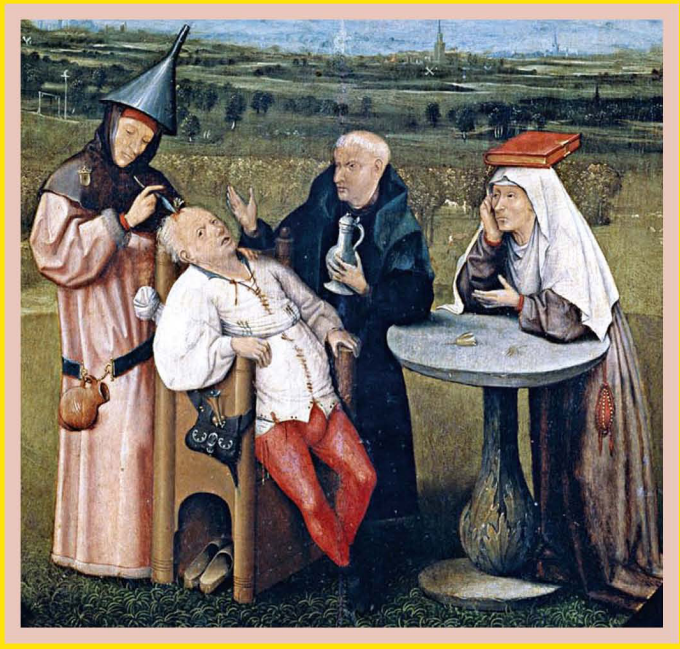
Update in Clinical Neurology

Editors: G. Comi, M. Arnaboldi, M. Guidotti



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UPDATE in CLINICAL NEUROLOGY

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M. Arnaboldi
M. Guidotti

NEW MAGAZINE EDIZIONI

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In copertina olio su tavola "Estrazione della pietra della follia" (48 × 35 cm) del pittore olandese Jeroen Anthoniszoon van Aken (1453-1516), detto Hieronymus Bosch. Dipinto completato nel 1494 o più tardi e conservato al Museo del Prado di Madrid.

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Editoriale

Prefazione

Per la sua XX riunione annuale la SIN-SNO Lombarda si presenta sul lago di Como, come da tradizione in concomitanza con gli Updates in Clinical Neurology, ospite di due Neurologie ed una Neurochirurgia ospedaliere che da sempre collaborano in grande sinergia al servizio del territorio e che per questo hanno creato un'associazione scientifica a taglio anche sociale, per meglio intercettare le richiesta di aiuto nel campo delle neuroscienze, "Comobrain".

La prima giornata è dedicata alla gestione individualizzata nel campo dei gliomi e della sclerosi multipla. L'individualizzazione del trattamento è una strategia terapeutica che inizia a configurarsi grazie ai potenti recenti sviluppi della medicina molecolare, che consente un approccio più mirato alle specifiche alterazione dei pathways metabolici.

La farmacogenetica e la farmacogenomica forniscono importanti indicazioni sulla modulazione individuale dell'efficacia delle terapie eziologiche.

La possibilità di una terapia più mirata si giova anche delle disponibilità di biomarkers che consentono una migliore definizione dello stato di malattia, una individuazione più precisa della prognosi ed un monitoraggio più accurato degli interventi terapeutici.

Nell'edizione di quest'anno degli Updates in Clinical Neurology si dibatte di trattamento individualizzato in due patologie: i gliomi cerebrali e la sclerosi multipla. Due tipi di patologie in cui si iniziano ad intravedere le opportunità offerte in ambito terapeutico sugli aspetti in ambito patogenetico.

Nella logica che vuole vedere la Neurologia sempre più orientata alla gestione delle urgenze, le prime due sessioni in programma il secondo giorno riguardano i farmaci antiepilettici di recente sintesi, che sembrano avere diverse indicazioni cliniche, coinvolgenti anche patologie e professionisti di altri settori, e le immunoglobuline endovena a elevato dosaggio, formidabile arma in mano ai neurologi soprattutto nelle fasi acutissime di gravi patologie a genesi disimmune. Questi farmaci pongono tuttavia problemi di utilizzo non solo dal punto di vista delle evidenze scientifiche, ma anche per vincoli amministrativi e legali. La XX riunione SIN-SNO sarà l'occasione per fare chiarezza su alcuni punti e per uniformarne il più possibile l'utilizzo da parte della classe neurologica lombarda, anche nel rispetto del corretto utilizzo delle risorse in Sanità.

Le sessioni pomeridiane sono, invece, mirate al problema del confronto della Neurologia con il sempre più evidente avanzamento della vita media, mirando a riprendere i progressi della ricerca e della terapia nel morbo di Alzheimer, senza tuttavia trascurare l'importanza di collegare i centri di cura ospedalieri con le esigenze territoriali e socio-assistenziali dei malati e delle loro famiglie.

I neurochirurghi presentano un loro contributo riguardante un argomento molto controverso.

Una lezione magistrale chiude la giornata, facendo il punto sui vari parkinsonismi e l'abbondante armamentario terapeutico attualmente in dotazione al neurologo ed al neurochirurgo in questo campo.

Benvenuti a Como, città del cervello

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Comunicazioni

SESSIONE EDUCAZIONALE:
“ICTUS CEREBRALE: ESPERIENZE A CONFRONTO”

SESSIONE EDUCAZIONALE:
“L’IMPIEGO DELLA IGVENA IN NEUROLOGIA”

SESSIONE EDUCAZIONALE:
“LA MALATTIA DI ALZHEIMER: A CHE PUNTO SIAMO?”

Abstract COMUNICAZIONE

□ Miastenia: Igvena o plasmaferesi

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Lo scambio plasmatico tradizionale e le immunoglobuline endovena ad alte dosi hanno un ruolo consolidato nel trattamento del paziente miastenico, soprattutto nelle fasi di riacutizzazione della malattia ed in particolare in caso di coinvolgimento del distretto bulbare ad innervazione bulbare. Pur con meccanismi molto diversi, entrambi gli approcci terapeutici risultano efficaci nel migliorare in modo significativo la sintomatologia bulbare e nel ridurre il tempo di degenza in ventilazione assistita nei pazienti affetti da insufficienza respiratoria.

Non disponiamo di studi RCT (Randomized Controlled Trial) sull'efficacia della plasmaferesi nel paziente miastenico, ma il parere degli esperti ha stabilito che esistono sufficienti evidenze cliniche sull'efficacia della procedura; inoltre, per motivi etici, non è proponibile lo studio verso placebo in pazienti affetti da forme gravi della malattia. L'efficacia della plasmaferesi è stata confrontata con quella delle immunoglobuline e gli studi disponibili sostengono l'equivalenza dei due trattamenti. Rimane sempre aperto il quesito se in determinate condizioni sia meglio il trattamento plasmatico rispetto alle immunoglobuline, ad esempio in caso di insufficienza respiratoria parziale o in pazienti in ventilazione assistita. Le informazioni disponibili non provengono da studi prospettici, ma l'analisi retrospettiva ha evidenziato un possibile vantaggio a favore della plasmaferesi sul recupero dalla ventilazione assistita, osservazione che meriterebbe ulteriori approfondimenti. Le immunoglobuline condividono le stesse indicazioni della plasmaferesi e presentano il vantaggio aggiuntivo di poter essere facilmente somministrate con ovvie conseguenze per quanto concerne i pazienti pediatrici, i pazienti senza adeguati accessi vascolari ed infine i pazienti con controindicazioni al trattamento aferetico per motivi cardiovascolari.

Molti quesiti rimangono aperti per entrambe le procedure, non essendo stato definito un protocollo di dosaggio ottimale per le immunoglobuline, se non lo schema classico universalmente adottato nelle malattie autoimmuni suddiviso in 3-5 giorni; più complesso è il trattamento plasmatico, per il quale esistono esperienze estremamente eterogenee con protocolli variabili da due sedute a schemi di trattamento particolarmente lunghi. Rimane, infine, aperto il problema del trattamento immunomodulante cronico con immunoglobuline o plasmaferesi: la letteratura in merito è molto limitata, ma entrambi i trattamenti possono essere utilizzati nel caso di pazienti che presentano scarsa risposta al trattamento farmacologico. In questi pazienti può essere preso in considerazione, se realizzabile, il trattamento selettivo di rimozione periodica delle immunoglobuline circolanti, procedura più complessa sul profilo tecnico destinata a pazienti selezionati, ma con sicuro vantaggio sul piano clinico e della tollerabilità da parte del paziente.

Nella nostra esperienza, preferiamo utilizzare in prima istanza lo scambio plasmatico; se inefficace si valuterà l'efficacia delle immunoglobuline e.v. ad alte dosi. In caso di provata farmaco-resistenza con persistenza di sintomatologia bulbare, o nel caso di pazienti che necessitano di frequenti scambi plasmatici per mantenere un quadro clinico soddisfacente, utilizziamo l'immunoassorbimento selettivo delle IgG circolanti.

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Abstract COMUNICAZIONE

□ Il territorio e il malato di Alzheimer

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Il *caregiver* del paziente con demenza di Alzheimer manifesta un *burden* fisico, emotivo, sociale ed economico molto rilevante[1,2,3]. Il Censis del 2006 ha rilevato che più dell'80% dei pazienti con demenza vive in famiglia[4]. Il protrarsi e l'aggravarsi del carico assistenziale conducono alla cosiddetta *sindrome del caregiver*[5]. Tale dato è stato replicato attraverso un'indagine epidemiologica svolta presso l'UVA (Unità di Valutazione Alzheimer) dell'Ospedale Niguarda[6]. Sulla base di questa evidenza il Centro di Neuropsicologia Cognitiva del Niguarda ha promosso un progetto multidisciplinare per il malato di Alzheimer e per i caregiver primari nell'ottica di un programma più generale di sviluppo di una organizzazione socio-assistenziale, dove l'ospedale e le UVA fungono da *rete* con i servizi territoriali esistenti. Un elemento rilevante di questa rete è lo sportello informativo e di ascolto gestito in collaborazione con i Consigli di Zona 2 e 9, le associazioni sindacali di volontariato e l'AIMA (Associazione Italiana Malattia di Alzheimer). La tipologia delle richieste comprende: supporto psicologico (52%), informazioni su servizi territoriali (Centri Diurni, Residenza Sanitaria Assistenziale: RSA) (12%), assistenza domiciliare (16%), miglioramento dell'accoglienza in Pronto Soccorso di pazienti appartenenti ad una categoria fragile e delle leggi a tutela dei pazienti.

Questo approccio multidisciplinare ha portato alla creazione di un servizio di sostegno psicologico di gruppo per i *caregiver*. Ad oggi sono stati realizzati circa dieci gruppi, per un totale di circa cento *caregiver*. Un'analisi preliminare ha mostrato una riduzione significativa ($p = 0,001$) dei bisogni relativi alla cura del proprio assistito e una riduzione significativa ($p = 0,045$) dell'ansia di stato tra l'inizio e la fine del trattamento di gruppo.

I risultati indicano la necessità di un intervento multistrutturato sul territorio per garantire maggiore continuità tra ospedale e territorio, alleviare il carico assistenziale del caregiver e migliorare la qualità del supporto familiare al paziente con l'effetto di ritardare il momento dell'istituzionalizzazione del paziente[7].

Bibliografia

1. Tognetti A.: Le problematiche del caregiver. G Gerontol 2004; 52: 505-510.
2. Marvardi M., Mattioli P., Spazzafumo L., Mastriforti R., Rinaldi P., Polidori M.C., Cherubini A., Quartesan R. et al.: The Caregiver Burden Inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study. Aging Clin Exp Res 2005; 17 (1): 46-53.
3. Sink K.M., Holden K.F., Yaffe K.: Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. Jama 2005; 293 (5): 596-608.
4. Spadin P., Vaccaro M. (a cura di): La vita riposta: i costi sociali ed economici della malattia di Alzheimer. Franco Angeli, Milano, 2007.
5. Gaugler J.E., Kane R.L., Kane R.A., Newcomer R.: The longitudinal effects of early behavior problems in the dementia caregiving career. Psychol Aging 2005; 20 (1): 100-116.
6. Passoni S., Mazzà M., Zanardi G., Bottini G.: Variazioni del caregiver burden in relazione al profilo clinico del paziente con demenza di Alzheimer. G Ital Med Lav Ergon 2010; 32 (3): B37-B42.
7. Teri L., McCurry S.M., Logsdon R., Gibbons L.E.: Training community consultants to help family members improve dementia care: a randomized controlled trial. Gerontologist 2005; 45 (6): 802-811.

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Abstract COMUNICAZIONE

□ L'impiego delle immunoglobuline endovena nelle neuropatie

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Da quando negli anni '80 sono state fatte le prime segnalazioni sulla loro efficacia nelle neuropatie, le immunoglobuline umane iperimmuni (Intravenous Immunoglobulin: IVIg) hanno acquisito sempre più spazio nei Centri per la diagnosi e terapia delle malattie neuromuscolari. Recenti trial clinici controllati hanno evidenziato la loro efficacia come farmaco di prima scelta nella Sindrome di Guillain Barrè (SGB), nella Polineuropatia Demielinizzante Cronica Infiammatoria (CIDP) e nella Neuropatia Motoria Multifocale (MMN).

Nella SGB le IVIg sono risultate efficaci anche sulla base di una revisione Cochrane, ma nonostante tutto sono approvate per tale indicazione solo da EMEA (European Medicines Agency) e non ancora da FDA (Food and Drug Administration).

L'utilizzo delle IVIg è in grado di ridurre la durata del ricovero ospedaliero dei pazienti, la durata della eventuale ventilazione assistita e riduce la possibile disabilità e quindi l'inabilità lavorativa dei pazienti.

Nonostante i protocolli di utilizzo del farmaco siano ormai consolidati (0,4 g/kg al die per 5 giorni consecutivi), poco si conosce sulla necessità o sulla possibilità di un secondo ciclo di IVIg in pazienti parzialmente responsivi e sul dosaggio di questo eventuale secondo ciclo. Inoltre, poco si conosce ancora sugli effetti delle IVIg sulle varianti di SGB (Acute Motor Axonal Neuropathy: AMAN, Acute Motor and Sensory Axonal Neuropathy: AMSAN, Miller Fisher syndrome: MFS).

Allo stesso modo non tutto appare chiarito nel trattamento della CIDP con IVIg. È ormai stabilito, sia da trial clinici controllati (IgIV CIDP Efficacy: ICE su tutti) che da revisioni Cochrane, che le IVIg sono efficaci e di prima scelta nella CIDP al dosaggio standard (2 g/kg). Non appare ancora chiaro quando i pazienti debbano essere nuovamente trattati ed a che dosaggio. Questo nasce dalla mancata conoscenza di un biomarker di attività della malattia. Alcuni quindi attendono un peggioramento del paziente clinicamente evidenziabile, altri trattano preventivamente i pazienti.

Nella MMN le IVIg appaiono efficaci ed in grado di migliorare i sintomi dei pazienti. Purtroppo nella maggior parte dei casi il loro effetto è di breve durata e necessita di ripetute somministrazioni. Anche in questa patologia si deve ancora definire il giusto dosaggio da somministrare e la frequenza delle somministrazioni.

Anche in altre neuropatie periferiche l'utilizzo delle IVIg appare efficace anche se sulla base di piccoli trial o di osservazioni anedottiche. Queste sono la polineuropatia demielinizzante in corso di MGUS (Monoclonal Gammopathy of Undetermined Significance) con anticorpi anti-MAG (Myelin-Associated Glycoprotein) e la radicoloplessopatia diabetica.

Numerosi studi sottolineano come alla base del dolore neuropatico presente in molte polineuropatie, soprattutto quella diabetica, vi sia una overespressione di citokine proinfiammatorie, tra cui il TNF (Tumour Necrosis Factor) alfa. Questo ha aperto la strada al trattamento di tale dolore con le IVIg. Sono quindi usciti diversi case reports che sottolineano l'efficacia delle IVIg nel trattamento del dolore neuropatico resistente alle terapie convenzionali, ed è stato portato a termine con buoni risultati (da confermare in studi controllati) un trial pilota randomizzato sulle polineuropatie dolorose.

In tutti i casi che sono stati qui riportati la tollerabilità e la sicurezza delle IVIg sono emerse come uno dei fattori di punta di tale trattamento.

Il vero problema riguarda il loro costo. Nonostante questo, dati di farmacoeconomia suggeriscono che vi siano vantaggi sia in termini di costi totali che di qualità della vita.

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Abstract COMUNICAZIONE

□ Symptomatic therapies in Alzheimer's disease

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■ **Acetylcholinesterase inhibitors in Alzheimer's disease.** In the last 15 years, symptomatic treatment for Alzheimer Disease (AD) has largely involved the replacement of neurotransmitters that are known to be lacking, mostly based on the "cholinergic hypothesis" of the disease. Different strategies have been investigated to improve cholinergic transmission, including the increase of acetylcholine synthesis or presynaptic release, the stimulation of cholinergic postsynaptic muscarinic and nicotinic receptors and the reduction of acetylcholine synaptic degradation with cholinesterase inhibitors. Acetylcholinesterase Inhibitors (AChEI) have been investigated for safety and efficacy in several double blind, randomised, controlled trials versus placebo, demonstrating various degrees of beneficial effect on cognitive, functional and behavioural symptoms.

To date, four AChEI are approved for the treatment of mild to moderate AD: tacrine (First Horizon Pharmaceuticals), donepezil (Pfizer), rivastigmine (Novartis), and galantamine (Janssen)[1]. Donepezil is now approved for severe AD as well. Although tacrine was the first drug approved for AD in 1993, it is rarely used due to hepatotoxicity[2].

The three AChEI currently used in the symptomatic treatment of AD, donepezil, rivastigmine and galantamine, are supported by many publications and their clinical efficacy is also confirmed by Cochrane systematic reviews[3-5]. Important issues in the management of dementia have been reviewed by the Quality Standard Subcommitee of the American Academy of Neurology[6]. Recent advances in the knowledge of AD pathogenesis are progressively shifting the timing of the treatment from the concept of "timely treatment", i.e. therapy initiated as soon as the diagnosis is made, to that of "early treatment", i.e. treatment initiated early in the disease course[7]; this derives from the neurodegenerative nature of AD, so that reasonable treatment expectations include short-term improvement, stabilization or, as established by an international working group at the World Alzheimer Congress in 2000, also a delay in the rate of progressive decline[8]. All these studies demonstrated benefits of early treatment in the population of patients with mild to moderate AD, probably even more pronounced if patients could be identified and treated before the onset of clinically evident dementia.

A recent article described results of a meta-analysis obtained through the Cochrane Dementia and Cognitive Improvement Group's Specialized Register[9]. Thirteen randomized, double blind, placebo controlled trials with donepezil, rivastigmine and galantamine were considered. Conclusions were that the three AChEI are efficacious for mild to moderate AD, although it is not possible to identify patients who will respond to treatment prior to treatment. Despite the slight variations in the mode of action of the three AChEI, there is no evidence of any difference among them with respect to efficacy. There appears to be less adverse effects associated with donepezil compared with rivastigmine. It may be that galantamine and rivastigmine match donepezil in tolerability if a careful and gradual titration routine over more than three months is used. Titration with donepezil is more straightforward and the lower dose may be worth consideration[9].

An important clinical matter is how to establish drug response in AD patients: in fact they experience not only an impairment in cognition and functionality, but also in behavior and activities of daily living. Several studies demonstrated that AChEI drugs are effective also on non-cognitive symptoms, in particular they may be considered

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a well-tolerated option for improving or preventing psychotic symptoms of AD[10,11]. Therefore, treatment decisions are not to be based on Mini Mental State Examination (MMSE) score or other cognitive tests only, because of the risk that a significant number patients are untreated. For a more complete picture of the drug response, it is necessary to have answers from the caregiver about patient's behaviour and global function in daily living, as an initial cognitive decline during therapy does not preclude benefits in other areas, and does not necessarily indicates a lack of response to treatment.

Despite the positive effects of such drugs, the real effectiveness of AChEI agents is still far from being universally accepted, and a strong debate is open, mainly concerning the cost-effectiveness ratio of these therapies. In march 2005, a report on the new draft guidance from the UK National Institute for Clinical Excellence (NICE) for Alzheimer's therapy has been published on BMJ[12]. NICE, the National Health Service (NHS) prescribing "watchdog", after reviewing the latest evidence on efficacy and cost effectiveness of AChEI, has retracted its previous guidance, issued in 2001, which supported the use of these drugs for Alzheimer's disease. According to the NICE assessment group, although donepezil, rivastigmine and galantamine have proven gains in cognitive and global scales compared with placebo in people with mild to moderate AD, there is "limited and largely inconclusive" evidence on important outcomes such as quality of life and time to admission to a nursing home. Therefore, in UK, according to these guidelines, these treatments should no longer be prescribed for AD patients, although patients currently receiving any of the drugs, can continue to do so.

Following the outcome of a judicial review in August 2007, NICE has amended and reissued the guidance as a quick reference guide[13]. According to this guidance donepezil, galantamine and rivastigmine are recommended as options in the management of patients with AD of moderate severity only (that is those patients with MMSE score between 10 and 20 points). The drug should only be continued while the patient's MMSE score, that must be reviewed every 6 months, remains at or above 10 points and their global, functional and behavioural condition are at a level of a conceivable drug effect. When the decision has been made to prescribe an AChEI, therapy should be started with a drug with the lowest acquisition cost. However, an alternative one could be prescribed where it is considered appropriate having regard to adverse profile, expectations around concordance, medical comorbidity, possibility of drug interactions and dosing profiles[13].

The under-investigation efficacy of cholinesterase agents in the treatment of behavioural and psychiatric symptoms in AD assumed greater importance in the last few years, when the results of clinical trials on safety and efficacy of atypical antipsychotic drugs in demented people showed an increased likelihood of serious cerebrovascular adverse events such as stroke and transient ischemic attack in elderly patients. This problem raised great concerns, because psychiatric and behavioural symptoms affect 60% to 90% of patients with dementia[14], and their treatment has a significant importance in reducing the number of institutionalized patients as well as the caregiver stress for patients who are nursed at home.

■ **AChEI in mild cognitive impairment.** Another important issue is whether AChEI may have effect in Mild Cognitive Impairment (MCI). MCI is still far to be a completely defined clinical entity, that refers to a transitional zone between normal ageing and dementia. Despite the uncertainty of the definition of MCI, some trials have been conducted in the attempt to study the role of AChEI currently approved for AD in preventing progression from MCI to AD. Unfortunately, as also published in Raschetti et al. (2007), the use of AChEI in MCI was not associated with any delay in the onset of AD or dementia. Moreover, the safety profile showed that the risks of these drugs are not negligible[15].

■ **Future perspectives.** A novel AChEI named dimebon has been tested in a randomised, double-blind, placebo-controlled study, demonstrating it is safe, well tolerated, and significantly able to improve the clinical course of patients with mild-to-moderate AD[16]. A number of additional compounds acting on cognition are under testing, including phenserine, muscarinic M1 agonists, M2, antagonists, nicotinic agonists, huperizine A[17].

References

1. Farlow M.: A clinical overview of cholinesterase inhibitors in Alzheimer's disease. Int Psychogeriatr 2002; 14 (Suppl. 1): 93-126.
2. Hansen R.A., Gartlehner G., Lohr K.N., Kaufer D.I.: Functional outcomes of drug treatment in Alzheimer's disease: A systematic review and meta-analysis. Drugs Aging 2007; 24 (2): 155-167.
3. Birks J.S., Harvey R.: Donepezil for dementia due to Alzheimer's disease. Cochrane Database Syst Rev 2003; (3): CD001190.
4. Olin J., Schneider L.: Galantamine for Alzheimer's disease. Cochrane Database Syst Rev 2002; (3): CD001747.
5. Birks J., Iakovidou V., Tsolaki M.: Rivastigmine for Alzheimer's disease. Cochrane Database Syst Rev 2000; (2): CD001191.
6. Doody R.S., Stevens J.C., Beck C., Dubinsky R.M., Kaye J.A., Gwyther L., Mohs R.C., Thal L.J. et al.: Practice parameter: management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2001; 56 (9): 1154-1166.
7. Gauthier S.G.: Alzheimer's disease: the benefits of early treatment. Eur J Neurol 2005; 12 (Suppl. 3): 11-16.
8. Winblad B., Brodaty H., Gauthier S., Morris J.C.,

Orgogozo J.M., Rockwood K., Schneider L., Takeda M. et al.: Pharmacotherapy of Alzheimer's disease: is there a need to redefine treatment success? Int J Geriatr Psychiatry 2001; 16 (7): 653-666.

9. Birks J.: Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006; (1): CD005593.
10. Finkel S.I.: Effects of rivastigmine on behavioral and psychological symptoms of dementia in Alzheimer's disease. Clin Ther 2004; 26 (7): 980-990.
11. Gauthier S., Feldman H., Hecker J., Vellas B., Emir B., Subbiah P.: Functional, cognitive and behavioral effects of donepezil in patients with moderate Alzheimer's disease. Curr Med Res Opin 2002; 18 (6): 347-354.
12. Kmietowicz Z.: NICE proposes to withdraw Alzheimer's drugs from NHS. Bmj 2005; 330 (7490): 495.
13. National Institute for Health and Clinical Excellence (NICE): Alzheimer's disease - donepezil, galantamine, rivastigmine (review) and memantine. NICE technology appraisal guidance 111 (amended). November 2006 (amended September 2007, August 2009). Available from: www.nice.org.uk/TA111.
14. Lyketsos C.G., Lopez O., Jones B., Fitzpatrick A.L., Breitner J., DeKosky S.: Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. Jama 2002; 288 (12): 1475-1483.
15. Raschetti R., Albanese E., Vanacore N., Maggini M.: Cholinesterase inhibitors in mild cognitive impairment: a systematic review of randomised trials. PLoS Med 2007; 4 (11): e338.
16. Doody R.S., Gavrilova S.I., Sano M., Thomas R.G., Aisen P.S., Bachurin S.O., Seely L., Hung D.: Effect of dimebon on cognition, activities of daily living, behaviour, and global function in patients with mild-to-moderate Alzheimer's disease: a randomised, double-blind, placebo-controlled study. Lancet 2008; 372 (9634): 207-215.
17. Barten D.M., Albright C.F.: Therapeutic strategies for Alzheimer's disease. Mol Neurobiol 2008; 37(2-3): 171-186.

Abstract COMUNICAZIONE

□ Management of acute stroke with organization of an emergency-urgency network and development of a connection between pre- and in-hospital settings: the Northern Lombardy Emergency Stroke Study

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Stroke is the leading cause of disability in adulthood. The principal aim of acute stroke management is to reduce mortality and disease-related disability. In the last decades several studies have demonstrated the efficacy of thrombolytic therapy in ischemic stroke, but up to 80% of cases cannot be treated because the diagnostic work-up exceeds the time limit, which is the principal factor for thrombolytic application. The aims of the study were the reduction of avoidable delay, the organization of an operative stroke emergency network and the identification of highly specialized structures. The study was conducted in the Northern Lombardy within the districts of Sondrio, Lecco, Como and Varese. All patients admitted to 19 hospitals of macro-area for acute stroke between November 2008 and January 2010 (phase 1) and between November 2009 and April 2010 (phase 3) were included into the Project. Pre-hospital, in-hospital and total time, gender, age, transport code, stroke subgroups, type of thrombolysis and clinical severity were registered. Statistical analysis was performed using chi-square test and Analysis of Variance (ANOVA). In the first phase 573 patients were observed with 43.5% using the Emergency System. The pre-hospital mean time was 292.91 minutes, while the in-hospital time was 226.84 minutes. Only 4 thrombolytic procedures were performed (0.7% of total cases). Analysing the results, we observed a significant difference in single step of acute management between the use of Emergency Service and not. Patients transported with this Service had lower value in pre-hospital ($p < 0.001$), in-hospital ($p < 0.05$) and consequently total time ($p < 0.001$). By these results some corrective factors were introduced in the management of acute stroke:

1. call the Emergency Service;
2. use of specific transport code (stroke code) to pre-alert the hospital of destination;
3. use of stroke code in the triage settings;
4. use of a "temporal" model for the acute stroke management;
5. regular updating of operators.

During the Study, the Regional Agency for the Emergency-Urgency approved the use of stroke code for the transport of patient with suspected stroke. Meetings into hospitals of the macro-area and with general population were organised to illustrate results of the first phase of the Project and to introduce corrective factors in the clinical practice, homogenizing the in-hospital activity. In the last phase we recorded the same data about the acute management of stroke, after the introduction of the disease-specific code (stroke code) to optimize the out- and in-hospital setting linkage. In this phase a total of 1,312 patients were observed with a mean age of 75 years. 56.3% of cases called the Emergency Service with a significative increase than the first phase ($p < 0.01$). We observed a significative time reduction in all steps of acute stroke management: pre-hospital, in-hospital and total time ($p < 0.001$). In this period thrombolytic procedures were performed on 49 patients (4.7% of ischemic strokes). This result is significantly higher than number of

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thrombolysis performed in Lombardy or in Italy for the same period ($p < 0.001$). The use of Emergency Service and the application of a stroke code during the transport and in all ischemic stroke patients could increase the number of thrombolytic procedures up to 190%.
In conclusion, for a better management of acute stroke, the results of the study suggest a closed interaction between Emergency Service and the Stroke Network, the efficacy of the stroke code use, the new in-hospital management model based on temporal variable and the need of a regular information for the population and the updating for hospital operators.

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Posters

Abstract POSTER

□ Natalizumab and cognitive impairment in multiple sclerosis: report of the therapeutical success in two patients

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Introduction. Cognitive impairment affects 40-65% of patients with multiple sclerosis and impairs their quality of life and employability[1]. Pathophysiology includes sensory deafferentation, involvement of white and gray matter, directs products of inflammation. Few studies described the effects of Disease Modifying Drugs (DMDs) on cognitive dysfunction[2]. Here we report two cases of improvement of cognitive performances after treatment with Natalizumab (NZB).

Case report. Two patients with Relapsing Remitting Multiple Sclerosis (RRMS) were treated with NZB 300 mg monthly for 22 months and 13 months respectively. Before starting NZB, patients underwent clinical evaluation (Expanded Disability Status Scale: EDSS), MRI lesion load and an extensive neuropsychological (NPS) evaluation, that included Trail Making Test (TMT), Digit Symbol Substitution Test (DSST), Verbal Fluency (FAS), Rey Test, Design Copy Test (CD), Wisconsin Card Sorting Test (WCST). At baseline, patient's 1 EDSS was 2.0; NPS evaluation showed an impairment in verbal abilities (FAS, Rey Test) and executive functions (WCST). Patient 2 scored pathologically in FAS and her EDSS was 2.5. Eighteen months later, lesion load on MRI was stable and EDSS improved (1.5) in both patients; NPS evaluations resulted within normal range of value.

Discussion. NZB has proved to be effective as DMD in RRMS[3], yet its efficacy on cognitive dysfunction has not been systematically investigated[2]. Our cases, responsive to NZB from clinical, radiological and neuropsychological point of view, confirm recent reports on this issue[4] and support the reliability of our NPS battery.

References

1. Amato M.P., Zipoli V., Portaccio E.: Multiple sclerosis-related cognitive changes: a review of cross-sectional and longitudinal studies. J Neurol Sci 2006; 245 (1-2): 41-46.
2. Comi G.: Effects of disease modifying treatments on cognitive dysfunction in multiple sclerosis. Neurol Sci 31 (Suppl. 2): 261-264.
3. Polman C.H., O'Connor P.W., Havrdova E., Hutchinson M., Kappos L., Miller D.H., Phillips J.T., Lublin F.D. et al.: A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med 2006; 354 (9): 899-910.
4. Mattioli F., Stampatori C., Bellomi F., Capra R.: Natalizumab efficacy on cognitive impairment in MS. Neurological Sciences 2011; 32 (Suppl. 3): 321-323.

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Abstract POSTER

□ Post-influenza vaccination encephalomyeloradiculoneuropathy: an adult case

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We present the case of a 70 years old male patient who, during the three weeks following influenza vaccination, presented a history of fever, increasing daytime somnolence, diplopia, peripheral facial palsy, hand paraesthesias, urinary retention and paraplegia.
On MRI multifocal white matter involvement of the cerebral hemispheres with two focal lesions, in the cervical and dorsal spinal cord respectively, were observed. After gadolinium administration there was enhancement of the nerve roots in the cauda equina.
The EMG and ENG confirmed the presence of acute motor axonopathy. The Cerebro-Spinal Fluid (CSF) analysis showed normal cell count and elevated protein concentration, with oligoclonal band of IgG.
PCR was negative for Varicella-Zoster Virus (VZV), Herpes Simplex Virus (HSV), Epstein-Barr Virus (EBV) and Cytomegalovirus (CMV) DNA in CSF.
Anti-ganglioside antibodies were negative.
Diagnosis of Acute Disseminated Encephalomyelitis (ADEM) with acute motor axonal neuropathy was made, and intravenous gammaglobulins were started in combination with steroids.
ADEM is a monophasic, immune-mediated demyelinating disorder following immunization or infection; multifocal central neurological dysfunctions can rapidly develop.
Guillain-Barré Syndrome (GBS) is characterized by an acute, symmetrical, progressive and inflammatory demyelinating peripheral neuropathy; axonal subtypes of GBS have been identified.
The present case may serve as a useful example of the association between central and peripheral neurological involvement in inflammatory neurological conditions, and the relationship of ADEM with GBS and its variants such as Bickerstaff Brainstem Encephalitis (BBE) and Fisher Syndrome (FS), as distinct nosological entities or part of the same clinical spectrum.

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Abstract POSTER

□ Subacute demyelinating polyneuropathy associated with B-cell lymphoma and IgM antibodies against myelin-associated glycoprotein

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Peripheral neuropathy associated with IgM Monoclonal Gammopathy of Unknown Significance (MGUS) is quite common[1]; about one half of patients with paraproteinaemic neuropathy show IgM monoclonal antibodies reacting with Myelin-Associated Glycoprotein (MAG). Paraproteinaemic neuropathies caused by haematological malignancies are far less frequent [2]. We report a 76-year-old patient with a subacute sensorimotor demyelinating polyneuropathy, monoclonal gammopathy and positivity of IgM autoantibodies against MAG, associated with a low grade B-cell lymphoma $CD20^{+}$, confirmed by bone marrow biopsy.

He presented with a two-months history of painful paraesthesias and walking difficulty. Neurological examination revealed marked ataxia, distal weakness in lower limbs, superficial and proprioceptive sensory deficit. Electroneurography documented reduced motor and sensory action potentials, prolonged distal motor latencies and slowed sensory and motor conduction velocities; cerebro-spinal fluid examination evidenced a slight proteinorrachia. Haematologic screening revealed a monoclonal gammopathy with high serum IgM and mild chain kappa proteinuria.

High titres of IgM anti-MAG antibodies were found. The patient was not responsive to a 5-days course of intravenous immunoglobulin treatment (0.4 g/kg/day), while chemotherapy for lymphoma (Fludarabine-Cyclophosphamide-Rituximab) determined clinical improvement.

This is an interesting association between paraproteinemic neuropathy and haematologic malignancy. Nevertheless, more observations are needed to clarify the causal relationship between anti-MAG antibodies and lymphoma, and the exact pathophysiology of nerve injury in these cases.

References

1. Bosch E.P., Smith B.E.: Peripheral neuropathies associated with monoclonal proteins. Med Clin North Am 1993; 77 (1): 125-139.
2. Donfrid M., Apostolski S., Suvajdzic N., Jankovic G., Cemerikic-Martinovic V., Atkinson H.D., Colovic M.: Monocytoid B cell lymphoma associated with antibodies to myelin-associated glycoprotein and sulphated glucuronyl paragloboside. Acta Haematol 2001; 106 (3): 130-132.

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Abstract POSTER

□ Effetto del Natalizumab sulle sottopopolazioni linfocitarie in pazienti affetti da sclerosi multipla: valore predittivo di efficacia?

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Introduzione. La Sclerosi Multipla (SM) è una malattia infiammatoria autoimmune demielinizzante multifattoriale del Sistema Nervoso Centrale (SNC).
Natalizumab è un anticorpo monoclonale che si lega alla subunità $\alpha 4$ delle integrine espresse dai linfociti T, impedendone così il passaggio attraverso la barriera emato-encefalica, momento cruciale nella patogenesi della malattia.
A fronte di una dimostrata efficacia, l'uso del Natalizumab è tuttora limitato dai dati sulla safety, in particolare in termini di infezioni.
Pazienti e Metodi. Sono stati studiati pazienti affetti da SM con forma Recidivante-Remittente (RR) aggressiva e candidati alla terapia con Natalizumab. Prima dell'inizio della terapia e quindi ogni 3 mesi sono stati eseguiti prelievi ematici per il controllo delle sottopopolazioni linfocitarie; la RM encefalo è stata effettuata ogni 6 mesi di trattamento.
Risultati e Conclusioni. Ad oggi sono stati arruolati 28 pazienti ed analizzati i dati di 19, con età media di 37 anni, durata media di malattia di 12,1 anno, punteggio alla Expanded Disability Status Scale (EDSS) medio-basale di 2,6 e con malattia in fase di attività clinica e radiologica.
Dopo una media di 13,3 infusioni di Natalizumab, il 68,4% dei pazienti è rimasto libero da attività di malattia (clinica e radiologica); a livello ematico è stato dimostrato un aumento statisticamente significativo ($p < 0,001$) di linfociti, eosinofili, linfociti natural killer ed in particolare dei linfociti B. Gli effetti collaterali sono stati di grado lieve/moderato e le infezioni più frequentemente registrate sono state quelle del tratto urinario.

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Abstract POSTER

□ Lesioni cerebrali in aree eloquenti: le innovazioni tecnologiche alla base di un miglior outcome clinico e radiologico

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Introduzione. Lesioni in aree cerebrali eloquenti quali i centri corticali del linguaggio o l'area somato-motrice primaria sono state considerate, in passato, non aggredibili chirurgicamente per i costi troppo elevati in termini di morbilità e deficit neurologici permanenti (dal 15 al 25,7%). L'uso in tempi recenti di tecniche di imaging con mappaggio funzionale pre- ed intra-operatorio riducono in maniera cospicua i rischi di danno neurologico permanente (5%), permettendo una maggiore aggressività chirurgica e garantendo un maggiore intervallo libero da malattia e contemporaneamente una migliore qualità di vita.
Caso clinico. Dal gennaio 2009 al gennaio 2011 sono stati operati 6 pazienti con lesioni cerebrali in area eloquente, sottoposti a studio di imaging con mappaggio funzionale non invasivo e stimolazione corticale intra-operatoria. Viene presentato il caso clinico di un paziente di 37 anni sottoposto ad asportazione di astrocitoma di grado II in area pre-motoria (4s) e seguito precedentemente in Neurologia per crisi comiziali resistenti alla terapia. Pre-operatoriamente è stata eseguita RM encefalo basale con mezzo di contrasto e con studio funzionale, che documentava la lesione frontale posteriore destra suggestiva per glioma a basso G° (confermato all'esame istologico definitivo). Durante l'intervento è stata eseguita la stimolazione corticale in anestesia generale prima e dopo la rimozione della lesione. Il paziente ha presentato nell'immediato post-operatorio un'emisindrome brachio-crurale sinistra regredita in poche ore.
Conclusioni. Una lesione gliale in adiacenza di area critica può essere trattata chirurgicamente con basso rischio di morbilità neurologica permanente a condizione di utilizzare tecniche di imaging funzionali pre-operatorie. Tuttavia, poiché le immagini neurofunzionali non sono in grado di distinguere fra un'area eloquente essenziale da un'area compensativa, la stimolazione funzionale intra-operatoria permette di definire meglio e "in vivo" i limiti della resezione chirurgica. In conclusione, l'uso di ecografo intra-operaotorio di ultima generazione, la stimolazione funzionale ed il planning pre- ed intra-operatorio con neuronavigatore, unitamente a tecniche di microchirurgia, garantiscono il miglior beneficio in termini di asportazione della lesione espansiva, riducendo significativamente il rischio di deficit neurologici permanenti post-operatori.

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Abstract POSTER

□ Inflammatory markers and oxidative status in patients with Alzheimer's disease treated with cholinesterase inhibitors

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Objectives. Alzheimer's disease (AD) is the most frequent neurodegenerative disorder in the elderly and at present no effective therapy exists. Both inflammation and oxidative stress play a role in AD. We investigated plasma oxidative status and PolyMorphoNuclear leukocyte (PMN) production of Reactive Oxygen Species (ROS) in AD patients on different anticholinesterase treatments.

Methods. 19 AD patients (75.4 ± 6,1 years; F/M = 17/2) treated with either donepezil (12) or rivastigmine (7) at currently recommended doses were studied at enrollement and after six weeks. At each visit, a blood sample was obtained. Plasma antioxidant capacity was assessed by both Ferric Reducing Ability of Plasma (FRAP) method and Oxygen Radical Absorbance Capacity (ORAC) assays. PMN production of ROS was induced by formyl-Methionyl-Leucyl-Phenylalanine (fMLP) 0.1 μM and assessed by spectrofluorimetry and expressed as fluorescence intensity in Arbitrary Units (AU).

Results. FRAP values were [mean (95% CI)] 523 (441-605) mmol/l in donepezil-treated patients and 623 (469-778) mmol/l in rivastigmine-treated patients ($p > 0.05$); the ORAC values were 1361 (1012-1711) in donepezil-treated patients and 4829 (2346-7313) in rivastigmine-treated patients ($p < 0.01$). PMN production of ROS was 155.2 (112.3-198.1) AU in donepezil-treated patients and 278.1 (146.0-410.2) AU in rivastigmine-treated patients ($p < 0.05$). Reference values obtained by retrospective analysis of historical data from a large cohort of healthy subject were 684 (526-843) mmol/l for FRAP, 3130 (1314-4946) mmol/l for ORAC and 248.7 (158.1-339.4) AU for PMN production of ROS.

Conclusions. In AD patients donepezil (but not rivastigmine) treatment is associated with decreased plasma antioxidant capacity and lower PMN oxidative burst. Future studies will assess whether such properties may be relevant for AD therapy.

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Abstract POSTER

□ Call-Center for cerebrovascular disease: a model for integration of treatment in the hospital-territory

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The progressive aging of the population and the growing incidence of patients with cerebrovascular disease with comorbidity and residual disability, motivates the need to make up organisational models to ensure continuity of treatment and care, protected discharge and a true Hospital County integration. This resulted in implementing a Call Center Clinic of multi-specialist care for Neurological and Internal Medicine by the Civic Hospital of Legnano.
The main objectives of the clinic are: support of the protected discharge of patients with cerebrovascular disease, continuity of treatment to reduce frequent hospital admissions, improvement of patient satisfaction, better share of care planning and reduction of sanitary costs. We report clinical data of 760 clinical interventions performed between September and December 2010 and 93 medical evaluations of patients.
The preliminary results regarding patient's satisfaction was encouraging. A rating scale ranging 1 to 7 showed a mean score equal to 6.31. Readmission for the same disease displayed a very small percentage.

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Abstract POSTER

□ Natural and Tr1 regulatory T cells (Treg) in multiple sclerosis patients treated with IFNβ

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In multiple sclerosis most research has focused on the role of natural Treg, while Tr1 were much less investigated.
Here, we simultaneously investigated the effect of Interferon beta (IFNβ) therapy on both types of Treg in blood samples of 44 patients who were studied before therapy start (T0), after 6 (T6) and 12 (T12) months of treatment, and from 43 patients treated for more than 24 months.
All patients were biologically responsive to IFNβ because MxA-induced. Flow cytometric analysis demonstrated that while $CD4^+CD45RA^+CCR7^+CD31^+$ lymphocytes, representing recent thymic emigrants, were increased after 12 months of therapy, natural $CD4^+CD25^+CD127^{low/-}$ Treg, as well as $CD4^+CD25^+CD127^{low/-}CD45RA^+CCR7^+CD31^+$ Treg which are the subset of Treg recently released from the thymus, did not change after therapy. However, in IFNβ treated patients, there is an increase of $CD4^+CD25^+CD127^{low/-}CD45RA^-CCR7^+$ "central memory" Treg, in which the presence of CCR7, regulating their trafficking to lymphoid and inflamed sites, confers the appropriate Treg localization for physiologic suppression. Furthermore, the stimulation of lymphocytes for 24 hours with anti-CD3 and anti-CD46 monoclonal antibodies, which is known to expand Tr1 cells, caused an increase of the RNA for Cyt-2, the pro-inflammatory cytoplasmic isoform of CD46 in a group of treated patients, while in the other group, Cyt-2 RNA level was comparable to that of controls. In the first of the two groups, a significant rise of mRNA for the anti-inflammatory cytokine IL-10 from T0 to T12 in co-stimulated cells was found. This indicated that, in patients with high Cyt-2, the increased level of IL-10 RNA could be the effect of a reaction carried on by IFNβ to offset the high expression of Cyt-2 pro-inflammatory isoform of CD46 molecule.

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Abstract POSTER

□ Complicanze dell'impianto di Gliadel nelle recidive dei glioblastomi

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La maggior parte dei pazienti affetti da glioblastoma multiforme decede entro i primi due anni dalla diagnosi, indipendentemente dall'approccio terapeutico. Inizialmente approvato dalla FDA (Food and Drug Administration) nel 1996 per la terapia delle recidive di glioblastoma, l'utilizzo del Gliadel è stato successivamente approvato anche per il trattamento in prima battuta di tutti i gliomi maligni ad alto grado. Studi recenti hanno, invece, dimostrato che l'impianto di carmustina non è consigliato per il trattamento dei gliomi ad alto grado in prima diagnosi, considerando l'attuale gold standard terapeutico la massima resezione chirurgica possibile seguita da radioterapia e chemioterapia con temozolomide. Il suo utilizzo nelle recidive di glioblastoma rappresenterebbe un valido approccio terapeutico, sebbene manchino solide evidenze scientifiche.

Presentiamo 15 casi di pazienti affetti da recidiva di glioblastoma multiforme giunti presso la nostra Clinica nel corso degli ultimi due anni e trattati mediante l'impianto di wafers di carmustina (Gliadel).

Tutti i pazienti erano stati sottoposti ad intervento chirurgico eseguito presso la nostra Clinica di asportazione di glioma maligno ad alto grado; successivamente seguiti presso il nostro Ambulatorio Neuro-Oncologico (Neurochirurgo, Oncologo, Radioterapista), una RM encefalo con gadolinio aveva dimostrato segni di recidiva di malattia.

I pazienti sono stati quindi sottoposti ad intervento chirurgico di asportazione di recidiva di malattia con impianto di wafers di carmustina nella cavità chirurgica.

In 11 pazienti la procedura è stata ben tollerata, senza complicanze post-operatorie legate alla diffusione all'interno del parenchima cerebrale del Gliadel.

In 2 pazienti si è assistito all'insorgenza di intensa cefalea associata a crisi epilettiche generalizzate, che hanno reso necessario introdurre in terapia anticomiziali e cortisonici ad alte dosi; in entrambi i casi una TC encefalo basale ha dimostrato la presenza di importante edema cerebrale.

Un paziente è stato trattato con terapia cortisonica per l'insorgenza di cefalea associata a nausea e vomito, successivamente seguiti da stato di sopore: anche in questo caso è stato dimostrato edema cerebrale.

In un paziente si è assistito al rapido decadimento neurologico, sino allo stato di coma; una RM ha dimostrato cerebrite a carico del sistema limbico e ad entrambi i poli temporali. Il paziente si presenta attualmente in stato vegetativo (GCS 7).

La sopravvivenza nei casi di recidiva di glioblastoma operati e trattati con wafers di Gliadel non è significativamente aumentata rispetto ai pazienti operati e sottoposti ad altri schemi terapeutici. Quindi l'utilizzo della carmustina in caso di recidiva può costituire un'opzione terapeutica qualora le altre modalità terapeutiche non siano praticabili, tenendo comunque conto degli effetti avversi anche gravi che abbiamo descritto.

La rimozione chirurgica totale dei gliomi ad alto grado rimane al giorno d'oggi fondamentale ai fini prognostici, indipendentemente dalle altre terapie post-operatorie.

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Abstract POSTER

□ Clinical features and classification of acute ischemic events among PFO-carriers

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Background. The association between Cryptogenic Stroke (CS) and Patent Foramen Ovale (PFO) supports the hypothesis that paradoxical embolism could be a relevant cause of stroke in young adults. The aim of the present study was to evaluate the features of acute ischemic events among PFO-carriers.

Patients. 60 patients with acute ischemic events and PFO: mean age 44.89 (± 11.21), M:F (27:33); 32% had dyslipidemia, 23.3% hypertension, 18.3% thrombofilia, and 8% cervical arteries stenosis.

Methods. ASCO (A for atherosclerosis, S for small vessel disease, C for cardiac source, O for other cause), OCSP (Oxfordshire Community Stroke Project), SSS-TOAST (Scandinavian Stroke Scale - Trial of Org 10172 (danaparoid) in Acute Stroke Treatment) classification, transesophageal ecocardiography, brain imaging.

Results. 50% of patients had stroke and 32% TIAs; 18% were recurrence. According to OCSP classification Partial Anterior Circulation Syndrome (PACS) occurred in 43.3%, Posterior Circulation Syndrome (POCS) in 31.7%, Lacunar Syndrome (LACS) in 23.3%, Total Anterior Circulation Syndrome (TACS) in 1.7%. At SSS-TOAST the events were classifiable as of cardioembolic origin in 6 (evident), 13 (probable) and 41 (possible) cases.

Conclusions. TOAST classification tends to underestimate the cardioembolic origin of ischemic events. Our PFO-patients rarely undergo major events, showing a prevalence of PACS and POCS; over 30% have at TC/MRI 2 or more lesions from previous events. PFO can be considered an important risk factor for CS, but it could be an incidental finding and other possible causes must be considered for subsequent therapeutic decision-making.

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Abstract POSTER

□ Relapsing cervical artery dissection in Ehlers-Danlos syndrome: case report

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Background. Cervical Artery Dissection (CAD) is a major cause of ischaemic stroke in young adults; its outcome is related to rare underlying diseases, cerebrovascular risk factors and the time for diagnosis and treatment.
Case report. A 22 yrs old woman presented with headache at right periorbital region, carotidodynia and paraesthesias involving the left arms, without significant recent trauma. Neurological examination revealed a left Horner-Syndrome and no common features of connective disorders including joint hypermobility. Brain MRI showed a hypodense right temporo-parietal lesion; MR and TC angiograms demonstrated CAD of the right Internal Carotid (ICA) and of homolateral vertebral artery. Screening for CardioVascular Risk Factors (CVRFs) was normal. Oral Anticoagulant Therapy (OAT) was started with good outcome and complete recanalization after 6 months. Three years after she presented a severe headache after a minor cervical trauma, without neurological impairment; MR angiogram showed occlusion of the left ICA due to CAD and a new ischaemic lesion. Despite OAT no recanalization was obtained. A mutation of COL3A1 gene consistent with Ehlers-Danlos syndrome type IV was documented.
Conclusions. Screening for underlying genetic conditions associated with CVD must be performed in young adults with stroke, also in absence of systemic somatic correlations.

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Abstract POSTER

□ Macroautophagy assessment in amyotrophic lateral sclerosis lymphomonocytes

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Amyotrophic lateral sclerosis (ALS) is a relentless neurodegenerative disorder for which currently no effective therapeutic options exist. Recent studies suggest a possible involvement for macroautophagy, a major cell pathway of protein catabolism, in the pathogenesis of ALS. Furthermore, lithium, a well-known autophagy inductor, is currently clinically tested on these patients. We decided to assess the hypothesis that a putative dysfunction of the autophagic pathway could be operative in Peripheral Blood Mononuclear Cells (PBMC) obtained from ALS patients, since these cells represent an accessible model for studying molecular pathogenesis of neuropsychiatric disorders. In this work we assessed beclin-1 and LC3-II immunoreactivity in PBMC from 15 ALS patients and 15 controls by Western blot analysis. The expression of Atg12 mRNA was assessed as well. No significant difference was observed for all these parameters between patients and controls. Since all recruited patients were treated with Riluzole we tried to exclude a putative interference of this drug quantifying LC3-II immunoreactivity in SH-SY5Y neuroblastoma cells treated with concentrations ranging from 2 to 50 μM for 8 hours. Riluzole failed to modify autophagy in this experimental paradigm. The results of this pilot study do not support the idea of a systemic autophagic dysfunction in ALS.

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Abstract POSTER

□ Acute visual loss and bilateral fixed mydriasis: an atypical case of giant cell arteritis

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Background. Giant Cell Arteritis (GCA) is an immune-mediated chronic vasculitis of large- and medium-sized vessels, usually occurring in individuals aged over 50 years. Characteristic findings include headache, jaw claudication, visual loss, and constitutional symptoms. The pathological hallmark of GCA is granulomatous inflammation of the involved vessels and Temporal Artery Biopsy (TAB) remains the gold standard for diagnosis. Additional diagnostic tests include blood tests (Erythrocyte Sedimentation Rate [ESR], C-reactive protein [CRP], platelets [PLT]) and imaging modalities (ultrasound of the arteries, fluorescein angiography, Computed Tomography [CT], and MRI). Since the prognosis for visual recovery is poor, the goal of treatment is to prevent ischemic damage and halt progression of visual loss.
Case report. A 67-year-old woman, with a history of hypertension, diabetes mellitus and with a pacemaker due to atrial fibrillation, presented to the Emergency Room of our hospital because of subacute and progressive visual loss. In 5 days, the patient became completely blind in her left eye (Oculus Sinister: OS), and just able to distinguish light and shadow with the right one (Oculus Dexter: OD). Simultaneously, her pupils became and remained mydriatic bilaterally. She was admitted to our neurological department, where the neurological examination revealed no abnormalities, except for the fixed bilateral mydriasis and routine blood tests showed an increase of PLT (589 x 10^9/L), ESR (58 mm/h), CRP (98.7 mg/L), fibrinogen (774 mg/dL), and Alkaline Phosphatase [AP] (161 U/L). A CT scan of orbits with contrast revealed no changes in optic nerves volume, morphology and/or pathological enhancement. The Cerebrospinal Fluid (CSF) examination was normal. A visual acuity of 0/10 in OS and fingers counting in OD, a fixed bilateral mydriasis and a bilateral optic disc edema were demonstrated with the neurophthalmological examination. A miotic response of the pupils was observed with the pilocarpine test at 2%, but also with a lower pilocarpine concentration (0.125%), suggesting a pupil denervation pattern. A Temporal Artery Biopsy (TAB) showed giant cell infiltration, supporting the hypothesis of GCA. Corticosteroid therapy (1 g solumedrol/day) was administered. During the next days, we could observe an improvement in OS visual acuity (until 3/10).
Conclusions. We presented a case of GCA diagnosed after a biopsy, with an atypical pattern of presentation, characterized by bilateral acute visual loss and fixed mydriasis. We supposed that, besides an involvement of large- and medium-size vessels, also small vessels might have been compromised, and/or in relation to a particularly extensive damage of the arterial wall, a lot of branches of the ophthalmic artery may be affected.

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Abstract POSTER

□ Adverse reaction to COMT inhibitors in Parkinson's disease patients: possible association with the UGT1A9 gene haplotype

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Entacapone and tolcapone are catechol-O-methyltransferase (COMT) inhibitors used for the treatment of patients with Parkinson's Disease (PD). Some of us provided evidence that the tolerability profile of COMT inhibitors could be related to individual genetic variations in drug metabolism[1], which occurs through UDP-GlucuronosylTransferase (UGT) 1A9. Expression and activity of UGT1A9 is affected by several Single Nucleotide Polymorphisms (SNPs), thus their combination effect should be taken into account. To assess the association between occurrence of Adverse Reactions (AR) COMT inhibitors-induced and allelic combination formed by common SNPs in UGT1A9 (UGT1A9*1b and UGT1A9*3) PD patients treated with COMT inhibitors were enrolled and screened for the occurrence of AR (defined as any events leading to COMT inhibitors therapy discontinuation).

Patients genotyping was performed by direct sequencing and patients phenotype were defined as: Rapid Metabolizers (RM); Intermediate Metabolizers (IM) and Slow Metabolizers (SM) according to specific combination of SNPs. 72 PD patients were enrolled in the study, of these, 11 presented AR. AR occurrence was not associated with individual SNPs, however in patient without AR phenotype were: RM = 33 (53%); IM = 26 (42%); SM = 3 (5%) and in patient with AR phenotype were: RM = 5 (45%); IM = 2 (18%); SM = 4 (27%), ($p < 0.003$) showing that patients with AR had statistically significant increased frequency of the PM phenotype.

PD patients with UGT1A9 SM phenotype seem at higher risk of AR leading to discontinuation of COMT inhibitors. Assessment of the cost-effectiveness of genetic screening as a tool to guide COMT inhibitor treatment is warranted.

Reference

1. Martignoni E., Cosentino M., Ferrari M., Porta G., Mattarucchi E., Marino F., Lecchini S., Nappi G.: Two patients with COMT inhibitor-induced hepatic dysfunction and UGT1A9 genetic polymorphism. Neurology 2005; 65 (11): 1820-1822.

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Abstract POSTER

□ Motor and visual imagery in amyotrophic lateral sclerosis

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Motor Imagery (MI) allows actions recall and movements programming without implying the concrete evoked movement execution[1]. It has been demonstrated that patients with selective damage to the descendent motor pathways showed an impaired M1[2,3]. However, in our knowledge, no study has systematically investigated MI in patients suffering of a progressive lost of the ability to move. Therefore, the aim of our work was to investigate the performance of Amyotrophic Lateral Sclerosis (ALS) patients in a MI tasks. Thirteen ALS patients and 13 neurologically unimpaired subjects participated in the study. We administered a modified version of the Hand Laterality Task (HLT)[4,5], in which participants were asked to judge the laterality (i.e. left or right) of a tilted hand and a control task, the Font Specularity Judgment (FSJ), in which subjects performed a visuo-spatial imagery processing in order to judge if a tilted alphabetic font was in its canonical or mirror-reversed form[6]. Hands (HLT) and fonts (FSJ) were presented with the same degrees of rotation (0°, 90°, 180 and 270°) in separate and counterbalanced blocks. Overall results were different comparing ALS patients with control subjects in both tasks ($p < 0.05$). More interesting, we analyzed the role of biomechanical constraints in HLT, defined as the advantage in judging hand orientated in 'comfortable' position compared with ones tilted in 'awkward' posture[7]. Only ALS patients did not show this effect at the HLT ($p > 0.05$), suggesting the hypothesis that these patients performed the task adopting a general rotation strategy and not a specific one for body parts as normals.

Taken together our results suggest that ALS patients might have an impaired access to the motor system due to the progressive atrophy of M1.

References

1. Tomasino B., Toraldo A., Rumiati R.I.: Dissociation between the mental rotation of visual images and motor images in unilateral brain-damaged patients. Brain Cogn 2003; 51 (3): 368-371.
2. Conson M., Sacco S., Sara M., Pistoia F., Grossi D., Trojano L.: Selective motor imagery defect in patients with locked-in syndrome. Neuropsychologia 2008; 46 (11): 2622-2628.
3. Conson M., Pistoia F., Sara M., Grossi D., Trojano L.: Recognition and mental manipulation of body parts dissociate in locked-in syndrome. Brain Cogn 2010; 73 (3): 189-193.
4. Sekiyama K.: Kinesthetic aspects of mental representations in the identification of left and right hands. Percept Psychophys 1982; 32 (2): 89-95.
5. Parsons L.M.: Imagined spatial transformations of one's hands and feet. Cogn Psychol 1987; 19 (2): 178-241.
6. Pelgrims B., Michaux N., Olivier E., Andres M.: Contribution of the primary motor cortex to motor imagery: A subthreshold TMS study. Hum Brain Mapp 2010, Nov 12 [Epub ahead of print].
7. Parsons L.M., Shimojo S.: Perceived spatial organization of cutaneous patterns on surfaces of the human body in various positions. J Exp Psychol Hum Percept Perform 1987; 13 (3): 488-504.

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Abstract POSTER

□ Causal fronto-temporal lobar degeneration mutations: a novel mutation in MAPT associated with non-fluent progressive aphasia phenotype

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A mutation scanning of Microtubule Associated Protein Tau gene (MAPT) was carried out in 67 patients with Fronto-Temporal Lobar Degeneration (FTLD) with an early onset and without mutations in progranulin gene. A novel variant has been found in a patient diagnosed clinically with non-fluent Progressive Aphasia (PA), with a positive familial history for dementia. At 65 years she started developing progressive language disturbance, characterized by verbal production deficit and articulation impairment. She came to our attention at 67 years. Her Mini-Mental State Examination (MMSE) score was 22/30. A brain CT scan showed ventricles' asymmetry (left > right) and signs of chronic vasculopathy. Cerebrospinal fluid analysis showed slightly decreased Abeta, slightly increased total tau and normal Ptau levels. She was diagnosed with PA according to current criteria.

A novel exon 10 MAPT variant was identified (g.123798G > A), which leads to an amino acidic change (p.Gly304Ser) in the second microtubule binding domain. In silico analysis predicted that this variant is damaging on protein structure and function.

Additional 168 FTLD patients and 503 controls screened did not carry the variant, suggesting that it is a mutation rather than a polymorphism. The aminoacid change could compromise the ability of tau to properly regulate the dynamic behaviour of microtubules.

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Abstract POSTER

□ Phenotypic heterogeneity of the GRN Asp22fs mutation in a large Italian kindred

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The Asp22fs(g.63_64insC) mutation in progranulin gene (GRN) has been reported in one patient with Fronto-Temporal Dementia (FTD).
Here, we describe the clinical heterogeneity associated with the GRN Asp22fs mutation in a large Italian family. Clinical and instrumental workup of two symptomatic carriers in two generations has been carried out, together with genetic analysis of probands and of nine asymptomatic family members. The first proband was a 47-year old male clinically diagnosed with FTD with a positive family history. Evaluation of plasma GRN levels was consistent with the presence of a mutation in its encoding gene, that was demonstrated by sequencing [Asp22fs(g.63_64insC)].
Brain MRI showed multiple T2 and FLAIR hyperintense areas in the frontal lobe white matter and right hemisphere cortical atrophy. The second proband was his 79 years old uncle, presenting with a mild cognitive impairment. Brain MRI showed small T2 hyperintense lesions and widespread cortical atrophy. Cerebrospinal fluid amyloid beta, tau and phosphotau protein levels were in both cases normal. Additional nine asymptomatic family members were studied.
This family's description expands the spectrum of clinical presentations of fronto-temporal lobar degeneration caused by GRN mutations, suggesting that the diagnosis could be missed in some individuals with an atypical presentation.

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Abstract POSTER

□ Transfer to clinical practice of Mixovirus protein A quantification to evaluate IFNβ bioactivity: 5 years experience

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Five years ago we have introduced a real-time PCR relative quantification assay for Mixovirus protein A (MxA) into routine clinical practice and, until now, we have measured MxA RNA levels in 718 samples from 625 unselected Beta Interferon (IFNβ)-treated Multiple Sclerosis (MS) patients. 180 of them were male (median age: 40, interquartile range: 33-48 years) and 445 were female (median age: 40, interquartile range: 33-46 years); 127 patients were referred to our laboratory from the MS Centre of our institution; 445 were from other MS Centres of our region and 53 from MS Centres in other Italian regions. Patients were considered MxA non-induced when MxA mRNA values were under the cut-off threshold of 3.83 Normalization Ratio (NR), which represent the 99th percentile of values obtained in healthy controls.

Our data show that the median MxA mRNA value, in MxA-induced samples, was 27.43 NR (interquartile range: 18.24-39.71) and that 84 of the 625 MS patients (13.4%) lacked MxA induction because MxA mRNA was below the cut-off value. The percentage and the cut-off threshold were consistent with values reported by other laboratories which, in most cases, analyzed samples from patients who were included in clinical protocols and had been previously screened for NAb positivity.

Our data further demonstrate that the measure of MxA transcripts in whole blood offers a practical method to monitoring IFNβ bioactivity, even if more recent results obtained in our laboratory indicated that IFNβ bioactivity loss is a dynamic process involving the recovery of MxA induction also after several months of MxA negativity.

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Abstract POSTER

□ Highly heterogeneous pattern of biological response to interferon-beta therapy in multiple sclerosis patients

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** Non solo Nab observational prospective trial: Bab, MxA, and characterization of IFNAR subunits and isoforms in the IFNβ bioactivity control in multiple sclerosis patients. Study code BD0106*

To identify the optimal marker of Interferon-β (IFNβ) bioactivity loss, 118 therapy-naïve Multiple Sclerosis (MS) patients were enrolled and their blood samples were obtained before and at 3, 6, 12, 18, 24, 30 and 36 months after IFNβ-1a and 1b therapy start. Binding antibodies (BAb) Neutralizing Antibodies (NAb), and Mixovirus protein A (MxA) RNA induction, quantified in samples obtained 12 hours after IFNβ injection, were therefore measured in a total of 735 samples. The study dropout rate was 28.8%.

The response to IFNβ treatment is highly heterogeneous, with individual patterns of reaction: 10 patients out 84 (11.9%) were respectively stably or transitorily biologically non-responder because $MxA^{-}BAb^{+}NAb^{+}$ (9.5%) or $MxA^{-}BAb^{-}NAb^{-}$ (2.4%), while 31 (36.9%) were biologically responsive to IFNβ for the entire period of the follow-up, because all samples were $MxA^{+}BAb^{-}NAb^{-}$. However, we regarded as responder also those patients that were MxA^{+} and NAb^{-} in all samples (10.7%), even if they were BAb^{+} at one or more time points of the follow up, and those that, in the absence of BAb and NAb, were MxA-non induced at one (14.3%), two (4.8%), or three (4.8%) non-consecutive time points. This last feature can be interpreted as a low patient's compliance and can be also the reason of the absence of MxA induction in one or two samples of 11 $BAb^{+}NAb^{-}$ patients (13.1%). Finally, 3 patients (3.6%) were considered responder because always MxA-induced despite the presence of BAb and NAb.

The data demonstrated the need to exactly check the moment of blood drawing and, due to the high heterogeneity of the biological response to IFNβ therapy, the requirement of a personalized therapy for each multiple sclerosis patient.

Disclosure of funding. *The study was sponsored by Biogen Dompé.*

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Abstract POSTER

□ Kinetics of anti-IFNβ antibodies production and IFNβ bioactivity loss in multiple sclerosis patients

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** Non solo Nab observational prospective trial: Bab, MxA, and characterization of IFNAR subunits and isoforms in the IFNβ bioactivity control in multiple sclerosis patients. Study code BD0106*

The kinetics of anti-IFNβ antibodies production and the interference with drug bioactivity were investigated in samples drawn before therapy start and at 3, 6, 12, 18, 24, 30 and 36 months of treatment from 8 Multiple Sclerosis (MS) patients who were biologically non responsive to IFNβ because Binding and Neutralizing Antibodies (BAb and NAb) were positive and MxA was non-induced in at least two consecutive samples. BAb, quantified by radioimmunoprecipitation, were detected at 3 months after therapy start in 6 patients, and after 6 months in 2. Furthermore, they were constantly present at all time points in 6 patients, and disappeared after 24 and 30 months of therapy in two. NAb, identified by cytopathic effect inhibition assay, were found in all BAb-positive patients, but their appearance was concomitant in 3 patients and delayed in 5 patients (in 2 patients at 6 months, in other 3 after 12, 18 and 36 months of therapy). Loss of IFNβ bioactivity measured with the quantification of MxA RNA by real-time PCR, occurred simultaneously to BAb and NAb appearance in 6 patients, but postponed of 12 and 30 months in two. In one patient, who resulted positive for BAb in all consecutive samples, the identification of NAb and the lack of MxA production arose only after 36 months of therapy. Finally, NAb disappeared before the BAb loss and the recovery of MxA-induction in 2 patients, while in one patient MxA values were over the cut-off at some time points of the follow up despite the presence of BAb and NAb.

The data demonstrated that the kinetics of BAb and NAb production and MxA induction are not strictly connected, and anti-IFNβ antibodies may appear more precociously than previously thought, and the loss of IFNβ bioactivity can be delayed at 3 years of therapy.

Disclosure of funding. *The study was sponsored by Biogen Dompé.*

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Abstract POSTER

□ Studio osservazionale: la sclerosi laterale amiotrofica nella provincia di Como

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La Sclerosi Laterale Amiotrofica (SLA) è una malattia neurodegenerativa e progressiva del sistema nervoso che colpisce selettivamente i motoneuroni. Si caratterizza per una progressiva paralisi muscolare dovuta alla degenerazione dei motoneuroni della corteccia motoria primaria, del tratto corticospinale e del midollo spinale.

La scelta di fare un intervento di sorveglianza nutrizionale sui pazienti affetti da questa patologia nasce dalla necessità di avere un quadro preciso dei dati epidemiologici sul territorio comasco e dello stato clinico-nutrizionale di tali pazienti affetti da patologia rara. Dalla letteratura vi è evidenza, infatti, che questi soggetti vanno spesso incontro a problemi nutrizionali. Una sensibilizzazione precoce e una presa in carico nella fase iniziale della malattia risulta indispensabile per prevenire l'insorgenza di un quadro di malnutrizione. L'obbiettivo a lungo termine è volto ad indagare se l'intervento nutrizionale possa prolungare l'aspettativa e/o migliorare la qualità di vita.

Lo studio ha preso avvio il 1 settembre 2009 e dopo un anno (31 agosto 2010) è stata fatta una prima analisi dei dati raccolti. Durante questo periodo sono stati seguiti 30 pazienti affetti da SLA in vari stadi della malattia e con età media di 65 anni.

Di questi pazienti 21 sono uomini e 9 sono donne, con un rapporto M:F di 2,3:1, che conferma la lieve prevalenza nel sesso maschile riportata in letteratura. La prevalenza dei pazienti affetti da SLA seguiti dal Servizio di Nutrizione Clinica e Dietetica di Como durante l'anno dello studio è stata pari a 5/100.000 abitanti mentre l'incidenza è stata di 1,7/100.000 abitanti, valori lievemente inferiori rispetto a quelli di prevalenza ed incidenza nazionali ma si tratta comunque solo dei pazienti seguiti dal Servizio. L'età media della diagnosi è di 60 anni (in accordo con la letteratura) con un'età minima di diagnosi di 30 anni ed un'età massima di 84 anni.

In letteratura la sopravvivenza media dei pazienti con SLA dal momento della diagnosi è stimata intorno ai 2-3 anni; i nostri dati mostrano una sopravvivenza media dalla diagnosi di 4,9 anni, con il 38% dei pazienti con una sopravvivenza maggiore di 3 anni, di cui 3 pazienti (10%) con una sopravvivenza maggiore di 10 anni e quindi possono essere considerati "atipici". Questi ultimi sono pazienti già seguiti da tempo dal Servizio pertanto sembra che un intervento di tipo nutrizionale sia molto importante.

Il Body Mass Index (BMI) medio dei pazienti in studio è di 21,6 Kg/m^2 e l'analisi dei dati mostra che 8 soggetti sono in malnutrizione lieve, 16 pazienti in normopeso, 5 in sovrappeso e solo 1 soggetto in obesità. Un altro parametro che è stato considerato è il valore AMA (Arm Muscle Area) ed il percentile ad esso associato. Il calcolo di questo valore ci ha permesso di rilevare che il 72% dei pazienti mostra una forte deplezione della massa muscolare (< 10 percentile).

Dei 30 pazienti in terapia, 24 sono in nutrizione enterale totale, 4 seguono una dieta per os con integratore e 2 solo una dieta per os.Tra i 24 pazienti in nutrizione enterale, 20 hanno la PEG (Percutaneous Endoscopic Gastrostomy), 2 la RIG (Radiologically Inserted Gastrostomy) e 2 il SNG (Sondino Naso-Gastrico). Il 55% dei pazienti entra in NE (Nutrizione Enterale) meno di due anni dopo la diagnosi, il 27% tra i 2 e i 5 anni ed il 18% ben dopo i 5 anni dall'esordio di malattia. Il tempo medio tra la diagnosi ed il posizionamento della PEG/RIG è stato di 2.9 ± 2.4 anni.

La letteratura indica casi di ipermetabolismo tra i pazienti affetti da SLA, mentre tra i pazienti in carico all'ASL non si sono riscontrati soggetti in ipermetabolismo, anzi dai dati raccolti si evidenzia che il metabolismo basale medio mi-

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surato con l'Armband è più basso rispetto al metabolismo basale medio basato con la formula di Harris Benedict.
Inoltre, abbiamo rilevato che il 17% dei pazienti mostravano o hanno riportato in precedenza piaghe da decubito; complicanza che in letteratura viene riportata come "atipica" in questa patologia. I decubiti sono più frequenti nei pazienti mantenuti a lungo in vita con la ventilazione assistita. È importante sottolineare, comunque, che il 80% di questi soggetti con piaghe a livello sacrale presenta il diabete come malattia concomitante.
Lo studio proseguirà mantenendo sotto osservazione questi soggetti e valutando se il loro stato nutrizionale migliorerà nel tempo e potrà portare persino ad un prolungamento della vita media.

Abstract POSTER

□ Symptomatic or prophylactic treatment of week-end migraine: an open label, non-randomized, comparison study of Frovatriptan *vs* Naproxen or no-therapy

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Background. Migraine is often triggered by a period of stress and overwork followed by relaxation. This particular form of migraine, called week-end migraine, has been poorly investigated over the years. Moreover, evidence of drug efficacy for this type of migraine is lacking.

Objective. To compare the efficacy of Frovatriptan (F) with that of Naproxen (N) or no-therapy, for the acute or prophylactic treatment of week-end migraineurs.

Methods. The study included 28 subjects (18 females, mean age 36 years, range 19-60 years) suffering from week-end migraine without aura. Subjects were followed up for 6 consecutive week-ends. During the first 2 week-ends no treatment was administered. On the third and fourth week-end patients were asked to take one 2.5 mg dose of F on saturday and one on sunday morning, regardless of the occurrence of migraine. On the fifth and sixth week-end patients were asked to take one 500 mg dose of N. All patients were allowed to take a rescue medication, consisting of any analgesic drug, in the afternoon (at least 6 hours after morning awakening). Efficacy was evaluated through a migraine diary, where patients had to report the severity of migraine, in a scale ranging between 0 (no migraine) and 10 (severe migraine), and the use of rescue medication.

Results. Score of migraine severity was significantly lower with F [4.8 (95% confidence interval: 3.8/5.9)] than with N [5.7 (5.1/6.4) $p < 0.05$ *vs* F] or no-therapy [6.6 (6.2/7.0) $p < 0.01$ *vs* F]. The difference in favor of F was more striking in patients not taking rescue medication [1.9 (1.5/2.3) *vs* 3.6 (3.0/4.2) $p < 0.001$ and *vs* no-therapy 5.1 (4.4/5.8) $p < 0.001$] and for the second day of treatment (sunday). The proportion of patients taking a rescue medication was significantly ($p < 0.05$) lower under F (12.5%) than under N (31.3%) or no-therapy (56.3%): in particular the chance of taking a rescue medication was 18% less with F than with N ($p < 0.01$).

Conclusions. This relatively small, open-label, non-randomized pilot study provides the first evidence of the efficacy of a last generation triptan either as symptomatic or prophylactic treatment of week-end migraine.

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Abstract POSTER

□ Un caso di sclerosi combinata subacuta in un paziente vegano

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Presentiamo il caso di un uomo di 44 anni, vegano, con anamnesi patologica remota non significativa.
Viene valutato dal neurologo per comparsa da circa 1 mese di sensazione tipo "scossa elettrica" lungo il rachide e parestesie a calza bilateralmente.
All'esame obiettivo neurologico si rilevano lieve ipostenia all'arto superiore sinistro, ipopallestesia con livello sensitivo medio-dorsale, lieve atassia nella deambulazione, fenomeno di Lhermitte.
Una RM del rachide cervico-dorsale documenta la presenza di un'alterazione di segnale estesa da C6 a D11 interessante prevalentemente i cordoni posteriori, senza significativa impregnazione di mezzo di contrasto; RM encefalo ed esame liquorale negativi.
Agli esami ematici rilievo di lieve anemia macrocitica (Mean Corpuscular Volume: MCV 124 fl), ipertrigliceridemia (582 mg/dl), modesto incremento degli indici di funzionalità epatica, deficit severo di vitamina B12.
Viene posta la diagnosi di sclerosi combinata ed impostata una terapia con cobalamina ad alto dosaggio (1 mg/die x 10 giorni, poi 1 volta/settimana x un mese, poi 1 volta/mese), oltre che una rivalutazione dello schema dietetico del paziente.
La dieta vegana esclude l'assunzione di prodotti di origine animale e, poiché questi ultimi sono la fonte principale di vitamina B12, i vegani sono più facilmente esposti alle conseguenze della carenza di tale vitamina, come confermato da alcuni casi riportati in letteratura.

BIBLIOGRAFIA

1. Brocadello F, Levedianos G, Piccione F, Manara R, Pesenti FF. Irreversibile subacute sclerotic combined degeneration of the spinal cord in a vegan subject. Nutrition. 2007; 23(7-8):622-4.
2. Cornejo W, González F, Toro ME, Cabrera D. Subacute combined degeneration. A description of the case of a strictly vegetarian child. Rev Neurol. 2001;33(12):1154-7.
3. Takahashi H, Ito S, Hirano S, Mori M, Suganuma Y, Hattori T. Subacute combined degeneration of the spinal cord in vegetarians: vegetarian's myelopathy. Intern Med. 2006;45(10):705-6.

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Abstract POSTER

□ Transient cortical blindness during right transradial cardiac catheterization

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The incidence of cortical blindness following cerebral angiography has been reported to be 1-4%.
Its occurrence after coronary angiography is far less common (< 0.005%).
The demonstration of contrast enhancement in the occipital cortex on CT scan confirms the diagnosis in most cases, which appears to be an adverse reaction to contrast agent. Patient outcome is excellent with complete recovery within 24-48 hours.
We describe a case of a 66 year old man with sudden cortical blindness during coronary angiography and bilateral occipital infarct detected at CT scan.

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Abstract POSTER

□ HIV-related cerebral toxoplasmosis mimicking Behçet neuro-vasculitis in a rheumatoid arthritis patient

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A 51 years old woman with a history of sieronegative Rheumatoid Arthritis (RA) and recent uveitis treated with azathioprine, was admitted to the General Medicine department due to significant weight loss, gait difficulties and recurrent lipothymia; a few months earlier a brain CT scan with contrast was normal.

Neurological examination was normal, patient was alert and oriented, although a fatuous attitude was noted. During hospitalization, she presented a rapid decline in alertness without focal neurological signs. She was not febrile and denied recent infectious diseases. EEG findings were unspecific. Cerebro-spinal fluid proteins were increased with few lymphocytes.

Brain MRI revealed multiple T2 hyperintense lesions involving right thalamo-capsular and pontine-midbrain area with contrast enhancement, and confluent lesions involving periventricular white matter, suggesting, along with medical history, of a Behçet neuro-vasculitis. Patient was treated accordingly, with corticosteroids (immediate benefit but subsequent recurrence) and cyclophosphamide. Ceftriaxone was associated, pending laboratory results, which eventually revealed HIV positivity with severe immune deficiency. MRI findings were re-discussed given this result, underlining a granulomatous nodule pattern possibly addressing multiple cerebral localization of Toxoplasma. Cotrimoxazole was introduced, but progressive worsening occurred until death. Brain pathology confirmed only the diagnosis of HIV related cerebral toxoplasmosis.

HIV infection should always be suspected in presence of cerebral lesions and neurological syndrome in the context of auto-immune disorders.

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Abstract POSTER

□ Mental acute performance in stroke: studio delle funzioni cognitive nell'ictus acuto

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Introduzione. Nella valutazione dei pazienti con ictus cerebrale in fase acuta è necessario indagare in modo breve ma accurato e attendibile le funzioni cognitive. Attualmente, lo strumento più utilizzato è il Mini Mental State Examination (MMSE), mutuato dalla valutazione dei pazienti con demenza e quindi non sufficientemente informativo per altre patologie. Abbiamo voluto costruire uno strumento di screening in lingua italiana breve ed esaustivo, specifico per l'ictus cerebrale in fase acuta (Mental Acute Performance (in) Stroke: MAPS) per esplorare in modo sistematico le funzioni cognitive nonché la fluttuazione dei deficit rilevati.

Materiali e metodi. Sono stati selezionati 37 soggetti con ictus cerebrale acuto (25 maschi e 12 femmine) presso la Stroke Unit dell'Ospedale Maggiore "Niguarda Ca' Granda" di Milano. L'età media è di 63,97 anni (DS 15,39), la scolarità media è di 9,6 anni (DS 4,18). Il gruppo di controllo bilanciato per età, sesso e scolarità si compone di 23 soggetti (7 femmine, 16 maschi). L'età media è di 62,97 anni (DS 15,39), la scolarità media è di 9,6 anni (DS 4,11). Ai soggetti è stato somministrato il MAPS, composto di dodici sub-test per indagare orientamento spazio-tempo, linguaggio, attenzione, memoria, prassia, funzioni esecutive e visuo-spaziali. Inoltre, è stato somministrato il MMSE secondo il disegno sperimentale ABBA (le condizioni AB sono applicate in un ordine la prima volta e nell'ordine inverso la seconda volta).

Risultati e conclusioni. Sia MMSE sia MAPS mostrano differenze significative nel discriminare normalità da patologia (MMSE - U = 189,500, p = 0,00; MAPS - U = 159,500, p = 0,00). Confrontando afasia e neglect MAPS risulta più specifico rispetto al MMSE che evidenzia solo deficit verbali. MAPS sembra pertanto un test clinico idoneo e specifico per lo *stroke* in fase acuta, nonostante richieda un tempo più lungo di somministrazione rispetto al MMSE (20 minuti *vs* 8 minuti). MAPS permette infatti uno screening sufficientemente accurato non che rappresenta un test adeguato anche per il follow up grazie alle forme parallele.

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Abstract POSTER

□ Risultati inaspettati dalla valutazione dello stato di nutrizione e delle abitudini dietetiche nei pazienti affetti da malattia di Parkinson in un Paese africano

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Background. L'analisi delle abitudini alimentari è importante nei pazienti affetti da malattia di Parkinson (PD), sia a scopo di ricerca, sia di cura. Infatti, la dieta è un fattore ambientale che potrebbe rientrare tra le concause che provocano la malattia. Inoltre, la composizione dei pasti (soprattutto l'assunzione di proteine animali) influenza in maniera importante l'assorbimento della levodopa e di conseguenza la risposta al farmaco. Ci siamo chiesti quali fossero lo stato di nutrizione e le abitudini dietetiche dei pazienti affetti da PD in aree geografiche diverse, in particolare in un paese in via di sviluppo.
Obiettivo. Valutare i parametri antropometrici e le abitudini alimentari in un gruppo di pazienti ghanesi (residenti a Sogakofe ed Accra) e affetti da PD, confrontandoli con un gruppo di controllo paragonabile per età e residente nella stessa area geografica.
Metodi. Abbiamo osservato un gruppo di 27 soggetti affetti da Malattia di Parkinson, di cui 17 maschi e 10 femmine e 10 controlli sani, 4 maschi e 6 femmine. Abbiamo raccolto le principali misure antropometriche e abbiamo indagato le abitudini dietetiche utilizzando un questionario di frequenza da noi redatto studiando la composizione dei piatti tipici locali ed un'anamnesi alimentare (recall delle 24 ore).
Risultati. L'intake calorico giornaliero medio è di circa 1.200 kcal al die, il Body Mass Index (BMI) medio è 22.3 ± 3.8 kg/m^2. L'apporto energetico è così ripartito tra i macronutrienti: il 60% deriva dai carboidrati, il 15% dalle proteine e il 25% dai lipidi. Il consumo di latte e derivati è molto modesto (circa 400 g alla settimana pro-capite). La principale fonte di calcio sembra essere l'acqua (consumo medio 1.000 ml al giorno). Non ci sono differenze significative nella dieta e nella composizione corporea dei pazienti PD rispetto ai controlli sani.
Discussione. L'assunzione giornaliera media di energia è inferiore, in entrambi i gruppi, rispetto ai livelli di assunzione raccomandata per i soggetti italiani di pari età (circa 1.800-1.900 kcal al die secondo i Livelli di Assunzione giornalieri Raccomandati di energia e Nutrienti per la popolazione italiana: LARN). Tuttavia, il BMI medio non è indicativo di malnutrizione. La composizione in macronutrienti è differente dalla dieta italiana, in cui l'energia deriva in misura maggiore dalle proteine (20%) e dai lipidi (36%) (dati dell'Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione: INRAN 2010). Il consumo di latte e derivati è notevolmente inferiore rispetto a quello italiano (200 g al giorno secondo i dati INRAN 2006).
Conclusioni. In Ghana esistono differenze sostanziali rispetto alla dieta italiana, soprattutto in merito a nutrienti e alimenti che hanno un ruolo accertato o potenziale nella PD (le proteine influenzano la risposta alla terapia, il consumo latte è stato recentemente studiato tra i possibili fattori concausali di PD, con risultati discordanti). Eclatante è il dato secondo cui, nonostante vi sia un apporto calorico molto basso, il BMI medio dei soggetti non è indicativo di uno stato di grave malnutrizione, a differenza di quanto ci si potrebbe aspettare. Probabilmente l'apporto calorico è sufficiente a soddisfare il fabbisogno energetico (verosimilmente dovuto ad uno scarso dispendio secondario ad una ridotta attività fisica).

Ringraziamenti. *Ringraziamo la Fondazione Grigioni per il Parkinson e il suo Presidente Prof. Gianni Pezzoli per aver organizzato, sostenuto e finanziato questo progetto in Africa. Ringraziamo la dott.ssa Giulia Privitera (Associazione di Dietetica e Nutrizione Clinica Italiana: ADI), per essersi resa disponibile a partire per il Ghana per collaborare a questo lavoro. Ringraziamo gli Istituti Clinici di Perfezionamento per aver autorizzato il proprio personale a rendere parte a questo progetto.*

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Abstract POSTER

□ Our first Natalizumab-treated patient: full recovery from highly active disease

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Case Report. We report the case of a 32 years-old man with Relapsing-Remitting Multiple Sclerosis (RR-MS). Clinical onset in June 1996 at the age of 18 with parestesie in right half-body. Magnetic Resonance Imaging (MRI) showed multiple T2 lesions in brain and cervical cord white matter, diagnosis of probable MS was made. He was free of relapses until May 2004, when he presented unbalance disturbances with objective evidence of ataxia and deep sensitivity alterations. A new brain MRI showed an increase of total lesion load with positive gadolinium enhancement of one lesion; cerebro-spinal fluid was positive for oligoclonal bands. Clinical remission after high IV steroids. Diagnosis of clinical defined MS was made. In October 2004 he started immunomodulating treatment with interferon beta 1a (Rebif®), but after one year he had a new relapse with left emiparesis (Expanded Disability Status Scale: EDSS 4.5), with MRI evidence of multiple new T2 lesions and positive gadolinium enhancement of 6 lesions. In 2006 two other relapses and evidence of high title of anti-interferon neutralizing antibodies, so the treatment was stopped. In 2007 two other relapses with partial remission after steroids, a new MRI showed 8 gadolinium-enhancing lesions. EDSS was 3.5. In May 2007 Natalizumab treatment was started and 49 infusions were administered.

Results. No more relapses after Natalizumab treatment. Brain MRI performed every 6 months showed neither new lesions appearance nor gd-enhancing lesions. Actual EDSS is 1.5, he has no disability and no cognitive deficit. His quality of life is very much better, he works and makes sports without any problems. He had no significant side effects, the treatment is very good tolerated.

Conclusions. The results of this case confirm that Natalizumab is a highly effective treatment for RR-MS patients with high disease activity.

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Abstract POSTER

□ Natalizumab treatment in a small multiple sclerosis Centre of Lombardia: our positive experience

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Introduction. Natalizumab treatment is very effective in highly active Multiple Sclerosis (MS) patients[1]. It is a second line treatment for both patients who failed Interferon or Copaxone treatment, and those with high clinical and magnetic resonance imaging (MRI) disease activity. (Agenzia Italiana del Farmaco: AIFA criteria)[2].

Aim of the study. To describe our personal experience in the treatment and management of Natalizumab in our MS Centre.

Material and methods. From May 2007 to January 2011 we enrolled 13 patients to Natalizumab treatment. 9 patients were enrolled according to AIFA criterion A, 4 according to AIFA criterion B[2]. All patients perform haematological exams before monthly Natalizumab infusions, and a brain MRI scan every 6 months.

Results. All patients are ongoing Natalizumab treatment. No patients worsened at Expanded Disability Status Scale (EDSS) score. Only one patient experienced a clinical relapse after the fifth infusion. One new T2 lesion appeared in MRI performed at sixth month in two patients and in MRI performed at one year in one patient. A MRI performed at sixth month showed the presence of 5 lesions with gadolinium enhancement in another patient. 8/13 patients are totally free from disease (61%). We had no significant side effects, no cases of Progressive Multifocal Leukoencephalopathy (PML).

Conclusions. Our data show a good clinical efficacy and a good tolerability of Natalizumab in our patients, with data similar to worldwide experience.

References

1. Polman C.H., O'Connor P.W., Havrdova E., Hutchinson M., Kappos L., Miller D.H., Phillips J.T., Lublin F.D. et al.: A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. N Engl J Med 2006; 354 (9): 899-910.
2. Nota AIFA 2006. Determinazione AIFA n. 115/2006.

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Abstract POSTER

□ Effects of Natalizumab on $CD4^+CD25^+FoxP3^+$ regulatory T lymphocytes in multiple sclerosis patients

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Introduction. Multiple Sclerosis (MS) is an inflammatory, disorder of the Central Nervous System (CNS) of unknown etiology. $CD4^+CD25^+FoxP3^+$ regulatory T cells (Tregs) play a key role in the mechanisms of autoimmunity and a loss of Treg suppressor function contributes to MS pathogenesis. Natalizumab is the first monoclonal antibody approved for the treatment of MS, based on improved efficacy in comparison to conventional therapies. Its long term safety is however still under investigation. The present study aimed at the monitoring of Treg in MS patients during treatment with Natalizumab. The study is part of a collaborative protocol coordinated by the Neurology Unit of "Valduce" Hospital (Como, Italy, P.I.: M. Guidotti).

Patients and methods. Patients with MS suitable for treatment with Natalizumab are enrolled and followed for 30 months with clinical, laboratory and radiological examination. Patients are studied before Natalizumab (baseline) and every 3 months after each infusion. Venous blood obtained at each visit is used for flow cytometric evaluation of Treg, as well as immunomagnetic separation of Treg and subsequent evaluation of FoxP3 gene expression by real-time PCR.

Results and conclusion. To date, 28 patients have been enrolled: 22 women and 6 men (mean age at the time of enrollment: 38 years; range: 20-52; mean disease duration: 11.6 years; range: 2-33). The mean ± SD EDSS (Expanded Disability Status Scale) score at the start of Natalizumab therapy was 2.6 ± 1.4. Only one patient so far dropped from the study due to recurrent urinary tract infections. Four patients reached the 22th infusion of the drug, others are still ongoing.

A preliminary evaluation of the data obtained in 14 patients all of whom already reached the 10th infusion shows a significant reduction in $CD4^+CD25^+FoxP3^+$ (from 2,4 ± 1,4% at enrollement to 1,3 ± 0,7% at the 10th infusion; $p = 0,04$), however with no significant modifications of FoxP3 mRNA levels 6,9 ± 6,8 x 10^{-5} at the 1th infusion to 5,1 ± 4,1 x 10^{-5} at the 10th infusion). The clinical significance of these findings will be carefully examined throughout the rest of the study.

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Abstract POSTER

□ Adrenergic and dopaminergic pathways in circulating lymphocytes as early markers of clinically isolated syndromes progressing to multiple sclerosis

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Multiple Sclerosis (MS) mainly begins as a Clinically Isolated Syndrome (CIS). Although the occurrence of a CIS does not necessarily imply a diagnosis of SM, it is strongly associated with the risk to develop this disease. Extensive evidence suggests the occurrence of dysregulated adrenergic/dopaminergic receptor-mediated mechanisms in lymphocytes from MS patients, which are partially restored by immunomodulating treatments. This study aims at investigating any association between alterations of adrenergic/dopaminergic pathways in lymphocytes from subject with CIS and their possible relationship with the eventual conversion to MS.

A multicentric longitudinal study will enroll 50 ambulatory patients affected with CIS and 15 healthy subject.

In the 12-month follow up 3 visits are scheduled. At each visit, a sample of venous blood is taken and lymphocyte expression of mRNA for β2-adrenoreceptor, dopaminergic receptors D2 and D5, and Tyrosine Hydroxylase (TH, the rate-limiting enzyme in the synthesis of dopamine, norepinephrine and epinephrine) is evaluated in both cultured lymphocytes and in purified $CD4^+CD25^+$ T regulatory cells (Treg).

At present, 6 patients (F/M: 3/3; age [mean ± SD]: 38,5 ± 14,0 years); and 4 healthy subject (F/M: 2/2; age: 37,5 ± 12,8 years) have been enrolled. Preliminary results are available for TH mRNA levels, which were $4,02 \pm 1,08 \times 10^{-6}$ in Phytohaemagglutinin (PHA) stimulated lymphocytes from patients and $2,07 \pm 1,13 \times 10^{-6}$ in cells from healthy subjects, and $1,05 \pm 0,30 \times 10^{-6}$ and $0,89 \pm 0,57 \times 10^{-6}$ in Treg from patients and healthy subjects, respectively.

Enrollement of all the scheduled patients and subsequent follow up will allow to establish the statistical significance of apparent differences and their eventual relationship with the clinical evolution of CIS.

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Abstract POSTER

□ Executive functions and attention/information processing rehabilitation in multifocal disease: clinical efficacy and fMRI correlates

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Multifocal diseases of the brain usually causes multiple, often interrelated cognitive deficits. We present data on the efficacy of intensive computer based training of attention/information processing speed and executive functions in Multiple Sclerosis (MS) patients and its fMRI correlates. 24 relapsing remitting MS patients with low motor disability were included in the study if they showed pathological scores in both Wisconsin Card Sorting Test (WCST) and Paced Auditory Serial Addition Test (PASAT) measures. They were randomized to have PC assisted rehabilitative treatment (Treatment Group: TG) (Rehacom Plan a day, Divided attention©; for three months 2 sessions/week) or no therapy. They underwent neuropsychological evaluation and MRI acquisition (dual-echo, 3D T1-weighted, diffusion tensor MRI and fMRI during Stroop task) at baseline and after three months; neuropsychological evaluation was repeated at 9 months follow up.

After rehabilitation TG showed significant improvement in attention/information processing and executive function tests, maintained at 9 months follow up. In a sub-group of patients, fMRI performed after three months disclosed treatment related modifications of the activity of the anterior cingulum, posterior cingulum/precuneus, left dorsolateral prefrontal cortex and right inferior parietal lobule, which correlated with cognitive improvement (r -0.88 to 0.88, $p < 0.05$).

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Abstract POSTER

□ Analysis of chaperone-mediated autophagy parameters in peripheral blood cells from patients with Parkinson's disease

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Recent studies demonstrate a key-role for Chaperone-Mediated Autophagy (CMA) impairment in the pathogenesis of Parkinson's Disease (PD). CMA represents the main degradative pathway for alpha-synuclein, which, in turn, is able to inhibit CMA when over-expressed or mutated. A significant reduction of protein levels of hsc70 and LAMP2A, the main components of CMA machinery, was found in the substantia nigra from PD patients, together with increased levels of MEF2D, a survival factor that qualifies as a CMA substrate.
Previous studies qualified Peripheral Blood Mononuclear Cells (PBMC) as reliable models of biochemical dysfunction occurring in PD brains. We assessed LAMP2A, hsc70 and MEF2D protein levels in PBMC from 15 PD patients and 15 age-matched controls by Western blot to identify a putative, easily accessible, peripheral biomarker of disease. No significant difference was observed in immunoreactivity of LAMP2A, hsc70 and MEF2D between PD patients and controls, suggesting that PBMC under basal conditions do not mirror alterations of CMA parameters observed in PD brains. We are assessing the expression of the same proteins after treatment of PBMC with several CMA modulators, in order to verify the existence of a possible different susceptibility between cells form patients and controls.

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Abstract POSTER

□ Acetyl-cholinesterase inhibitors influence on endogenous immune response against beta amyloid in Alzheimer's disease

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Acetyl-Colinesterase Inhibitors (AChEI) are drugs frequently prescribed for the treatment of Alzheimer's Disease (AD) in patients with mild to moderate dementia, exerting effects on cognition and neuropsychiatric symptoms as well as daily living.

We performed ELISA tests on plasma samples of 66 AD patients treated or not with AChEI and we found significantly ($p < 0.01$) increased selective plasma levels of anti-Abeta 1-42 in treated AD patients (344 ± 180 ng/ml) with respect to untreated AD (211 ± 77 ng/ml). To support a potential role of AChEI in the modulation of the immune response against Abeta we are now evaluating, in *ex vivo* linfo-monocytes from a subgroup of the same subjects, mRNA levels of the transcription factor GATA-3 involved in the differentiation towards Th2 line. Moreover we have set up lymphocytes cultures for the stimulation with PHA and donepezil to evaluate GATA3 mRNA levels both in patients and controls. The modulation to Th2 form stimulates the proliferation of B lymphocytes, increasing their activity in antibody production.

A potential pharmacological strategy aimed at increasing the endogenous immune response against Abeta peptide might represent an interesting therapeutic target in Alzheimer disease.

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Abstract POSTER

□ Determinants of locomotor disability in multiple sclerosis: an immunological and diffusion tensor MRI study

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Objectives. To assess the contribution of inflammatory and degenerative features to the pathobiology of locomotor disability in Multiple Sclerosis (MS), by investigating both immunological indices related to T-cell activation and tract-specific Diffusion Tensor (DT) MRI-derived markers of irreversible tissue damage in patients with benign MS (BMS), secondary progressive MS (SPMS) and early Relapsing-Remitting MS (RRMS).

Methods. Forty patients [15 with BMS, 15 SPMS and 10 with early, non-disabled (i.e., having disease duration shorter than 3 years and Expanded Disability Status Scale (EDSS) score ≤ 3.0) RRMS] underwent immunophenotypic and functional analysis of Myelin Basic Protein (MBP)-stimulated T lympho-monocytes (obtained from blood sampling) and DT MRI of the brain. Post-contrast T1-weighted images were also acquired in the same imaging session and the presence of contrast-enhancing lesions was assessed. DT-derived measures of right and left Cortico-Spinal Tract (CST) integrity were computed through the elastic co-registration of patients' Fractional Anisotropy (FA) and Mean Diffusivity (MD) maps to a probabilistic atlas constructed from the DT data of 15 age-matched healthy volunteers.

Results. The percentage of MBP-stimulated-RORγτ transcriptional factor-expressing $CD4^+$, IL-10 and IL-23-producing $CD14^+$ cells were significantly higher in SPMS ($CD4^+$ and IL-23 $CD14^+$) and early RRMS (IL-10 and IL-23 $CD14^+$) compared with BMS patients ($p < 0.05$). Conversely, significantly less IL-6-producing $CD14^+$ cells were present in SPMS and early RRMS than in BMS patients ($p < 0.05$). The presence of one or more contrast-enhancing lesions was more frequent in SPMS (6/15) than in BMS (1/15) patients. The mean values of right and left CST FA and MD were respectively lower and higher in SPMS than in both RRMS and BMS patients ($p < 0.05$), but did not significantly differ between RRMS and BMS patients. The best discrimination between SPMS and BMS patients was achieved by a multivariable model including both IL-6 $CD14^+$ cell and average right CST MD values.

Conclusion. In BMS patients, who are still not disabled after a long-lasting disease, the severity of CST damage remains as low as in the earlier stages of MS and an immunological pattern suggestive of reduced inflammatory activity is observed. Our findings are consistent with a "dual action" of persistent inflammation and irreversible tissue damage of clinically eloquent sites in the pathogenesis of MS-related locomotor disability.

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Abstract POSTER

□ Acute bilateral sciatica in "migration" of traumatic subarachnoid pontine haematoma: a case report

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A 43 years-old man was admitted in Neurosurgery Unit after road accident in which he reported cranial trauma. He became unconscious initially. In Emergency Room (ER) he was submitted to brain CT that revealed intracranial pontine Subarachnoid Pontine Haematoma (SAH). In a few days the CT imaging improved and the patient was discharged, complaining only of moderate headache. Seven days after traumatic event, headache worsened and an exacerbated lower back pain extending at lower limbs appeared. The patient was admitted in Neurological department again. He showed bilateral 10° Lasègue sign and positive Lhermitte sign, being the neurological examination otherwise unremarkable with head and lumbar CT normal. The spinal cord RM showed a hyper-intense lesion on T1W1 at the lower end of lumbar sac with a moderate haemorrhage. All haematological tests and angioMR of head and spinal cord are normal. Pain and clinical signs disappeared after steroidal therapy. A circumscribed collection of blood in spinal subarachnoid space after traumatic intracranial SAH was very unusual, since most traumatic spinal SAH have a blood coagulation defect or occur as a complication of spinal procedures. A literature review confirms that this is a rare clinical event. In fact only another similar clinical case was previously reported.

Reference

1. Chen H.C., Hsu P.W., Tzaan W.C.: "Migration" of traumatic subarachnoid hematoma? A case report. Surg Neurol 2008; 70 (2): 213-216.

Corrispondenza: Dr.ssa Patrizia Perrone, U.O. di Neurologia, Ospedale Civile, via Candiani 2, 20025 Legnano (MI), tel. 0331-449551, fax 0331-449558, e-mail: patrizia.perrone@ao-legnano.it
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Abstract POSTER

□ Lack of a role of interferon receptor in IFNβ bioactivity loss in multiple sclerosis patients lacking MxA induction in the absence of anti-IFNβ antibodies

C. ZANOTTI, R. CAPRA*, M. ZAFFARONI*, M. ROTTOLI*, V. MARTINELLI*, L. PROVINCIALI*, C. GASPERINI*, M. VECCHIO*, G. ROSATI*, M. AMATO*, G. MANCARDI*, L. IMBERTI

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** Non solo Nab observational prospective trial: Bab, MxA, and characterization of IFNAR subunits and isoforms in the IFNβ bioactivity control in multiple sclerosis patients. Study code BD0106*

RNA for the Interferon Receptor subunit IFNAR1 and IFNAR2, as well as for the IFNAR2.1 (inactive), IFNAR2.2 (active) and IFNAR2.3 (soluble) isoforms was quantified by real-time PCR in two patients that resulted repeatedly negative for anti-IFNβ antibodies, both of the binding (BAb, measured by radioimmunoprecipitation) and neutralizing (NAb, identified by cytopathic effect inhibition assay) type. They were also Mixovirus protein-A (MxA)-non induced (quantified by real-time PCR) respectively in three consecutive samples taken over one year period, and in four samples obtained over two years period. Data were compared to those of patients in which IFNβ was stably bioactive ($MxA^+BAb^-NAb^-$ for the entire period of study: 31 patients), or stably non-bioactive ($MxA^-BAb^+NAb^+$: 8 patients). Analysis by repeated measures ANOVA (Analysis of Variance) did not show any significant differences in IFNAR subunits and isoforms RNA expression between the three groups over time. However, if the analysis was performed by comparing only stably non-bioactive patients to the two subjects lacking MxA induction and repeatedly negative for anti-IFNβ antibodies, in the latter a significant increased IFNAR2.2 active isoform expression was surprisingly found.

Taken altogether, these results question the proposed detrimental role of IFNAR RNA modulation in determining IFNβ bioactivity loss in the absence of anti-IFNβ antibodies.

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