognitive deficits in patients with neurodegenerative diseases, e.g. Alzheimer's disease (AD). Nevertheless the tDCS-induced modulation on cortical excitability still remains to be investigated. To this aim, we investigated the tDCS-induced effects on spontaneous and evoked cortical activity, combining transcranial magnetic stimulation (TMS) and electroencephalography (EEG).

Fourteen AD patients were randomly assigned to two groups. The first group underwent a 2-week real tDCS treatment, while the second group underwent a 2-week placebo treatment. Anodal tDCS (2mA) was delivered for 25 minutes above the left dorsolateral prefrontal cortex (DLFPC). The EEG activity and TMS-evoked cortical potentials (TEPs) were recorded from 19 scalp electrodes before and after treatment. The statistical analyses were performed to reveal cortical changes after tDCS treatment in comparison with baseline measure. We didn't find significant changes in cortical measures after anodal tDCS.

These results show that applying anodal tDCS treatment during the resting state doesn't induce a specific modulation on the cortical excitability neither improves cognitive performance. This study supports the combination of TMS-EEG as a tool for examining the non invasive brain stimulation induced effects in clinical protocols.

TRANSCRANIAL MAGNETIC STIMULATION OF PRIMARY MOTOR CORTEX CAN RESET ORTHOSTATIC TREMOR: A CASE REPORT

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Orthostatic tremor (OT) is a rare but well-defined condition characterized by rapid (13-18 Hz), highly coherent tremor activity of both leg muscles, causing unsteadiness when standing.

Tremor is thought to be generated by supraspinal oscillators but it's unknown if these tremor generators involve cortical circuits. Some authors reported a modulation of OT by transcranial magnetic stimulation (TMS).

We described a 65 years-old female suffering from 18 Hz primary orthostatic tremor. Suprathreshold TMS applied over the primary motor cortex demonstrated to reset tremor activity of the controlateral vastus medialis muscle.

Magnetic stimulation of the lumbar spine failed to induce any modification of the tremor. Our TMS data, even if from a single-case, support the hypothesis that primary motor cortex is involved in the modulation of OT.

NOCICEPTIVE EVOKED POTENTIALS (LEPs) MODULATION BY CORTICAL rTMS: COMPARISON BETWEEN MOTOR AND DORSOLATERAL PREFRONTAL (DLPFC) CORTEX STIMULATION

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Evidence by functional imaging studies suggests the role of motor cortex (M1) and left dorsolateral prefrontal cortex (DLPFC) in the inhibitory control of nociceptive transmission system.

Repetitive transcranial magnetic stimulation (rTMS) is able to modulate experimentally induced acute and chronic pains. In particular the motor cortex rTMS delivered at high frequency (10 Hz) is able to reduce LEP amplitude in patients with acute and chronic neuropathic pain. Less is known about the ability of high frequence rTMS on DLPFC to modulate LEP amplitude.

Objective

In the present study, we evaluated the effect of DLPFC and M1 activation (through rTMS) on nociceptive control in a model of Tm:YAG laser stimulation induced pain.

Methods

In 10 healthy subjects laser-evoked potentials (LEPs) (N2 and P2 components) were recorded in response to laser stimulation of the right hand, before and after active or sham rTMS. Were administered 20 trains of 100 stimuli on the left M1 or on the ipsilateral DLPFC at 10-Hz frequency. The intensity of stimulation was 100% of the motor threshold (MT). Laser-induced pain was scored on a visual analogue scale (0-10 VAS).

Results

Active rTMS on the M1 and on DLPFC reduced N2–P2 amplitude of the LEPs in response to the controlateral hand stimulation, without a homogeneous decrement of pain produced by laser stimulation in right hand. By contrast sham rTMS on the left DLPFC or M1 didn't reduce N2-P2 amplitude of the LEPs.

Conclusion

The present support the hypothesis of the different ability of M1 and DLPFC to interfere with the processing of acute provoked pain. Besides, the dissociation between the N2-P2 amplitude and the subjective reduction of the perception of the laser induced pain confirm the cognitive elaboration of the LEP. This could open new perspectives to non-invasive brain stimulation protocols of alternative target area for pain treatment.

VIDEOSESSIONE
MIOCLONO

COMUNICAZIONI ORALI

POST-TRAUMATIC PERIPHERAL MYOCLONUS WITH CAUSALGIC PAIN SUPPRESSIBLE BY TOXIN TYPE A INJECTION

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The concept of peripheral myoclonus is not yet fully accepted by the medical community because of the difficulty in establishing a cause-and-effect relationship between trauma and subsequent movement disorders.

Here we describe a 47-year-old man who developed involuntary dorsal movements after spinal trauma with D7 vertebral body fracture without spinal cord injury**.**Abnormal bursts of muscle activity, semi-rhythmic involuntary muscle spasms, appeared one month after surgery (vertebral stabilization with fusion procedure) and EMG techniques identified prolonged contraction of right D4-D8 paraspinal and major rhomboid muscles. A hypoaesthesia and slight dysaesthesia involved an area overlying D4-D8 paraspinal muscles with dynamic tactile allodynia and deep pain. A Tinel's sign was found near the proximal surface of the hypoaesthetic area. Gentle pressure of the hypoaesthetic skin surface consistently suppressed the rhythmic contractions, which resumed immediately after cessation of compression.

Central nervous system functions (spine and brain imaging, motor and somatosensory evoked potentials, EEG back-averaging) were normal. Lidocaine injection into these muscles resulted in complete cessation of the involuntary movements, and the patient was successfully treated with botulinum toxin type A, but without pain control. The neurophysiological polygraphic study was useful to determine the therapeutic target muscles.

These findings raise the possibility that the peripheral myoclonus was primarily caused by ectopic firing of the injured posterior spinal nerves and dorsal scapular nerve, then spreading to adjacent muscles possibly via a central mechanism mediated by group Ia afferents or inducing central (spinal) generator activity. Other possible mechanisms are proposed in Literature: loss of inhibitory function of local dorsal horn interneurons, abnormal hyperactivity of local anterior horn neurons, aberrant local axons re-excitations and loss of inhibition from suprasegmentar descending pathways.

BACK-AVERAGING STUDY OF MYOCLONUS IN A CASE OF EARLY MYOCLONIC ENCEPHALOPATHY

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Early myoclonic encephalopathy (EME) is characterized by fragmentary myoclonus, erratic focal seizures and tonic spasms, with a pattern of suppression-burst on the EEG. There are few cases reported in literature, especially regarding the neurophysiology of myoclonus. EEG-EMG polygraphyc recordings are the only tests able to prove the cortical origin of myoclonus. Sometimes is not clear the exact correlation between jerks and the specific cortical activity. We report the clinical and neurophysiological features of a patient with early myoclonic encephalopathy studied with EEG/EMG back-averaging.

A 3-months year old male developed progressively myoclonus and tonic spasms. Other clinical features was nystagmus. A brain MRI study showed a mild diffuse cerebral demyelination. No metabolic disorders were found. A video-EEG was performed with EMG study of bilateral deltoids and also EKG-PNG poligraphy.

The EEG was characterized by suppression burst pattern with periods of flat activity lasting 3-6 sec. Bilateral jerks were recorded during burst activity with a back-averaging correlation.

Early myoclonic encephalopathy is a dreadful fortunately rare epileptic encephalopathy without effective treatment. Myoclonic jerks are mandatory to prompt diagnosis of this syndrome, but sometimes there is no clear correlation with cortical activity. In literature there are few data regarding EEG/EMG correlation in EME. In our case back-averaging examination showed a strict correlation between EEG spike and EMG burst, identifying a direct cortical origin of myoclonus.

CASI CLINICI SNC

POSTER

INTER-HEMISPHERIC FUNCTIONAL COUPLING OF ELECTROENCEPHALOGRAPHIC ALPHA RHYTHMS IN EPILEPTIC PATIENTS COULD BE INCREASED BY MOBILE PHONE EMISSION

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GSM electromagnetic fields (GSM-EMFs) of mobile phones could modulate -after a prolonged exposure- inter-hemispheric synchronization of temporal and frontal resting electroencephalographic (EEG) rhythms in normal young and elderly subjects.

Here we tested the it could be more evident in epileptic patients, who typically suffer from abnormal mechanisms governing synchronization of rhythmic firing of cortical neurons. Eyes-closed resting EEG data were recorded in ten patients affected by focal epilepsy. These data were compared with those obtained from 15 age-matched normal subjects. The GSM device was turned on (45 minutes) in the “GSM” condition and was turned off (45 minutes) in the other condition (“Sham”). The mobile phone was always positioned on the left side in both patients and control subjects. Spectral coherence evaluated the inter-hemispheric synchronization of EEG rhythms at the frequency bands: delta (about 2-4Hz), theta (about 4-6Hz), alpha1 (about 6-8Hz), alpha2 (about 8-10Hz), and alpha3 (about 10-12Hz). The effects on the patients were investigated comparing the inter-hemispheric EEG coherence. Compared with the control subjects, epileptic patients showed a statistically significant higher inter-hemispheric coherence of temporal and frontal alpha rhythms (about 8-12 Hz) in the GSM than “Sham” condition.

These results suggest that GSM-EMFs of mobile phone may affect inter-hemispheric synchronization of the dominant (alpha) EEG rhythms in epileptic patients. If confirmed by future studies on a larger group of epilepsy patients, the modulation of the inter-hemispheric alpha coherence due to the GSM-EMFs could have clinical implications and be related to changes in cognitive-motor function.

ELECTROPHYSIOLOGICAL EVALUATION AND SKIN BIOPSY IN THE DIAGNOSIS OF SENSORY NEUROPATHY

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Electrophysiological evaluation of sensory nerves represents the standard test to diagnose a sensory neuropathy. Nerve electrical stimulation, however, bypasses the extreme periphery, so it doesn't offer any information about last endings of myelinated fibers and mechanoreceptors that can be investigated instead by skin biopsy. Skin biopsy is a minimally invasive tool that allows quantification of free and corpusculated sensory receptors and their afferences.

In order to evaluate if the assessment of distal cutaneous sensory endings may improve diagnostic accuracy in sensory neuropathy evaluation we retrospectively compared electrophysiological data and Meissner corpuscle (MC) and intrapapillary myelinated fiber (IMF) density in a group of 119 patients affected by sensory neuropathy of different etiology.

We observed a significant correlation between electrophysiological and morphological data. Moreover among patients with normal electrophysiological evaluation, about 20% showed a reduction of IMF and over 50% showed a reduction of MC density.

We conclude that the immunohistochemical evaluation of cutaneous nerves, allowing the visualization of the last nerve endings, is a more sensitive tool, compared to standard electrophysiology, to diagnose sensory neuropathy.

THE SLEEP-DEPRIVED BRAIN IN NORMALS AND PATIENTS WITH JUVENILE MYOCLONIC EPILEPSY: A PERTURBATIONAL APPROACH TO MEASURING CORTICAL REACTIVITY

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Simultaneous electroencephalography-transcranial magnetic stimulation (EEG-TMS) investigates cortical reactivity to external perturbations. TMS evoked potentials (TEPs) have been described in normals during sleep and wake but not after sleep deprivation or in pathologically enhanced excitability, i.e., epilepsy.

The aim of our study was to identify TEPs and their modifications via EEG-TMS co-registration in healthy controls and patients with juvenile myoclonic epilepsy (JME) during wake, sleep deprivation and sleep conditions. Focal TMS was administered to the primary motor cortex in 12 healthy controls and 10 patients with JME. At least 150 TMS were delivered randomly every 8-15 sec during wake, sleep deprivation and sleep conditions. EEG was simultaneously acquired from 32 scalp electrodes.

A significant increase in late peak amplitudes (P100 and N190) was observed in all subjects during the sleep-deprived condition, with a marked anterior increase and overall higher amplitude potentials in the JME patients.

We demonstrated an overall higher cortical excitability in the JME patients, particularly over the anterior cortex after sleep deprivation and rebound sleep. This phenomenon could be related to the cortico-thalamic circuit dysfunctions believed to cause myoclonic epilepsy and a higher susceptibility of the frontal and prefrontal areas to the effects of sleep deprivation.

A CASE OF ISOLATED AND PROLONGED GLOBAL APHASIA: THE ROLE OF EEG AND FDG-PET IN DIFFERENTIAL DIAGNOSIS

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The most common cause of sudden isolated and prolonged global aphasia is stroke, affecting the cortical or subcortical language network. However, an aphasic status epilepticus (ASE) has to be considered as a possible differential diagnosis in awake patients presenting with acute and prolonged language impairment.

ASE is suggestive of a localized dysfunction of language processing in the dominant hemisphere. ASE is a rare phenomenon and to our knowledge a few cases are described in the literature. In the differential diagnosis between ASE and stroke with aphasia, FDG-PET imaging should be used when EEG shows no clear evidence of ictal activity. We described a case of a 74 year-old woman who presented sudden onset of both isolated and prolonged global aphasia 5 months after a left temporo-occipital haemorrhage and 20 days after a left hemispheric ischaemic stroke. A new ischaemic and haemorragic event was excluded by neuroimaging (CT and MRI, including DWI).

Since several EEGs showed atypical patterns in the left temporal region, an FDG-PET was performed, resulting in two hypermetabolic areas in the left temporal and occipital lobes. The aphasia improved after anti-epileptic therapy.

In conclusion, this is a case of post-stroke ASE, in which the evidence of hypermetabolism on FDG-PET allowed a definite diagnosis of epilepsy.

DEEP BRAIN STIMULATION MAY IMPROVE COGNITIVE FUNCTIONS IN THE LOGOPENIC VARIANT OF PRIMARY PROGRESSIVE APHASIA (LPPA)

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Background

No therapies are available for the logopenic variant of primary progressive aphasia (LPPA). Nevertheless deep brain stimulation may improve cognitive functions in some neurodegenerative disorders, no previous studies investigated deep brain stimulation effects in patients with LPPA.

Objective

Our aim was to investigate the effects on cognitive function of high frequency repetitive transcranial magnetic stimulation (hf-rTMS) delivered deeply over the dorso-lateral prefrontal cortex (DLPFC) in a patient with LPPA.

Materials and methods

The patient was a 50 years-old right-handed man with a diagnosis of LPPA due to progressive language impairment (phonological errors in speech and naming, impaired single word retrieval and sentences repetition) and predominant left perisylvian atrophy and hypoperfusion. Deep hf-rTMS was delivered over the left DLPFC. The patient received four stimulation cycles (two REAL and two SHAM) each of whom lasted 20 minutes for 5 consecutive days. Patient's performances in frontal, visuo-spatial and linguistic tasks were evaluated before and after each stimulation session. Test scores after REAL were compared with those obtained at baseline and after SHAM.

Results

We found a temporary, but highly significant improvement in the linguistic skills (either oral and written tasks) but not in the other cognitive domains tested, after REAL, but not SHAM stimulations.

Discussion

Hf-rTMS delivered over the left DLPFC could improve language in LPPA by enhancing long term potentiation and synaptic plasticity within the stimulated and interconnected areas involved in language network. Our findings might prompt future researches into the feasibility and efficacy of deep hf-rTMS as a therapeutic tool in progressive aphasia syndromes and other neurodegenerative disorders.

SPONTANEOUS BRAIN FUNCTIONING ALTERATIONS IN OBSTRUCTIVE SLEEP APNEA SYNDROME: A RESTING-STATE FMRI STUDY

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Objectives

Obstructive sleep apnea (OSA) syndrome is a frequent, impairing and risky medical condition. Repeated episodes of upper airway obstruction lead to sleep fragmentation and possible effects of hypoxia, as well as objective sleepiness and cognitive disturbances. Resting-State fMRI (RS-fMRI) has been proven to be useful into characterizing network level brain alterations underlying pathological cognition. Here we investigated for the first time changes in RS-fMRI brain connectivities in OSA patients.

Materials

20 severe OSA patients (age 55yrs+/-8, BMI 28+/-1) and age-BMI matched control subjects underwent RS-fMRI. Patients underwent clinical evaluation and polysomnography.

Methods

Individual connectivity matrices, extracted from 100 anatomically defined brain regions, entered network analysis involving Default Mode Network (DMN), Attentional Network (AN) and Parieto-Frontal Integration Theory (P-Fit) network. We tested (1) the impact of OSA on a wide set of cognition and attention relevant brain regions and (2) the relation of connectivity measures with the clinical burden, represented by 4 different polysomnography indices.

Results

We found differences between OSA and controls located in bilateral frontal and temporal regions; an increased connectivity between P-Fit frontal regions (p=.036); a correlation between Apnea-Hypopnea Index (AHI) and overall frontal lobe functioning (r=.510, p .025); an increased connectivity between DMN and the rest of the brain (r= .522, p =.038).

Discussion

OSA seems to be accompanied by a global reorganization of the connectivities between regions relevant to attention and cognition.

Conclusion

RS-fMRI analysis can provide information about brain functioning changes that underlies OSA symptomatology, leading to a better understanding of its complex pathophysiology.

THE ROLE OF TRANSCRANIAL B-MODE SONOGRAPHY IN PARKINSON'S DISEASE AND PARKINSONISM

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Background

Transcranial B-mode sonography (TCS) to assess brainstem has become an important tool for the diagnosis of movement disorders. Although substantia nigra (SN) hyperechogenicity can be found in more than 90% of idiopathic Parkinson's disease (IPD) patients, it is very rarely found in patients with atypical parkinsonism. Purpose

The aim was to evaluate the effectiveness of TCS in diagnosis of IPD and parkinsonism. TCS was performed in 46 patients. Twenty-five patients (54%) had a clinical diagnosis of IPD; 21 patients (46%) had parkinsonism, of which 12 multiple system atrophy (MSA), 2 progressive supranuclear palsy (PSP), 2 vascular parkinsonism and 3 iatrogenic parkinsonism.

Results

In 20 patients with IPD (80%), in 1 patient with MSA (8%), in 1 patient with PSP (33%), and in 3 patients with iatrogenic parkinsonism (100%) TCS showed an increased SN hyperechogenicity. Sensitivity of TCS was of 77% in IPD and 93% in parkinsonism.

Conclusion

Although the limitation due to the bone window, TCS represents a non invasive and available approach and it provides information about the morphology of the brain for refinement of the diagnosis of several movement disorders.

LONG TERM NEUROPHYSIOLOGICAL MONITORING IN VEGETATIVE AND MINIMALLY CONSCIOUSNESS PATIENTS: PROTOCOL DESCRIPTION AND PRELIMINARY DATA

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Vegetative and minimally consciousness patients have been taken, in the last years, an increasing attention in the social and scientific community.

The neurophysiology is probably the best adapted disciplines for the long term observation of these clinic cases.

The low expensive and the few invasive neurophysiological methods are particularly effectiveness to give objective data, easy to compare in the time.

So the project CORE is planed. Its aim is choosing, monitoring and studying vegetative and minimally consciousness patients, by a standardised protocol serially applied.

10 patients were chosen for this plan. The time spent by injury had to be more 3 months and less than 18. The aetiology of their clinical condition is various: 3 are traumatic patients, 7 post-anoxic patients. They will monitor for two year. During this time some neurophysiological diagnostic tests, organized in battery, are performing (EEG, short-latency PES, long-latency PES, BAEP and P300-MN) and for some of these are using also the complex paradigms. Moreover also f-MRI is included in CORE protocol, in particular one evaluation was made at the beginning of the project and the second one will repeated at the end. Finally these patients are periodically submitted to a clinical evaluation based on Coma Recovery Scale - Revised (CRS-R).

After two years the clinical data, f-MRI date and the neurophysiological ones will elaborated and compared to determine which of these will be the most reliable and effective tools.

CROSSING THE LINE BETWEEN LAPAROSCOPIC AND ROBOTIC SURGERY: WHAT DOES HAPPEN IN A SURGEON'S BRAIN?

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Introduction

In human, both primary and non-primary motor areas are involved in the control of voluntary movements. However, the dynamics of functional coupling among different motor areas has not been fully clarified yet. There is to date no research looking the functional variations in the brain of surgeons operating in laparoscopy compared with those trained in robotic surgery.

Materials and Methods

We enrolled 16 right-handed surgeons, with the same experience in the field of robotic and laparoscopic surgery; we evaluated modifications in intra and inter-hemispheric EEG coherence with a 32-channels device during the same, simplified motor task with either a robotic or a laparoscopic approach. Estimates of auto and coherence spectra were calculated by a fast Fourier transform algorithm implemented on Matlab 5.3.

Results

We found increase of coherence in surgeons performing laparoscopy, in beta and gamma-banda activity, in all experimental conditions (M1 vs SMA, S1 vs SMA, S1 vs pre-SMA and M1 vs S1; $p<0.01$). Conversely, an increase in inter-hemispheric coherence was found in surgeons using the robotic procedure (left pre-SMA vs right M1, left pre-SMA vs right S1, right pre-SMA vs left M1, right pre-SMA vs left S1; $p<0.01$).

Discussion

Our data provide a semi-quantitative evaluation of dynamics in functional coupling among different cortical areas in surgeons performing laparoscopy or robotic surgery. We detected a wider activation of motor and non-motor areas in volunteers using a laparoscopic approach compared with those operating with the robot. Analysis of inter-hemispheric coherence proved a more effective synchronization between homologous areas in surgeons using a robotic approach, likely reflecting the induction of early-onset transcallosal plasticity phenomena.

NEUROPHYSIOLOGICAL STUDY OF 2 SISTERS AFFECTED BY RETINAL DYSTROPHY IN ALSTRÖM SYNDROME

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Introduction

The Alström syndrome is characterized by an autosomal recessive inheritance, obesity, mental retardation, cardiomyopathy and retinopathy. Research has not yet characterized the retinal disorder. The aim of this study is to evaluate visual electrophysiology in two sisters with Alström Syndrome.

Case Report

Two sisters HY (F, 4 y) and HS (F, 2 y), both have nystagmus, photophobia, visual impairment, obesity and mental retardation. Both are homozygous carriers of a variation of intronic sequence between exons 9 and 10 in a splice site of chromosome 2. The flash visual evoked potential (VEP) were abnormal in both patients, worse in HY. The electroretinogram (ERG) showed a severe impairment of the photoreceptors. Combining ERG and PEV allowed to hypothesize a greater involvement of the responses generated by the system of cones.

Conclusions

The reported cases, which present the typical clinical picture of Alström Syndrome, confirmed by genetic defect, support the important role of electrophysiological study of the visual system in this pathology, which allowed the diagnosis of retinal dystrophy "cone-rod" type in both patients. The finding of a different clinical stage in the two sisters of different ages suggests that retinal damage begins with photopic system involvement and then extends to the scotopic system.

ONABOTULINUMTOXIN A FOR TREATMENT OF CHRONIC DAILY HEADACHE ACCORDING TO PREEMPT PROTOCOL

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Chronic daily headache (CDH) is a group of disorders characterized by very frequent headaches (>/= 15 days a month), including headaches associated with drug overuse.

When headache duration is greater than 4 hours, the most frequent disorders are chronic migraine (CM), chronic tension-type headache (CTTH), hemicrania continua and new daily persistent headache. Long duration CDH is a significant public health concern, as patients have a significant diminished quality of life. OnabotulinumtoxinA has shown efficacy in relieving pain in chronic migraine (PREEMPT Clinical program, Dodick et al, 2010).

We examined 4 female patients, mean age 47, affected by CDH with overuse of acute headache drugs. The mean frequency of headache days was 21,7 per month. 2 patients had CM and the other 2 patients had CTTH and multiple sclerosis. Preventative treatments and common pain medication have been ineffective for all the patients. OnabotulinumtoxinA 155 UI was administered to every patient according to PREEMPT protocol. After 12 weeks we repeated the treatment. At the end of the observation the mean frequency of headache days was largely reducted: 9,5. No substantial side effects, except for hair loss in a patient, has been reported.

Conclusions

OnabotulimuntoxinA according to PREEMPT protocol seems to be promising in the treatment of CDH. Larger studies are needed to confirm the efficacy of onabotulinumtoxinA in relieving pain, expecially for CTTH, in which PREEMPT protocol has not been tested yet.

REFRACTORY FOCAL MOTOR STATUS EPILEPTICUS RESPONSIVE TO INTRAVENOUS LACOSAMIDE

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We report a refractory focal motor status epilepticus (SE), responsive to treatment with lacosamide.

The patient (male, 39) was operated for a right fronto-temporo-parietal chronic subdural haematoma and ten days after he was admitted to ER for onset of recurrent focal motor seizures of left upper limb, leftward gaze deviation and brief impairment of consciousness. Seizures constituted a focal motor SE, which was not responsive to first-line treatment (intravenous midazolam and levetiracetam). A CT scan showed relapse of haematoma and surgical treatment was decided. As the patient awakened from anaesthesia, focal motor seizures still occurred and a continuous myoclonus of left wrist extensor muscles was observed. Intravenous phenytoin did not interrupt myoclonus nor focal motor seizures. An EEG showed both a myoclonus-related right centro-parietal periodic paroxysmal activity (PLEDs), and ictal focal epileptiform discharges arising from the same areas. Intravenous lacosamide (200mg iv/12h) interrupted motor seizures by the first hour, whereas myoclonus persisted 24h more associated with PLEDs of attenuated amplitude. A subsequent video-EEG showed further PLEDs amplitude attenuation and disappearance of positive myoclonus which was replaced by a negative myoclonus of the same muscles lasted about 24h. An EEG one month afterwards showed disappearance of PLEDs with a normal background activity. The patient is still seizure-free at six months.

Efficacy of lacosamide in treatment of refractory focal SE has been recently reported in literature.

The case we observed confirms such efficacy and has the peculiarity of showing a progressive effect on different epileptic manifestations.

ACUTE LATE ONSET MYELOPATHY: CLINICAL AND NEUROPHYSIOLOGICAL ASPECTS

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Introduction

Acute late onset myelopathy (LOM) is an unusual entity, poorly characterised in clinical and neurophysiological aspects.

Objective

In this retrospective study we review a series of patients with acute late onset myelopathy (presentation of the first symptom of disease after the age of 50 years) admitted to our hospital from June 2011 to February 2012.

Methods

Investigation is concerning with clinical, laboratory, magnetic resonance imaging (MRI), motor and somatosensory evoked potentials (MEPs and SEPs), NVC and EMG, of patients with acute LOM of various origins; we attempt to draw the more appropriate and useful neurophysiological approach to achieve information in the underlying pathophysiology.

Results and conclusions

We included 8 patients (4 F and 4 M) with acute LOM. The most frequent first symptoms were motors deficits (8/8). Inflammation within the spinal cord was turn out in 6 cases by MRI or CSF examination (1 Clinically Isolated Syndrome, 1 Multiple Sclerosis, 1 Neuromyelitis Optica, 3 idiopatic myelitis). In one case the aetiology of LOM was neoplastic and in the other one probably paraneoplastic.

Severe clinical onset and poor outcome were related with central-located spinal lesions, extending more than 3 vertebral segments.

Diagnostic contribution of neurophysiology was relevant in MRI-negative patients (2/8): diagnosis of myelopathy was confirmed by increased central motor and somato-sensory conduction time and by inflammatory features based on CSF. MEPs were found to be more affected than SEPs in patients who had more severe paraparesis at onset. Associated abnormalities of peripheral nervous system were showed in three patients.

SPASTICITY IN PATIENTS WITH SEVERE ACQUIRED BRAIN INJURY: AN IMPAIRMENT THAT IS POORLY UNDERSTOOD AND POORLY MEASURED

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Objective

The aim of this interventional evaluation study was to assess the acknoledgment of spasticity secondary to severe brain injury by observing 27 patients recovered in our Neurological Rehabilitation Section of the Clinical Institute Città di Brescia (Italy). The study will thus investigate any parametric and non-parametric correlations that might influence the development of spasticity in these patients in order to optimize their clinical and rehabilitative approach.

Material and method

27 patients (14 males, 13 females; mean age 65+/-15yy), affected by severe acquired brain injury and recovered in our Neurological Rehabilitation Section from february to october 2009, were recruited in this study. In accordance with our inclusion criteria (GCS < or = 8, LCF < or = 3, DRS < or = 22), patients were divided in 4 observational groups (post-stroke group, post-haemorragic group, post-anoxic group, post-traumatic group) and evaluated under an epidemiological, clinical and functional point of view. Patients had been undergoing physiotherapy during the recovery and observational period, 6 days a week, in 2-hour session, consisting in passive limb kinesis, neurodynamic limb exercises and postural control exercises.

Results

Our data showed that 85% of patients recruited developed an upper and/or lower limb spasticity, never demonstrated in other clinical evidences. In a particular way, we observed that a) post-haemorragic group showed an higher incidence of limb spasticity, b) spasticity will develop earlier in post-stroke and traumatic patients, c) spasticity severity is stronger in post-anoxic and traumatic brain injury. However, these parametric data were not statistically significant ($p > 0.05$). All patients received drug and physiotherapic treatment (in line with our National Consensus Conference protocol) but only 30% of them will not develop limb spasticity. In line with our non- parametric statistical analysis, no correlation between the development of limb spasticity and nutritional and co-morbidity patients status was observed.

Conclusions

Our observational and investigational study demonstrated that to date, there is no clinical advanced evidence about the pathophysiological mechanisms underlying the development of spasticity in patients affected by vegetative state secondary to severe acquired brain injury. Moreover, a comprehensive clinical and rehabilitative review is needed in order to optimize the complex managment in patients affected by cognitive and motor disorders related to severe acquired brain injury.

LATE-TERM NEUROPHYSIOLOGICAL EVALUATION OF PRES IN 5 YOUNG PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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PRES is a syndrome characterized by specific clinical symptoms and neuroradiological signs which are often reversible. PRES occurs in different chronic diseases. Its pathogenesis is not well known but always presents vasogenic edema.

Aim of the study is the retrospective evaluation of all PRES whose diagnosis has been made for 2 years.

From december 2011 to february 2012, we examined 5 patients suffering from ALL (3 M, 2 F, mean age: 11 years) who developed PRES during induction chemotherapy.

PRES lasted 3-10 days and symptoms were altered mental state (5), hypertension (4), epileptic seizures (3), headache and visual disturbances (3).

At the admission, EEG, CT scan, MRI and angio-MRI were performed.

After almost 3 months since the beginning of PRES, clinical examination, brain MRI, EEG and patter-VEP were performed.

Neurological examination was normal in 4/5; only one showed blurred right emiparesis; Brain MRI was normal in everyone.

VEPs were normal in 2/5, 3 presented mild and moderate abnormalities.

EEG abnormalities were related to the first MRI results and hypertension in every patient and were reduced in the following check-up after discharge (2/5) .

Neurophysiologic investigations – EEG and VEP- after 3 months of PRES, evidenced a functional damage in CNS albeit normal MRI. We related alterations to symptoms, therapy, MRI, finding a direct link only with intrathecal methotrexate (MTX).

EEG and VEP, should be considered first-choice investigations in short- and long-term follow-up of PRES to uncover functional damage whether imaging diagnosis is negative.

POTENZIALI EVOCATI E MONITORAGGIO

POSTER

EXPLORING BRAINSTEM FUNCTIONS IN MS PATIENTS BY COMBINING NEUROPHYSIOLOGICAL AND NEURORADIOLOGICAL APPROACHES

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Objective

To examine sensitivity of brainstem reflexes (BSRs) and to correlate BSRs with multimodal evoked potentials (mEPs) and brain MRI lesion burden in relapsing-remitting multiple sclerosis patients (RRMS).

Methods

Sixty RRMS patients (aged 33.3±8.3, range 20-50, disease duration 8.2±6.4 yrs, EDSS score 1.8±1.1) underwent visual, acoustic, upper and lower somatosensory EP recordings (respectively VEP, ABR, median SEP–mSEP- and tibial SEP-tSEP) and brain MRI. BSRs of interest were: the vestibulo-collic (VCR), trigemino-cervical (TCR), vestibulo-masseteric (VMR) and acoustic-masseteric (AMR) reflexes. Neurological examination was rated according to the EDSS scale. mPE, BSRs, brain MRI and EDSS data were quantified according to a conventional score.

Results

EP abnormalities were recorded in 84.5% of patients distributed as follows: VEP 43.1%, ABR 37.3%, mSEP 60.3%, tSEP 58.6%. BSRs were impaired in 90% of patients specifically with the following percentage frequency: VEMP 38.3%, TCR 83.4%, VMR 81.6% and AMR 83.3%. Brain RM revealed 71.7% of patients with BS lesion. Abnormalities of mEPs significantly correlated with: impaired BSRs (r=0.342 p=0.008), BS MRI lesion burden (r=0.501 p=0.0001) and EDSS score (r=0.472 p=0.0001).

BSR alterations significantly correlated with BS lesion burden (r=0.335 p=0.009) and EDSS score (r=0.352 p=0.006). No correlations were found between disease duration and the above mentioned variables.

Conclusions

Comparing BSR data with EP findings, MRI lesion burden and EDSS score it emerges that BSR recording may represent a useful, additional tool in providing evidence of BS dysfunction in MS with high sensitivity compared to the conventional paraclinical tests.

EVOKED POTENTIALS MAY PREDICT RESPONSE TO IMMUNOMODULATING TREATMENT IN MULTIPLE SCLEROSIS

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Objective

Early diagnosis and treatment of multiple sclerosis-MS is now granted after the advent of magnetic resonance imaging-MRI, raising the need of biomarkers for monitoring and predicting treatment response and disability. Evoked potentials-EPs are a good candidate since they explore functional involvement of eloquent pathways.

Methods

Disability-EDSS and multimodal EPs were assessed in patients with RRMS (96) before immunomodulating treatment and after 2.5 $\pm$ 0.8 years follow-up (75), when patients were classified as non-responders (<50% relapse rate reduction, or >2 MRI enhancing lesions, or >4 new lesions), full-responders (no MRI /clinical activity), or partial responders. The severity of all EPs abnormalities was scored using a 0-3 conventional scale from normal to absent and summed to obtain a global EPs score.

Results

EPs score and EDSS at baseline was significantly correlated with EDSS at baseline ($r=0.511$, $p<0.001$) and even more at follow-up ($r=0.686$ $p<0.001$), and was significantly higher in non responders subgroup vs the other subgroups. At follow-up, the EPs score significantly increased in the whole group, more significantly in the non-responders vs other subgroups, while EDSS significantly increased in non-responders. Moreover, 34% of full responders had a global EPs score increase >2. Patients with baseline global EPs score >6 had increased risk (OR=5.82) of worsened follow-up EDSS (positive predictive value-PPV 78 %, negative PV 67.5%, chi square $p=0.001$).

Conclusions

If performed early, EPs may help predicting and monitoring treatment response better than clinical or MRI assessment alone, suggesting their validation as surrogate biomarker in MS.

OPTICAL COHERENCE TOMOGRAPHY AND VISUAL EVOKED POTENTIALS: WHICH IS MORE SENSITIVE IN MULTIPLE SCLEROSIS?

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Objectives

The aim of this study is to evaluate differences between optical coherence tomography (OCT) and visual evoked potentials (VEP) in multiple sclerosis (MS) and clinically isolated syndrome (CIS) patients.

Methods

Cross-sectional study of 40 subjects with MS (6 CIS, 30 relapsing-remitting–RRMS, 4 secondary progressive–SPMS; age 37±9, disease duration (DD) 6.3±6.4, females 22, Expanded Disability Status Scale –EDSS- median 2.0 range 0.0-7.5) of whom 18 with clinical history of optic neuritis (ON) in a single eye and 5 in both eyes at least 3 months prior. Visual Acuity (VA), OCT retinal nerve fiber layer (RNFL) thickness , VEP(checkerboard,15') and EDSS were performed in all patients. The severity VEP abnormalities were quantified according to a 4-graded conventional score (0 normal, 3 absent).

Results

In eyes with previous ON, the sensitivity of OCT was 68% for global RNFL thickness (64%for temporal quadrant) vs 71% for VEP Only 61% eyes were abnormal at both examinations. Abnormal VEPs only were found in 11% and OCT only in 7%, while the combination of the two detected abnormalities in 79% of eyes. In eyes without previous ON the sensitivity of OCT was 19% for global RNFL thickness, (17%for temporal quadrant) vs 31% for VEP. Only 15% eyes were abnormal at both examinations. Abnormal VEPs only were found in 15% and OCT only in 4%, while the combination of the two detected abnormalities in 35% of eyes. No significant difference was found between OCT and VEP sensitivity (McNemar Test $p<0.05$) also when classifying patients as CIS/early MS (DD ≤ 2yrs, N=14) and with longer DD (>5yrs, N=23). In eyes without previous ON, DD was significantly correlated with temporal RNFL quadrant thickness (Pearson's r=-0.3, p=0.02) and not with global RNFL thickness or VEP. VEP score and RNFL thickness were significantly correlated with EDSS (global RNFL: Spearman rs=-0.43, p=0.001; temporal RNFL: rs=-0.33, p= 0.01; VEP score: rs=0.45, p=0.0002) and with VA (global RNFL: rs=0.30, p=0.03; temporal RNFL: rs=0.42, p=0.002; VEP score: rs=-0.43, p= 0.001).

Conclusion

The present findings of similar OCT and VEP sensitivity in detecting clinical and subclinical alterations in CIS/MS patients underline their complementary usefulness in clinical evaluation which, when used in combination, help increasing sensitivity in detecting abnormalities in the visual pathways. The correlation with disability, VA and DD support the role of the two tests in monitoring MS patients.

CONJUGATED LINOLEIC ACID (CLA) DIETARY TREATMENT IN X-LINKED ADRENOLEUKODYSTROPHY

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Introduction

Some evidence shows that a dietary treatment with Lorenzo's oil (LO) and Conjugated Linoleic Acid (CLA) is able to stabilize the worsening of Somatosensory Evoked Potentials (SEPs) abnormalities in X-ALD carriers.

Objectives: Aim of this study was to evaluate the effect of the LO + CLA treatment in X-ALD patients, by means of SEP.

Methods

Ten X-ALD patients underwent clinical examination and 4 arms SEP study before and after 6 months of a mixture of LO (40 g/day) with CLA (5 g/day) dietary therapy. SEPs latencies and amplitudes were compared before and after treatment.

Results

Median nerve SEPs worsened at follow-up due to a significant increase of N13 latency (p = 0.000), N20 latency (p=0.005) and N9-N20 interpeak interval. Tibial nerve SEPs findings worsened at follow-up. In particular after treatment, when compared with before: 1) the N22 latency (P = 0.047) and the N37 latency (P = 0.046) increased significantly; 2) the N22-N37 interpeak interval increased significantly (P = 0.012). Overall only four patients showed substantially unchanged neurophysiologic features after therapy.

Conclusions

Conversely to the evidences obtained in X-ALD carriers, the dietary treatment with LO + CLA in X-ALD patients does not modify significantly the natural course of the disease. These data permit to hypothesize that, in X-ALD patients, the mechanisms of somatosensory system impairment are partially different from those underlying the somatosensory pathways abnormalities in X-ALD carriers, and confirm that inflammatory mechanism, crucial in determining severe disability, plays a predominant role in the late stages of the disease.

Keywords

X-linked adrenoleukodystrophy, somatosensory evoked potentials, Lorenzo's oil, Conjugated Linoleic Acid.

TRIGEMINAL LASER-EVOKED POTENTIALS: AN USEFUL TOOL TO DETECT POST-SURGICAL OUTCOME IN TRIGEMINOVASCULAR CONFLICT NEURALGIA

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Introduction

Trigeminal laser-evoked potentials (T-LEPs) can explore the nociceptive pathways not assessed by the conventional exteroceptive trigeminal reflexes and differentiate neuropathic from nociceptive pain, representing an useful diagnostic tool to study the orofacial pain syndromes.

Patients and methods

We studied seven patients (median age 58 years, six women, one man) affected from trigeminal neuralgia caused by trigeminovascular conflict and 6 age-matched controls (five women, one man).

Each group underwent conventional trigeminal reflexes (bilateral Blink Reflex and Masseter Inhibitory Reflex (MIR) and trigeminal LEPs. The patients were also submitted to neurophysiological testing one week after surgery.

Results

R1 and R2 blink reflex latency, SP1 and SP2 duration, were not statistically different between subjects and patients and between healthy and affected sides before and after surgery. Intriguingly, the affected side T-LEPs amplitude of the patient group was significantly reduced respect healthy side before surgery (17,07µV; 29,96µV; p=0,02). Moreover, after surgery, the patient T-LEPs amplitude of the affected side increased and the pre/post-operative difference was significant.

(17,07µV; 24,93µV; p=0,03)

Conclusions

Trigeminal neuralgia caused by trigeminovascular conflict may be related to Aδ fibers impairment, and T-LEPs are more sensitive than conventional trigeminal reflexes in monitoring the post-surgical outcome in trigeminovascular conflict.

PRE-OPERATORY "IN-LAB" NEUROPHYSIOLOGICAL EVALUATIONS TO OPTIMISE ION IN SKULL-BASE SURGERY PROCEDURES

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Actually the skull-base surgery is a quite frequent procedure in the neurosurgical context. These operations are continuously improving, but they are still considered a at high-risk practice. For these reasons the intra-operatory neurophysiology (ION) has becoming essential for the success of neurosurgery.

However the successful of an intra-operatory neurophysiology evaluation is based on a careful, reliable and accurate pre-operatory in-lab evaluation.

The skull base neurosurgical procedures are most frequently applied to brain tumours, malformation and traumatic injury. Those can involve the vital functions of the brainstem witch a different (clinical or subclinical) grade of damage.

Few neurophysiology diagnostic tests can be used (PES, PEM, BAEP and EMG techniques), but their execution and interpretation must be finalized to the ION. So in these preparatory step the figure of the Neurophysiology Technician became fundamental.

The first aim of the pre-operatory evaluation is obviously to understand the grade of the cerebral impairment, witch are the brain's anatomic parts more involved and which of the parts of this are more a risk during the intra-operatory monitoring.

By the pre-operatory evaluation is possible to set up the ION protocol: choosing the procedures to record, testing the feasibility, identifying the best position for the electrodes (not necessary the standard one), evaluating the needing time to the acquisition of some procedures relatively to that specific patient.

Finally the pre-operatory tests give the basal data about the brain electric activities to evaluate both intra-operatory and post-operatory records and they are essential for the follow-up.

INTRAOPERATIVE NEUROPHYSIOLOGY AND THE PEDIATRIC PATIENT

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Background

The goal of surgery is to maximize results avoiding jatrogenic damage. This is particularly true in children: the use of Intraoperative Neurophysiology is therefore expanding in the pediatric population. The aim of our study was to report our experience about Intraoperative Monitoring (IOM) in a series of pediatric patient.

Methods

We report the data of 122 consecutive surgeries in 103 patients aged below 18 years in whom intraoperative neurophysiologic techniques were applied. Data were compared with 2031 IOM in adult patients.

Results

Surgery involved the spinal cord in 27.9% of the pediatric population and 36.4% of adults, posterior fossa in 54.9% of children (11.4% of adults). Finally supratentorial surgery represented 17.2% of pediatric surgeries and 52.1% of adult surgeries. Mapping/testing techniques were applied in 50% of pediatric surgeries and in 19.4% of adult surgeries. The rate of transient or persistent modification of neurophysiologic parameters was 18.9%. Transient modifications occurred in 12 patients: only 1 of them showed a persistent, mild deficit of VII nerve. In 11 surgeries (9%) persistent alteration were observed: however, only 2 patients had a worsening of a pre-existing deficit. None of our patients reported any of the IOM related complications that have been described in literature.

Conclusions

Our study provides evidence as to the relevance, impact and safety of IOM in pediatric neurosurgery. The specificity of intraoperative neurophysiology in children is due to different types of surgery and to a more widespread use of mapping/testing in comparison with adults.

SOMATOSENSORY EVOKED POTENTIALS IN THE PAEDIATRIC CARDIOSURGICAL INTENSIVE CARE UNIT

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Introduction

Somatosensory Evoked Potentials (SEPs) have proved to be a reliable indicator of outcome in comatose adults with severe head injury or in post-anoxic coma. However, the value as a prognostic tool in children is still under debate. This is at least in part due to the low grade of homogeneity of the series, that often group together adult and paediatric patients and different etiologies. The aim of this study is to evaluate the predictive value SEPs in the specific setting of comatose children with anoxic encephalopathy in the paediatric cardio-surgical intensive care unit.

Methods

17 paediatric patients with hypoxic-ischemic encephalopathy were included. Median nerve SEPs were recorded within 24 hrs. from the admission; subsequent recordings were made if clinically indicated. SEPs were scored with a 3 grade scale (0 bilateral absence of N20; 1 unilateral absence of N20 or uni/bilateral increase of central conduction time; 2 normal).

Results

Overall 11 patients died and 7 survived (1 with cognitive and motor deficit). At time of first recording the cortical and/or subcortical SEPs were bilaterally absent in 7 patients: they all died. Of the remaining 10, 6 had normal recordings persistent in time and they all recovered. In 3 patients SEPs deteriorated at 2nd or 3rd recording: none of them recovered. Finally 1 patient with normal SEPs persistent in time deceased of cardiac death.

Conclusions

Somatosensory Evoked Potentials are powerful predictors of outcome, particularly poor outcome, in children with anoxic encephalopathy in the paediatric cardio-surgical intensive care unit. The predictive value of SEPs is increased by seriate recordings.

INTRAOPERATIVE MONITORING IN NEUROSURGICAL CASES: OUR EXPERIENCE

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Introduction

Intraoperative monitoring (IOM) is a new method to guide neurosurgical operations for a better result and complications reduction. We used this procedure during neurosurgical removal of acoustic neuroma, medulla tumours, particularly intra-dural and cauda, in patients attending Neuroscience Department of AOS S. Maria of Terni, between January 2011 and March 2012.

Description of cases

We examined 9 patients with acoustic neuroma, 18 with intra-dural medulla tumours and 3 with neoplasias of cauda.

During asportation of acoustic neuroma, we used Free Run EMG, Blink Reflex and bipolar electrical stimulation to monitor 7° nerve course. Among these neurophysiological methods, Free-Run EMG gave better results to alert the neurosurgeon during operation. Only 2 patients showed 7° nerve paresis at the end of operation, with a partial recovery after four months.

At this moment, we didn't use electrical PEM, but we obtained similar results with Blink Reflex.

For medulla, we used PES cortical signal during intra-dural tumours treatment, while Free Run EMG and sacral reflex were utilized for cauda monitoring. None of patients treated showed motor deficit.

Conclusions

Considering our positive experience with IOM during neurosurgical operation, we will use it also for experimental implantation of stem cells in motor neuron disesase. We wish to continue our experience with IOM also with improvement of new equipment, like electrical PEM.

SOMATOSENSORY EVOKED POTENTIAL RECORDED DURING THERAPEUTIC HYPOTHERMIA RETAINS ITS PREDICTIVE VALUE FOR POOR NEUROLOGICAL OUTCOME AFTER CARDIAC ARREST

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Purpose

Early prediction of neurologic outcome for patients resuscitated from cardiac arrest (CA) is a challenging task. Therapeutic hypothermia (TH) has been shown to improve neurologic outcome after CA. TH may confound established predictors of neurologic outcome in comatose survivors of CA. The aims of the study were to evaluate if: 1) amplitude of cortical somatosensory evoked potentials (SEPs) is influenced by TH in comatose patients after CA 2) patients with bilaterally absent (BA) SEPs during TH can recover cortical responses after rewarming 3) BA SEPs recorded during TH retains its prediction value for poor neurological outcome as in normothermic patients.

Methods

Prospective cohort study including comatose adults resuscitated from in- or out-of-hospital CA treated with TH. SEPs were recorded during TH (6-24 hrs after CA) and after rewarming in those patients who remained comatose. Neurologic outcome was assessed 6 months after CA by Glasgow Outcome Scale.

Results

Forty-six patients were included. No significant differences were found between mean amplitude of N20 recorded during TH with respect to normothermia. During TH, 21 patients showed bilaterally absent cortical N20. No patients with bilaterally absent SEPs during TH recovered cortical responses during normothermia. All patients with absent SEPs during TH did not recover consciousness.

Conclusions

1) TH has not significantly influenced N20 amplitude with respect to normothermic condition; 2) BA SEPs obtained in early recordings during TH is a good predictor for persistence of their absence after rewarming; 3) BA SEPs during TH retains its prognostic value for poor neurological outcome as in normothermic patients.

DETECTION OF SHORT-TERM HABITUATION IN HEALTHY SUBJECTS AND IN PATIENTS WITH DISORDER OF CONSCIOUSNESS (DOC)

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Objective

Short-term habituation is a fundamental component of attention, a "bottom-up" filtering for salient stimuli and a prerequisite for subsequent "top-down" processing. It can be detected using simple passive paradigm in which trains of stimuli of identical or different or modality are presented. In order to verify the test applicability in patients with DOC (disorder of consciousness), we obtained normative data in healthy subjects.

Methods

Long latency evoked potentials (N1-P2) were recorded in 16 healthy subjects receiving trains of stimuli (S1–S2–S3). S1 and S2 always belonged to the same sensory modality (auditory or somatosensory) whereas S3 belonged either to the same modality as S1 and S2 (triplet "same") or to the other modality (triplet "different"). We also recorded 4 patients with DOC with different levels of consciousness (valued according "CRS-R" coma recovery scale-revised).

Results

In healthy subjects the amplitude of S3/N1-P2 was, in triplet "same", significantly lower than S1/N1-P2 ($p<0.0001$), whereas in triplet "different" habituation of S3/ N1-P2 was not observed. Short-term habituation was absent in 2 VS (vegetative state) patients (CRS-R scores 3/23, 4/23) while it was found in a MCS (minimally conscious state) patient (CRS-R score 20/23) and in one post-anoxic VS patient (CRS-R 6/23) who later became minimally conscious.

Significance

Short term habituation process is a reproducible and substantial phenomenon in healthy subjects. We found the lack of this process in some VS patients while it was preserved in one MCS patient. Our "triplet" protocol could be able to pick-up preserved information processing capacities in patients with DOC.

CASI CLINICI SNP

POSTER

ULTRASOUND FOLLOW-UP OF IMMUNE-MEDIATED NEUROPATHIES: CONSISTENCY AND DISCREPANCY WITH CLINICAL FEATURES

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Nerve ultrasound (US), as a complement to clinical and electrophysiological investigations, is becoming a widely accepted tool in assessment of several peripheral nerve disorders, especially entrapment syndromes and traumatic nerve injury. Attention has been focused lately also on immune-mediated neuropathies. Few US reports have focused on demyelinating polyneuropathies, mainly on chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), and Guillain-Barré syndrome (GBS). To the best of our knowledge, longitudinal US studies in immune-mediated neuropathies has never been performed. We report on four cases of immune-mediated neuropathies (2 MMN, 1 GBS, and 1 CIDP) with serial US follow-up.

In the 2 MMN patients, US findings completely recovered after one year of intravenous immunoglobulin therapy (IVIg) in one patient, while in the second one, also undergoing IVIg treatment US normalization never occurred. US findings were consistent with clinical response and neurophysiologic features.

The patient with GBS had clinical and electrophysiology improvement after IVIg and plasma exchange; a progressive improvement of US changes was seen in serial follow-up evaluations up to complete normalization.

In the patient affected with CIDP, on IVIg therapy, clinical improvement was followed by almost complete neurophysiologic improvement, but complete US normalization never occurred. These preliminary data show that modifications of US findings often mirror clinical and neurophysiologic changes/pattern and may help monitor disease evolution. Follow-up studies in larger populations will help confirm these data.

USEFULNESS OF ULTRASOUND IN DIAGNOSING NERVE DAMAGES DUE TO OSTEOSYNTHESIS TOOLS: 6 CASES AND REVIEW OF LITERATURE

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Ultrasound (US) is useful to identify the relationships between the nerves and the surrounding structures such as muscles, bones and tendons. This is crucial in several chronic compression/entrapment syndromes and also in trauma. Nerves may be damaged by direct contusion or laceration, by fracture fragments, by the interposition between fragments, by traction when the bone ends are forcedly separated, or they may be affected by iatrogenic damage such as interposition between osteosynthesis plate and screw or contact with them. The main distinction between primary (fracture) and secondary damage (iatrogenic) is based on the timing of onset of symptoms and, therefore, on its close relationship to the trauma (pre-surgery) or treatment (post-surgery).

Metallic tools are well depicted by US that is able to provide additional information to the clinical and electrophysiological examinations. We present the cases of 6 patients with upper limb fractures who underwent surgery for reduction and fixation by osteosynthesis. After surgery patients complained of motor or sensory deficit and sometimes neuropathic pain. US examination, performed from 1 to 8 months after surgery, showed the close anatomical and dynamic relationship between the nerve and the metallic tool revealing mechanisms of compression, friction or stretching.

NERVE ENTRAPMENT INTO BONY TUNNEL: A RARE COMPLICATION OF BONE FRACTURES DIAGNOSED BY ULTRASOUND AND LITERATURE REVIEW

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Nerve palsy due to callus osseous incorporating a nerve is a very rare but possible complication after bone fractures. It is a difficult diagnosis to make and it is usually an accidental finding during surgical exploration. X-rays or CT scans usually show the presence of a callus osseous, and they can show defects or other abnormalities in callus formation and bone morphology. We report four cases of nerve entrapment into callus osseous following bone fractures and diagnosed through ultrasound (US). We then reviewed the literature for cases of bony nerve entrapment into callus osseous.

The first patient is a 45-year old man who developed ulnar nerve palsy four months after a traumatic olecranon epiphyseal fracture due to a callus osseous developed around the nerve. The second patient is a 13-year-old girl with a radial nerve palsy developed after a diaphyseal humeral fracture: the nerve was entrapped into the bone, but it spontaneously improved after few months. The third patient is a 14-year-old girl with a worsening left median neuropathy due to a cominutive humeral fracture occurred four years earlier: US showed that the median nerve was entrapped into a bony canal. The fourth patient is a 27-year-old girl who reported with a complete radial nerve palsy after a humeral fracture. US performed one year after the fracture showed the nerve enceased into the callus, with the presence of a huge neuroma.

It is important to describe these cases and perform follow up to take the best therapeutic decision.

EXTRATERRITORIAL SPREAD OF PAIN SYMPTOMS IN PATIENTS WITH ULNAR NEUROPATHY AT THE ELBOW

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Background

Extraterritorial neuropathic pain (NP) is common in carpal tunnel syndrome (CTS) but data from other nerve entrapment conditions are lacking.

Objectives

The aims of the study are to examine (1) the frequency of extraterritorial symptoms in ulnar neuropathy at the elbow (UNE), and (2) which clinical features are associated with this phenomenon.

Methods

Consecutive UNE patients were enrolled. Inclusion criteria: age 18-65, clinical and electrodiagnostic criteria for UNE, minimal symptoms duration of two months. Exclusion criteria: previous UNE surgery, CTS, radiculopathy, plexopathy, thoracic outlet syndrome, upper-limb pain conditions, neurological, orthopedic, rheumatologic, endocrine disease, pregnancy, severe systemic diseases, renal failure, diabetes mellitus, cognitive and psychiatric conditions. Pain severity was measured with a 0-10 visual analogue scale (VAS). UNE symptoms distribution was marked with an upper-limb diagram. Demographic, clinical, objective, and electrodiagnostic variables were recorded.

Results

We recruited 121 consecutive UNE patients. After selection to exclude coexistent

confounding conditions, 44 patients were included. Extraulnar symptoms were found in 18 patients (36.3%), and they were more frequent in women. Pain VAS was significantly higher and cold hyperalgesia was significantly more frequent in patients with extraulnar symptoms. Male sex and tactile hypaesthesia significantly reduced, while pain VAS and cold hyperalgesia significantly increased the risk of extraulnar symptoms.

Discussion

Extraulnar symptoms are frequent in UNE. These data extend the notion that NP may spread outside the anatomical boundaries of affected peripheral nerves.

Conclusions

Pain-related mechanisms of central sensitization may underlie this phenomenon. Our data may help to reduce UNE misdiagnosis and to better apply the NP revised definition.

INDIRECT DISCHARGES AS EARLY NEUROPHYSIOLOGICAL MARKER IN AN ATYPICAL GBS PRESENTATION

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We describe a rare case of Guillain-Barré syndrome (GBS) with clinical signs of small fibers involvement at onset and with indirect discharges (iDs) as early neurophysiological signs of focal demyelination.

A 53-year-old man who frequently travelled to eastern countries, with negative past medical history, presented acute onset of diffuse dysaesthesias with cold fluids contact, subjective feature of metallic taste, bladder, bowel and sexual dysfunction. In the next 3-4 days he developed weakness of both lower limbs which made the patient unable to run and walk without assistance. On day 10 he was admitted to our department and neurological examination revealed symmetrical leg weakness, absence of tendon reflexes and moderate distal decreased deep sensation of lower limbs. The cerebrospinal fluid (CSF) showed a slight elevation of proteins. Electrophysiological examination, performed in very early stages of the disease, did not fulfill the electrodiagnostic criteria for GBS. During the initial nerve conduction studies several abnormal late responses, distinct from F weaves, were observed. These iDs are possibly related to marked focal conduction slowing due to demyelination. The patient was treated with IVIg, 0.4 g/Kg bodyweight for 5 consecutive days, with initial clinical improvement after five weeks. At fourth week from the clinical onset an electrodiagnostic study was performed and now the patient fulfilled neurophysiological criteria for GBS.

We emphasize the key role of early nerve conduction abnormalities, like the late responses, to recognize early neurophysiological signs of demyelination supporting the diagnosis of GBS when both clinical and neurophysiological picture are not still confirmative of GBS diagnosis.

SKIN BIOPSY AND QST IN FRIEDREICH'S PATIENTS: A FOLLOW-UP STUDY

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Friedreich ataxia (FA) is a genetically determined disease, where the large fiber sensory neuropathy is the most characteristic feature, although an involvement of small fibers has been also demonstrated by skin biopsy.

To better understand the course of small fibers neuropathy in FA, we performed a follow-up study on seven patients (3 females and 4 male, age range 30 to 51years old) studying over time morphology and function of small nerve fibers in the skin. All patient underwent a baseline evaluation. Follow-up was done after a period among three and five years; 3/7 patients underwent a third evaluation after eleven years. All patients underwent 3 mm punch skin biopsy from thigh, leg and fingertip. At the same time-points they underwent Quantitative Sensory Testing (QST). Cutaneous nerve fibers and mechanoreceptors were visualised using antibodies to the pan-neuronal marker protein gene product 9.5 and to myelin basic protein. Quantification of epidermal nerve fibers (ENFs) was performed on skin sections using digitized images acquired by non-laser confocal microscopy (CARV) and Neurolucida software. The count of Meissner corpuscles (MCs) and intradermal myelinated endings (IME) per mm^2 was performed on an epifluorescent microscope with the aid of ScionImage image analysis software. We detected in our patients a loss of MCs and IME and ENFs over time. In 3 out of seven patients we observed a preservation or an improvement of ENFs in thigh and leg.

Our findings confirm the involvement of small fibers in FA. Physical and rehabilitative therapy could explain the improvement of ENFs that doesn't seem, however, to reflect a significant functional recovery.

RILUZOLE BLOCKS HUMAN MUSCLE ACETYLCHOLINE RECEPTORS

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Introduction

Riluzole, the only drug available against amyotrophic lateral sclerosis (ALS), has recently been shown to block muscle ACh receptors (AChR), raising concerns about possible negative side-effects on neuromuscular transmission in treated patients. In this work we studied riluzole impact on the function of muscle AChR in vitro and on neuromuscular transmission in ALS patients, using electrophysiological techniques.

Materials and methods

Human recombinant AChR composed by α1β1δ subunits plus γ or ε subunits (γ - or ε-AChR) were expressed in HEK cells or Xenopus oocytes. In both preparations, riluzole 0.5 μM, a clinically relevant concentration, reversibly reduced the amplitude and accelerated the decay of ACh-evoked current if applied before coapplication with ACh.

Results

The action on γ-AChR was more potent and faster than on ε-AChR. In HEK outside-out patches, riluzole-induced block of macroscopic ACh-evoked current gradually developed during the initial milliseconds of ACh presence. Single channel recordings in HEK cells and in human myotubes from ALS patients showed that riluzole prolongs channel closed time, but has no effect on channel conductance and open duration. Finally, compound muscle action potentials (CMAPs) evoked by nerve stimulation in ALS patients remained unaltered after a 1-week suspension of riluzole treatment.

Conclusions

These data indicate that riluzole, while apparently safe on synaptic transmission, may affect the function of AChR expressed in denervated muscle fibres of ALS patients, with biological consequences that remain to be investigated.

EFFECTS OF ESCITALOPAM ON CUTANEOUS SILENT PERIOD: EVIDENCE OF SEROTONINERGIC MODULATION?

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Introduction

Painful cutaneous nerve stimulation leads to transient suppression of voluntary muscle contraction, this phenomenon is called the cutaneous silent period (CSP). The neurotransmitters potentially involved in mediating this suppression remain unknown**.**

Objective

To investigate the central nervous system circuitry of this inhibitory reflex, we study the effects of 20mg oral dose of escitalopram, a selective serotonin reuptake inhibitor, in 7 healthy volunteers.

Method

We elicited CSP in the first dorsal interosseus muscle from the right hand through surface electrodes. The fifth digit of the right hand was stimulated by electrical shock with intensity set at 20 times perception threshold. We performed the electrophysiological recordings before and 3 hours after the administration of escitalopram. Subjects rated the subjective intensity of the peripheral painful sensation, after every recordings, on an 11-point numerical scale (11PNS) scale, graded from 0 = no pain to 10 = unbearable pain.

Results

Escitalopram significantly increased CSP duration, but left unchanged both onset latency and subjective pain perception.

Conclusion

We suggest that escitalopram reinforces supraspinal descending serotonergic activity on spinal inhibitory interneurons controlling α-motoneurons for the hand muscles.

THE ROLE OF NEUREGULIN 1 AND LAMININ PATHWAYS IN SC DEVELOPEMENT: A NEUROPHYSIOLOGICAL STUDY IN MOUSE MODELS

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Introduction

During development of the peripheral nervous system (PNS), the neuronal key molecule that regulates SC development is Neuregulin 1(Nrg1). Nrg1 type III contains a cysteine rich domain (CRD) and triggers myelination as a juxtracine signal from the neuronal membrane.. Haploinsufficency of Nrg1 typeIII cause hypomyelintion in PNS. Beyond Nrg1 an important ligand/receptor interaction for SC myelination is played by laminins/integrins. The Lm211 deficient mice(Lm) are a Model of Congenital Muscular Dystrophy(MDC1A) in which the absence of laminin causes a peripheral neuropathy which contributes to the disease.

Aim of the study

To understand if the Neuregulin 1 and Laminin pathways cooperate in myelination in vivo, we performed a genetic interaction experiment. To ask if hypomyelination in Nrg1 type III mice PNS was aggravated by the complete removal of Lm211, we generated compound–heterozygous mice expressing half of Nrg1 typeIII (CRD) and null for Lm211. To look for myelin defects we first perform electrophysiological analysis on 15 pnd mice because Lm211-/- die 21 days after birth.

Results

In comparison to the wild type group we observed a statistical significant increase of cMAP and F wave latency in CRD, Lm 211 -/- and compound mice; the nerve conduction velocity in CRD +/- mice is reduced by 20%, in Lm211-/- by 41,5% while in CRD+/- Lm211-/- by 42%. Electrophysiological analysis showed a statistically significant more severe demyelinating neuropathy in Lm211-/- and CRD+/-Lm211-/- as compared to CRD +/- mice but it does not reveal additional hypomyelination effect between Lm211 -/- and the compound CRD+/- Lm211 mice.

Discussion

These results suggest that both laminin and Nrg1 reduce nerve conduction velocity, but their action is not synergistic. Morphological studies are now underway to understand if the absence of the 2 molecules impairs nerve conduction velocity by the same or different mechanisms (i.e. regulation of myelin thickness versus regulation of internodal length.

MICRONEUROGRAPHIC RECORDING OF SYMPATHETIC NERVE ACTIVITY IN A PATIENT WITH DOPAMINE BETA-HYDROXYLASE DEFICIENCY

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Introduction

Dopamine beta-hydroxylase (DbetaH) deficiency is a very rare form of primary autonomic failure characterized by minimal or undetectable plasma noradrenaline and adrenaline together with increased dopamine plasma levels and by a severe orthostatic hypotension.

Objective

To study sympathetic nerve activity by microneurography ans skin biopsy in a patient with suspected DbetaH and orthostatic hypotension.

Methods

The patient was a 34 years-old man complaining of orthostatic hypotension and muscle hypotonia from the birth. Symptoms worsen progressively during late adolescence and early adulthood with severe orthostatic hypotension. DbetaH deficiency was suggested by minimal or undetectable plasma norepinephrine. The patient underwent skin biopsy to study peripheral somatic and autonomic innervation and an extensive microneurographic examination with the recording of muscle (MSNA) and skin (SSNA) sympathetic nerve activities. Thirty-two age-matched subjects without signs of neurological dysfunction served as controls.

Results

Skin biopsy disclosed normal somatic and sudomotor cholinergic innervation. Skin adrenergic innervation evaluated by a panneuronal marker (PGP) was normal but DbetaH staining was absent. MSNA displayed an increased incidence (91 bursts/100HB; n.v. 54±16 bursts/100 HB) and frequency (58 bursts/min; n.v. 38±14 bursts/min). SSNA showed normal frequency (10 bursts/min; n.v. 11±5 bursts/min) and latency (0.7 sec; n.v. 0.7±0.07 sec).

Conclusion

This patient showed a DbetaH deficiency as confirmed by skin biopsy. Furthermore, microneurography showed a peculiar picture with increased MSNA in presence of a severe orthostatic hypotension.

SHORT AND MIDDLE TERM OUTCOME OF PERIPHERAL NERVE STIMULATION OF BRACHIAL PLEXUS FOR TREATMENT OF CHRONIC POST TRAUMATIC NEUROPATHIC PAIN

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Objectives

Aim of study was to evaluate the effect on *pain relief* in patients with peripheral neuropathic pain after brachial plexus lesions using an implanted peripheral nerve stimulator applied on nerve branch using a peculiar surgical technique.

Methods

Seven patients with post-traumatic lesion of brachial plexus or distal peripheral nerve complaining severe intractable pain. Neuropathic pain diagnosis according with redefinition and the grading system (2008) was assessed. Conventional drugs and surgical treatment were not effective. Patients were enrolled in a single centre, open-label trial after institutional review board approval. Patients underwent clinical evaluation with careful neuroalgological evaluation recording negative signs and positive phenomena, pain questionnaires (NRS and NPSI), quality of life scale (SF 36), and quality of sleep. Then at baseline evaluation Quantitative Sensory Testing was performed to quantify thermal and pain thresholds. Surgical treatment consists in a new surgical technique: quadripolar electrocatheters were placed directly on the sensory peripheral branch of nerve mainly involved (on sensitive portion of median nerve in 5 and on radial nerve in 2) into the axillary cavity. We performed a 2 years followup evaluation (scalses, clinica evaluation, QST). We assessed a double blind control with Neurstimulation turned off after 6-24 h.

Results

All patients but one at baseline experienced severe pain with severe positive phenomena in the median (5) and radial (2) territory. Only one patient showed ongoing pain with paroxisms and complete anaesthesia for all modalities. After switch on the neurostimulator system all patients experienced pain relief (>50%, and >95% in most), and positive phenomena in particular tactile and thermal (both cold and warm) were almost disappeared. Peripheral nerve stimulation improved quality of life and sleep. No significant or unexpected adverse events occurred. Mean patient study satisfaction was 95%.

Discussion

We propose and encourage this surgical technique because safety and effective and in our experienced is the first choice after post traumatic nerve lesion.

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