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CORTICAL WHITE-MATTER MICROSTRUCTURE IN SCHIZOPHRENIA

British Journal of Psychiatry 2007;191:113-119

Andreone N, Tansella M, Cerini R, Versace A, Rambaldelli G, Perlini C, Dusi N, Pelizza L, Balestrieri M, Barbui C, Nosè M, Gasparini A, Brambilla P.

I.F. 2006: 5,436

BACKGROUND: Several, although not all, of the previous small diffusion-weighted imaging (DWI) studies have shown cortical white-matter disruption in schizophrenia. AIMS: To investigate cortical white-matter microstructure with DWI in a large community-based sample of people with schizophrenia. METHOD: Sixty-eight people with schizophrenia and 64 healthy controls underwent a session of DWI to obtain the apparent diffusion coefficient (ADC) of white-matter water molecules. Regions of interest were placed in cortical lobes. RESULTS: Compared with controls, the schizophrenia group had significantly greater ADCs in frontal, temporal and occipital white matter (analysis of covariance, $P < 0.05$). CONCLUSIONS: Our findings confirm the presence of cortical white-matter microstructure disruption in frontal and temporo-occipital lobes in the largest sample of people with schizophrenia thus for studied with this technique. Future brain imaging studies, together with genetic investigations, should further explore white-matter integrity and genes encoding myelin-related protein expression in people with first-episode schizophrenia and those at high risk of developing the disorder.

ANTERIOR CINGULATE VOLUMES IN SCHIZOPHRENIA: A SYSTEMATIC REVIEW AND A META-ANALYSIS OF MRI STUDIES

Schizophrenia Research 2007;93(1-3):1-12

Baiano M, David A, Versace A, Churchill R, Balestrieri M, Brambilla P.

I.F. 2006: 4,264

OBJECTIVES: Several MRI studies have investigated the anterior cingulate in schizophrenia, as this is a key region for emotional processing and higher executive performances. A systematic review of structural MRI studies and a meta-analysis were conducted to explore whether anterior cingulate volumes are abnormal in patients with schizophrenia. METHOD: A systematic search strategy was used to identify eligible MRI studies. Thereafter, a meta-analysis was carried out by using a random effect model. Also, a meta-regression analysis was used to assess the influence of age, gender and slice thickness on effect sizes. RESULTS: The meta-analysis was performed on seven studies. These results showed that the anterior cingulate volumes were significantly reduced in patients compared to healthy controls. Significant heterogeneity between these studies was observed. The meta-regression demonstrated that the effect size was significantly related only to slice thickness. CONCLUSIONS: Our work confirmed the presence of abnormally reduced anterior cingulate volumes in schizophrenia. However, several methodological issues limited the interpretation of these findings. Among these were different MR acquisition parameters and the small size of the sample, which was mostly composed of chronic patients. Future MRI studies should be planned to better understand the functional expression of anterior cingulate structural abnormalities.

THE BEHAVIOURAL PHENOTYPE OF CORNELIA DE LANGE SYNDROME: A STUDY OF 56 INDIVIDUALS

Journal of Intellectual Disability Research 2007;51(9):671-681

Basile E, Villa L, Selicorni A, Molteni M.

I.F. 2006: 1,068

Background Few studies have investigated functional and behavioural variables of Cornelia de Lange Syndrome (CdLS) in a large sample of individuals. The aim of this study is to provide greater insight into the clinical, behavioural and cognitive characteristics that are associated with CdLS. Methods In total, 56 individuals with CdLS participated in the study. During hospitalization, their mothers received a number of questionnaires to complete. The behavioural phenotype was investigated using

the following scales: Developmental Behaviour Scale Primary Carer Version; Autism Behaviour Checklist; Childhood Autism Rating Scale. Results Our participants demonstrated some behavioural characteristics that are frequently associated with CdLS (hyperactivity, attention disorder, anxiety, compulsive disorders, self-injurious behaviour and autistic-like features). Our findings demonstrate the variability of behavioural characteristics in CdLS in addition to highlighting the contribution of some variables to both the CdLS behavioural profile and the developmental trajectory of the behavioural pattern. Conclusions The behavioural characteristics identi- fied in our sample were correlated with some clinical and functional aspects (chronological age, cognitive level and clinical phenotype). The variability of the behavioural profile in CdLS reflected the wide variability in cognitive and adaptive functioning across individuals and led us to conclude that there may be multiple behavioural phenotypes associated with the syndrome. Further comparative studies between CdLS and individuals with intellectual disability or other genetic syndromes may help to provide further understanding of the behavioural phenotype of CdLS.

EFFECT OF THE CATECHOL-O-METHYLTRANSFERASE VALMET GENOTIPE ON CHILDREN'S EARLY PHASES OF FACIAL STIMULI PROCESSING

Genes, Brain and Behavior 2007;6(4):364-374

Battaglia M, Zanoni A, Giorda R, Pozzoli U, Citterio A, Beri S, Ogliari A, Nobile M, Marino C, Molteni M.

I.F. 2006: 4,385

The ability to process and identify human faces matures early in life, is universal and is mediated by a distributed neural system. The temporal dynamics of this cognitive-emotional task can be studied by cerebral visual event-related potentials (ERPs) that are stable from midchildhood onwards. We hypothesized that part of individual variability in the parameters of the N170, a waveform that specifically marks the early, precategorical phases of human face processing, could be associated with genetic variation at the functional polymorphism of the catechol-O-methyltransferase (val(158)met) gene, which influences information processing, cognitive control tasks and patterns of brain activation during passive processing of human facial stimuli. Forty-nine third and fourth graders underwent a task of implicit processing of other children's facial expressions of emotions while ERPs were recorded. The N170 parameters (latency and amplitude) were insensitive to the type of expression, stimulus repetition, gender or school grade. Although limited by the absence of met- homozygotes among boys, data showed shorter N170 latency associated with the presence of 1-2 met158 alleles, and family-based association tests (as implemented in the PBAT version 2.6 software package) confirmed the association. These data were independent of the serotonin transporter promoter polymorphism and the N400 waveform investigated in the same group of children in a previous study. Some electrophysiological features of face processing may be stable from midchildhood onwards. Different waveforms generated by face processing may have at least partially independent genetic architectures and yield different implications toward the understanding of individual differences in cognition and emotions.

A GENETIC STUDY OF THE ACUTE ANXIOUS RESPONSE TO CARBON DIOXIDE STIMULATION IN MAN

Journal of Psychiatric Research 2007;41(11):906-917

Battaglia M, Ogliari A, Harris J, Spatola CAM, Pesenti-Gritti P, Reichborn-Kjennerud T, Torgersen S, Kringlen E, Tambs K.

I.F. 2006: 3,700

People with panic disorder-agoraphobia and their relatives often react anxiously to CO2-enriched gas mixtures. Available data are not suited to disentangle genetic from common environmental causes of familial aggregation of CO2 reactivity, nor provide quantitative estimations of the sources of trait variation. Three-hundred-forty-six twin pairs belonging to the general population-based Norwegian NIPH Mental Health Study underwent selfassessments of anxiety and of DSM-IV panic symptoms after inhalation of a 35%CO2–65%O2 mixture. Two thresholds were employed – at sample's 75th and 90th percentiles of responses – to define provoked panic attacks and to calculate polychoric correlations. Variance components were estimated by structural equation modelling (SEM). For definitions of responses based on the sum of all 13 panic symptoms, SEM could not discriminate between shared environmental versus genetic causes of familial resemblance for provoked attacks. For definitions of responses based on global anxiety, or on the sums of those symptoms (dyspnea, dizziness, palpitations) with highest variance post-CO2, the best-fitting models indicated additive genetic factors as the sole cau-

ses for within-family resemblance. Best-fit heritability estimates ranged from 0.42 to 0.57. Genetic and idiosyncratic environmental factors explain most of individual differences in reactivity to hypercapnia. Within-family similarities for this trait are largely explained by genetic determinants.

GREATER CORTICAL GRAY MATTER DENSITY IN LITHIUM-TREATED PATIENTS WITH BIPOLAR DISORDER

Biological Psychiatry 2007;62(1):7-16

Bearden CE, Thompson PM, Dalwani M, Hayashi KM, Lee AD, Nicoletti M, Trakhenbroit M, Glahn DC, Brambilla P, Sassi RB, Mallinger AG, Frank EK, David J, Soares JC.

I.F. 2006: 7,154

BACKGROUND: The neurobiological underpinnings of bipolar disorder are not well understood. Previous neuroimaging findings have been inconsistent; however, new methods for three-dimensional (3-D) computational image analysis may better characterize neuroanatomic changes than standard volumetric measures. METHODS: We used high-resolution magnetic resonance imaging and cortical pattern matching methods to map gray matter differences in 28 adults with bipolar disorder, 70% of whom were lithium-treated (mean age = 36.1 +/- 10.5; 13 female subject), and 28 healthy control subjects (mean age = 35.9 +/- 8.5; 11 female subjects). Detailed spatial analyses of gray matter density (GMD) were conducted by measuring local proportions of gray matter at thousands of homologous cortical locations. RESULTS: Gray matter density was significantly greater in bipolar patients relative to control subjects in diffuse cortical regions. Greatest differences were found in bilateral cingulate and paralimbic cortices, brain regions critical for attentional, motivational, and emotional modulation. Secondary region of interest (ROI) analyses indicated significantly greater GMD in the right anterior cingulate among lithium-treated bipolar patients (n = 20) relative to those not taking lithium (n = 8). CONCLUSIONS: These brain maps are consistent with previous voxel-based morphometry reports of greater GMD in portions of the anterior limbic network in bipolar patients and suggest neurotrophic effects of lithium as a possible etiology of these neuroanatomic differences.

DEVELOPMENT OF OROFACIAL PRAXIS OF CHILDREN FROM 4 TO 8 YEARS OF AGE

Perceptual and Motor Skills 2007;104:1355-1366

Bearzotti F, Tavano A, Fabbro F.

I.F. 2006: 0,333

Orofacial praxis is the ability to pian and execute movements or sequences of voluntary movements, meaningful or not, using the muscles 'of the pharyngo- buccofacial system or the orofacial region. An' original test was developed, the Orofacial Praxis Test, consisting of 36 gestures, 24 single and 12 complex, elicited through verbal and imitative request. The test was administered to 93 normal1y developing Italian children ages 4 to 8 yr. to assess devdopment of orofacial praxis. Analysis showed a progressive development of the orofacial praxic ability by type of gesture and examiner's request: (1) the imitation modality is more facilitating than a verbal request modality, especial1y for children ages 4 or 5 years; (2) a consistent mastery of sequences of gestures and oroverbal movements is in place by age 6 years. T}J.eanalysis of the orofacial region may be helpful in identifying persistent speech difficulties and developmental coordination disorders.

DNA METHYLATION REGULATES TISSUE SPECIFIC EXPRESSION OF SHANK3

Journal of Neurochemistry 2007;101(5):1380-1391

Beri S*, Tonna N*, Menozzi G, Bonaglia MC, Sala C, Giorda R.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 4,260

Tissue-specific gene expression can be controlled by epigenetic modifications such as DNA methylation. SHANK3, together with its homologues SHANK1 and SHANK2, has a central functional and structural role in excitatory synapses and is involved in the human chromosome 22q13 deletion syndrome. In this report, we show by DNA methylation analysis in lymphocytes, brain cortex, cerebellum and heart that the three SHANK genes possess several methylated CpG boxes, but only SHANK3 CpG islands are highly methylated in tissues where protein expression is low or absent and unmethylated where expression is present. SHANK3 protein expression is significantly reduced in hippocampal neurons after treatment with methionine, while HeLa cells become able to express SHANK3 after treatment with 5-Aza-2¢-deoxycytidine. Altogether, these data suggest the existence of a specific epigenetic control mechanism regulating SHANK3, but not SHANK1 and SHANK2, expression.

OVEREXPRESSION OF THE C-TYPE NATRIURETIC PEPTIDE (CNP) IS ASSOCIATED TO OVERGROWTH AND BONE ANOMALIES IN AN INDIVIDUAL WITH BALANCED T(2;7) TRANSLOCATION

Human Mutation 2007;28(7):724-731

Bocciardi R*, Giorda R*, Buttgereit J*, Gimelli S, Divizia MT, Beri S, Garofalo S, Tavella S, Lerone M, Zuffardi O, Bader M, Ravazzolo R, Gimelli G.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 6,473

Longitudinal bone growth is determined by the process of endochondral ossification in the cartilaginous growth plate, which is located at both ends of vertebrae and long bones and involves many systemic hormones and local regulators. We report the molecular characterization of a de novo balanced t(2;7)(q37.1;q21.3) translocation in a young female with Marfanoid habitus and skeletal anomalies. The translocation was characterized by fluorescence in situ hybridization (FISH), checked for other abnormalities by array-comparative genomic hybridization (CGH), and finally, the breakpoints were cloned, sequenced, and compared. Biochemical dosage was applied to study the possible mechanisms that may cause the proposita's phenotype. The breakpoint on chromosome 2 disrupts the hypothetical gene MGC42174 (HUGO-approved symbol DIS3L2) and is located in the proximity of the NPPC gene coding for C-type natriuretic peptide (CNP), a molecule that regulates endochondral bone growth. CNP plasma concentration was doubled in the proband compared to five normal controls, while NPPC was substantially overexpressed in her fibroblasts. A transgenic mouse generated to target NPPC overexpression in bone showed a phenotype highly reminiscent of the patient's phenotype. The breakpoint on chromosome 7 is localized proximally at about 75 kb from the COL1A2 gene. The COL1A2 allele on the derivative chromosome was strongly underexpressed in fibroblasts, but total collagen was not significantly different from controls. Several evidences support the conclusion that the proband's abnormal phenotype is associated with C-type natriuretic peptide overexpression. (c) 2007 Wiley-Liss, Inc.

SUBTELOMERIC TRISOMY 21Q: A NEW BENIGN CHROMOSOMAL VARIANT

European Journal of Medical Genetics 2007;50(1):54-59

Bonaglia MC, Marelli S, Gottardi G, Zucca C, Pramparo T, Giorda R, Grasso R, Borgatti R, Zuffardi O.

I. F. 2006: 1,614

The diagnosis of a subtelomeric rearrangement has immediate impact on counseling, particularly in the case of familial rearrangements. However, the existence of subtelomeric imbalances with absent phenotypic effects may hamper genetic counseling, particularly when the rearrangement has not been previously described. We report on a new subtelomeric polymorphism, consisting of a familial subtelomeric rearrangement of chromosome 19 resulting in distal trisomy for 21q, detected in a child with Angelman Syndrome (AS) due to an UBE3A mutation. This report shows that new, previously unknown, benign subtelomeric variants may complicate the correct clinical diagnosis.

CONTEXT PROCESSING PERFORMANCE IN BIPOLAR DISORDER PATIENTS

Bipolar Disorders 2007;9(3):230-237

Brambilla P, MacDonald III AW, Sassi RB, Johnson MK, Mallinger AG, Carter CS, Soares J.

I.F. 2006: 3,494

Objectives: Context processing is the adaptive control of current behavior through the use of prior context information. It has been found to be impaired in schizophrenia. Some studies have indicated that, compared with patients with schizophrenia, those with bipolar disorder (BPD) display a similar but less severe neuropsychological pattern of impairment. However, this cognitive dimension has not yet been examined in BPD patients in the existing literature. Methods: An expectancy version of the AX continuous performance test (AX-CPT) was administered to 15 bipolar outpatients and 26 healthy controls. Patients with schizophrenia, in which context processing deficits are known to occur, were used as a reference group. Results: Bipolar patients showed a context processing deficit relative to healthy controls, although this was less severe and generalized than in schizophrenia patients. Conclusions: These findings suggest there are milder impairments in context processing in BPD compared with schizophrenia. However, the severity of possible context processing deficits in BPD may have been underestimated in our sample of mostly euthymic outpatients.

CAN NEUROIMAGING STUDIES HELP US IN UNDERSTANDING THE BIOLOGICAL

CAUSES OF SCHIZOPHRENIA?

International Review of Psychiatry 2007;19(4):313-314 - Editoriale

Brambilla P, Tansella M.

I.F. 2006: 0,908

Abstract non disponibile.

THE ROLE OF WHITE MATTER FOR THE PATHOPHYSIOLOGY OF SCHIZOPHRENIA

International Review of Psychiatry 2007;19(4):459-468

Brambilla P, Tansella M.

I.F. 2006: 0,908

Inter- and intra-hemispheric connectivity disturbances have been suggested to play a major role in schizophrenia. To this extent, diffusion weighted imaging (DWI) is a relatively new technique examining subtle white matter microstructure organization. DWI studies in schizophrenia strongly suggest that white matter communication is disrupted. This supports the hypothesis that there is a cortico-cortical and transcallosal altered connectivity in schizophrenia, which may be relevant for the pathophysiology and the cognitive disturbances of the disorder. Future longitudinal diffusion and functional imaging studies targeting brain communication together with genetic investigations should further characterize white matter pathology in schizophrenia and its relevance for the development of the illness.

NITRIC OXIDE: EMERGING CONCEPTS ABOUT ITS USE IN CELL-BASED THERAPIES

Expert Opinion on Investigational Drugs 2007;16(1):33-43

Brunelli S, Rovere-Querini P, Sciorati C, Manfredi AA, Clementi E.

I.F. 2006: 3,174

Regenerative medicine is an emerging clinical discipline in which cell-based therapies are used to restore the functions of damaged or defective tissues and organs. Along with the well-established use of cells derived from bone marrow or pancreatic islets, novel approaches of cell therapy have recently emerged that appear particularly promising; that is, those using cell-based vaccines and stem cells. This review focuses on the recent developments of these experimental therapeutic approaches and their drawbacks, with specific focus on dendritic cell vaccines in tumours and mesoangioblasts in muscular dystrophies. The authors discuss how the unique properties of a gaseous messenger, NO, may be exploited to overcome some of the drawbacks of these cell-based approaches in combined therapies based on NO-releasing drugs and cell delivery.

NITRIC OXIDE RELEASE COMBINED WITH NONSTEROIDAL ANTIINFLAMMATORY ACTIVITY PREVENTS MUSCULAR DYSTROPHY PATHOLOGY AND ENHANCES STEM CELL THERAPY

Proceedings of the National Academy of Sciences of the United States of America (PNAS) 2007;104(1):264-269

Brunelli S*, Sciorati C*, D'Antona G, Innocenzi A, Covarello D, Galvez BG, Perrotta C, Monopoli A, Sanvito F, Bottinelli R, Ongini E, Cossu G, Clementi E.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 9,643

Duchenne muscular dystrophy is a relatively common disease that affects skeletal muscle, leading to progressive paralysis and death. There is currently no resolutive therapy. We have developed a treatment in which we combined the effects of nitric oxide with nonsteroidal antiinflammatory activity by using HCT 1026, a nitric oxide-releasing derivative of flurbiprofen. Here, we report the results of long-term (1-year) oral treatment with HCT 1026 of two murine models for limb girdle and Duchenne muscular dystrophies (alpha-sarcoglycan-null and mdx mice). In both models, HCT 1026 significantly ameliorated the morphological, biochemical, and functional phenotype in the absence of secondary effects, efficiently slowing down disease progression. HCT 1026 acted by reducing inflammation, preventing muscle damage, and preserving the number and function of satellite cells. HCT 1026 was significantly more effective than the corticosteroid prednisolone, which was analyzed in parallel. As an additional beneficial effect, HCT 1026 enhanced the therapeutic efficacy of arterially delivered donor stem cells, by increasing 4-fold their ability to migrate and reconstitute muscle fibers. The therapeutic strategy we propose is not selective for a subset of mutations; it provides ground for immediate clinical experimentation with HCT 1026 alone, which is approved for use in humans; and it sets the stage for combined therapies with donor or autologous, genetically corrected stem cells.

ARE PATIENTS WITH HEREDITARY SPASTIC PARAPLEGIA DIFFERENT FROM PATIENTS WITH SPASTIC DIPLEGIA DURING WALKING? GAIT EVALUATION USING 3D GAIT ANALYSIS

Functional Neurology 2007;22(1):23-28

Cimolin V, Piccinini L, D'Angelo MG, Turconi AC, Berti M, Crivellini M, Albertini G, Galli M.

I.F. 2006: 0,569

Patients with hereditary spastic paraplegia (HSP) often resemble patients with mild spastic diplegia (SD), although their motor limitations differ. The aim of this study was to analyse quantitatively the gait of HSP and SD subjects in order to define the gait pattern in HSP and the differences between the two conditions. Fifteen subjects with HSP, 40 patients with SD and 20 healthy subjects underwent gait analysis (GA). The spatio-temporal and kinematic parameters at the proximal joints were found to be similar in HSP and SD, whereas the most significant differences were found at the knee and ankle joints. Both groups displayed a tendency for knee hyperextension in the midstance phase, but the duration of this hyperextension was longer in the HSP patients. This study shows that GA complements traditional clinical evaluations, making it possible to distinguish, clearly, between motor ability in HSP and in SD patients; the duration of the knee hyperextension during midstance was found to discriminate between the two gait patterns.

ISOLATION AND CHARACTERIZATION OF MURINE NEURAL STEM/PROGENITOR CELLS BASED ON PROMININ-1 EXPRESSION

Experimental Neurology 2007;205(2):547-562

Corti S, Nizzardo M, Nardini M, Donadoni C, Locatelli F, Papadimitriou D, Salani S, Del Bo R, Ghezzi S, Strazzer S, Bresolin N, Comi GP.

I.F. 2006: 4,156

The identification of strategies for the isolation of neural stem cells (NSCs) has important implications for the understanding of their biology and the development of therapeutic applications. It has been previously described that human neural stem and progenitor cells (NSPCs) can be isolated from the central nervous system (CNS) using antibodies to prominin (CD133) and fluorescence-activated cell sorting (FACS). Although this antigen displayed an identical membrane topology in several human and murine tissues there was uncertainty as to the relationship between human and mouse prominin because of the low level of amino acid identity. Here we show that prominin expression can be used to identify and isolate also murine NSPCs from the developing or adult brain. Prominin is co-expressed with known neural stem markers like SOX 1-2, Musashi and Nestin. Moreover, neurosphere-forming cells with multipotency and self-renewal capacity reside within the prominin-positive fraction. Transplantation experiments show that CD133-positive cells give rise to neurons and glial cells in vivo, and that many neurons display appropriate phenotypic characteristics of the recipient tissues. The demonstration that CD133 is a stem cell antigen for murine NSPCs as it is for human NSPCs is useful for the investigation of mammal neurogenesis and development of preclinical tests of NSPCs transplantation in mouse analogues of human diseases.

NEURAL STEM CELLS LEWISX+CXCR4+ MODIFY DISEASE PROGRESSION IN AN AMYOTROPHIC LATERAL SCLEROSIS MODEL

Brain 2007;130:1289-1305

Corti S, Locatelli F, Papadimitriou D, Del Bo R, Nizzardo M, Nardini M, Donadoni C, Salani S, Fortunato F, Strazzer S, Bresolin N, Comi GP.

I.F. 2006: 7,617

Amyotrophic lateral sclerosis (ALS) is a fatal neurological disease characterized by the degeneration of the motor neurons. We tested whether treatment of superoxide dismutase (SOD1)-G93A transgenic mouse, a model of ALS, with a neural stem cell subpopulation double positive for Lewis X and the chemokine receptor CXCR4 (LeX1CXCR4þ) can modify the disease's progression. In vitro, after exposure to morphogenetic stimuli, LeX1CXCR41 cells generate cholinergic motor neuron-like cells upon differentiation. LeX1CXCR41 cells deriving from mice expressing Green Fluorescent Protein in all tissues or only in motor neurons, after a period of priming in vitro, were grafted into spinal cord of SOD1-G93A mice. Transplanted transgenic mice exhibited a delayed disease onset and progression, and survived significantly longer than non-treated animals by 23 days. Examination of the spinal cord revealed integration of donorderived cells that differentiated mostly in neurons and in a lower proportion in motor neuron-like cells. Quantification of motor neurons of the spinal cord suggests a significant neuroprotection by LeX1CXCR41 cells.

BothVEGF- and IGF1-dependent pathwayswere significantlymodulated in transplanted animals compared to controls, suggesting a role of these neurotrophins in MN protection. Our results support the therapeutic potential of neural stem cell fractions through both neurogenesis and growth factors release in motor neuron disorders.

CRIPTIC DELETIONS ARE A COMMON FINDING IN "BALANCED" RECIPROCAL AND COMPLEX CHROMOSOME REARRANGEMENTS: A STUDY OF 59 CASES

Journal of Medical Genetics 2007;44:750–762

De Gregori M, Ciccone R, Magini P, Pramparo T, Gimelli S, Messa J, Novara F, Vetro A, Rossi E, Maraschio P, Bonaglia MC, Anichini C, Ferrero GB, Silengo M, Fazzi E, Zatterale A, Fischetto R, Previderè C, Belli S, Turci A, Calabrese G, Bernardi F, Meneghelli E, Riegel M, Rocchi M, Guerneri S, Lalatta F, Zelante L, Romano C, Fichera M, Mattina T, Arrigo GZollino M, Giglio S, Lonardo F, Bonfante A, Ferlini A, Cifuentes F, Van Esch H, Liesbeth B, Schinzel A, Vermeesch JR, Zuffardi O.

I.F. 2006: 5,087

Using array comparative genome hybridisation (CGH) 41 de novo reciprocal translocations and 18 de novo complex chromosome rearrangements (CCRs) were screened. All cases had been interpreted as ''balanced'' by conventional cytogenetics. In all, 27 cases of reciprocal translocations were detected in patients with an abnormal phenotype, and after array CGH analysis, 11 were found to be unbalanced. Thus 40% (11 of 27) of patients with a ''chromosomal phenotype'' and an apparently balanced translocation were in fact unbalanced, and 18% (5 of 27) of the reciprocal translocations were instead complex rearrangements with .3 breakpoints. Fourteen fetuses with de novo, apparently balanced translocations, all but two with normal ultrasound findings, were also analysed and all were found to be normal using array CGH. Thirteen CCRs were detected in patients with abnormal phenotypes, two in women who had experienced repeated spontaneous abortions and three in fetuses. Sixteen patients were found to have unbalanced mutations, with up to 4 deletions. These results suggest that genome-wide array CGH may be advisable in all carriers of ''balanced'' CCRs. The parental origin of the deletions was investigated in 5 reciprocal translocations and 11 CCRs; all were found to be paternal. Using customised platforms in seven cases of CCRs, the deletion breakpoints were narrowed down to regions of a few hundred base pairs in length. No susceptibility motifs were associated with the imbalances. These results show that the phenotypic abnormalities of apparently balanced de novo CCRs are mainly due to cryptic deletions and that spermatogenesis is more prone to generate multiple chaotic chromosome imbalances and reciprocal translocations than oogenesis.

SPG11: A CONSISTENT CLINICAL PHENOTYPE IN A FAMILY WITH HOMOZYGOUS SPATACSIN TRUNCATING MUTATION

Neurgenetics 2007;8:301–305

Del Bo R, Di Fonzo A, Ghezzi S, Locatelli F, Stevanin G, Costa A, Corti S, Bresolin N, Comi GP.

I.F. 2006 4,250

Hereditary spastic paraplegias (HSP) are a heterogeneous group of neurodegenerative disorders leading to progressive spasticity of the lower limbs. Here, we descrive clinical and genetic features in an Italian family affected by autosomal recessive HSP (ARHSP) with mental impairment and thin corpus callosum (TCC). In both affected subjects, genetic analysis revealed the presence of a homozygous small deletion (733_734delAT) leading to a frameshift (M245VfsX) within the coding region of SPG11 gene, encoding spatacsin. This finding is the first independent confirmation that spatacsin loss of function mutations cause ARHPS-TCC.

HIGH-FREQUENCY ECoG OSCILLATIONS IN THE SITE OF ONSET OF EPILEPTIC SEIZURES DURING SLEEP

Sleep Medicine 2007;8(1):96-97

Della Marca G, Vollovo C, Barba. C, Fuggetta MF, Restuccia D, Colicchio G.

I.F. 2006: 2,926

Abstract non disponibile.

NECTID MEDIATES SKELETAL MUSCLE REGENERATION BY PROMOTING MYOBLAST SURVIVAL AND DIFFERENTIATION

The Journal of Cell Biology 2007;179(2):305-319

Deponti D, Francois S, Baesso S, Sciorati C,

Innocenzi A, Broccoli V, Muscatelli F, Meneveri R, Clementi E, Cossu G, Brunelli S.

I.F. 2006: 10,152

Regeneration of muscle fi bers that are lost during pathological muscle degeneration or after injuries is sustained by the production of new myofi bers. An important cell type involved in muscle regeneration is the satellite cell. Necdin is a protein expressed in satellite cell–derived myogenic precursors during perinatal growth. However, its function in myogenesis is not known. We compare transgenic mice that overexpress necdin in skeletal muscle with both wild-type and necdin null mice. After muscle injury the necdin null mice show a considerable defect in muscle healing, whereas mice that overexpress necdin show a substantial increase in myofi ber regeneration. We also fi nd that in muscle, necdin increases myogenin expression, accelerates differentiation, and counteracts myoblast apoptosis. Collectively, these data clarify the function and mechanism of necdin in skeletal muscle and show the importance of necdin in muscle regeneration.

SPHINGOSINE 1-PHOSPHATE MEDIATES PROLIFERATION AND SURVIVAL OF MESOANGIOBLASTS

Stem Cells 2007;25:1713-1719

Donati C, Cencetti F, Nincheri P, Bernacchioni C, Brunelli S, Clementi E, Cossu G, Bruni P.

I.F. 2006: 7,924

Mesoangioblasts are stem cells capable of differentiating in various mesodermal tissues and are presently regarded as suitable candidates for cell therapy of muscle degenerative diseases, as well as myocardial infarction. The enhancement of their proliferation and survival after injection in vivo could greatly improve their ability to repopulate damaged tissues. In this study, we show that the bioactive sphingolipid sphingosine 1-phosphate (S1P) regulates critical functions of mesoangioblast cell biology. S1P evoked a full mitogenic response in mesoangioblasts, measured by labeled thymidine incorporation and cell counting. Moreover, S1P strongly counteracted the apoptotic process triggered by stimuli as diverse as serum deprivation, C2-ceramide treatment, or staurosporine treatment, as assessed by cell counting, as well as histone-associated fragments and caspase-3 activity determinations. S1P acts both as an intracellular messenger and through specific membrane receptors. Realtime polymerase chain reaction analysis revealed that mesoangioblasts express the S1P-specific receptor S1P3 and, to a minor extent, S1P1 and S1P2. By using S1P receptor subtype-specific agonists and antagonists, we found that the proliferative response to S1P was mediated mainly by S1P2. By contrast, the antiapoptotic effect did not implicate S1P receptors. These findings demonstrate an important role of S1P in mesoangioblast proliferation and survival and indicate that targeting modulation of S1P-dependent signalling pathways may be used to improve the efficiency of muscle repair by these cells. Disclosure of potential conflicts of interest is found at the end of this article.

LANGUAGE DISTURBANCES IN A GROUP OF PARTICIPANTS SUFFERING FROM DUCHENNE MUSCULAR DYSTROPHY: A PILOT STUDY

Perceptual and Motor Skills 2007;104(2):663-676

Fabbro F, Marini A, Felisari G, Comi GP, D'Angelo MG, Turconi AC, Bresolin N.

I.F. 2006: 0,333

Results from several studies suggest that the process of language acquisition may be altered in patients suffering from Duchenne Muscular Dystrophy. In this study, a group of 8 male participants with Duchenne Muscular Dystrophy (M age = 16 yr., SD = 4.7) underwent an extensive neuropsychological and language assessment. They also performed a discourse production task. Results showed mild mental retardation associated with a specific deficit in Verbal rather than Performance IQ. At the linguistic assessment, 7 of 8 participants showed moderate to severe difficulties on oral language processing with particularly impaired morphosyntactic competence.

MID1 MUTATION SCREENING IN A LARGE COHORT OF OPITZ G/BBB SYNDROME PATIENTS: 29 NOVEL MUTATIONS IDENTIFIED

Human Mutation 2007;28(2):206-207

Ferrentino R, Bassi MT, Chitayat D, Tabolacci E, Meroni G.

I.F. 2006: 6,473

Opitz G/BBB Syndrome (OS) is a multiple congenital anomaly disorder characterized by defects along the body midline. The disease is characterized by variable expressivity of signs that include hypertelorism, cleft lip and/or palate, laryngo-tracheo-esophageal abnormalities, cardiac defects, and hypospadias. OS patients also present with mental retardation and brain anatomical abnormalities. An autosomal

dominant form mapping to chromosome 22 and an X-linked form of OS are known. The gene responsible for the X-linked form of OS, MID1, codes for a member of the Tripartite Motif family of E3 ubiquitin ligases. Here we report 29 novel mutations in 29 unrelated patients of a cohort of 140 male OS cases. These mutations are found in both familial and sporadic cases. They are scattered along the entire length of the gene and are represented by missense and nonsense mutations, insertions and deletions causing frame shift mutations, and deletion of either single exons or the entire gene. The variety of the mutations found confirms that loss-of-function is the mechanism underlying the OS phenotype. Moreover, the low percentage of MID1-mutated OS patients, 47% of the familial and 13% of the sporadic cases, suggests a wider genetic heterogeneity underlying the OS phenotype. (c) 2006 Wiley-Liss, Inc.

EVOLUTION OF NEUROLOGIC FEATURES IN WILLIAMS SYNDROME

Pediatric Neurology 2007;36(5):301-306

Gagliardi C, Martelli S, Burt Michael D, Borgatti R.

I.F. 2006: 1,542

As a part of a large multidisciplinary clinical and research follow-up study, 47 Williams syndrome patients underwent detailed neurologic testing. Because previous studies have documented the absence of major neurologic signs in Williams syndrome, the neurologic testing focused on soft signs. Previous findings of impairment of both gross and fine motor coordination were confirmed, and the presence of mild cerebellar and extrapyramidal signs was documented. In a 4-year follow-up study, an age-related pattern was revealed: soft extrapyramidal signs became more evident from 8 years of age and increased in the 14+ age group. The results are discussed according to a hypothesis related to the dopaminergic system involvement in Williams syndrome: anomalous organization or accelerated ageing process.

A LARGE ANALPHOID INVDUP(3)(Q22.3QTER) MARKER CHROMOSOME CHARACTERIZED BY ARRAY-CGH IN A CHILD WITH MALFORMATIONS, MENTAL RETARDATION, AMBIGUOUS GENITALIA AND BLASCHKO'S LINES

European Journal of Medical Genetics 2007;50(4):264-273

Gimelli G, Giorda R, Beri S, Gimelli S, Zuffardi O.

I.F. 2006: 1,614

We report a new case of mosaic chromosome 3-derived marker chromosome, present in fibroblasts but not in lymphocytes, found in a child with malformations, mental retardation and ambiguous genitalia. Cytogenetic and molecular analysis showed that the supernumerary invdup(3)(q22.3qter) chromosome was negative at FISH with alpha satellite probe. The presence of a functional neocentromere was confirmed by immunofluorescence with antibodies to centromere proteins (CENPs). Definition of the marker breakpoints has been done through array-CGH. The skin of the patient presented dyschromic areas ordered along Blaschko's lines. The invdup(3q) marker chromosome was present only in fibroblasts from the dark skin biopsy, while lymphocytes and fibroblasts from the normal skin showed a normal male karyotype. Expression of the HPS3 gene (MIM: 606118) was more than two times higher in dark skin fibroblasts. Neocentromeres are most often observed on chromosomal arm fragments that have separated from an endogenous centromere, and therefore actually confer mitotic stability to what would have been acentric fragments. To our knowledge, this invdup(3q) analphoid marker is the largest among the several reported so far. Parental origin and possible mode of formation have been defined by DNA polymorphisms studies. The size of the duplicated marker chromosome and its frequency and tissue distribution may be relevant to the severity of the propositus' phenotype.

TWO CLASSES OF LOW COPY REPEATS CO-MEDIATE A NEW RECURRENT REARRANGEMENT CONSISTING IN DUPLICATION AT 8p23.1 AND TRIPLICATION AT 8p23.2

Human Mutation 2007;28(5):459-468

Giorda R, Ciccone R, Gimelli G, Pramparo T, Beri S, Bonaglia MC, Giglio S, Genuardi M, Argente J, Rocchi M, Zuffardi O.

I.F. 2006: 6,473

We describe a new type of rearrangement consisting of the duplication of 8p23.1 and the triplication of 8p23.2 [dup trp(8p)] in two patients affected by mental retardation and minor facial dysmorphisms. Array-comparative genomic hybridization (CGH), fluorescence in situ hybridization (FISH), and genotyping of polymorphic loci allowed us to demonstrate that this rearrangement is mediated by the combined effects of two unrelated low-copy

repeats (LCRs). The first set of LCRs consists of the two clusters of olfactory receptor genes (OR-REPs) lying at 8p23.1. The second type of LCRs consists of a 15-kb segmental duplication, lying in inverted orientation at 8p23.2 and enclosing a non-repeated sequence of approximately 130 kb, named MYOM2-REP because of its proximity to the MYOM2 gene. The molecular characterization of a third case with a dicentric chromosome 8 demonstrated that the rearrangement had been generated by nonallelic homologous recombination between the two MYOM2-REPs. Based on our findings, we propose a model showing that a second recombination event at the level of the OR-REPs leads to the formation of the dup trp(8p) chromosome. This rearrangement can only arise during meiosis in heterozygous carriers of the polymorphic 8p23.1 inversion, whereas in subjects with noninverted chromosomes 8 or homozygous for the inversion only the dicentric chromosome can be formed. Our study demonstrates that nonallelic homologous recombination involving multiple LCRs can generate more complex rearrangements and cause a greater variety of genomic diseases. 2007 Wiley-Liss, Inc.

REORGANISATION OF THE SOMATOSENSORY SYSTEM AFTER EARLY BRAIN DAMAGE

Clinical Neurophysiology 2007;118(5):1110-1121

Guzzetta A, Bonanni P, Biagi L, Tosetti M, Montanaro D, Guerrini R, Cioni G.

I.F. 2006: 2,718

OBJECTIVE: To examine the reorganisation of the somatosensory system after early brain lesions. METHODS: We studied 12 young patients with congenital hemiplegia. Causative lesions were brain malformations, periventricular injuries and cortico-subcortical lesions. We explored the somatosensory system using evoked potentials, fMRI during sensory stimulation and clinical assessment of sensory function. To correlate sensory and motor function, we also performed transcranial magnetic stimulation, fMRI of hand movement and assessment of motor function by means of Melbourne test. RESULTS: Eleven patients showed a perilesional reorganisation of primary somatosensory function, as expressed by short latency potentials following stimulation of the paretic hand; in a remaining patient, delayed latency responses (N27.1) were only elicited over the ipsilateral undamaged hemisphere. Five of the eleven patients with perilesional somatosensory representation of the affected hand showed contralesional shifting of motor function, thus exhibiting sensory-motor dissociation. Significant correlation was found between sensory deficit and fMRI activation during sensory stimulation. CONCLUSIONS: In subjects with early brain lesions, somato-sensory function is generally reorganised within the affected hemisphere. A contralesional shifting is uncommon and poorly efficient in function restoration. SIGNIFICANCE: This study confirms and further explores the difference in reorganisation capabilities of the motor and sensory system following early brain injury of different etiologies and timing.

TESTING THE 8-SYNDROME STRUCTURE OF THE CHILD BEHAVIOR CHECKLIST IN 30 SOCIETIES

Journal of Clinical Child & Adolescent Psychology 2007;36(3):405-417

Ivanova MY, Dobrean A, Dopfner M, Erol N, Fombonne E, Fonseca A. Castro, Frigerio A, Grietens H, Hannesdottir H, Kanbayashi Y, Lambert MC, Achenbach TM, Larsson B, Leung P, Liu X, Minaei A, Mulatu MS, Novik T, Ja Oh K, Roussos A, Sawyer M, Simsek Z, Dumenci L, Steinhausen HC, Winkler MC, Wolanczyk T, Yang H-J, Zilber NZR, Verhulst FC, Rescorla LA, Almqvist F, Weintraub S, Bilenberg N, Bird H, Chen WJ.

I.F. 2006: 2,338

There is a growing need for multicultural collaboration in child mental health services, training, and research. To facilitate such collaboration, this study tested the 8-syndrome structure of the Child Behavior Checklist (CBCL) in 30 societies. Parents' CBCL ratings of 58,051 6- to 18-year-olds were subjected to confirmatory factor analyses, which were conducted separately for each society. Societies represented Asia; Africa; Australia; the Caribbean; Eastern, Western, Southern, and Northern Europe; the Middle East; and North America. Fit indices strongly supported the correlated 8-syndrome structure in each of 30 societies. The results support use of the syndromes in diverse societies.

TESTING THE TEACHER'S REPORT FORM SYNDROMES IN 20 SOCIETIES

School Psychology Review 2007;36(3):468-483

Ivanova MY, Achenbach TM, Rescorla LA, Dumenci L, Almqvist F, Bathiche M, Bilenberg N, Bird H, Domuta A, Erol N, Fombonne E, Fonseca A. Castro, Frigerio A, Kanbayashi Y,

Lambert MC, Leung P, Liu X, Minaei A, Roussos A, Simsek Z, Weintraub S, Wolanczyk T, Zubrick SR, Zukauskiene R, Verhulst F.

I.F. 2006: 0,905

Standardized assessment instrument developed in one society are often used in other societies. However it is important to determinate empirically how assessment instruments developed in one society function in others. The present study tested the fit of the Teacher's Report form syndrome structures in 20 diverse societies using data for 30,030 6- to 15-year-old students from Asia; Australia; the Caribbean; eastern, western, southern and northern Europe; and the Middle East. A correlated seven-syndrome model and a hierarchical Attention Problems Model were tested separately in each of the 20 societies via confirmatory factor analyses.The result supported the fit of the models in the tested societies.

CLINICAL AND MOLECULAR HETEROGENEITY IN ITALIAN PATIENTS AFFECTED BY COHEN SYNDROME

Journal of Human Genetics 2007;52(12):1011-1017

Katzaki E, Pescucci C, Uliana V, Papa FT, Ariani F, Meloni I, Priolo M, Selicorni A, Milani D, Fischetto R, Celle ME, Grasso R, Dallapiccola B, Brancati F, Bordignon M, Tenconi R, Federico A, Mari F, Renieri A, Longo I.

I.F. 2006: 2,205

Cohen syndrome is an autosomal recessive disorder with variability in the clinical manifestations, characterized by developmental delay, visual disability, facial dysmorphisms and intermittent neutropenia. We described a cohort of 10 patients affected by Cohen syndrome from nine Italian families ranging from 5 to 52 years at assessment. Characteristic age related facial changes were well documented. Visual anomalies, namely retinopathy and myopia, were present in 9/10 patients (retinopathy in 9/10 and myopia in 8/10). Truncal obesità has been described in all patients older than 6 years (8/8). DNA samples from all patients were analyzed for mutations in COH1 by DHPLC. We detected 15 COH1 alterations most of them were truncating mutations, only one being a missense change. Partial gene deletions have been found in two families. Most mutations were private. Two were already reported in the literature just once. A single base deletion leading to p.T3708fs3769, never reported before, was found in three apparently unrelated families deriving from a restricted area of the Veneto's lowland, between Padova town and Tagliamento river, in heterozygous state. Given the geographical conformation of this region, which is neither geographically or culturally isolated, a recent origin of the mutation could be hypothesized.

INHIBITORY EFFECT OF VOLUNTARY MOVEMENT PREPARATION ON CUTANEOUS HEAT PAIN AND LASER-EVOKED POTENTIALS

European Journal of Neuroscience 2007;25(6):1900-1907

Le Pera D, Brancucci A, De Armas L, Del Percio C, Miliucci R, Babiloni C, Restuccia D, Rossini PM, Valeriani M.

I.F. 2006: 3,709

In our study, preparation of voluntary movement was used to physiologically activate the motor cortex areas and the effect of this activation on CO2 laser-evoked potentials (LEPs) was explored. LEPs were recorded from 31 scalp electrodes in 10 healthy subjects after painful stimulation of the right C6–C7 skin dermatomes. LEP stimuli were delivered in the time interval between a visual warning stimulus followed after 1 s. by an imperative stimulus. The imperative stimulus triggered: (i) no task in the baseline condition (Pain); (ii) flexion–extension movements of the second finger of the right hand in the movement condition (Pain + Movement); (iii) cognitive task (mathematic computation) in the distraction condition (Pain + Cognition). The experimental conditions were also repeated durino application of laser stimuli on the left C6–C7 skin dermatomes. Compared with the baseline condition (no task required), durino preparation of right-hand voluntary movement there was a significant reduction in LEP amplitude and subjective pain rating after right- but not after left-hand stimulation, which suggests that the observed effect cannot be attributed to a nonspecific reduction in attention toward painful stimulus. During preparation of a cognitive task, LEP amplitude was reduced compared to baseline. Our results represent the first neurophysiological suggestion that physiological activation of the motor cortex, occurring during movement preparation, inhibits cortical pain processing by a centrifugal mechanism.

TRANSGENIC FRUIT-FLIES EXPRESSING A FRET-BASED SENSOR FOR IN VIVO IMAGING OF CAMP DYNAMICS

Cellular Signalling 2007;2296–2303

Lissandron V, Rossetto MG, Erbguth K, Fiala A, Daga A, Zaccolo M.

I.F. 2006: 4,887

3'–5'-cyclic adenosine monophosphate (cAMP) is a ubiquitous intracellular second messenger that mediates the action of various hormones and neurotransmitters and influences a plethora of cellular functions. In particular, multiple neuronal processes such as synaptic plasticity underlying learning and memory are dependent on cAMP signalling cascades. It is now well recognized that the specificity and fidelity of cAMP downstream effects are achieved through a tight temporal as well as spatial control of the cAMP signals. Approaches relying on real-time imaging and Fluorescence Resonance Energy Transfer (FRET)-based biosensors for direct visualization of cAMP changes as they happen in intact living cells have recently started to uncover the fine details of cAMP spatio-temporal signalling patterns. Here we report the generation of transgenic fruit-flies expressing a FRET-based, GFP-PKA sensor and their use in real-time optical recordings of cAMP signalling both ex vivo and in vivo in adult and developing organisms. These transgenic animals represent a novel tool for understanding the physiology of the cAMP signalling pathway in the context of a functioning body.

FAS SMALL INTERFERING RNA REDUCES MOTONEURON DEATH IN AMYOTROPHIC LATERAL SCLEROSIS MICE

Annals of Neurology 2007;62(1):81-92

Locatelli F*, Corti S*, Papadimitriou D, Fortunato F, Del Bo R, Donadoni C, Nizzardo M, Nardini M, Salani S, Ghezzi S, Strazzer S, Bresolin N, Comi GP.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 8,051

OBJECTIVE: Amyotrophic lateral sclerosis (ALS) is a progressive, fatal neurodegenerative disease characterized by selective motoneuron death. Understanding of the molecular mechanisms that trigger and regulate motoneuron degeneration could be relevant to ALS and other motoneuron disorders. This study investigates the role of Fas-linked motoneuron death in the pathogenesis of ALS. METHODS: We performed in vitro and in vivo small interfering RNA-mediated interference, by silencing the Fas receptor on motoneurons that carry the superoxide dismutase-1 (SOD1)-G93A mutation. RESULTS: We observed a significant reduction in Fas expression at messenger RNA ($p < 0.001$) and protein levels. Treated motoneurons demonstrated an increase in survival and a reduction in cytochrome c release from mitochondria. In vivo, continuous intrathecal administration of Fas small interfering RNA by an osmotic minipump improved motor function and survival in SOD1-G93A mice (mean increase, 18 days; $p < 0.0001$). Treated mice showed a significant reduction in Fas and Fas mediators p38 mitogen-activated protein kinase, neuronal nitric oxide synthase, and caspase-8. INTERPRETATION: Fas silencing interferes with motoneuron-specific downstream death pathways and results in increased motoneuron survival and amelioration of the SOD1-G93A phenotype, suggesting new possible strategies for molecular therapy of ALS.

ENDOSCOPIC ANATOMY OF THE CEREBRAL AQUEDUCT

Neurosurgery 2007;61(Operative Neurosurgery - Supplement):ONS-1-ONS-6

Longatti P, Fiorindi A, Perin A, Martinuzzi A.

I.F. 2006: 2,692

OBJECTIVE: What is known about the cerebral aqueduct is derived mainly from the legacy of classic histology and from the most recent advanced neuroimaging technologies. In fact, although this important structure is frequently glimpsed by neurosurgeons, only limited anatomic contributions have been added by microsurgery to its direct in vivo description. A review of our surgical experience in navigating the fourth ventricle prompted us to revisit the classical anatomic descriptions of the aqueduct and compare them using the novel perspective of neuroendoscopy. METHODS: We reviewed video recordings of 65 transaqueductal explorations of the fourth ventricle using flexible endoscopes, which were performed in our center to treat various pathological conditions. Forty-one patients were selected as being more informative for anatomic description. They include 21 patients with communicating normal pressure hydrocephalus, 6 patients with intraventricular hemorrhage, 5 patients with membranous obstruction of the foramen of Magendie, 5 patients with trapped fourth ventricle as evidenced after aqueductoplasty, 3 patients with colloid cysts, and 1 patient with craniopharyngioma with apparently normal aqueduct, which was navigated to aspirate small fragments of colloid and tiny clots. RESULTS: Patients with normal-sized third ventricles confirmed the typical triangular shape of the aqueductal adytum, whereas all pa-

thological aqueducts invariably had an oval contour. The posterior commissure, a faint trace of the median sulcus, and the rubral eminences were the structures invariably noticed. Five segments of the aqueduct were always identifiable: the adytum, first constriction, ampulla, second constriction, and posterior part or egressus. CONCLUSION: Neuroendoscopy provides a novel perspective into the inner aqueductal wall and supplies an incomparable view of the intracanalicular anatomic structures.

INDICATORS OF THEORY OF MIND IN NARRATIVE PRODUCTION: A COMPARISON BETWEEN INDIVIDUALS WITH GENETIC SYNDROMES AND TYPICALLY DEVELOPING CHILDREN

Clinical Linguistics & Phonetics 2007;21(1):37-53

Lorusso ML, Galli R, Libera L, Gagliardi C, Borgatti R, Hollebrandse B.

I.F. 2006: 0,693

It is a matter of debate whether the development of theory of mind (ToM) depends on linguistic development or is, rather, an expression of cognitive development. The study of genetic syndromes,

which are characterized by intellectual impairment as well as by different linguistic profiles, may provide useful information with respect to this issue. The present study compares indicators of ToM

in the narrative production of individuals with Cornelia de Lange syndrome, Down syndrome, Williams syndrome and typically developing children, matched on sex and mental age. Statistical comparisons of data obtained from a qualitative analysis of the narrative production of the different

groups confirm the presence of distinctive patterns, mainly related to the effective use of personal pronouns. The analysis of correlations among storytelling variables and other cognitive and linguistic variables suggests that the relationship between language development, cognitive development, and the emergence of ToM cannot be reduced to unidirectional causal links.

EVALUATION OF NARRATIVE ABILITIES IN PATIENTS SUFFERING FROM DUCHENNE MUSCULAR DYSTROPHY

Brain and Language 2007;102(1):1-12

Marini A, Lorusso ML, D'Angelo MG, Civati F, Turconi AC, Fabbro F, Bresolin N.

I.F. 2006: 2,317

The present work investigated cognitive, linguistic and narrative abilities in a group of children suffering from Duchenne Muscular Dystrophy, an allelic X-linked recessive disorder caused by mutations in the gene encoding dystrophin. The patients showed mildly reduced IQ with lower Verbal than Performance Intelligence Quotient and were mildly affected in visual attention and short-term memory processing. At the linguistic assessment, neither receptive (word comprehension) nor expressive (naming tasks and fluency) lexical abilities were impaired. However, their narratives were qualitatively inferior with respect to those produced by a group of typically developing children. Their speech samples were characterized by the presence of fewer verbs and complete sentences. It is suggested that the reduced production of complete sentences is due to a selective problem in verb argument structure generation. Since the lack of dystrophin is assumed to produce effects on the maturation of the cerebellum, whose involvement has been recently suggested in verb and syntactic processing, these findings may lend indirect support to the hypothesis of a cerebellar-cortical circuit specialized in verb and sentence production.

PATTERNS OF LANGUAGE IMPROVEMENT IN ADULTS WITH NON-CHRONIC NON-FLUENT APHASIA AFTER SPECIFIC THERAPIES

Aphasiology 2007;21(2):164-186

Marini A, Caltagirone C, Pasqualetti P, Carlomagno S.

I.F. 2006: 0,882

Abstract non disponibile.

ASSOCIATION OF SHORT-TERM MEMORY WITH A VARIANT WITHIN DYX1C1 IN DEVELOPMENTAL DYSLEXIA

Genes, Brain and Behavior 2007;6:640-646

Marino C, Citterio A, Giorda R, Facoetti A, Menozzi G, Vanzin L, Lorusso ML, Nobile M, Molteni M.

I.F. 2006: 4,385

A substantial genetic contribution in the etiology of developmental dyslexia (DD) has been well documented with independent groups reporting a susceptibility locus on chromosome 15q. After the identification of the DYX1C1 gene as a potential candidate for DD, several independent association studies reported controversial results. We

performed a family-based association study to determine whether the DYX1C1 single nucleotide polymorphisms (SNPs) that have been associated with DD before, that is SNPs '23GA' and '1249GT', influence a broader phenotypic definition of DD. A significant linkage disequilibrium was observed with 'Single Letter Backward Span' (SLBS) in both single-marker and haplotype analyses. These results provide further support to the association between DD and DYX1C1 and it suggests that the linkage disequilibrium with DYX1C1 is more saliently explained in Italian dyslexics by short-term memory, as measured by 'SLBS', than by the categorical diagnosis of DD or other related phenotypes.

CHRONIC THERAPY FOR MCARDLE DISEASE: THE RANDOMIZED TRIAL WITH ACE INHIBITOR

Acta Myologica 2007;26(1):64-66

Martinuzzi A, Liava A, Trevisi E, Antoniazzi L, Frare M.

I.F. 2006: 0,000

Abstract non disponibile.

SEVERE HEAD INJURY IN EARLY INFANCY: ANALYSIS OF CAUSES AND POSSIBLE PREDICTIVE FACTORS FOR OUTCOME

Childs Nervous System 2007;23(8):873-880

Marton E, Mazzucco M, Nascimben E, Martinuzzi A, Longatti P.

I.F. 2006: 1,257

OBJECT: The aim of this study was to analyse the causes and prognostic factors for outcome in severe traumatic brain injuries (TBI) in early infancy. MATERIALS AND METHODS: We present a retrospective study on 16 infants aged less than 12 months observed over the last 20 years in our department for severe brain injury. Infants were evaluated by the Children Coma Scale (CCS). We assessed Glasgow Outcome Scale (GOS) at discharge and at 12 months after discharge. CONCLUSIONS: The main causes of trauma were domestic accidents followed by car accidents. The highest positive correlation was found between the GOS score at 1 year and the presence of hypoxia and hypotension at admission, the presence of hyperglycaemia at 24 h and the occurrence of major clotting disorders. A significant but weaker correlation was found with the CCS at admission, the occurrence of early post-traumatic seizures and the length of stay in the intensive care unit.

ANALYSIS OF THE DYNAMICAL BEHAVIOUR OF THE EEG RHYTHMS DURING A TEST OF SUSTAINED ATTENTION

Conf Proc IEEE Eng Med Biol Soc. 2007;2007:1298-301

Molteni E, Bianchi AM, Butti M, Reni G, Zucca C.

I.F 2006: 0,94

In clinical routine, the evaluation of sustained attention is often performed analyzing behavioral data collected during specific tests. It is not common to match such analyses with a detailed examination of the subject's simultaneous electroencephalographic (EEG) activity, and particularly its frequency content. In this study, 9 healthy volunteers underwent a modified Conners' CPT test, while their EEG were contemporarily recorded. Spectral power was calculated for each of the recorded EEG signals, with particular attention to frequency bands that are traditionally reported in literature. Then Compressed Spectral Array (CSA) sequence of spectra was plotted, and the analysis of the variability of the rhythms was carried out. Evaluation of the obtained results shows that the nine subjects shared a progressive backshift of alpha rhythm during the accomplishment of the CPT test. Moreover, beta and gamma activities were stronger in the right than in the left hemisphere. An intense and widespread decrease in EEG spectral power during test performing became visible in many subjects. Statistical analysis provided evidence that EEG activity correlates with the test behavioral results in many cerebral areas. For this reason, we encourage further investigations of the combined employment of tests and EEG recording during the clinical assessment of sustained attention performance.

FRONTO-LIMBIC BRAIN STRUCTURES IN SUICIDAL AND NON-SUICIDAL FEMALE PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Molecular Psychiatry 2007;12(4):360-366

Monkul ES, Hatch JP, Nicoletti M, Spence S, Brambilla P, Lacerda ALT, Sassi RB, Mallinger AG, Keshavan MS, Soares JC.

I.F. 2006: 11,804

Our knowledge about the neurobiology of suicide is limited. It has been proposed that suicidal behavior generally requires biological abnormalities concomitant with the personality trait of impulsivity/aggression, besides an acute psychiatric illness or

psychosocial stressor. We investigated fronto-limbic anatomical brain abnormalities in suicidal and non-suicidal adult female patients with unipolar depression. Our sample consisted of seven suicidal unipolar patients, 10 non-suicidal unipolar patients and 17 healthy female comparison subjects. The criterion for suicidality was one or more documented lifetime suicide attempts. A 1.5T GE Signa Imaging System running version Signa 5.4.3 software was used to acquire the magnetic resonance imaging images. All anatomical structures were measured blindly, with the subjects' identities and group assignments masked. We used analysis of covariance with age and intracranial volume as covariates and the Tukey–Kramer procedure to compare suicidal patients, non-suicidal patients and healthy comparison subjects. Suicidal patients had smaller right and left orbitofrontal cortex gray matter volumes compared with healthy comparison subjects. Suicidal patients had larger right amygdala volumes than non-suicidal patients. Abnormalities in the orbitofrontal cortex and amygdala in suicidal patients may impair decision-making and predispose these patients to act more impulsively and to attempt suicide.

PREFRONTAL GRAY MATTER INCREASES IN HEALTHY INDIVIDUALS AFTER LITHIUM TREATMENT: A VOXEL-BASED MORPHOMETRY STUDY

Neuroscience Letters 2007;429(1):7-11

Monkul ES, Matsuo K, Nicoletti MA, Dierschke N, Hatch JP, Dalwani M, Brambilla P, Caetano S, Sassi RB, Mallinger AG, Soares JC.

I.F. 2006: 2,092

The objective of this study was to test the hypothesis that 4 weeks of lithium administration would be associated with changes in brain gray and white matter volumes in healthy individuals. Thirteen right-handed healthy volunteers (6 females, mean age = 25.9±10.0 years) were studied. 3D SPGR MRIs (TR = 25 ms, TE = 5 ms, slice-thickness = 1.5 mm) were acquired using a 1.5 T GE Signa Imaging System, at baseline and after 4 weeks of lithium administration at therapeutically relevant doses. Optimized voxel-based morphometry (VBM) analyses were conducted. Left and right dorsolateral prefrontal cortex and left anterior cingulate gray matter volumes increased significantly following lithium administration. Total white matter volume was increased, whereas total brain volume and total gray matter volume were not significantly changed following 4 weeks of lithium. Lithium treatment resulted in prefrontal regional gray matter volume increases in healthy volunteers, as well as increases in total white matter volume. Whether these changes are mediated by neurotrophic/neuroprotective or osmotic effects remains unknown.

DEFECTIVE MITOCHONDRIAL BIOGENESIS: A HALLMARK OF THE HIGH CARDIOVASCULAR RISK IN THE METABOLIC SYNDROME?

Circulation Research 2007;100:795-806

Nisoli E, Clementi E, Carruba MO, Moncada S.

I.F. 2006: 9,854

The metabolic syndrome is a group of risk factors of metabolic origin that are accompanied by increased risk for type 2 diabetes mellitus and cardiovascular disease. These risk factors include atherogenic dyslipidemia, elevated blood pressure and plasma glucose, and a prothrombotic and proinflammatory state. The condition is progressive and is exacerbated by physical inactivity, advancing age, hormonal imbalance, and genetic predisposition. The metabolic syndrome is a particularly challenging clinical condition because its complex molecular basis is still largely undefined. Impaired cell metabolism has, however, been suggested as a relevant pathophysiological process underlying several clinical features of the syndrome. In particular, defective oxidative metabolism seems to be involved in visceral fat gain and in the development of insulin resistance in skeletal muscle. This suggests that mitochondrial function may be impaired in the metabolic syndrome and, thus, in the consequent cardiovascular disease. We have recently found that mitochondrial biogenesis and function are enhanced by nitric oxide in various cell types and tissues, including cardiac muscle. Increasing evidence suggests that this mediator acts as a metabolic sensor in cardiomyocytes. This implies that a defective production of nitric oxide might be linked to dysfunction of the cardiomyocyte metabolism. Here we summarize some recent findings and propose a hypothesis for the high cardiovascular risk linked to the metabolic syndrome.

SOCIOECONOMIC STATUS MEDIATES THE GENETIC CONTRIBUTION OF THE DRD4 AND 5-HTTLPR POLYMORPHISMS TO EXTERNALIZATION IN PRE-ADOLESCENCE

Development and Psychopathology 2007;19

(2007), 1147–1160

Nobile M, Giorda R, Marino C, Carlet O, Pastore V, Vanzin L, Bellina M, Molteni M, Battaglia M.

I.F. 2006: 2,709

The impact of socioeconomic status (SES) and genetic polymorphisms on individual differences for externalized behaviors have often been investigated separately in studies of children and adults. In a general population sample of 607 Italian preadolescents, we examined the independent and joint effects of SES and the dopamine receptor D4 (DRD4) and serotonin transporter linked promoter region (5-HTTLPR) polymorphisms upon rule-breaking and aggressive behaviors measured with the Child Behavior CheckList/6–18. We found evidence, which was based on both one locus and two-loci genotype analyses, that low SES and DRD4 long and 5-HTTLPR long alleles, both alone and in interaction, are associated with higher aggressive behavior scores. The effects were similar but more modest and limited to one locus genotype analyses for rule-breaking behavior. Consistent with studies that showed the effects of societal moderators on the heritability of externalized behaviors across different segments of the population, we suggest that diminished social constraints associated with low parental SES may act as enhancers of the genetic influence of specific DRD4 and 5-HTTLPR alleles over aggressive behaviors in preadolescence.

NITRIC OXIDE BOOSTS CHEMOIMMUNOTHERAPY VIA INHIBITION OF ACID SPHINGOMYELINASE IN A MOUSE MODEL OF MELANOMA

Cancer Research 2007;67(16):7559-7564

Perrotta C, Bizzozero L, Falcone S, Rovere-Querini P, Prinetti A, Schuchman EH, Sonnino S, Manfredi A, Clementi E.

I.F. 2006: 7,656

Cisplatin is one of the most effective anticancer drugs, but its severe toxic effects, including depletion of immune-competent cells, limit its efficacy. We combined the systemic treatment with cisplatin with intratumor delivery of dendritic cells (DC) previously treated ex vivo with a pulse of nitric oxide (NO) released by the NOdonors (z)-1-[2-(2-aminoethyl)-N-(2- ammonioethyl)amino]-diazen-1-ium-1,2-diolate or isosorbide dinitrate. We found that this chemoimmunotherapy, tested in the B16 mouse model of melanoma, was significantly more efficacious than cisplatin alone, leading to tumor regression and animal survival at low doses of cisplatin that alone had no effect. Tumor cure was not observed when combining cisplatin with DCs not exposed to NOdonors, indicating the key role of the pretreatment with NO. We investigated the mechanisms responsible for the synergic effect of NO-treated DCs and cisplatin and found that NO-treated DCs were protected both in vitro and in vivo from cisplatin-induced cytotoxicity.Cisplatin triggered DC apoptosis through increased expression and activation of acid sphingomyelinase; pretreatment of DCs with NOdonors prevented such activation and inhibited activation of the downstream proapoptotic events, including generation of ceramide, activation of caspases 3 and 9, and mitochondrial depolarization. The effects of NOwer e mediated through generation of its physiologic messenger, cyclic GMP. We conclude that NOand NOgener ating drugs represent promising tools to increase the efficacy of chemoimmunotherapies in vivo, promoting the survival and increasing the function of injected cells by targeting a key pathway in cisplatin-induced cytotoxicity.

THE ITALIAN XLMR BANK: A CLINICAL AND MOLECULAR DATABASE

Human Mutation 2007;28(1):13-18

Pescucci C, Caselli R, Mari F, Speciale C, Ariani E, Bruttini M, Sampieri K, Mencarelli MA, Scala E, Longo I, Artuso R, Renieri A, Meloni I, XLMR Italian Network (Bassi MT, Borgatti R)

I.F. 2006: 6,473

Mental retardation (MR) is a nonprogressive condition characterized by a significant impairment of intellectual capabilities with deficit of cognitive and adaptive functioning and onset before 18 years. Mental retardation occurs in about 2 to 3% of the general population and it is estimated that 25 to 35% of the cases may be due to genetic causes. Among these ''genetic'' MR, 25 to 30% are probably due to mutations in a gene on the X chromosome (X-linked mental retardation, XLMR). Given the genetic heterogeneity of XLMR, the availability of a considerable number of patients with accurate phenotypic classification is a crucial factor for research. The X-linked Mental Retardation Italian Network, which has been active since 2003, has collected detailed clinical information and biological samples from a vast number of MR patients. Collected samples and clinical information are inserted within the XLMR bank, a comprehensive molecular and clinical web-based database available at the address http://xlmr.unisi.

it. The database is organized in three distinct parts. Part I and II contain several electronic schedules to register information on the family, the phenotypic description, the photographs, and a 20 sec movie of the patient. Part III allows the registration of molecular analyses performed on each case; samples and clinical data are usable via password-restricted access. Clinical and molecular centers interested in joining the network may request a password by simply contacting the Medical Genetics of the University of Siena. The XLMR bank is an innovative biological database that allows the collection of molecular and clinical data, combines descriptive and iconographic resources, and represents a fundamental tool for researchers in the field of mental retardation.

QUANTIFICATION OF ENERGY EXPENDITURE DURING GAIT IN CHILDREN AFFECTED BY CEREBRAL PALSY

Europa Medicophysica 2007;43:7-12

Piccinini L, Cimolin V, Galli M, Berti M, Crivellini M, Turconi AC.

I.F. 2006: 0,000

AIM: Children affected by cerebral palsy (CP) are generally characterised by some movement limitations and abnormalities that compromised gait pattern. These disabilities during deambulation may lead to excessive energy cost and so to a compromised energy efficiency. METHODS: In this study oxygen expenditure was evaluated during walking in 20 children affected by CP and in 20 healthy children, using Cosmed K4b2 (Cosmed, Italy). From obtained data about energy consumption, some parameters (heart rate, energy expenditure index, oxygen consumption, oxygen cost) were extracted, first in order to quantify energy cost during gait in pathological and healthy subjects and then to underline differences between the 2 groups of children. RESULTS: In particular, the results obtained revealed that heart rate (bpm) and oxygen consumption (mL/kg/min) mean values didn't differ significantly between normal subjects and those with CP; instead, energy expenditure index (b/m) and oxygen cost (mL/kg/m) presented higher mean values rather than control group at a statistically level and so they revealed to be significant parameters, in order characterized energy expenditure in children affected by CP. CONCLUSIONS: This inefficiency characteristic of CP deambulation is probably directly connected to the presence of simultaneous contraction of agonist and antagonist muscle in these patients.

INTRON SIZE IN MAMMALS: COMPLEXITY COMES TO TERMS WITH ECONOMY

Trends in Genetics 2007;23(1):20-24

Pozzoli U, Menozzi G, Comi GP, Cagliani R, Bresolin N, Sironi M.

I.F. 2006: 9,95

Different and contrasting models have been proposed to explain intron size evolution in mammals. Here, we demonstrate that intron and intergenic size per se has no adaptive role in gene expression regulation but reflects the need to preserve conserved intronic elements. Although the amount of non-coding functional elements explains the within-genome size variation of intergenic spacers, we show that an additional, additive pressure has been acting on highly expressed introns to reduce the cost of their transcription.

CONSISTENCY OF TEACHER-REPORTED PROBLEMS FOR STUDENTS IN 21 COUNTRIEST

School Psychology Review 2007;36(1):91-110

Rescorla LA, Achenbach TM, Ginzburg S, Ivanova MY, Dumenci L, Almqvist F, Bathiche M, Bilenberg N, Bird H, Domuta A, Erol N, Fombonne E, Fonseca AC, Frigerio A, Kanbayashi Y, Lambert MC, Liu X, Leung P, Minaei A, Roussos A, Simsek Z, Weintraub S, Weisz J, Wolanczyk T, Zubrick SR, Zukauskiene R, Verhulst F.

I.F. 2006: 0,905

This study compared teachers' ratings of behavioral and emotional problems on the Teacher's Report Form for general population samples in 21 countries {N = 30,957). Correlations between internal consistency coefficients in different countries averaged .90. Effect.s of country on scale scores ranger from 3% to 13%. Gender effects ranged from < 1% to 5%. and age effects were all <1%. With great consistency across countries, scores were higher for boys than for girls on eight scales: Total Problems; Externalizing; the Attentino Problems, Rule-Breaking Behavior, and Aggressive Behavior syndromes; and Diagnostic and Statistical Manual (DSM)-onented Attention Deficit Hyperactivity Problems, Oppositional Defiant Problems, and Conduct Problems. Correlations between mean item ratings in different countries averaged .74. Teacher's Report Form results were thus similar across 21 very diverse countries, despite differences across these countries in school systems, models of pedagogy, and curricula.

BEHAVIORAL AND EMOTIONAL PROBLEMS REPORTED BY PARENTS OF CHILDREN AGES 6 TO 16 IN 31 SOCIETIES

Journal of Emotional and Behavioral Disorders 2007;15(3):130-142

Rescorla LA, Achenbach TM, Ivanova MY, Dumenci L, Almqvist FK, Bilenberg N, Bird H, Chen WJ, Dobrean A, Dopfner M, Erol N, Fombonne E, Fonseca AC, Frigerio A, Grietens H, Hannesdottir H, Kanbayashi Y, Lambert MC, Larsson B, Leung P, Liu X, Minaei A, Mulatu MS, Novik T, Oh Kyung-J, Roussos A, Sawyer M, Simsek Z, Steinhausen H-C, Weintraub S, Weisz J, Winkler MC, Wolanczyk T, Yang H.-J, Zilber N, Zukauskiene R, Verhulst F.

I.F. 2006: 1,143

This study compared parents' ratings of behavioral and emotional problems on the Child Behavior Checklist (Achenbach, 1991; Achenbach & Rescorla, 2001) for general population samples of children ages 6 to 16 from 31 societies (N = 55,508). Effect sizes for society ranged from .03 to .14. Effect sizes for gender were ≤ .01, with girls generally scoring higher on Internalizing problems and boys generally scoring higher on Externalizing problems. Effect sizes for age were ≤ .01 and varied across types of problems.Total Problems scores for 19 of 31 societies were within 1 SD of the overall mean of 22.5. Bisociety correlations for mean item scores averaged .74. The findings indicate that parents' reports of children's problems were similar in many ways across highly diverse societies. Nonetheless, effect sizes for society were larger than those for gender and age,indicating the need to take account of multicultural variations in parents' reports of children's problems.

MODULATION OF HIGH-FREQUENCY (600 HZ) SOMATOSENSORY-EVOKED POTENTIALS AFTER rTMS OF THE PRIMARY SENSORY CORTEX

European Journal of Neuroscience 2007;26(8):2349–2358

Restuccia D, Ulivelli M, De Capua A, Bartalini S, Rossi S.

I.F. 2006: 3,709

Somatosensory inputs to the primary sensory cortex (S1) after median nerve stimulation include temporally overlapping parallel processing, as reflected by standard low-frequency somatosensory-evoked potentials (LF-SEPs) and high-frequency SEPs (HF-SEPs), the latter being more sensitive to arousal and to other rapid adaptive changes. Experimental data suggest that cortical HFSEPs are formed by two successive pre- and postsynaptic components, respectively, generated in the terminal part of thalamocortical radiation (early burst) and in specialized neuronal pools within S1 (later burst).In eight healthy subjects, slow (1 Hz) or rapid (10 Hz) repetitive transcranial magnetic stimulations (rTMS), which are known to induce opposite changes on cortical excitability, applied on S1 did not modify LF-SEPs, while HF-SEPs showed a series of dissociate changes in the early and later high-frequency burst, moreover occurring with a different time-course. Slow rTMS caused an immediate and lasting decrease of the later burst activity, coupled with an immediate increase of the earlier part of the burst, suggesting that inhibition of cortical excitability triggered opposite, compensatory effects at subcortical levels; rapid rTMS induced a delayed increase of later HF-SEPs, leaving unaltered the earlier subcortical burst.Findings causally demonstrate that LF- and HF-SEPs reflect two distinct functional pathways for somatosensory input processing, and that early and late high-frequency burst do actually reflect the activity of different generators, as suggested by experimental data. Possible underlying neurophysiological phenomena are discussed.

CEREBELLAR DAMAGE IMPAIRS DETECTION OF SOMATOSENSORY INPUT CHANGES. A SOMATOSENSORY MISMATCH-NEGATIVITY STUDY

Brain 2007;130(1):276-287

Restuccia D, Della Marca G, Valeriani M, Leggio MG, Molinari M.

I.F. 2006: 7,617

Several recent studies support the view that the cerebellum's contribution to sensory processing is not limited tomovement regulation. In a previous paper (Restuccia D, Valeriani M, Barba C, Le Pera D, Capecci M, Filippini V, Molinari M. Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. Brain 2001; 124: 757–68) we showed that the cerebellum influences somatosensory input processing at very early stages. The present study was aimed at verifying whether an analogous influence is also exerted at higher levels. For some time it has been known that in the auditory modality a specific event-related potential (ERP), that is, mismatch negativity (MMN), reflects preattentive detection of changes in the

incoming stimulus by comparing the new stimulus with sensory memory traces. To test the cerebellar influence on the processing of incoming somatosensory stimuli we first verified whether the electrical stimulation of fingers, according to an 'oddball' paradigm within a stimulus-ignored condition, was able to elicit event-related components specifically linked to the preattentive detection of change. We analysed scalp responses obtained from eight healthy volunteers during frequent and rare electrical stimulation of the first and fifth finger of the left hand, respectively. To ensure that responses to deviant stimuli were due to changes in detection mechanisms, rather than to activation of new afferents, we also analysed responses to rare stimulation alone ('standard-omitted' condition). The 'oddball' stimulation was able to elicit a parieto-occipital extra negativity that was different in scalp

distribution and latency from the N140 response to the 'standard-omitted' stimulation. We considered that this response was related to changes in detection mechanisms and labelled it somatosensory mismatch negativity (S-MMN). When the same procedure was applied to six patients with unilateral cerebellar lesions we found that the S-MMN was clearly abnormal after stimulation of the affected hand (ipsilateral to the affected cerebellar hemisphere). Earlier ERPs, as well as ERPs elicited during the 'standard-omitted' condition, were fully normal. Present data indicate that cerebellar processing is involved in preattentive detection of somatosensory input changes. In conclusion, this study demonstrates the reliability of S-MMN recordings and indicates that subjects with cerebellar damage may be impaired in the cortical processing of incoming somatosensory inputs.

GIANT SUBCORTICAL HIGH-FREQUENCY SEPS IN IDIOPATHIC GENERALIZED EPILEPSY: A PROTECTIVE MECHANISM AGAINST SEIZURES?

Clinical Neurophysiology 2007;118(1):60-68

Restuccia D, Valeriani M, Della Marca G.

I.F. 2006: 2,718

OBJECTIVE: Recently, we found that high-frequency somatosensory evoked potentials (HF-SEPs), which are modulated by arousal-related structures, were abnormally enhanced during N-REM sleep in two seizure-free IGE patients [Restuccia D, Rubino M, Valeriani M, Della Marca G. Increase of brainstem high-frequency SEP subcomponents during light sleep in seizure-free epileptic patients. Clin Neurophysiol 2005; 116: 1774-1778]. Here, we aimed at verifying whether similar HF-SEP abnormalities were significantly correlated to the clinical outcome in a larger population of untreated IGE patients. METHODS: Patients were classified as Juvenile Myoclonic epilepsy (JME; six patients) and Childhood or Juvenile Absence epilepsy (CAE and JAE, six patients). They were untreated because newly diagnosed, or because seizure-free. HF-SEPs from patients were compared with those obtained from 21 healthy volunteers. RESULTS: HF-SEPs were abnormally enhanced in all seizure-free CAE-JAE patients, whereas they were normal in all JME patients and in CAE-JAE patients with frequent seizures. Not only scalp distribution, but also dipolar source analysis suggested a subcortical origin for these enhanced subcomponents, possibly in the brainstem. CONCLUSIONS: The enhancement of HF-SEPs might reflect the hyperactivity of arousal-related brainstem structures; such an enhancement was found in all seizure-free CAE-JAE patients, while it was never observed in JME patients. SIGNIFICANCE: We speculate that the hyperactivity of arousal-related brainstem structures might account for the different clinical outcome among IGE subsyndromes.

A GENERAL POPULATION TWIN STUDY OF THE CBCL/6-18 DSM-ORIENTED SCALES

Journal of the American Academy of Child and Adolescent Psychiatry 2007;46(5):619-627

Spatola CAM, Fagnani C, Pesenti-Gritti P, Ogliari A, Stazi MA, Battaglia M.

I.F. 2006: 4,767

OBJECTIVE: To explore the contributions of genetic and environmental influences to individual variation and covariation of the Child Behavior Checklist (CBCL) DSM-oriented scales (DOS) originally proposed by Achenbach and associates in 2001. Method: A classic twin study of 398 twin pairs ages 8 to 17 years belonging to the population-based Italian Twin Registry, assessed by parents using the CBCL for Ages 6 to 18 (CBCL/6Y18). Results: Univariate analyses showed that compared with the classic CBCL/6Y18 empirical subscales, the DOS have higher heritability (lowest 0.54 for Anxiety Problems, highest 0.71 for Conduct Problems) and simpler causal structure in that the phenotypic variance was satisfactorily explained by additive genetic and unique environmental factors only. Multivariate analyses showed that the causes of phe-

notypic correlation among the different DOS can be attributed to one common genetic factor and to two idiosyncratic environmental factors, each loading differently on the Internalizing (Anxiety and Affective Problems) and the Externalizing (Attention-Deficit/Hyperactivity, Oppositional Defiant, and Conduct Problems) CBCL/6Y18 DOS. CONCLUSIONS: Several common risk factors of both genetic and environmental nature can simultaneously affect a child_s proneness to develop the psychopathological signs and symptoms captured by the CBCL/6Y18 DOS.

LANGUAGE AND SOCIAL COMMUNICATION IN CHILDREN WITH CEREBELLAR DYSGENESIS

Folia Phoniatrica et Logopedia 2007;59(4):201-209

Tavano A, Fabbro F, Borgatti R.

I.F. 2006: 0,655

OBJECTIVE: Acquired cerebellar lesions in children and adults may determine deficits of executive functions, visuoperceptual skills, expressive language and modulation of affect; a complex pattern termed 'cerebellar cognitive affective syndrome'. However, the long-term sequelae of malformative cerebellar lesions have yet to be systematically investigated, particularly in children. The purpose of this study was to present preliminary longitudinal data on the development of language and social communication skills in children with congenital malformations confined to the cerebellum. PATIENTS AND METHODS: Five children (3 males, 2 females) with cerebellar malformations confined to the cerebellum were selected. Three patients presented with cerebellar hypoplasia involving the vermis and the hemispheres, while the remaining 2 had a malformation affecting only the cerebellar hemispheres. Neurobehavioral and language development were traced through access to available clinical data. RESULTS: In the patients with cerebellar vermis malformation, language and social communicative skills were affected to a variable extent: 1 patient did not present with social disturbances during development. Those with hemispheric cerebellar lesions presented with selective linguistic impairments. CONCLUSIONS: The neurobehavioral profile of children with cerebellar malformations supports a key role of the cerebellum in language acquisition and affect regulation as distinguished functional domains. Copyright 2007 S. Karger AG, Basel.

DISORDERS OF COGNITIVE AND AFFECTIVE DEVELOPMENT IN CEREBELLAR MALFORMATIONS

Brain 2007;130:2646-2660

Tavano A, Grasso R, Gagliardi C, Triulzi F, Bresolin N, Fabbro F, Borgatti R.

I.F. 2006: 7,617

Acquired cerebellar lesions in adults and children can lead to the development of a complex behavioural pattern termed 'Cerebellar Cognitive Affective Syndrome' (Schmahmann and Sherman, Brain, 1998; 121: 561 ^ 79), which is characterized by reduced cognitive efficiency associated with specific neuropsychological deficits (executive and visuospatial disorders), expressive language disorders (mild agrammatism and anomia) and affective disorders with blunting of affect. It is not known whether a symptomatological picture such as this can also be found in congenital cerebellar malformations.We studied the behavioural developmental profile of 27 patients including children and adults with congenital malformations confined to the cerebellum, the largest studied sample to date. Extensive clinical and neuropsychological investigations highlight the presence of a wide range of disorders supporting the important role played by the cerebellumin the acquisition of higher-order cognitive and affective skills.The type and extent of cerebral reorganization processes in the presence of malformative lesions are difficult to predict andmay possibly account for the variability of clinical phenotypes. It is, therefore, more difficult to identify a syndromic picture defined as exactly as is the case with acquired lesions.However, the pattern of deficits that we document is in remarkable agreement with the general profile of the Cerebellar Cognitive Affective Syndrome. Malformations affecting the cerebellar vermis induce affective and social disorders and evolve towards more unfavourable pictures often associated with an autistic symptomatology. Malformations of cerebellar hemispheres are more frequently associated with selective neuropsychological deficits involving mainly executive functions and visuospatial and linguistic abilities. Motor deficits are generally less severe, and tend to improve slowly and progressively, in some cases reaching almost complete functionality. Finally, the overall favourable evolution with an onset of skills in advanced age in a consistent subset of subjects suggests that individual follow-ups should be performed in order to monitor the quality and stability of impairments and acquired abilities over time.

AMINO ACID CHANGES IN THE AMINO TERMINUS OF THE NA, K-ATPASE ALPHA-2 SUBUNIT ASSOCIATED TO FAMILIAL AND SPORADIC HEMIPLEGIC MIGRAINE

Clinical Genetics 2007;72:517-523 – Short Report

Tonelli A, Gallanti A, Bersano A, Cardin V, Ballabio E, Airoldi G, Redaelli F, Candelise L, Bresolin N, Bassi MT.

I.F. 2006: 3,140

Familial hemiplegic migraine (FHM) is a rare subtype of migraine with aura inherited with an autosomal dominant pattern. Here, we report the genetic analysis of four families and one sporadic case with hemiplegic migraine (HM) in whom we searched for mutations in the three genes associated with the disease CACNA1A, ATP1A2 and SCN1A. Two novel amino acid changes p.Arg65Trp and p.Tyr9Asn, in the Na,K-adenosine triphosphatase (ATPase) alpha-2 subunit encoded by the ATP1A2 gene, were found in one FHM family and in the sporadic case, respectively. These mutations are peculiar for their location in the extreme Nterminus, an uncommon mutation target in this protein. Low frequency of migraine attacks in all our mutant patients with low complexity of the associated aura symptoms in the sporadic case is also observed. Besides the two novel mutations, the data here reported confirm the involvement of ATP1A2 gene in the sporadic form of HM, while the negative results on the other families tested for all genes known in HM strengthen the hypothesis of the existence of at least another locus involved in FHM.

AUTOLOGOUS TRANSPLANTATION OF MUSCLE-DERIVED CD133+ STEM CELLS IN DUCHENNE MUSCLE PATIENTS

Cell Transplantation 2007;16(6):563-577

Torrente Y, Belicchi M, Marchesi C, D'Antona G, Cogiamanian F, Pisati F, Gavina M, Giordano R, Tonlorenzi R, Fagiolari G, Lamperti C, Porretti L, Lopa R, Sampaolesi M, Vicentini L, Grimoldi N, Tiberio F, Songa V, Baratta P, Prelle A, Forzenigo L, Guglieri M, Pansarasa O, Rinaldi C, Mouly V, Butler-Browne GS, Comi GP, Biondinetti P, Moggio M, Gaini SM, Stocchetti N, Priori A, D'Angelo MG, Turconi AC, Bottinelli R, Cossu G, Rebulla P, Bresolin N.

I.F. 2006: 3,482

Duchenne muscular dystrophy (DMD) is a lethal X-linked recessive muscle disease due to defect on the gene encoding dystrophin. The lack of a functional dystrophin in muscles results in the fragility of the muscle fiber membrane with progressive muscle weakness and premature death. There is no cure for DMD and current treatment options focus primarily on respiratory assistance, comfort care, and delaying the loss of ambulation. Recent works support the idea that stem cells can contribute to muscle repair as well as to replenishment of the satellite cell pool. Here we tested the safety of autologous transplantation of muscle-derived CD133+ cells in eight boys with Duchenne muscular dystrophy in a 7-month, double-blind phase I clinical trial. Stem cell safety was tested by measuring muscle strength and evaluating muscle structures with MRI and histological analysis. Timed cardiac and pulmonary function tests were secondary outcome measures. No local or systemic side effects were observed in all treated DMD patients. Treated patients had an increased ratio of capillary per muscle fibers with a switch from slow to fast myosin-positive myofibers.

LEVETIRACETAM IN NON-CONVULSIVE STATUS EPILEPTICUS IN CHILDHOOD: A CASE REPORT

Journal of Child Neurology 2007;22(5):639-641

Trabacca A, Profice P, Costanza MC, Gesualdi ME, De Rinaldis M.

I.F. 2006: 1,350

The authors report the case of a child with cerebral palsy and refractory epilepsy who developed nonconvulsive status epilepticus without acute medical cause treated successfully with levetiracetam. In accordance with other studies whose authors hypothesized that aggressive treatment may worsen the prognosis in elderly patients with nonconvulsive status epilepticus, the present authors successfully used a more conservative approach to the treatment of nonconvulsive status epilepticus in their patient. This case suggests that levetiracetam is a useful option for the treatment of nonconvulsive status epilepticus in childhood, in accordance with some authors who have described the anticonvulsant effects of levetiracetam in experimental status epilepticus and in status epilepticus in adults and in children with continuous spike waves during slow sleep.

HUNTINGTON'S DISEASE AND HDACI: WOULD SULPIRIDE AND VALPROATE BE OF THERAPEUTIC VALUE?

Medical Hypotheses 2007;69(4):964-965

Tremolizzo L, Rodriguez-Menendez V, Di

Francesco J, Sala G, Galbussera A, Appollonio I, Ferrarese C.

I.F. 2006: 1,299

Abstract non disponibile.

MULTIPLE BRAIN LESIONS WITH CENTRAL CALCIFICATIONS: CAN YOU HIT THE TARGET?

Neurological Sciences 2007;28 (5):285-286

Tremolizzo L, Galbussera A, Frigo M, Apale P, Fumagalli C, Appollonio I, Ferrarese C.

I.F. 2006: 0,894

Abstract non disponibile.

AN APPARENTLY SPORADIC CASE OF OCULOPHARYNGEAL MUSCULAR DYSTROPHY: THE FIRST ITALIAN REPORT

Neurological Sciences 2007;28:339-341

Tremolizzo L, Galbussera A, Tagliabue E, Fermi S, Bruttini M, Lamperti C, Moggio M, Appollonio I, Ferrarese C.

I.F. 2006: 0,894

Here we report the case of a 73-year-old Italian woman affected by genetically confirmed oculopharyngeal muscular dystrophy (OPMD) with a negative family history. As OPMD is usually transmitted as an autosomal-dominant meiotically stable trait, this case allows us to suggest that putative de novo OPMD mutations might occur more frequently than previously thought; moreover, when compatible with a proper clinical phenotype, OPMD might be included in the differential diagnosis even in the absence of a positive family history.

REPRESENTATION OF BODY IDENTITY AND BODY ACTIONS IN EXTRASTRIATE BODY AREA AND VENTRAL PREMOTOR CORTEX

Nature Neuroscience 2007;10(1):30-31

Urgesi C, Candidi M, Ionta S, Aglioti S.

I.F. 2006: 14,805

Although inherently linked, body form and body action may be represented in separate neural substrates. Using repetitive transcranial magnetic stimulation in healthy individuals, we show that interference with the extrastriate body area impairs the discrimination of bodily forms, and interference with the ventral premotor cortex impairs the discrimination of bodily actions. This double dissociation suggests that whereas extrastriate body area mainly processes actors' body identity, premotor cortex is crucial for visual discriminations of actions.

TRANSCRANIAL MAGNETIC STIMULATION REVEALS TWO CORTICAL PATHWAYS FOR VISUAL BODY PROCESSING

Journal of Neuroscience 2007;27(30):8023-8030

Urgesi C, Calvo-MB, Haggard P, Aglioti S.

I.F. 2006: 7,453

Visual recognition of human bodies is more difficult for upside down than upright presentations. This body inversion effect implies that body perception relies on configural rather than local processing. Although neuroimaging studies indicate that the visual processing of human bodies engages a large fronto-temporo-parietal network, information about the neural underpinnings of configural body processing is meager. Here, we used repetitive transcranial magnetic stimulation (rTMS) to study the causal role of premotor, visual, and parietal areas in configural processing of human bodies. Eighteen participants performed a delayed matching-to-sample task with upright or inverted static body postures. Event-related, dual-pulse rTMS was applied 150 ms after the sample stimulus onset, over left ventral premotor cortex (vPMc), right extrastriate body area (EBA), and right superior parietal lobe (SPL) and, as a control site, over the right primary visual cortex (V1). Interfering stimulation of vPMc significantly reduced accuracy of matching judgments for upright bodies. In contrast, EBA rTMS significantly reduced accuracy for inverted but not for upright bodies. Furthermore, a significant body inversion effect was observed after interfering stimulation of EBA and V1 but not of vPMc and SPL. These results demonstrate an active contribution of the fronto-parietal mirror network to configural processing of bodies and suggest a novel, embodied aspect of visual perception. In contrast, the local processing of the body, possibly based on the form of individual body parts instead of on the whole body unit, appears to depend on EBA. Therefore, we propose two distinct cortical routes for the visual processing of human bodies.

PARALLEL SPINAL PATHWAYS GENERATE THE MIDDLE-LATENCY N1 AND THE LATE P2 COMPONENTS OF THE LASER EVOKED POTENTIALS

Clinical Neurophysiology 2007;118(5):1097-1104

Valeriani M, Le Pera D, Restuccia D, De Armas L, Miliucci R, Betti V, Vigevano F, Tonali P.

I.F. 2006: 2,718

OBJECTIVE: To investigate the possible presence of multiple spino-thalamic pathways with different conduction velocities (CVs) in the human spinal cord. METHODS: Laser evoked potentials (LEPs) were recorded in 10 healthy subjects after stimulation of the dorsal midline at four vertebral level: C5, T2, T6, and T10. This method allowed us to minimize the influence of the conduction in the peripheral fibers and to calculate the spinal CV in two different ways: (1) the reciprocal of the slope of the regression line was obtained from the latencies of the different LEP components, and (2) the distance between C5 and T10 was divided by the latency difference of the responses at the two sites. In particular, we considered the middle-latency N1 potential (latencies of around 135, 150, 157, and 171 ms after stimulation at C5, T2, T6, and T10 levels, respectively), which is generated in the second somatosensory (SII) area, and the late P2 response (latencies of around 336, 344, 346, and 362 ms after stimulation at C5, T2, T6, and T10 levels, respectively), which is generated in the anterior cingulate cortex (ACC). RESULTS: The calculated CV of the spinal fibers generating the N1 potential (around 9 m/s) was significantly different ($P < 0.05$) from the one of the pathway producing the P2 response (around 13 m/s). CONCLUSIONS: Our results suggest that the N1 and the P2 LEP components are generated by two parallel spinal pathways. Significance: Both the N1 and P2 potentials should be recorded in the clinical routine since a dissociated abnormality of either response may be found in lesions of the nociceptive system not only in the brain, but also at spinal cord level.

MRI STUDY OF CORPUS CALLOSUM IN PATIENTS WITH BORDERLINE PERSONALITY DISORDER - A PILOT STUDY

Progress in Neuro-Psychopharmacology and Biological Psychiatry 2007;31:1519-1525

Zanetti MV, Soloff PLH, Nicoletti MA, Hatch JP, Brambilla P, Keshavan MS, Soares JC.

I.F. 2006: 2,584

This pilot study examined the integrity of the corpus callosum in a sample of patients with borderline personality disorder (BPD), as abnormalities in inter-hemispheric communication could possibly be involved in illness pathophysiology. We utilized magnetic resonance imaging (MRI) signal intensity (SI) and morphometric measures. Ten BPD and 20 healthy control subjects were assessed for current and past Axis I and Axis II comorbidities and histories of childhood abuse. Regional CC SI and areas were measured with semi-automated software from threedimensional gradient echo imaging scans. Analysis of covariance was conducted to evaluate the results. No significant differences were observed between BPD and controls in the SI or area of any CC region. Abnormalities in interhemispheric connectivity do not appear necessary for the development of BPD. Further studies with larger samples are needed to confirm this preliminary finding.

CORTICAL WHITE-MATTER MICROSTRUCTURE IN SCHIZOPHRENIA

British Journal of Psychiatry 2007;191:113-119

Andreone N, Tansella M, Cerini R, Versace A, Rambaldelli G, Perlini C, Dusi N, Pelizza L, Balestrieri M, Barbui C, Nosè M, Gasparini A, Brambilla P.

I.F. 2006: 5,436

BACKGROUND: Several, although not all, of the previous small diffusion-weighted imaging (DWI) studies have shown cortical white-matter disruption in schizophrenia. AIMS: To investigate cortical white-matter microstructure with DWI in a large community-based sample of people with schizophrenia. METHOD: Sixty-eight people with schizophrenia and 64 healthy controls underwent a session of DWI to obtain the apparent diffusion coefficient (ADC) of white-matter water molecules. Regions of interest were placed in cortical lobes. RESULTS: Compared with controls, the schizophrenia group had significantly greater ADCs in frontal, temporal and occipital white matter (analysis of covariance, $P < 0.05$). CONCLUSIONS: Our findings confirm the presence of cortical white-matter microstructure disruption in frontal and temporo-occipital lobes in the largest sample of people with schizophrenia thus for studied with this technique. Future brain imaging studies, together with genetic investigations, should further explore white-matter integrity and genes encoding myelin-related protein expression in people with first-episode schizophrenia and those at high risk of developing the disorder.

ANTERIOR CINGULATE VOLUMES IN SCHIZOPHRENIA: A SYSTEMATIC REVIEW AND A META-ANALYSIS OF MRI STUDIES

Schizophrenia Research 2007;93(1-3):1-12

Baiano M, David A, Versace A, Churchill R,

Balestrieri M, Brambilla P.

I.F. 2006: 4,264

OBJECTIVES: Several MRI studies have investigated the anterior cingulate in schizophrenia, as this is a key region for emotional processing and higher executive performances. A systematic review of structural MRI studies and a meta-analysis were conducted to explore whether anterior cingulate volumes are abnormal in patients with schizophrenia. METHOD: A systematic search strategy was used to identify eligible MRI studies. Thereafter, a meta-analysis was carried out by using a random effect model. Also, a meta-regression analysis was used to assess the influence of age, gender and slice thickness on effect sizes. RESULTS: The meta-analysis was performed on seven studies. These results showed that the anterior cingulate volumes were significantly reduced in patients compared to healthy controls. Significant heterogeneity between these studies was observed. The meta-regression demonstrated that the effect size was significantly related only to slice thickness. CONCLUSIONS: Our work confirmed the presence of abnormally reduced anterior cingulate volumes in schizophrenia. However, several methodological issues limited the interpretation of these findings. Among these were different MR acquisition parameters and the small size of the sample, which was mostly composed of chronic patients. Future MRI studies should be planned to better understand the functional expression of anterior cingulate structural abnormalities.

THE BEHAVIOURAL PHENOTYPE OF CORNELIA DE LANGE SYNDROME: A STUDY OF 56 INDIVIDUALS

Journal of Intellectual Disability Research 2007;51(9):671-681

Basile E, Villa L, Selicorni A, Molteni M.

I.F. 2006: 1,068

Background Few studies have investigated functional and behavioural variables of Cornelia de Lange Syndrome (CdLS) in a large sample of individuals. The aim of this study is to provide greater insight into the clinical, behavioural and cognitive characteristics that are associated with CdLS. Methods In total, 56 individuals with CdLS participated in the study. During hospitalization, their mothers received a number of questionnaires to complete. The behavioural phenotype was investigated using the following scales: Developmental Behaviour Scale Primary Carer Version; Autism Behaviour Checklist; Childhood Autism Rating Scale. Results Our participants demonstrated some behavioural characteristics that are frequently associated with CdLS (hyperactivity, attention disorder, anxiety, compulsive disorders, self-injurious behaviour and autistic-like features). Our findings demonstrate the variability of behavioural characteristics in CdLS in addition to highlighting the contribution of some variables to both the CdLS behavioural profile and the developmental trajectory of the behavioural pattern. Conclusions The behavioural characteristics identi- fied in our sample were correlated with some clinical and functional aspects (chronological age, cognitive level and clinical phenotype). The variability of the behavioural profile in CdLS reflected the wide variability in cognitive and adaptive functioning across individuals and led us to conclude that there may be multiple behavioural phenotypes associated with the syndrome. Further comparative studies between CdLS and individuals with intellectual disability or other genetic syndromes may help to provide further understanding of the behavioural phenotype of CdLS.

EFFECT OF THE CATECHOL-O-METHYLTRANSFERASE VALMET GENOTIPE ON CHILDREN'S EARLY PHASES OF FACIAL STIMULI PROCESSING

Genes, Brain and Behavior 2007;6(4):364-374

Battaglia M, Zanoni A, Giorda R, Pozzoli U, Citterio A, Beri S, Ogliari A, Nobile M, Marino C, Molteni M.

I.F. 2006: 4,385

The ability to process and identify human faces matures early in life, is universal and is mediated by a distributed neural system. The temporal dynamics of this cognitive-emotional task can be studied by cerebral visual event-related potentials (ERPs) that are stable from midchildhood onwards. We hypothesized that part of individual variability in the parameters of the N170, a waveform that specifically marks the early, precategorical phases of human face processing, could be associated with genetic variation at the functional polymorphism of the catechol-O-methyltransferase (val(158)met) gene, which influences information processing, cognitive control tasks and patterns of brain activation during passive processing of human facial stimuli. Forty-nine third and fourth graders underwent a task of implicit processing of other children's facial expressions of emotions while ERPs were recorded. The N170 parameters (latency and amplitude) were insensitive to the type of expression, stimulus repetition, gender or school grade. Although limited by the absence of met- homozygotes among boys, data showed

shorter N170 latency associated with the presence of 1-2 met158 alleles, and family-based association tests (as implemented in the PBAT version 2.6 software package) confirmed the association. These data were independent of the serotonin transporter promoter polymorphism and the N400 waveform investigated in the same group of children in a previous study. Some electrophysiological features of face processing may be stable from midchildhood onwards. Different waveforms generated by face processing may have at least partially independent genetic architectures and yield different implications toward the understanding of individual differences in cognition and emotions.

A GENETIC STUDY OF THE ACUTE ANXIOUS RESPONSE TO CARBON DIOXIDE STIMULATION IN MAN

Journal of Psychiatric Research 2007;41(11):906-917

Battaglia M, Ogliari A, Harris J, Spatola CAM, Pesenti-Gritti P, Reichborn-Kjennerud T, Torgersen S, Kringlen E, Tambs K.

I.F. 2006: 3,700

People with panic disorder-agoraphobia and their relatives often react anxiously to CO2-enriched gas mixtures. Available data are not suited to disentangle genetic from common environmental causes of familial aggregation of CO2 reactivity, nor provide quantitative estimations of the sources of trait variation. Three-hundred-forty-six twin pairs belonging to the general population-based Norwegian NIPH Mental Health Study underwent selfassessments of anxiety and of DSM-IV panic symptoms after inhalation of a 35%CO2–65%O2 mixture. Two thresholds were employed – at sample's 75th and 90th percentiles of responses – to define provoked panic attacks and to calculate polychoric correlations. Variance components were estimated by structural equation modelling (SEM). For definitions of responses based on the sum of all 13 panic symptoms, SEM could not discriminate between shared environmental versus genetic causes of familial resemblance for provoked attacks. For definitions of responses based on global anxiety, or on the sums of those symptoms (dyspnea, dizziness, palpitations) with highest variance post-CO2, the best-fitting models indicated additive genetic factors as the sole causes for within-family resemblance. Best-fit heritability estimates ranged from 0.42 to 0.57. Genetic and idiosyncratic environmental factors explain most of individual differences in reactivity to hypercapnia. Within-family similarities for this trait are largely explained by genetic determinants.

GREATER CORTICAL GRAY MATTER DENSITY IN LITHIUM-TREATED PATIENTS WITH BIPOLAR DISORDER

Biological Psychiatry 2007;62(1):7-16

Bearden CE, Thompson PM, Dalwani M, Hayashi KM, Lee AD, Nicoletti M, Trakhenbroit M, Glahn DC, Brambilla P, Sassi RB, Mallinger AG, Frank EK, David J, Soares JC.

I.F. 2006: 7,154

BACKGROUND: The neurobiological underpinnings of bipolar disorder are not well understood. Previous neuroimaging findings have been inconsistent; however, new methods for three-dimensional (3-D) computational image analysis may better characterize neuroanatomic changes than standard volumetric measures. METHODS: We used high-resolution magnetic resonance imaging and cortical pattern matching methods to map gray matter differences in 28 adults with bipolar disorder, 70% of whom were lithium-treated (mean age = 36.1 +/- 10.5; 13 female subject), and 28 healthy control subjects (mean age = 35.9 +/- 8.5; 11 female subjects). Detailed spatial analyses of gray matter density (GMD) were conducted by measuring local proportions of gray matter at thousands of homologous cortical locations. RESULTS: Gray matter density was significantly greater in bipolar patients relative to control subjects in diffuse cortical regions. Greatest differences were found in bilateral cingulate and paralimbic cortices, brain regions critical for attentional, motivational, and emotional modulation. Secondary region of interest (ROI) analyses indicated significantly greater GMD in the right anterior cingulate among lithium-treated bipolar patients (n = 20) relative to those not taking lithium (n = 8). CONCLUSIONS: These brain maps are consistent with previous voxel-based morphometry reports of greater GMD in portions of the anterior limbic network in bipolar patients and suggest neurotrophic effects of lithium as a possible etiology of these neuroanatomic differences.

DEVELOPMENT OF OROFACIAL PRAXIS OF CHILDREN FROM 4 TO 8 YEARS OF AGE

Perceptual and Motor Skills 2007;104:1355-1366

Bearzotti F, Tavano A, Fabbro F.

I.F. 2006: 0,333

Orofacial praxis is the ability to pian and execute movements or sequences of voluntary movements, meaningful or not, using the muscles 'of the pharyngo- buccofacial system or the orofacial region. An' original test was developed, the Orofacial Praxis Test, consisting of 36 gestures, 24 single and 12 complex, elicited through verbal and imitative request. The test was administered to 93 normal1y developing Italian children ages 4 to 8 yr. to assess devdopment of orofacial praxis. Analysis showed a progressive development of the orofacial praxic ability by type of gesture and examiner's request: (1) the imitation modality is more facilitating than a verbal request modality, especial1y for children ages 4 or 5 years; (2) a consistent mastery of sequences of gestures and oroverbal movements is in place by age 6 years. T}J.eanalysis of the orofacial region may be helpful in identifying persistent speech difficulties and developmental coordination disorders.

DNA METHYLATION REGULATES TISSUE SPECIFIC EXPRESSION OF SHANK3

Journal of Neurochemistry 2007;101(5):1380-1391

Beri S*, Tonna N*, Menozzi G, Bonaglia MC, Sala C, Giorda R.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 4,260

Tissue-specific gene expression can be controlled by epigenetic modifications such as DNA methylation. SHANK3, together with its homologues SHANK1 and SHANK2, has a central functional and structural role in excitatory synapses and is involved in the human chromosome 22q13 deletion syndrome. In this report, we show by DNA methylation analysis in lymphocytes, brain cortex, cerebellum and heart that the three SHANK genes possess several methylated CpG boxes, but only SHANK3 CpG islands are highly methylated in tissues where protein expression is low or absent and unmethylated where expression is present. SHANK3 protein expression is significantly reduced in hippocampal neurons after treatment with methionine, while HeLa cells become able to express SHANK3 after treatment with 5-Aza-2¢-deoxycytidine. Altogether, these data suggest the existence of a specific epigenetic control mechanism regulating SHANK3, but not SHANK1 and SHANK2, expression.

OVEREXPRESSION OF THE C-TYPE NATRIURETIC PEPTIDE (CNP) IS ASSOCIATED TO OVERGROWTH AND BONE ANOMALIES IN AN INDIVIDUAL WITH BALANCED T(2;7) TRANSLOCATION

Human Mutation 2007;28(7):724-731

Bocciardi R*, Giorda R*, Buttgereit J*, Gimelli S, Divizia MT, Beri S, Garofalo S, Tavella S, Lerone M, Zuffardi O, Bader M, Ravazzolo R, Gimelli G.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 6,473

Longitudinal bone growth is determined by the process of endochondral ossification in the cartilaginous growth plate, which is located at both ends of vertebrae and long bones and involves many systemic hormones and local regulators. We report the molecular characterization of a de novo balanced t(2;7)(q37.1;q21.3) translocation in a young female with Marfanoid habitus and skeletal anomalies. The translocation was characterized by fluorescence in situ hybridization (FISH), checked for other abnormalities by array-comparative genomic hybridization (CGH), and finally, the breakpoints were cloned, sequenced, and compared. Biochemical dosage was applied to study the possible mechanisms that may cause the proposita's phenotype. The breakpoint on chromosome 2 disrupts the hypothetical gene MGC42174 (HUGO-approved symbol DIS3L2) and is located in the proximity of the NPPC gene coding for C-type natriuretic peptide (CNP), a molecule that regulates endochondral bone growth. CNP plasma concentration was doubled in the proband compared to five normal controls, while NPPC was substantially overexpressed in her fibroblasts. A transgenic mouse generated to target NPPC overexpression in bone showed a phenotype highly reminiscent of the patient's phenotype. The breakpoint on chromosome 7 is localized proximally at about 75 kb from the COL1A2 gene. The COL1A2 allele on the derivative chromosome was strongly underexpressed in fibroblasts, but total collagen was not significantly different from controls. Several evidences support the conclusion that the proband's abnormal phenotype is associated with C-type natriuretic peptide overexpression. (c) 2007 Wiley-Liss, Inc.

SUBTELOMERIC TRISOMY 21Q: A NEW BENIGN CHROMOSOMAL VARIANT

European Journal of Medical Genetics 2007;50(1):54-59

Bonaglia MC, Marelli S, Gottardi G, Zucca C, Pramparo T, Giorda R, Grasso R, Borgatti R, Zuffardi O.

I. F. 2006: 1,614

The diagnosis of a subtelomeric rearrangement has immediate impact on counseling, particularly in the case of familial rearrangements. However, the existence of subtelomeric imbalances with absent phenotypic effects may hamper genetic counseling, particularly when the rearrangement has not been previously described. We report on a new subtelomeric polymorphism, consisting of a familial subtelomeric rearrangement of chromosome 19 resulting in distal trisomy for 21q, detected in a child with Angelman Syndrome (AS) due to an UBE3A mutation. This report shows that new, previously unknown, benign subtelomeric variants may complicate the correct clinical diagnosis.

CONTEXT PROCESSING PERFORMANCE IN BIPOLAR DISORDER PATIENTS

Bipolar Disorders 2007;9(3):230-237

Brambilla P, MacDonald III AW, Sassi RB, Johnson MK, Mallinger AG, Carter CS, Soares J.

I.F. 2006: 3,494

Objectives: Context processing is the adaptive control of current behavior through the use of prior context information. It has been found to be impaired in schizophrenia. Some studies have indicated that, compared with patients with schizophrenia, those with bipolar disorder (BPD) display a similar but less severe neuropsychological pattern of impairment. However, this cognitive dimension has not yet been examined in BPD patients in the existing literature. Methods: An expectancy version of the AX continuous performance test (AX-CPT) was administered to 15 bipolar outpatients and 26 healthy controls. Patients with schizophrenia, in which context processing deficits are known to occur, were used as a reference group. Results: Bipolar patients showed a context processing deficit relative to healthy controls, although this was less severe and generalized than in schizophrenia patients. Conclusions: These findings suggest there are milder impairments in context processing in BPD compared with schizophrenia. However, the severity of possible context processing deficits in BPD may have been underestimated in our sample of mostly euthymic outpatients.

CAN NEUROIMAGING STUDIES HELP US IN UNDERSTANDING THE BIOLOGICAL CAUSES OF SCHIZOPHRENIA?

International Review of Psychiatry 2007;19(4):313-314 - Editoriale

Brambilla P, Tansella M.

I.F. 2006: 0,908

Abstract non disponibile.

THE ROLE OF WHITE MATTER FOR THE PATHOPHYSIOLOGY OF SCHIZOPHRENIA

International Review of Psychiatry 2007;19(4):459-468

Brambilla P, Tansella M.

I.F. 2006: 0,908

Inter- and intra-hemispheric connectivity disturbances have been suggested to play a major role in schizophrenia. To this extent, diffusion weighted imaging (DWI) is a relatively new technique examining subtle white matter microstructure organization. DWI studies in schizophrenia strongly suggest that white matter communication is disrupted. This supports the hypothesis that there is a cortico-cortical and transcallosal altered connectivity in schizophrenia, which may be relevant for the pathophysiology and the cognitive disturbances of the disorder. Future longitudinal diffusion and functional imaging studies targeting brain communication together with genetic investigations should further characterize white matter pathology in schizophrenia and its relevance for the development of the illness.

NITRIC OXIDE: EMERGING CONCEPTS ABOUT ITS USE IN CELL-BASED THERAPIES

Expert Opinion on Investigational Drugs 2007;16(1):33-43

Brunelli S, Rovere-Querini P, Sciorati C, Manfredi AA, Clementi E.

I.F. 2006: 3,174

Regenerative medicine is an emerging clinical discipline in which cell-based therapies are used to restore the functions of damaged or defective tissues and organs. Along with the well-established use of cells derived from bone marrow or pancreatic islets, novel approaches of cell therapy have recently emerged that appear particularly promising; that is, those using cell-based vaccines and stem cells. This review focuses on the recent developments of these experimental therapeutic approaches and their drawbacks, with specific focus on dendritic cell vaccines in tumours and mesoangioblasts in muscular dystrophies. The authors discuss how the unique properties of a gaseous messenger, NO, may be exploited to overcome some of the drawbacks of these cell-based approaches in combined therapies based on NO-releasing drugs and cell delivery.

NITRIC OXIDE RELEASE COMBINED WITH NONSTEROIDAL ANTIINFLAMMATORY ACTIVITY PREVENTS MUSCULAR DYSTROPHY PATHOLOGY AND ENHANCES STEM CELL THERAPY

Proceedings of the National Academy of Sciences of the United States of America (PNAS) 2007;104(1):264-269

Brunelli S*, Sciorati C*, D'Antona G, Innocenzi A, Covarello D, Galvez BG, Perrotta C, Monopoli A, Sanvito F, Bottinelli R, Ongini E, Cossu G, Clementi E.

*Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 9,643

Duchenne muscular dystrophy is a relatively common disease that affects skeletal muscle, leading to progressive paralysis and death. There is currently no resolutive therapy. We have developed a treatment in which we combined the effects of nitric oxide with nonsteroidal antiinflammatory activity by using HCT 1026, a nitric oxide-releasing derivative of flurbiprofen. Here, we report the results of long-term (1-year) oral treatment with HCT 1026 of two murine models for limb girdle and Duchenne muscular dystrophies (alpha-sarcoglycan-null and mdx mice). In both models, HCT 1026 significantly ameliorated the morphological, biochemical, and functional phenotype in the absence of secondary effects, efficiently slowing down disease progression. HCT 1026 acted by reducing inflammation, preventing muscle damage, and preserving the number and function of satellite cells. HCT 1026 was significantly more effective than the corticosteroid prednisolone, which was analyzed in parallel. As an additional beneficial effect, HCT 1026 enhanced the therapeutic efficacy of arterially delivered donor stem cells, by increasing 4-fold their ability to migrate and reconstitute muscle fibers. The therapeutic strategy we propose is not selective for a subset of mutations; it provides ground for immediate clinical experimentation with HCT 1026 alone, which is approved for use in humans; and it sets the stage for combined therapies with donor or autologous, genetically corrected stem cells.

ARE PATIENTS WITH HEREDITARY SPASTIC PARAPLEGIA DIFFERENT FROM PATIENTS WITH SPASTIC DIPLEGIA DURING WALKING? GAIT EVALUATION USING 3D GAIT ANALYSIS

Functional Neurology 2007;22(1):23-28

Cimolin V, Piccinini L, D'Angelo MG, Turconi AC, Berti M, Crivellini M, Albertini G, Galli M.

I.F. 2006: 0,569

Patients with hereditary spastic paraplegia (HSP) often resemble patients with mild spastic diplegia (SD), although their motor limitations differ. The aim of this study was to analyse quantitatively the gait of HSP and SD subjects in order to define the gait pattern in HSP and the differences between the two conditions. Fifteen subjects with HSP, 40 patients with SD and 20 healthy subjects underwent gait analysis (GA). The spatio-temporal and kinematic parameters at the proximal joints were found to be similar in HSP and SD, whereas the most significant differences were found at the knee and ankle joints. Both groups displayed a tendency for knee hyperextension in the midstance phase, but the duration of this hyperextension was longer in the HSP patients. This study shows that GA complements traditional clinical evaluations, making it possible to distinguish, clearly, between motor ability in HSP and in SD patients; the duration of the knee hyperextension during midstance was found to discriminate between the two gait patterns.

ISOLATION AND CHARACTERIZATION OF MURINE NEURAL STEM/PROGENITOR CELLS BASED ON PROMININ-1 EXPRESSION

Experimental Neurology 2007;205(2):547-562

Corti S, Nizzardo M, Nardini M, Donadoni C, Locatelli F, Papadimitriou D, Salani S, Del Bo R, Ghezzi S, Strazzer S, Bresolin N, Comi GP.

I.F. 2006: 4,156

The identification of strategies for the isolation of neural stem cells (NSCs) has important implications for the understanding of their biology and the development of therapeutic applications. It has been previously described that human neural stem and progenitor cells (NSPCs) can be isolated from the central nervous system (CNS) using antibodies to prominin (CD133) and fluorescence-activated cell sorting (FACS). Although this antigen displayed an identical membrane topology in several human and murine tissues there was uncertainty as to the relationship between human and mouse prominin because of the low level of amino acid identity. Here we show that prominin expression can be used to identify and isolate also murine NSPCs from the developing or adult brain. Prominin is co-expressed with known neural stem markers like SOX 1-2, Musashi and Nestin. Moreover, neu-

rosphere-forming cells with multipotency and self-renewal capacity reside within the prominin-positive fraction. Transplantation experiments show that CD133-positive cells give rise to neurons and glial cells in vivo, and that many neurons display appropriate phenotypic characteristics of the recipient tissues. The demonstration that CD133 is a stem cell antigen for murine NSPCs as it is for human NSPCs is useful for the investigation of mammal neurogenesis and development of preclinical tests of NSPCs transplantation in mouse analogues of human diseases.

NEURAL STEM CELLS LEWISX+CXCR4+ MODIFY DISEASE PROGRESSION IN AN AMYOTROPHIC LATERAL SCLEROSIS MODEL

Brain 2007;130:1289-1305

Corti S, Locatelli F, Papadimitriou D, Del Bo R, Nizzardo M, Nardini M, Donadoni C, Salani S, Fortunato F, Strazzer S, Bresolin N, Comi GP.

I.F. 2006: 7,617

Amyotrophic lateral sclerosis (ALS) is a fatal neurological disease characterized by the degeneration of the motor neurons. We tested whether treatment of superoxide dismutase (SOD1)-G93A transgenic mouse, a model of ALS, with a neural stem cell subpopulation double positive for Lewis X and the chemokine receptor CXCR4 (LeX1CXCR4þ) can modify the disease's progression. In vitro, after exposure to morphogenetic stimuli, LeX1CXCR41 cells generate cholinergic motor neuron-like cells upon differentiation. LeX1CXCR41 cells deriving from mice expressing Green Fluorescent Protein in all tissues or only in motor neurons, after a period of priming in vitro, were grafted into spinal cord of SOD1-G93A mice. Transplanted transgenic mice exhibited a delayed disease onset and progression, and survived significantly longer than non-treated animals by 23 days. Examination of the spinal cord revealed integration of donorderived cells that differentiated mostly in neurons and in a lower proportion in motor neuron-like cells. Quantification of motor neurons of the spinal cord suggests a significant neuroprotection by LeX1CXCR41 cells. BothVEGF- and IGF1-dependent pathwayswere significantlymodulated in transplanted animals compared to controls, suggesting a role of these neurotrophins in MN protection. Our results support the therapeutic potential of neural stem cell fractions through both neurogenesis and growth factors release in motor neuron disorders.

CRIPTIC DELETIONS ARE A COMMON FINDING IN "BALANCED" RECIPROCAL AND COMPLEX CHROMOSOME REARRANGEMENTS: A STUDY OF 59 CASES

Journal of Medical Genetics 2007;44:750–762

De Gregori M, Ciccone R, Magini P, Pramparo T, Gimelli S, Messa J, Novara F, Vetro A, Rossi E, Maraschio P, Bonaglia MC, Anichini C, Ferrero GB, Silengo M, Fazzi E, Zatterale A, Fischetto R, Previderè C, Belli S, Turci A, Calabrese G, Bernardi F, Meneghelli E, Riegel M, Rocchi M, Guerneri S, Lalatta F, Zelante L, Romano C, Fichera M, Mattina T, Arrigo GZollino M, Giglio S, Lonardo F, Bonfante A, Ferlini A, Cifuentes F, Van Esch H, Liesbeth B, Schinzel A, Vermeesch JR, Zuffardi O.

I.F. 2006: 5,087

Using array comparative genome hybridisation (CGH) 41 de novo reciprocal translocations and 18 de novo complex chromosome rearrangements (CCRs) were screened. All cases had been interpreted as ''balanced'' by conventional cytogenetics. In all, 27 cases of reciprocal translocations were detected in patients with an abnormal phenotype, and after array CGH analysis, 11 were found to be unbalanced. Thus 40% (11 of 27) of patients with a ''chromosomal phenotype'' and an apparently balanced translocation were in fact unbalanced, and 18% (5 of 27) of the reciprocal translocations were instead complex rearrangements with .3 breakpoints. Fourteen fetuses with de novo, apparently balanced translocations, all but two with normal ultrasound findings, were also analysed and all were found to be normal using array CGH. Thirteen CCRs were detected in patients with abnormal phenotypes, two in women who had experienced repeated spontaneous abortions and three in fetuses. Sixteen patients were found to have unbalanced mutations, with up to 4 deletions. These results suggest that genome-wide array CGH may be advisable in all carriers of ''balanced'' CCRs. The parental origin of the deletions was investigated in 5 reciprocal translocations and 11 CCRs; all were found to be paternal. Using customised platforms in seven cases of CCRs, the deletion breakpoints were narrowed down to regions of a few hundred base pairs in length. No susceptibility motifs were associated with the imbalances. These results show that the phenotypic abnormalities of apparently balanced de novo CCRs are mainly due to cryptic deletions and that spermatogenesis

is more prone to generate multiple chaotic chromosome imbalances and reciprocal translocations than oogenesis.

SPG11: A CONSISTENT CLINICAL PHENOTYPE IN A FAMILY WITH HOMOZYGOUS SPATACSIN TRUNCATING MUTATION

Neurgenetics 2007;8:301–305

Del Bo R, Di Fonzo A, Ghezzi S, Locatelli F, Stevanin G, Costa A, Corti S, Bresolin N, Comi GP.

I.F. 2006 4,250

Hereditary spastic paraplegias (HSP) are a heterogeneous group of neurodegenerative disorders leading to progressive spasticity of the lower limbs. Here, we descrive clinical and genetic features in an Italian family affected by autosomal recessive HSP (ARHSP) with mental impairment and thin corpus callosum (TCC). In both affected subjects, genetic analysis revealed the presence of a homozygous small deletion (733_734delAT) leading to a frameshift (M245VfsX) within the coding region of SPG11 gene, encoding spatacsin. This finding is the first independent confirmation that spatacsin loss of function mutations cause ARHPS-TCC.

HIGH-FREQUENCY ECoG OSCILLATIONS IN THE SITE OF ONSET OF EPILEPTIC SEIZURES DURING SLEEP

Sleep Medicine 2007;8(1):96-97

Della Marca G, Vollovo C, Barba. C, Fuggetta MF, Restuccia D, Colicchio G.

I.F. 2006: 2,926

Abstract non disponibile.

NECTID MEDIATES SKELETAL MUSCLE REGENERATION BY PROMOTING MYOBLAST SURVIVAL AND DIFFERENTIATION

The Journal of Cell Biology 2007;179(2):305-319

Deponti D, Francois S, Baesso S, Sciorati C, Innocenzi A, Broccoli V, Muscatelli F, Meneveri R, Clementi E, Cossu G, Brunelli S.

I.F. 2006: 10,152

Regeneration of muscle fi bers that are lost during pathological muscle degeneration or after injuries is sustained by the production of new myofi bers. An important cell type involved in muscle regeneration is the satellite cell. Necdin is a protein expressed in satellite cell–derived myogenic precursors during perinatal growth. However, its function in myogenesis is not known. We compare transgenic mice that overexpress necdin in skeletal muscle with both wild-type and necdin null mice. After muscle injury the necdin null mice show a considerable defect in muscle healing, whereas mice that overexpress necdin show a substantial increase in myofi ber regeneration. We also fi nd that in muscle, necdin increases myogenin expression, accelerates differentiation, and counteracts myoblast apoptosis. Collectively, these data clarify the function and mechanism of necdin in skeletal muscle and show the importance of necdin in muscle regeneration.

SPHINGOSINE 1-PHOSPHATE MEDIATES PROLIFERATION AND SURVIVAL OF MESOANGIOBLASTS

Stem Cells 2007;25:1713-1719

Donati C, Cencetti F, Nincheri P, Bernacchioni C, Brunelli S, Clementi E, Cossu G, Bruni P.

I.F. 2006: 7,924

Mesoangioblasts are stem cells capable of differentiating in various mesodermal tissues and are presently regarded as suitable candidates for cell therapy of muscle degenerative diseases, as well as myocardial infarction. The enhancement of their proliferation and survival after injection in vivo could greatly improve their ability to repopulate damaged tissues. In this study, we show that the bioactive sphingolipid sphingosine 1-phosphate (S1P) regulates critical functions of mesoangioblast cell biology. S1P evoked a full mitogenic response in mesoangioblasts, measured by labeled thymidine incorporation and cell counting. Moreover, S1P strongly counteracted the apoptotic process triggered by stimuli as diverse as serum deprivation, C2-ceramide treatment, or staurosporine treatment, as assessed by cell counting, as well as histone-associated fragments and caspase-3 activity determinations. S1P acts both as an intracellular messenger and through specific membrane receptors. Realtime polymerase chain reaction analysis revealed that mesoangioblasts express the S1P-specific receptor S1P3 and, to a minor extent, S1P1 and S1P2. By using S1P receptor subtype-specific agonists and antagonists, we found that the proliferative response to S1P was mediated mainly by S1P2. By contrast, the antiapoptotic effect did not implicate S1P receptors. These findings demonstrate an important role of S1P in mesoangioblast proliferation and survival and indicate that targeting

modulation of S1P-dependent signalling pathways may be used to improve the efficiency of muscle repair by these cells. Disclosure of potential conflicts of interest is found at the end of this article.

LANGUAGE DISTURBANCES IN A GROUP OF PARTICIPANTS SUFFERING FROM DUCHENNE MUSCULAR DYSTROPHY: A PILOT STUDY

Perceptual and Motor Skills 2007;104(2):663-676

Fabbro F, Marini A, Felisari G, Comi GP, D'Angelo MG, Turconi AC, Bresolin N.

I.F. 2006: 0,333

Results from several studies suggest that the process of language acquisition may be altered in patients suffering from Duchenne Muscular Dystrophy. In this study, a group of 8 male participants with Duchenne Muscular Dystrophy (M age = 16 yr., SD = 4.7) underwent an extensive neuropsychological and language assessment. They also performed a discourse production task. Results showed mild mental retardation associated with a specific deficit in Verbal rather than Performance IQ. At the linguistic assessment, 7 of 8 participants showed moderate to severe difficulties on oral language processing with particularly impaired morphosyntactic competence.

MID1 MUTATION SCREENING IN A LARGE COHORT OF OPITZ G/BBB SYNDROME PATIENTS: 29 NOVEL MUTATIONS IDENTIFIED

Human Mutation 2007;28(2):206-207

Ferrentino R, Bassi MT, Chitayat D, Tabolacci E, Meroni G.

I.F. 2006: 6,473

Opitz G/BBB Syndrome (OS) is a multiple congenital anomaly disorder characterized by defects along the body midline. The disease is characterized by variable expressivity of signs that include hypertelorism, cleft lip and/or palate, laryngo-tracheo-esophageal abnormalities, cardiac defects, and hypospadias. OS patients also present with mental retardation and brain anatomical abnormalities. An autosomal dominant form mapping to chromosome 22 and an X-linked form of OS are known. The gene responsible for the X-linked form of OS, MID1, codes for a member of the Tripartite Motif family of E3 ubiquitin ligases. Here we report 29 novel mutations in 29 unrelated patients of a cohort of 140 male OS cases. These mutations are found in both familial and sporadic cases. They are scattered along the entire length of the gene and are represented by missense and nonsense mutations, insertions and deletions causing frame shift mutations, and deletion of either single exons or the entire gene. The variety of the mutations found confirms that loss-of-function is the mechanism underlying the OS phenotype. Moreover, the low percentage of MID1-mutated OS patients, 47% of the familial and 13% of the sporadic cases, suggests a wider genetic heterogeneity underlying the OS phenotype. (c) 2006 Wiley-Liss, Inc.

EVOLUTION OF NEUROLOGIC FEATURES IN WILLIAMS SYNDROME

Pediatric Neurology 2007;36(5):301-306

Gagliardi C, Martelli S, Burt Michael D, Borgatti R.

I.F. 2006: 1,542

As a part of a large multidisciplinary clinical and research follow-up study, 47 Williams syndrome patients underwent detailed neurologic testing. Because previous studies have documented the absence of major neurologic signs in Williams syndrome, the neurologic testing focused on soft signs. Previous findings of impairment of both gross and fine motor coordination were confirmed, and the presence of mild cerebellar and extrapyramidal signs was documented. In a 4-year follow-up study, an age-related pattern was revealed: soft extrapyramidal signs became more evident from 8 years of age and increased in the 14+ age group. The results are discussed according to a hypothesis related to the dopaminergic system involvement in Williams syndrome: anomalous organization or accelerated ageing process.

A LARGE ANALPHOID INVDUP(3)(Q22.3QTER) MARKER CHROMOSOME CHARACTERIZED BY ARRAY-CGH IN A CHILD WITH MALFORMATIONS, MENTAL RETARDATION, AMBIGUOUS GENITALIA AND BLASCHKO'S LINES

European Journal of Medical Genetics 2007;50(4):264-273

Gimelli G, Giorda R, Beri S, Gimelli S, Zuffardi O.

I.F. 2006: 1,614

We report a new case of mosaic chromosome 3-derived marker chromosome, present in fibroblasts but not in lymphocytes, found in a child with malformations, mental retardation and ambiguous ge-

nitalia. Cytogenetic and molecular analysis showed that the supernumerary invdup(3)(q22.3qter) chromosome was negative at FISH with alpha satellite probe. The presence of a functional neocentromere was confirmed by immunofluorescence with antibodies to centromere proteins (CENPs). Definition of the marker breakpoints has been done through array-CGH. The skin of the patient presented dyschromic areas ordered along Blaschko's lines. The invdup(3q) marker chromosome was present only in fibroblasts from the dark skin biopsy, while lymphocytes and fibroblasts from the normal skin showed a normal male karyotype. Expression of the HPS3 gene (MIM: 606118) was more than two times higher in dark skin fibroblasts. Neocentromeres are most often observed on chromosomal arm fragments that have separated from an endogenous centromere, and therefore actually confer mitotic stability to what would have been acentric fragments. To our knowledge, this invdup(3q) analphoid marker is the largest among the several reported so far. Parental origin and possible mode of formation have been defined by DNA polymorphisms studies. The size of the duplicated marker chromosome and its frequency and tissue distribution may be relevant to the severity of the propositus' phenotype.

TWO CLASSES OF LOW COPY REPEATS CO-MEDIATE A NEW RECURRENT REARRANGEMENT CONSISTING IN DUPLICATION AT 8p23.1 AND TRIPLICATION AT 8p23.2

Human Mutation 2007;28(5):459-468

Giorda R, Ciccone R, Gimelli G, Pramparo T, Beri S, Bonaglia MC, Giglio S, Genuardi M, Argente J, Rocchi M, Zuffardi O.

I.F. 2006: 6,473

We describe a new type of rearrangement consisting of the duplication of 8p23.1 and the triplication of 8p23.2 [dup trp(8p)] in two patients affected by mental retardation and minor facial dysmorphisms. Array-comparative genomic hybridization (CGH), fluorescence in situ hybridization (FISH), and genotyping of polymorphic loci allowed us to demonstrate that this rearrangement is mediated by the combined effects of two unrelated low-copy repeats (LCRs). The first set of LCRs consists of the two clusters of olfactory receptor genes (OR-REPs) lying at 8p23.1. The second type of LCRs consists of a 15-kb segmental duplication, lying in inverted orientation at 8p23.2 and enclosing a nonrepeated sequence of approximately 130 kb, named MYOM2-REP because of its proximity to the MYOM2 gene. The molecular characterization of a third case with a dicentric chromosome 8 demonstrated that the rearrangement had been generated by nonallelic homologous recombination between the two MYOM2-REPs. Based on our findings, we propose a model showing that a second recombination event at the level of the OR-REPs leads to the formation of the dup trp(8p) chromosome. This rearrangement can only arise during meiosis in heterozygous carriers of the polymorphic 8p23.1 inversion, whereas in subjects with noninverted chromosomes 8 or homozygous for the inversion only the dicentric chromosome can be formed. Our study demonstrates that nonallelic homologous recombination involving multiple LCRs can generate more complex rearrangements and cause a greater variety of genomic diseases. 2007 Wiley-Liss, Inc.

REORGANISATION OF THE SOMATOSENSORY SYSTEM AFTER EARLY BRAIN DAMAGE

Clinical Neurophysiology 2007;118(5):1110-1121

Guzzetta A, Bonanni P, Biagi L, Tosetti M, Montanaro D, Guerrini R, Cioni G.

I.F. 2006: 2,718

OBJECTIVE: To examine the reorganisation of the somatosensory system after early brain lesions. METHODS: We studied 12 young patients with congenital hemiplegia. Causative lesions were brain malformations, periventricular injuries and cortico-subcortical lesions. We explored the somatosensory system using evoked potentials, fMRI during sensory stimulation and clinical assessment of sensory function. To correlate sensory and motor function, we also performed transcranial magnetic stimulation, fMRI of hand movement and assessment of motor function by means of Melbourne test. RESULTS: Eleven patients showed a perilesional reorganisation of primary somatosensory function, as expressed by short latency potentials following stimulation of the paretic hand; in a remaining patient, delayed latency responses (N27.1) were only elicited over the ipsilateral undamaged hemisphere. Five of the eleven patients with perilesional somatosensory representation of the affected hand showed contralesional shifting of motor function, thus exhibiting sensory-motor dissociation. Significant correlation was found between sensory deficit and fMRI activation during sensory stimulation. CONCLUSIONS: In subjects with early

brain lesions, somato-sensory function is generally reorganised within the affected hemisphere. A contralesional shifting is uncommon and poorly efficient in function restoration. SIGNIFICANCE: This study confirms and further explores the difference in reorganisation capabilities of the motor and sensory system following early brain injury of different etiologies and timing.

TESTING THE 8-SYNDROME STRUCTURE OF THE CHILD BEHAVIOR CHECKLIST IN 30 SOCIETIES

Journal of Clinical Child & Adolescent Psychology 2007;36(3):405-417

Ivanova MY, Dobrean A, Dopfner M, Erol N, Fombonne E, Fonseca A. Castro, Frigerio A, Grietens H, Hannesdottir H, Kanbayashi Y, Lambert MC, Achenbach TM, Larsson B, Leung P, Liu X, Minaei A, Mulatu MS, Novik T, Ja Oh K, Roussos A, Sawyer M, Simsek Z, Dumenci L, Steinhausen HC, Winkler MC, Wolanczyk T, Yang H-J, Zilber NZR, Verhulst FC, Rescorla LA, Almqvist F, Weintraub S, Bilenberg N, Bird H, Chen WJ.

I.F. 2006: 2,338

There is a growing need for multicultural collaboration in child mental health services, training, and research. To facilitate such collaboration, this study tested the 8-syndrome structure of the Child Behavior Checklist (CBCL) in 30 societies. Parents' CBCL ratings of 58,051 6- to 18-year-olds were subjected to confirmatory factor analyses, which were conducted separately for each society. Societies represented Asia; Africa; Australia; the Caribbean; Eastern, Western, Southern, and Northern Europe; the Middle East; and North America. Fit indices strongly supported the correlated 8-syndrome structure in each of 30 societies. The results support use of the syndromes in diverse societies.

TESTING THE TEACHER'S REPORT FORM SYNDROMES IN 20 SOCIETIES

School Psychology Review 2007;36(3):468-483

Ivanova MY, Achenbach TM, Rescorla LA, Dumenci L, Almqvist F, Bathiche M, Bilenberg N, Bird H, Domuta A, Erol N, Fombonne E, Fonseca A. Castro, Frigerio A, Kanbayashi Y, Lambert MC, Leung P, Liu X, Minaei A, Roussos A, Simsek Z, Weintraub S, Wolanczyk T, Zubrick SR, Zukauskiene R, Verhulst F.

I.F. 2006: 0,905

Standardized assessment instrument developed in one society are often used in other societies. However it is important to determinate empirically how assessment instruments developed in one society function in others. The present study tested the fit of the Teacher's Report form syndrome structures in 20 diverse societies using data for 30,030 6- to 15-year-old students from Asia; Australia; the Caribbean; eastern, western, southern and northern Europe; and the Middle East. A correlated seven-syndrome model and a hierarchical Attention Problems Model were tested separately in each of the 20 societies via confirmatory factor analyses.The result supported the fit of the models in the tested societies.

CLINICAL AND MOLECULAR HETEROGENEITY IN ITALIAN PATIENTS AFFECTED BY COHEN SYNDROME

Journal of Human Genetics 2007;52(12):1011-1017

Katzaki E, Pescucci C, Uliana V, Papa FT, Ariani F, Meloni I, Priolo M, Selicorni A, Milani D, Fischetto R, Celle ME, Grasso R, Dallapiccola B, Brancati F, Bordignon M, Tenconi R, Federico A, Mari F, Renieri A, Longo I.

I.F. 2006: 2,205

Cohen syndrome is an autosomal recessive disorder with variability in the clinical manifestations, characterized by developmental delay, visual disability, facial dysmorphisms and intermittent neutropenia. We described a cohort of 10 patients affected by Cohen syndrome from nine Italian families ranging from 5 to 52 years at assessment. Characteristic age related facial changes were well documented. Visual anomalies, namely retinopathy and myopia, were present in 9/10 patients (retinopathy in 9/10 and myopia in 8/10). Truncal obesità has been described in all patients older than 6 years (8/8). DNA samples from all patients were analyzed for mutations in COH1 by DHPLC. We detected 15 COH1 alterations most of them were truncating mutations, only one being a missense change. Partial gene deletions have been found in two families. Most mutations were private. Two were already reported in the literature just once. A single base deletion leading to p.T3708fs3769, never reported before, was found in three apparently unrelated families deriving from a restricted area of the Veneto's lowland, between Padova town and Tagliamento river, in heterozygous state. Given the geographical conformation of this region, which is

neither geographically or culturally isolated, a recent origin of the mutation could be hypothesized.

INHIBITORY EFFECT OF VOLUNTARY MOVEMENT PREPARATION ON CUTANEOUS HEAT PAIN AND LASER-EVOKED POTENTIALS

European Journal of Neuroscience 2007;25(6):1900-1907

Le Pera D, Brancucci A, De Armas L, Del Percio C, Miliucci R, Babiloni C, Restuccia D, Rossini PM, Valeriani M.

I.F. 2006: 3,709

In our study, preparation of voluntary movement was used to physiologically activate the motor cortex areas and the effect of this activation on CO2 laser-evoked potentials (LEPs) was explored. LEPs were recorded from 31 scalp electrodes in 10 healthy subjects after painful stimulation of the right C6–C7 skin dermatomes. LEP stimuli were delivered in the time interval between a visual warning stimulus followed after 1 s. by an imperative stimulus. The imperative stimulus triggered: (i) no task in the baseline condition (Pain); (ii) flexion–extension movements of the second finger of the right hand in the movement condition (Pain + Movement); (iii) cognitive task (mathematic computation) in the distraction condition (Pain + Cognition). The experimental conditions were also repeated durino application of laser stimuli on the left C6–C7 skin dermatomes. Compared with the baseline condition (no task required), durino preparation of right-hand voluntary movement there was a significant reduction in LEP amplitude and subjective pain rating after right- but not after left-hand stimulation, which suggests that the observed effect cannot be attributed to a nonspecific reduction in attention toward painful stimulus. During preparation of a cognitive task, LEP amplitude was reduced compared to baseline. Our results represent the first neurophysiological suggestion that physiological activation of the motor cortex, occurring during movement preparation, inhibits cortical pain processing by a centrifugal mechanism.

TRANSGENIC FRUIT-FLIES EXPRESSING A FRET-BASED SENSOR FOR IN VIVO IMAGING OF CAMP DYNAMICS

Cellular Signalling 2007;2296–2303

Lissandron V, Rossetto MG, Erbguth K, Fiala A, Daga A, Zaccolo M.

I.F. 2006: 4,887

3'–5'-cyclic adenosine monophosphate (cAMP) is a ubiquitous intracellular second messenger that mediates the action of various hormones and neurotransmitters and influences a plethora of cellular functions. In particular, multiple neuronal processes such as synaptic plasticity underlying learning and memory are dependent on cAMP signalling cascades. It is now well recognized that the specificity and fidelity of cAMP downstream effects are achieved through a tight temporal as well as spatial control of the cAMP signals. Approaches relying on real-time imaging and Fluorescence Resonance Energy Transfer (FRET)-based biosensors for direct visualization of cAMP changes as they happen in intact living cells have recently started to uncover the fine details of cAMP spatio-temporal signalling patterns. Here we report the generation of transgenic fruit-flies expressing a FRET-based, GFP-PKA sensor and their use in real-time optical recordings of cAMP signalling both ex vivo and in vivo in adult and developing organisms. These transgenic animals represent a novel tool for understanding the physiology of the cAMP signalling pathway in the context of a functioning body.

FAS SMALL INTERFERING RNA REDUCES MOTONEURON DEATH IN AMYOTROPHIC LATERAL SCLEROSIS MICE

Annals of Neurology 2007;62(1):81-92

Locatelli F*, Corti S*, Papadimitriou D, Fortunato F, Del Bo R, Donadoni C, Nizzardo M, Nardini M, Salani S, Ghezzi S, Strazzer S, Bresolin N, Comi GP.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 8,051

OBJECTIVE: Amyotrophic lateral sclerosis (ALS) is a progressive, fatal neurodegenerative disease characterized by selective motoneuron death. Understanding of the molecular mechanisms that trigger and regulate motoneuron degeneration could be relevant to ALS and other motoneuron disorders. This study investigates the role of Fas-linked motoneuron death in the pathogenesis of ALS. METHODS: We performed in vitro and in vivo small interfering RNA-mediated interference, by silencing the Fas receptor on motoneurons that carry the superoxide dismutase-1 (SOD1)-G93A mutation. RESULTS: We observed a significant reduction in Fas expression at messenger RNA ($p < 0.001$) and protein levels. Treated motoneurons demonstrated an increase in survival and a reduction in cytochrome c release from mi-

tochondria. In vivo, continuous intrathecal administration of Fas small interfering RNA by an osmotic minipump improved motor function and survival in SOD1-G93A mice (mean increase, 18 days; $p < 0.0001$). Treated mice showed a significant reduction in Fas and Fas mediators p38 mitogen-activated protein kinase, neuronal nitric oxide synthase, and caspase-8. INTERPRETATION: Fas silencing interferes with motoneuron-specific downstream death pathways and results in increased motoneuron survival and amelioration of the SOD1-G93A phenotype, suggesting new possible strategies for molecular therapy of ALS.

ENDOSCOPIC ANATOMY OF THE CEREBRAL AQUEDUCT

Neurosurgery 2007;61(Operative Neurosurgery - Supplement):ONS-1-ONS-6

Longatti P, Fiorindi A, Perin A, Martinuzzi A.

I.F. 2006: 2,692

OBJECTIVE: What is known about the cerebral aqueduct is derived mainly from the legacy of classic histology and from the most recent advanced neuroimaging technologies. In fact, although this important structure is frequently glimpsed by neurosurgeons, only limited anatomic contributions have been added by microsurgery to its direct in vivo description. A review of our surgical experience in navigating the fourth ventricle prompted us to revisit the classical anatomic descriptions of the aqueduct and compare them using the novel perspective of neuroendoscopy. METHODS: We reviewed video recordings of 65 transaqueductal explorations of the fourth ventricle using flexible endoscopes, which were performed in our center to treat various pathological conditions. Forty-one patients were selected as being more informative for anatomic description. They include 21 patients with communicating normal pressure hydrocephalus, 6 patients with intraventricular hemorrhage, 5 patients with membranous obstruction of the foramen of Magendie, 5 patients with trapped fourth ventricle as evidenced after aqueductoplasty, 3 patients with colloid cysts, and 1 patient with craniopharyngioma with apparently normal aqueduct, which was navigated to aspirate small fragments of colloid and tiny clots. RESULTS: Patients with normal-sized third ventricles confirmed the typical triangular shape of the aqueductal adytum, whereas all pathological aqueducts invariably had an oval contour. The posterior commissure, a faint trace of the median sulcus, and the rubral eminences were the structures invariably noticed. Five segments of the aqueduct were always identifiable: the adytum, first constriction, ampulla, second constriction, and posterior part or egressus. CONCLUSION: Neuroendoscopy provides a novel perspective into the inner aqueductal wall and supplies an incomparable view of the intracanalicular anatomic structures.

INDICATORS OF THEORY OF MIND IN NARRATIVE PRODUCTION: A COMPARISON BETWEEN INDIVIDUALS WITH GENETIC SYNDROMES AND TYPICALLY DEVELOPING CHILDREN

Clinical Linguistics & Phonetics 2007;21(1):37-53

Lorusso ML, Galli R, Libera L, Gagliardi C, Borgatti R, Hollebrandse B.

I.F. 2006: 0,693

It is a matter of debate whether the development of theory of mind (ToM) depends on linguistic development or is, rather, an expression of cognitive development. The study of genetic syndromes,

which are characterized by intellectual impairment as well as by different linguistic profiles, may provide useful information with respect to this issue. The present study compares indicators of ToM

in the narrative production of individuals with Cornelia de Lange syndrome, Down syndrome, Williams syndrome and typically developing children, matched on sex and mental age. Statistical comparisons of data obtained from a qualitative analysis of the narrative production of the different

groups confirm the presence of distinctive patterns, mainly related to the effective use of personal pronouns. The analysis of correlations among storytelling variables and other cognitive and linguistic variables suggests that the relationship between language development, cognitive development, and the emergence of ToM cannot be reduced to unidirectional causal links.

EVALUATION OF NARRATIVE ABILITIES IN PATIENTS SUFFERING FROM DUCHENNE MUSCULAR DYSTROPHY

Brain and Language 2007;102(1):1-12

Marini A, Lorusso ML, D'Angelo MG, Civati F, Turconi AC, Fabbro F, Bresolin N.

I.F. 2006: 2,317

The present work investigated cognitive, linguistic and narrative abilities in a group of children suffe-

ring from Duchenne Muscular Dystrophy, an allelic X-linked recessive disorder caused by mutations in the gene encoding dystrophin. The patients showed mildly reduced IQ with lower Verbal than Performance Intelligence Quotient and were mildly affected in visual attention and short-term memory processing. At the linguistic assessment, neither receptive (word comprehension) nor expressive (naming tasks and fluency) lexical abilities were impaired. However, their narratives were qualitatively inferior with respect to those produced by a group of typically developing children. Their speech samples were characterized by the presence of fewer verbs and complete sentences. It is suggested that the reduced production of complete sentences is due to a selective problem in verb argument structure generation. Since the lack of dystrophin is assumed to produce effects on the maturation of the cerebellum, whose involvement has been recently suggested in verb and syntactic processing, these findings may lend indirect support to the hypothesis of a cerebellar-cortical circuit specialized in verb and sentence production.

PATTERNS OF LANGUAGE IMPROVEMENT IN ADULTS WITH NON-CHRONIC NON-FLUENT APHASIA AFTER SPECIFIC THERAPIES

Aphasiology 2007;21(2):164-186

Marini A, Caltagirone C, Pasqualetti P, Carlomagno S.

I.F. 2006: 0,882

Abstract non disponibile.

ASSOCIATION OF SHORT-TERM MEMORY WITH A VARIANT WITHIN DYX1C1 IN DEVELOPMENTAL DYSLEXIA

Genes, Brain and Behavior 2007;6:640-646

Marino C, Citterio A, Giorda R, Facoetti A, Menozzi G, Vanzin L, Lorusso ML, Nobile M, Molteni M.

I.F. 2006: 4,385

A substantial genetic contribution in the etiology of developmental dyslexia (DD) has been well documented with independent groups reporting a susceptibility locus on chromosome 15q. After the identification of the DYX1C1 gene as a potential candidate for DD, several independent association studies reported controversial results. We performed a family-based association study to determine whether the DYX1C1 single nucleotide polymorphisms (SNPs) that have been associated with DD before, that is SNPs '23GA' and '1249GT', influence a broader phenotypic definition of DD. A significant linkage disequilibrium was observed with 'Single Letter Backward Span' (SLBS) in both single-marker and haplotype analyses. These results provide further support to the association between DD and DYX1C1 and it suggests that the linkage disequilibrium with DYX1C1 is more saliently explained in Italian dyslexics by short-term memory, as measured by 'SLBS', than by the categorical diagnosis of DD or other related phenotypes.

CHRONIC THERAPY FOR MCARDLE DISEASE: THE RANDOMIZED TRIAL WITH ACE INHIBITOR

Acta Myologica 2007;26(1):64-66

Martinuzzi A, Liava A, Trevisi E, Antoniazzi L, Frare M.

I.F. 2006: 0,000

Abstract non disponibile.

SEVERE HEAD INJURY IN EARLY INFANCY: ANALYSIS OF CAUSES AND POSSIBLE PREDICTIVE FACTORS FOR OUTCOME

Childs Nervous System 2007;23(8):873-880

Marton E, Mazzucco M, Nascimben E, Martinuzzi A, Longatti P.

I.F. 2006: 1,257

OBJECT: The aim of this study was to analyse the causes and prognostic factors for outcome in severe traumatic brain injuries (TBI) in early infancy. MATERIALS AND METHODS: We present a retrospective study on 16 infants aged less than 12 months observed over the last 20 years in our department for severe brain injury. Infants were evaluated by the Children Coma Scale (CCS). We assessed Glasgow Outcome Scale (GOS) at discharge and at 12 months after discharge. CONCLUSIONS: The main causes of trauma were domestic accidents followed by car accidents. The highest positive correlation was found between the GOS score at 1 year and the presence of hypoxia and hypotension at admission, the presence of hyperglycaemia at 24 h and the occurrence of major clotting disorders. A significant but weaker correlation was found with the CCS at admission, the occurrence of early post-traumatic seizures and the length of stay in the intensive care unit.

ANALYSIS OF THE DYNAMICAL BEHAVIOUR OF THE EEG RHYTHMS DURING A TEST OF SUSTAINED ATTENTION

Conf Proc IEEE Eng Med Biol Soc. 2007;2007:1298-301

Molteni E, Bianchi AM, Butti M, Reni G, Zucca C.

I.F 2006: 0,94

In clinical routine, the evaluation of sustained attention is often performed analyzing behavioral data collected during specific tests. It is not common to match such analyses with a detailed examination of the subject's simultaneous electroencephalographic (EEG) activity, and particularly its frequency content. In this study, 9 healthy volunteers underwent a modified Conners' CPT test, while their EEG were contemporarily recorded. Spectral power was calculated for each of the recorded EEG signals, with particular attention to frequency bands that are traditionally reported in literature. Then Compressed Spectral Array (CSA) sequence of spectra was plotted, and the analysis of the variability of the rhythms was carried out. Evaluation of the obtained results shows that the nine subjects shared a progressive backshift of alpha rhythm during the accomplishment of the CPT test. Moreover, beta and gamma activities were stronger in the right than in the left hemisphere. An intense and widespread decrease in EEG spectral power during test performing became visible in many subjects. Statistical analysis provided evidence that EEG activity correlates with the test behavioral results in many cerebral areas. For this reason, we encourage further investigations of the combined employment of tests and EEG recording during the clinical assessment of sustained attention performance.

FRONTO-LIMBIC BRAIN STRUCTURES IN SUICIDAL AND NON-SUICIDAL FEMALE PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Molecular Psychiatry 2007;12(4):360-366

Monkul ES, Hatch JP, Nicoletti M, Spence S, Brambilla P, Lacerda ALT, Sassi RB, Mallinger AG, Keshavan MS, Soares JC.

I.F. 2006: 11,804

Our knowledge about the neurobiology of suicide is limited. It has been proposed that suicidal behavior generally requires biological abnormalities concomitant with the personality trait of impulsivity/aggression, besides an acute psychiatric illness or psychosocial stressor. We investigated fronto-limbic anatomical brain abnormalities in suicidal and non-suicidal adult female patients with unipolar depression. Our sample consisted of seven suicidal unipolar patients, 10 non-suicidal unipolar patients and 17 healthy female comparison subjects. The criterion for suicidality was one or more documented lifetime suicide attempts. A 1.5T GE Signa Imaging System running version Signa 5.4.3 software was used to acquire the magnetic resonance imaging images. All anatomical structures were measured blindly, with the subjects' identities and group assignments masked. We used analysis of covariance with age and intracranial volume as covariates and the Tukey–Kramer procedure to compare suicidal patients, non-suicidal patients and healthy comparison subjects. Suicidal patients had smaller right and left orbitofrontal cortex gray matter volumes compared with healthy comparison subjects. Suicidal patients had larger right amygdala volumes than non-suicidal patients. Abnormalities in the orbitofrontal cortex and amygdala in suicidal patients may impair decision-making and predispose these patients to act more impulsively and to attempt suicide.

PREFRONTAL GRAY MATTER INCREASES IN HEALTHY INDIVIDUALS AFTER LITHIUM TREATMENT: A VOXEL-BASED MORPHOMETRY STUDY

Neuroscience Letters 2007;429(1):7-11

Monkul ES, Matsuo K, Nicoletti MA, Dierschke N, Hatch JP, Dalwani M, Brambilla P, Caetano S, Sassi RB, Mallinger AG, Soares JC.

I.F. 2006: 2,092

The objective of this study was to test the hypothesis that 4 weeks of lithium administration would be associated with changes in brain gray and white matter volumes in healthy individuals. Thirteen right-handed healthy volunteers (6 females, mean age = 25.9±10.0 years) were studied. 3D SPGR MRIs (TR = 25 ms, TE = 5 ms, slice-thickness = 1.5 mm) were acquired using a 1.5 T GE Signa Imaging System, at baseline and after 4 weeks of lithium administration at therapeutically relevant doses. Optimized voxel-based morphometry (VBM) analyses were conducted. Left and right dorsolateral prefrontal cortex and left anterior cingulate gray matter volumes increased significantly following lithium administration. Total white matter volume was increased, whereas total brain volume and total gray matter volume were not significantly changed following 4 weeks of lithium. Lithium

treatment resulted in prefrontal regional gray matter volume increases in healthy volunteers, as well as increases in total white matter volume. Whether these changes are mediated by neurotrophic/neuroprotective or osmotic effects remains unknown.

DEFECTIVE MITOCHONDRIAL BIOGENESIS: A HALLMARK OF THE HIGH CARDIOVASCULAR RISK IN THE METABOLIC SYNDROME?

Circulation Research 2007;100:795-806

Nisoli E, Clementi E, Carruba MO, Moncada S.

I.F. 2006: 9,854

The metabolic syndrome is a group of risk factors of metabolic origin that are accompanied by increased risk for type 2 diabetes mellitus and cardiovascular disease. These risk factors include atherogenic dyslipidemia, elevated blood pressure and plasma glucose, and a prothrombotic and proinflammatory state. The condition is progressive and is exacerbated by physical inactivity, advancing age, hormonal imbalance, and genetic predisposition. The metabolic syndrome is a particularly challenging clinical condition because its complex molecular basis is still largely undefined. Impaired cell metabolism has, however, been suggested as a relevant pathophysiological process underlying several clinical features of the syndrome. In particular, defective oxidative metabolism seems to be involved in visceral fat gain and in the development of insulin resistance in skeletal muscle. This suggests that mitochondrial function may be impaired in the metabolic syndrome and, thus, in the consequent cardiovascular disease. We have recently found that mitochondrial biogenesis and function are enhanced by nitric oxide in various cell types and tissues, including cardiac muscle. Increasing evidence suggests that this mediator acts as a metabolic sensor in cardiomyocytes. This implies that a defective production of nitric oxide might be linked to dysfunction of the cardiomyocyte metabolism. Here we summarize some recent findings and propose a hypothesis for the high cardiovascular risk linked to the metabolic syndrome.

SOCIOECONOMIC STATUS MEDIATES THE GENETIC CONTRIBUTION OF THE DRD4 AND 5-HTTLPR POLYMORPHISMS TO EXTERNALIZATION IN PRE-ADOLESCENCE

Development and Psychopathology 2007;19 (2007), 1147–1160

Nobile M, Giorda R, Marino C, Carlet O, Pastore V, Vanzin L, Bellina M, Molteni M, Battaglia M.

I.F. 2006: 2,709

The impact of socioeconomic status (SES) and genetic polymorphisms on individual differences for externalized behaviors have often been investigated separately in studies of children and adults. In a general population sample of 607 Italian preadolescents, we examined the independent and joint effects of SES and the dopamine receptor D4 (DRD4) and serotonin transporter linked promoter region (5-HTTLPR) polymorphisms upon rule-breaking and aggressive behaviors measured with the Child Behavior CheckList/6–18. We found evidence, which was based on both one locus and two-loci genotype analyses, that low SES and DRD4 long and 5-HTTLPR long alleles, both alone and in interaction, are associated with higher aggressive behavior scores. The effects were similar but more modest and limited to one locus genotype analyses for rule-breaking behavior. Consistent with studies that showed the effects of societal moderators on the heritability of externalized behaviors across different segments of the population, we suggest that diminished social constraints associated with low parental SES may act as enhancers of the genetic influence of specific DRD4 and 5-HTTLPR alleles over aggressive behaviors in preadolescence.

NITRIC OXIDE BOOSTS CHEMOIMMUNOTHERAPY VIA INHIBITION OF ACID SPHINGOMYELINASE IN A MOUSE MODEL OF MELANOMA

Cancer Research 2007;67(16):7559-7564

Perrotta C, Bizzozero L, Falcone S, Rovere-Querini P, Prinetti A, Schuchman EH, Sonnino S, Manfredi A, Clementi E.

I.F. 2006: 7,656

Cisplatin is one of the most effective anticancer drugs, but its severe toxic effects, including depletion of immune-competent cells, limit its efficacy. We combined the systemic treatment with cisplatin with intratumor delivery of dendritic cells (DC) previously treated ex vivo with a pulse of nitric oxide (NO) released by the NOdonors (z)-1-[2-(2-aminoethyl)-N-(2- ammonioethyl)amino]-diazen-1-ium-1,2-diolate or isosorbide dinitrate. We found that this chemoimmunotherapy, tested in the B16 mouse model of melanoma, was significantly more efficacious than cisplatin alone, leading to tumor

regression and animal survival at low doses of cisplatin that alone had no effect. Tumor cure was not observed when combining cisplatin with DCs not exposed to NOdonors, indicating the key role of the pretreatment with NO. We investigated the mechanisms responsible for the synergic effect of NO-treated DCs and cisplatin and found that NO-treated DCs were protected both in vitro and in vivo from cisplatin-induced cytotoxicity.Cisplatin triggered DC apoptosis through increased expression and activation of acid sphingomyelinase; pretreatment of DCs with NOdonors prevented such activation and inhibited activation of the downstream proapoptotic events, including generation of ceramide, activation of caspases 3 and 9, and mitochondrial depolarization. The effects of NOwer e mediated through generation of its physiologic messenger, cyclic GMP. We conclude that NOand NOgener ating drugs represent promising tools to increase the efficacy of chemoimmunotherapies in vivo, promoting the survival and increasing the function of injected cells by targeting a key pathway in cisplatin-induced cytotoxicity.

THE ITALIAN XLMR BANK: A CLINICAL AND MOLECULAR DATABASE

Human Mutation 2007;28(1):13-18

Pescucci C, Caselli R, Mari F, Speciale C, Ariani E, Bruttini M, Sampieri K, Mencarelli MA, Scala E, Longo I, Artuso R, Renieri A, Meloni I, XLMR Italian Network (Bassi MT, Borgatti R)

I.F. 2006: 6,473

Mental retardation (MR) is a nonprogressive condition characterized by a significant impairment of intellectual capabilities with deficit of cognitive and adaptive functioning and onset before 18 years. Mental retardation occurs in about 2 to 3% of the general population and it is estimated that 25 to 35% of the cases may be due to genetic causes. Among these ''genetic'' MR, 25 to 30% are probably due to mutations in a gene on the X chromosome (X-linked mental retardation, XLMR). Given the genetic heterogeneity of XLMR, the availability of a considerable number of patients with accurate phenotypic classification is a crucial factor for research. The X-linked Mental Retardation Italian Network, which has been active since 2003, has collected detailed clinical information and biological samples from a vast number of MR patients. Collected samples and clinical information are inserted within the XLMR bank, a comprehensive molecular and clinical web-based database available at the address http://xlmr.unisi.it. The database is organized in three distinct parts. Part I and II contain several electronic schedules to register information on the family, the phenotypic description, the photographs, and a 20 sec movie of the patient. Part III allows the registration of molecular analyses performed on each case; samples and clinical data are usable via password-restricted access. Clinical and molecular centers interested in joining the network may request a password by simply contacting the Medical Genetics of the University of Siena. The XLMR bank is an innovative biological database that allows the collection of molecular and clinical data, combines descriptive and iconographic resources, and represents a fundamental tool for researchers in the field of mental retardation.

QUANTIFICATION OF ENERGY EXPENDITURE DURING GAIT IN CHILDREN AFFECTED BY CEREBRAL PALSY

Europa Medicophysica 2007;43:7-12

Piccinini L, Cimolin V, Galli M, Berti M, Crivellini M, Turconi AC.

I.F. 2006: 0,000

AIM: Children affected by cerebral palsy (CP) are generally characterised by some movement limitations and abnormalities that compromised gait pattern. These disabilities during deambulation may lead to excessive energy cost and so to a compromised energy efficiency. METHODS: In this study oxygen expenditure was evaluated during walking in 20 children affected by CP and in 20 healthy children, using Cosmed K4b2 (Cosmed, Italy). From obtained data about energy consumption, some parameters (heart rate, energy expenditure index, oxygen consumption, oxygen cost) were extracted, first in order to quantify energy cost during gait in pathological and healthy subjects and then to underline differences between the 2 groups of children. RESULTS: In particular, the results obtained revealed that heart rate (bpm) and oxygen consumption (mL/kg/min) mean values didn't differ significantly between normal subjects and those with CP; instead, energy expenditure index (b/m) and oxygen cost (mL/kg/m) presented higher mean values rather than control group at a statistically level and so they revealed to be significant parameters, in order characterized energy expenditure in children affected by CP. CONCLUSIONS: This inefficiency characteristic of CP deambulation is probably directly connected to the presence of simultaneous contraction of agonist and antagonist muscle in these patients.

INTRON SIZE IN MAMMALS: COMPLEXITY COMES TO TERMS WITH ECONOMY

Trends in Genetics 2007;23(1):20-24

Pozzoli U, Menozzi G, Comi GP, Cagliani R, Bresolin N, Sironi M.

I.F. 2006: 9,95

Different and contrasting models have been proposed to explain intron size evolution in mammals. Here, we demonstrate that intron and intergenic size per se has no adaptive role in gene expression regulation but reflects the need to preserve conserved intronic elements. Although the amount of non-coding functional elements explains the within-genome size variation of intergenic spacers, we show that an additional, additive pressure has been acting on highly expressed introns to reduce the cost of their transcription.

CONSISTENCY OF TEACHER-REPORTED PROBLEMS FOR STUDENTS IN 21 COUNTRIEST

School Psychology Review 2007;36(1):91-110

Rescorla LA, Achenbach TM, Ginzburg S, Ivanova MY, Dumenci L, Almqvist F, Bathiche M, Bilenberg N, Bird H, Domuta A, Erol N, Fombonne E, Fonseca AC, Frigerio A, Kanbayashi Y, Lambert MC, Liu X, Leung P, Minaei A, Roussos A, Simsek Z, Weintraub S, Weisz J, Wolanczyk T, Zubrick SR, Zukauskiene R, Verhulst F.

I.F. 2006: 0,905

This study compared teachers' ratings of behavioral and emotional problems on the Teacher's Report Form for general population samples in 21 countries {N = 30,957). Correlations between internal consistency coefficients in different countries averaged .90. Effect.s of country on scale scores ranger from 3% to 13%. Gender effects ranged from < 1% to 5%. and age effects were all <1%. With great consistency across countries, scores were higher for boys than for girls on eight scales: Total Problems; Externalizing; the Attentino Problems, Rule-Breaking Behavior, and Aggressive Behavior syndromes; and Diagnostic and Statistical Manual (DSM)-onented Attention Deficit Hyperactivity Problems, Oppositional Defiant Problems, and Conduct Problems. Correlations between mean item ratings in different countries averaged .74. Teacher's Report Form results were thus similar across 21 very diverse countries, despite differences across these countries in school systems, models of pedagogy, and curricula.

BEHAVIORAL AND EMOTIONAL PROBLEMS REPORTED BY PARENTS OF CHILDREN AGES 6 TO 16 IN 31 SOCIETIES

Journal of Emotional and Behavioral Disorders 2007;15(3):130-142

Rescorla LA, Achenbach TM, Ivanova MY, Dumenci L, Almqvist FK, Bilenberg N, Bird H, Chen WJ, Dobrean A, Dopfner M, Erol N, Fombonne E, Fonseca AC, Frigerio A, Grietens H, Hannesdottir H, Kanbayashi Y, Lambert MC, Larsson B, Leung P, Liu X, Minaei A, Mulatu MS, Novik T, Oh Kyung-J, Roussos A, Sawyer M, Simsek Z, Steinhausen H-C, Weintraub S, Weisz J, Winkler MC, Wolanczyk T, Yang H.-J, Zilber N, Zukauskiene R, Verhulst F.

I.F. 2006: 1,143

This study compared parents' ratings of behavioral and emotional problems on the Child Behavior Checklist (Achenbach, 1991; Achenbach & Rescorla, 2001) for general population samples of children ages 6 to 16 from 31 societies (N = 55,508). Effect sizes for society ranged from .03 to .14. Effect sizes for gender were ≤ .01, with girls generally scoring higher on Internalizing problems and boys generally scoring higher on Externalizing problems. Effect sizes for age were ≤ .01 and varied across types of problems.Total Problems scores for 19 of 31 societies were within 1 SD of the overall mean of 22.5. Bisociety correlations for mean item scores averaged .74. The findings indicate that parents' reports of children's problems were similar in many ways across highly diverse societies. Nonetheless, effect sizes for society were larger than those for gender and age,indicating the need to take account of multicultural variations in parents' reports of children's problems.

MODULATION OF HIGH-FREQUENCY (600 HZ) SOMATOSENSORY-EVOKED POTENTIALS AFTER rTMS OF THE PRIMARY SENSORY CORTEX

European Journal of Neuroscience 2007;26(8):2349–2358

Restuccia D, Ulivelli M, De Capua A, Bartalini S, Rossi S.

I.F. 2006: 3,709

Somatosensory inputs to the primary sensory cortex (S1) after median nerve stimulation include temporally overlapping parallel processing, as reflected by standard low-frequency somatosensory-evoked potentials (LF-SEPs) and high-frequency

SEPs (HFSEPs), the latter being more sensitive to arousal and to other rapid adaptive changes. Experimental data suggest that cortical HFSEPs are formed by two successive pre- and postsynaptic components, respectively, generated in the terminal part of thalamocortical radiation (early burst) and in specialized neuronal pools within S1 (later burst).In eight healthy subjects, slow (1 Hz) or rapid (10 Hz) repetitive transcranial magnetic stimulations (rTMS), which are known to induce opposite changes on cortical excitability, applied on S1 did not modify LF-SEPs, while HF-SEPs showed a series of dissociate changes in the early and later high-frequency burst, moreover occurring with a different time-course. Slow rTMS caused an immediate and lasting decrease of the later burst activity, coupled with an immediate increase of the earlier part of the burst, suggesting that inhibition of cortical excitability triggered opposite, compensatory effects at subcortical levels; rapid rTMS induced a delayed increase of later HF-SEPs, leaving unaltered the earlier subcortical burst.Findings causally demonstrate that LF- and HF-SEPs reflect two distinct functional pathways for somatosensory input processing, and that early and late high-frequency burst do actually reflect the activity of different generators, as suggested by experimental data. Possible underlying neurophysiological phenomena are discussed.

CEREBELLAR DAMAGE IMPAIRS DETECTION OF SOMATOSENSORY INPUT CHANGES. A SOMATOSENSORY MISMATCH-NEGATIVITY STUDY

Brain 2007;130(1):276-287

Restuccia D, Della Marca G, Valeriani M, Leggio MG, Molinari M.

I.F. 2006: 7,617

Several recent studies support the view that the cerebellum's contribution to sensory processing is not limited tomovement regulation. In a previous paper (Restuccia D, Valeriani M, Barba C, Le Pera D, Capecci M, Filippini V, Molinari M. Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. Brain 2001; 124: 757–68) we showed that the cerebellum influences somatosensory input processing at very early stages. The present study was aimed at verifying whether an analogous influence is also exerted at higher levels. For some time it has been known that in the auditory modality a specific event-related potential (ERP), that is, mismatch negativity (MMN), reflects preattentive detection of changes in the incoming stimulus by comparing the new stimulus with sensory memory traces. To test the cerebellar influence on the processing of incoming somatosensory stimuli we first verified whether the electrical stimulation of fingers, according to an 'oddball' paradigm within a stimulus-ignored condition, was able to elicit event-related components specifically linked to the preattentive detection of change. We analysed scalp responses obtained from eight healthy volunteers during frequent and rare electrical stimulation of the first and fifth finger of the left hand, respectively. To ensure that responses to deviant stimuli were due to changes in detection mechanisms, rather than to activation of new afferents, we also analysed responses to rare stimulation alone ('standard-omitted' condition). The 'oddball' stimulation was able to elicit a parieto-occipital extra negativity that was different in scalp

distribution and latency from the N140 response to the 'standard-omitted' stimulation. We considered that this response was related to changes in detection mechanisms and labelled it somatosensory mismatch negativity (S-MMN). When the same procedure was applied to six patients with unilateral cerebellar lesions we found that the S-MMN was clearly abnormal after stimulation of the affected hand (ipsilateral to the affected cerebellar hemisphere). Earlier ERPs, as well as ERPs elicited during the 'standard-omitted' condition, were fully normal. Present data indicate that cerebellar processing is involved in preattentive detection of somatosensory input changes. In conclusion, this study demonstrates the reliability of S-MMN recordings and indicates that subjects with cerebellar damage may be impaired in the cortical processing of incoming somatosensory inputs.

GIANT SUBCORTICAL HIGH-FREQUENCY SEPS IN IDIOPATHIC GENERALIZED EPILEPSY: A PROTECTIVE MECHANISM AGAINST SEIZURES?

Clinical Neurophysiology 2007;118(1):60-68

Restuccia D, Valeriani M, Della Marca G.

I.F. 2006: 2,718

OBJECTIVE: Recently, we found that high-frequency somatosensory evoked potentials (HF-SEPs), which are modulated by arousal-related structures, were abnormally enhanced during N-REM sleep in two seizure-free IGE patients [Restuccia D, Rubino M, Valeriani M, Della Marca G. Increase of brainstem high-frequency SEP subcomponents

during light sleep in seizure-free epileptic patients. Clin Neurophysiol 2005; 116: 1774-1778]. Here, we aimed at verifying whether similar HF-SEP abnormalities were significantly correlated to the clinical outcome in a larger population of untreated IGE patients. METHODS: Patients were classified as Juvenile Myoclonic epilepsy (JME; six patients) and Childhood or Juvenile Absence epilepsy (CAE and JAE, six patients). They were untreated because newly diagnosed, or because seizure-free. HF-SEPs from patients were compared with those obtained from 21 healthy volunteers. RESULTS: HF-SEPs were abnormally enhanced in all seizure-free CAE-JAE patients, whereas they were normal in all JME patients and in CAE-JAE patients with frequent seizures. Not only scalp distribution, but also dipolar source analysis suggested a subcortical origin for these enhanced subcomponents, possibly in the brainstem. CONCLUSIONS: The enhancement of HF-SEPs might reflect the hyperactivity of arousal-related brainstem structures; such an enhancement was found in all seizure-free CAE-JAE patients, while it was never observed in JME patients. SIGNIFICANCE: We speculate that the hyperactivity of arousal-related brainstem structures might account for the different clinical outcome among IGE subsyndromes.

A GENERAL POPULATION TWIN STUDY OF THE CBCL/6-18 DSM-ORIENTED SCALES

Journal of the American Academy of Child and Adolescent Psychiatry 2007;46(5):619-627

Spatola CAM, Fagnani C, Pesenti-Gritti P, Ogliari A, Stazi MA, Battaglia M.

I.F. 2006: 4,767

OBJECTIVE: To explore the contributions of genetic and environmental influences to individual variation and covariation of the Child Behavior Checklist (CBCL) DSM-oriented scales (DOS) originally proposed by Achenbach and associates in 2001. Method: A classic twin study of 398 twin pairs ages 8 to 17 years belonging to the population-based Italian Twin Registry, assessed by parents using the CBCL for Ages 6 to 18 (CBCL/6Y18). Results: Univariate analyses showed that compared with the classic CBCL/6Y18 empirical subscales, the DOS have higher heritability (lowest 0.54 for Anxiety Problems, highest 0.71 for Conduct Problems) and simpler causal structure in that the phenotypic variance was satisfactorily explained by additive genetic and unique environmental factors only. Multivariate analyses showed that the causes of phenotypic correlation among the different DOS can be attributed to one common genetic factor and to two idiosyncratic environmental factors, each loading differently on the Internalizing (Anxiety and Affective Problems) and the Externalizing (Attention-Deficit/Hyperactivity, Oppositional Defiant, and Conduct Problems) CBCL/6Y18 DOS. CONCLUSIONS: Several common risk factors of both genetic and environmental nature can simultaneously affect a child_s proneness to develop the psychopathological signs and symptoms captured by the CBCL/6Y18 DOS.

LANGUAGE AND SOCIAL COMMUNICATION IN CHILDREN WITH CEREBELLAR DYSGENESIS

Folia Phoniatrica et Logopedia 2007;59(4):201-209

Tavano A, Fabbro F, Borgatti R.

I.F. 2006: 0,655

OBJECTIVE: Acquired cerebellar lesions in children and adults may determine deficits of executive functions, visuoperceptual skills, expressive language and modulation of affect; a complex pattern termed ‘cerebellar cognitive affective syndrome’. However, the long-term sequelae of malformative cerebellar lesions have yet to be systematically investigated, particularly in children. The purpose of this study was to present preliminary longitudinal data on the development of language and social communication skills in children with congenital malformations confined to the cerebellum. PATIENTS AND METHODS: Five children (3 males, 2 females) with cerebellar malformations confined to the cerebellum were selected. Three patients presented with cerebellar hypoplasia involving the vermis and the hemispheres, while the remaining 2 had a malformation affecting only the cerebellar hemispheres. Neurobehavioral and language development were traced through access to available clinical data. RESULTS: In the patients with cerebellar vermis malformation, language and social communicative skills were affected to a variable extent: 1 patient did not present with social disturbances during development. Those with hemispheric cerebellar lesions presented with selective linguistic impairments. CONCLUSIONS: The neurobehavioral profile of children with cerebellar malformations supports a key role of the cerebellum in language acquisition and affect regulation as distinguished functional domains. Copyright 2007 S. Karger AG, Basel.

DISORDERS OF COGNITIVE AND AFFECTIVE DEVELOPMENT IN CEREBELLAR MALFORMATIONS

Brain 2007;130:2646-2660

Tavano A, Grasso R, Gagliardi C, Triulzi F, Bresolin N, Fabbro F, Borgatti R.

I.F. 2006: 7,617

Acquired cerebellar lesions in adults and children can lead to the development of a complex behavioural pattern termed 'Cerebellar Cognitive Affective Syndrome' (Schmahmann and Sherman, Brain, 1998; 121: 561 ^ 79), which is characterized by reduced cognitive efficiency associated with specific neuropsychological deficits (executive and visuospatial disorders), expressive language disorders (mild agrammatism and anomia) and affective disorders with blunting of affect. It is not known whether a symptomatological picture such as this can also be found in congenital cerebellar malformations.We studied the behavioural developmental profile of 27 patients including children and adults with congenital malformations confined to the cerebellum, the largest studied sample to date. Extensive clinical and neuropsychological investigations highlight the presence of a wide range of disorders supporting the important role played by the cerebellumin the acquisition of higher-order cognitive and affective skills.The type and extent of cerebral reorganization processes in the presence of malformative lesions are difficult to predict andmay possibly account for the variability of clinical phenotypes. It is, therefore, more difficult to identify a syndromic picture defined as exactly as is the case with acquired lesions.However, the pattern of deficits that we document is in remarkable agreement with the general profile of the Cerebellar Cognitive Affective Syndrome. Malformations affecting the cerebellar vermis induce affective and social disorders and evolve towards more unfavourable pictures often associated with an autistic symptomatology. Malformations of cerebellar hemispheres are more frequently associated with selective neuropsychological deficits involving mainly executive functions and visuospatial and linguistic abilities.Motor deficits are generally less severe, and tend to improve slowly and progressively, in some cases reaching almost complete functionality. Finally, the overall favourable evolution with an onset of skills in advanced age in a consistent subset of subjects suggests that individual follow-ups should be performed in order to monitor the quality and stability of impairments and acquired abilities over time.

AMINO ACID CHANGES IN THE AMINO TERMINUS OF THE NA, K-ATPASE ALPHA-2 SUBUNIT ASSOCIATED TO FAMILIAL AND SPORADIC HEMIPLEGIC MIGRAINE

Clinical Genetics 2007;72:517-523 – Short Report

Tonelli A, Gallanti A, Bersano A, Cardin V, Ballabio E, Airoldi G, Redaelli F, Candelise L, Bresolin N, Bassi MT.

I.F. 2006: 3,140

Familial hemiplegic migraine (FHM) is a rare subtype of migraine with aura inherited with an autosomal dominant pattern. Here, we report the genetic analysis of four families and one sporadic case with hemiplegic migraine (HM) in whom we searched for mutations in the three genes associated with the disease CACNA1A, ATP1A2 and SCN1A. Two novel amino acid changes p.Arg65Trp and p.Tyr9Asn, in the Na,K-adenosine triphosphatase (ATPase) alpha-2 subunit encoded by the ATP1A2 gene, were found in one FHM family and in the sporadic case, respectively. These mutations are peculiar for their location in the extreme Nterminus, an uncommon mutation target in this protein. Low frequency of migraine attacks in all our mutant patients with low complexity of the associated aura symptoms in the sporadic case is also observed. Besides the two novel mutations, the data here reported confirm the involvement of ATP1A2 gene in the sporadic form of HM, while the negative results on the other families tested for all genes known in HM strengthen the hypothesis of the existence of at least another locus involved in FHM.

AUTOLOGOUS TRANSPLANTATION OF MUSCLE-DERIVED CD133+ STEM CELLS IN DUCHENNE MUSCLE PATIENTS

Cell Transplantation 2007;16(6):563-577

Torrente Y, Belicchi M, Marchesi C, D'Antona G, Cogiamanian F, Pisati F, Gavina M, Giordano R, Tonlorenzi R, Fagiolari G, Lamperti C, Porretti L, Lopa R, Sampaolesi M, Vicentini L, Grimoldi N, Tiberio F, Songa V, Baratta P, Prelle A, Forzenigo L, Guglieri M, Pansarasa O, Rinaldi C, Mouly V, Butler-Browne GS, Comi GP, Biondinetti P, Moggio M, Gaini SM, Stocchetti N, Priori A, D'Angelo MG, Turconi AC, Bottinelli R, Cossu G, Rebulla P, Bresolin N.

I.F. 2006: 3,482

Duchenne muscular dystrophy (DMD) is a lethal X-linked recessive muscle disease due to defect on the gene encoding dystrophin. The lack of a func-

tional dystrophin in muscles results in the fragility of the muscle fiber membrane with progressive muscle weakness and premature death. There is no cure for DMD and current treatment options focus primarily on respiratory assistance, comfort care, and delaying the loss of ambulation. Recent works support the idea that stem cells can contribute to muscle repair as well as to replenishment of the satellite cell pool. Here we tested the safety of autologous transplantation of muscle-derived CD133+ cells in eight boys with Duchenne muscular dystrophy in a 7-month, double-blind phase I clinical trial. Stem cell safety was tested by measuring muscle strength and evaluating muscle structures with MRI and histological analysis. Timed cardiac and pulmonary function tests were secondary outcome measures. No local or systemic side effects were observed in all treated DMD patients. Treated patients had an increased ratio of capillary per muscle fibers with a switch from slow to fast myosin-positive myofibers.

LEVETIRACETAM IN NON-CONVULSIVE STATUS EPILEPTICUS IN CHILDHOOD: A CASE REPORT

Journal of Child Neurology 2007;22(5):639-641

Trabacca A, Profice P, Costanza MC, Gesualdi ME, De Rinaldis M.

I.F. 2006: 1,350

The authors report the case of a child with cerebral palsy and refractory epilepsy who developed nonconvulsive status epilepticus without acute medical cause treated successfully with levetiracetam. In accordance with other studies whose authors hypothesized that aggressive treatment may worsen the prognosis in elderly patients with nonconvulsive status epilepticus, the present authors successfully used a more conservative approach to the treatment of nonconvulsive status epilepticus in their patient. This case suggests that levetiracetam is a useful option for the treatment of nonconvulsive status epilepticus in childhood, in accordance with some authors who have described the anticonvulsant effects of levetiracetam in experimental status epilepticus and in status epilepticus in adults and in children with continuous spike waves during slow sleep.

HUNTINGTON'S DISEASE AND HDACI: WOULD SULPIRIDE AND VALPROATE BE OF THERAPEUTIC VALUE?

Medical Hypotheses 2007;69(4):964-965

Tremolizzo L, Rodriguez-Menendez V, Di Francesco J, Sala G, Galbussera A, Appollonio I, Ferrarese C.

I.F. 2006: 1,299

Abstract non disponibile.

MULTIPLE BRAIN LESIONS WITH CENTRAL CALCIFICATIONS: CAN YOU HIT THE TARGET?

Neurological Sciences 2007;28 (5):285-286

Tremolizzo L, Galbussera A, Frigo M, Apale P, Fumagalli C, Appollonio I, Ferrarese C.

I.F. 2006: 0,894

Abstract non disponibile.

AN APPARENTLY SPORADIC CASE OF OCULOPHARYNGEAL MUSCULAR DYSTROPHY: THE FIRST ITALIAN REPORT

Neurological Sciences 2007;28:339-341

Tremolizzo L, Galbussera A, Tagliabue E, Fermi S, Bruttini M, Lamperti C, Moggio M, Appollonio I, Ferrarese C.

I.F. 2006: 0,894

Here we report the case of a 73-year-old Italian woman affected by genetically confirmed oculopharyngeal muscular dystrophy (OPMD) with a negative family history. As OPMD is usually transmitted as an autosomal-dominant meiotically stable trait, this case allows us to suggest that putative de novo OPMD mutations might occur more frequently than previously thought; moreover, when compatible with a proper clinical phenotype, OPMD might be included in the differential diagnosis even in the absence of a positive family history.

REPRESENTATION OF BODY IDENTITY AND BODY ACTIONS IN EXTRASTRIATE BODY AREA AND VENTRAL PREMOTOR CORTEX

Nature Neuroscience 2007;10(1):30-31

Urgesi C, Candidi M, Ionta S, Aglioti S.

I.F. 2006: 14,805

Although inherently linked, body form and body action may be represented in separate neural substrates. Using repetitive transcranial magnetic stimulation in healthy individuals, we show that interference with the extrastriate body area impairs the discrimination of bodily forms, and interference with the ventral premotor cortex impairs the discrimination of bodily actions. This double dissociation suggests

that whereas extrastriate body area mainly processes actors' body identity, premotor cortex is crucial for visual discriminations of actions.

TRANSCRANIAL MAGNETIC STIMULATION REVEALS TWO CORTICAL PATHWAYS FOR VISUAL BODY PROCESSING

Journal of Neuroscience 2007;27(30):8023-8030

Urgesi C, Calvo-MB, Haggard P, Aglioti S.

I.F. 2006: 7,453

Visual recognition of human bodies is more difficult for upside down than upright presentations. This body inversion effect implies that body perception relies on configural rather than local processing. Although neuroimaging studies indicate that the visual processing of human bodies engages a large fronto-temporo-parietal network, information about the neural underpinnings of configural body processing is meager. Here, we used repetitive transcranial magnetic stimulation (rTMS) to study the causal role of premotor, visual, and parietal areas in configural processing of human bodies. Eighteen participants performed a delayed matching-to-sample task with upright or inverted static body postures. Event-related, dual-pulse rTMS was applied 150 ms after the sample stimulus onset, over left ventral premotor cortex (vPMc), right extrastriate body area (EBA), and right superior parietal lobe (SPL) and, as a control site, over the right primary visual cortex (V1). Interfering stimulation of vPMc significantly reduced accuracy of matching judgments for upright bodies. In contrast, EBA rTMS significantly reduced accuracy for inverted but not for upright bodies. Furthermore, a significant body inversion effect was observed after interfering stimulation of EBA and V1 but not of vPMc and SPL. These results demonstrate an active contribution of the fronto-parietal mirror network to configural processing of bodies and suggest a novel, embodied aspect of visual perception. In contrast, the local processing of the body, possibly based on the form of individual body parts instead of on the whole body unit, appears to depend on EBA. Therefore, we propose two distinct cortical routes for the visual processing of human bodies.

PARALLEL SPINAL PATHWAYS GENERATE THE MIDDLE-LATENCY N1 AND THE LATE P2 COMPONENTS OF THE LASER EVOKED POTENTIALS

Clinical Neurophysiology 2007;118(5):1097-1104

Valeriani M, Le Pera D, Restuccia D, De Armas L, Miliucci R, Betti V, Vigevano F, Tonali P.

I.F. 2006: 2,718

OBJECTIVE: To investigate the possible presence of multiple spino-thalamic pathways with different conduction velocities (CVs) in the human spinal cord. METHODS: Laser evoked potentials (LEPs) were recorded in 10 healthy subjects after stimulation of the dorsal midline at four vertebral level: C5, T2, T6, and T10. This method allowed us to minimize the influence of the conduction in the peripheral fibers and to calculate the spinal CV in two different ways: (1) the reciprocal of the slope of the regression line was obtained from the latencies of the different LEP components, and (2) the distance between C5 and T10 was divided by the latency difference of the responses at the two sites. In particular, we considered the middle-latency N1 potential (latencies of around 135, 150, 157, and 171 ms after stimulation at C5, T2, T6, and T10 levels, respectively), which is generated in the second somatosensory (SII) area, and the late P2 response (latencies of around 336, 344, 346, and 362 ms after stimulation at C5, T2, T6, and T10 levels, respectively), which is generated in the anterior cingulate cortex (ACC). RESULTS: The calculated CV of the spinal fibers generating the N1 potential (around 9 m/s) was significantly different ($P < 0.05$) from the one of the pathway producing the P2 response (around 13 m/s). CONCLUSIONS: Our results suggest that the N1 and the P2 LEP components are generated by two parallel spinal pathways. Significance: Both the N1 and P2 potentials should be recorded in the clinical routine since a dissociated abnormality of either response may be found in lesions of the nociceptive system not only in the brain, but also at spinal cord level.

MRI STUDY OF CORPUS CALLOSUM IN PATIENTS WITH BORDERLINE PERSONALITY DISORDER - A PILOT STUDY

Progress in Neuro-Psychopharmacology and Biological Psychiatry 2007;31:1519-1525

Zanetti MV, Soloff PLH, Nicoletti MA, Hatch JP, Brambilla P, Keshavan MS, Soares JC.

I.F. 2006: 2,584

This pilot study examined the integrity of the corpus callosum in a sample of patients with borderline personality disorder (BPD), as abnormalities in inter-hemispheric communication could possibly be involved in illness pathophysiology. We utilized

magnetic resonance imaging (MRI) signal intensity (SI) and morphometric measures. Ten BPD and 20 healthy control subjects were assessed for current and past Axis I and Axis II comorbidities and histories of childhood abuse. Regional CC SI and areas were measured with semi-automated software from threedimensional gradient echo imaging scans. Analysis of covariance was conducted to evaluate the results. No significant differences were observed between BPD and controls in the SI or area of any CC region. Abnormalities in interhemispheric connectivity do not appear necessary for the development of BPD. Further studies with larger samples are needed to confirm this preliminary finding.

LAVORI PER ESTESO PUBBLICATI SU RIVISTE RECENSITE Anno 2008

INCREASED FRONTO-TEMPORAL PERFUSION IN BIPOLAR DISORDER

Journal of Affective Disorders 2008;110(1-2):106-114

Agarwal N, Bellani M, Perlini C, Rambaldelli G, Atzori M, Cerini R, Vecchiato F, Pozzi Mucelli R, Andreone N, Balestrieri M, Tansella M, Brambilla P.

I.F. 2007: 3,144

OBJECTIVES: Previous imaging reports showed over-activation of fronto-limbic structures in bipolar patients, particularly in response to emotional stimuli. In this study, for the first time, we used perfusion weighted imaging (PWI) to analyze lobar cerebral blood volume (CBV) in bipolar disorder to further explore the vascular component to its pathophysiology. METHODS: Fourteen patients with DSM-IV bipolar disorder (mean age+/-SD=49.00+/-12.30 years; 6 males, 8 females) and 29 normal controls (mean age+/-SD=45.07+/-10.30 years; 13 males, 16 females) were studied. PWI images were obtained following intravenous injection of paramagnetic contrast agent (Gadolinium-DTPA), with a 1.5 T Siemens magnet using an echo-planar sequence. The contrast of enhancement (CE), was calculated pixel by pixel as the ratio of the maximum signal intensity drop during the passage of contrast agent (Sm) by the baseline pre-bolus signal intensity (So) (CE=Sm/So*100) for frontal, temporal, parietal, and occipital lobes, bilaterally, on two axial images. Higher CE values correspond to lower CBV and viceversa. RESULTS: Bipolar patients had significantly lower CE values in left frontal and temporal lobes (p=0.01 and p=0.03, respectively) and significantly inverse laterality index for frontal lobe (p=0.017) compared to normal controls. No significant correlations between CE measure and age or clinical variables were found (p>0.05). CONCLUSION: This study found increased left frontal and temporal CBV in bipolar disorder. Fronto-temporal hyper-perfusion may sustain over-activation of these structures during emotion modulation, which have been observed in patients with bipolar illness.

ACTION ANTICIPATION AND MOTOR RESONANCE IN ELITE BASKETBALL PLAYERS

Nature Neuroscience 2008;11(9):1109-1116

Aglioti S, Cesari P, Romani M, Urgesi C.

I.F. 2007: 15,664

We combined psychophysical and transcranial magnetic stimulation studies to investigate the dynamics of action anticipation and its underlying neural correlates in professional basketball players. Athletes predicted the success of free shots at a basket earlier and more accurately than did individuals with comparable visual experience (coaches or sports journalists) and novices. Moreover, performance between athletes and the other groups differed before the ball was seen to leave the model's hands, suggesting that athletes predicted the basket shot's fate by reading the body kinematics. Both visuo-motor and visual experts showed a selective increase of motor-evoked potentials during observation of basket shots. However, only athletes showed a time-specific motor activation during observation of erroneous basket throws. Results suggest that achieving excellence in sports may be related to the fine-tuning of specific anticipatory 'resonance' mechanisms that endow elite athletes' brains with the ability to predict others' actions ahead of their realization.

A CLINICAL, GENETIC AND BIOCHEMICAL CHARACTERIZATION OF SPG7 MUTATIONS IN A LARGE COHORT OF PATIENTS WITH HEREDITARY SPASTIC PARAPLEGIA

Human Mutation 2008;29(4):522-531

Arnoldi A, Tonelli A, Crippa F, Villani G, Pacelli C, Sironi M, Pozzoli U, D'Angelo MG, Meola G, Martinuzzi A, Crimella C, Redaelli F, Panzeri C, Renieri A, Comi GP, Turconi AC, Bresolin N, Bassi MT.

I.F. 2007: 6,273

Mutations in the SPG7 gene encoding a mitochondrial protein termed paraplegin, are responsible for a recessive form of hereditary spastic paraparesis. Only few studies have so far been performed in lar-

ge groups of hereditary spastic paraplegia (HSP) patients to determine the frequency of SPG7 mutations. Here, we report the result of a mutation screening conducted in a large cohort of 135 Italian HSP patients with the identification of six novel point mutations and one large intragenic deletion. Sequence analysis of the deletion breakpoint, together with secondary structure predictions of the deleted region, indicate that a complex rearrangement, likely caused by extensive secondary structure formation mediated by the short interspersed nuclear element (SINE) retrotransposons, is responsible for the deletion event. Biochemical studies performed on fibroblasts from three mutant patients revealed mild and heterogeneous mitochondrial dysfunctions that would exclude a specific association of a complex I defect with the pathology at the fibroblast level. Overall, our data confirm that SPG7 point mutations are rare causes of HSP, in both sporadic and familial forms, while underlying the puzzling and intriguing aspects of histological and biochemical consequences of paraplegin loss. Copyright 2008 Wiley-Liss, Inc.

DECREASED ENTORHINAL CORTEX VOLUMES IN SCHIZOPHRENIA

Schizophrenia Research 2008;102(1-3):171-180

Baiano M, Perlini C, Rambaldelli G, Cerini R, Dusi N, Bellani M, Spezzapria G, Versace A, Balestrieri M, Pozzi Mucelli R, Tansella M, Brambilla P.

I.F. 2007: 4,240

BACKGROUND: The entorhinal cortex is located in the medial temporal lobe and is involved in memory and learning. Previous MRI studies reported conflicting findings in schizophrenia, showing normal or reduced entorhinal size. OBJECTIVES: To explore entorhinal cortex volumes in a large sample of patients with schizophrenia recruited from the geographically defined catchment area of South Verona (i.e. 100,000 inhabitants). We also investigated the size of hippocampus as part of the medial temporal lobe. METHODS: 70 patients with schizophrenia and 77 normal controls underwent a session of MRI (TR=2060 ms, TE=3.9 ms, slice thickness=1.25 mm). Entorhinal and hippocampal volumes were explored using the Brains2 software. RESULTS: A significant group effect was found for total entorhinal cortex but not for hippocampus, with patients suffering from schizophrenia having smaller entorhinal volumes compared to normal subjects (F=6.24, p=0.01), particularly on the right side (F=9.76, p=0.002). Also, the laterality index for entorhinal cortex was higher in normal individuals than in patients with schizophrenia (F=5.45, p=0.02). CONCLUSIONS: Consistent with some of the previous reports, our study confirmed the presence of abnormally decreased entorhinal volumes, particularly on the right side, in a large number of patients with schizophrenia and also found altered asymmetry. This may play a major role in the psychopathology and cognitive disturbances of the disease. Future longitudinal MRI studies including high-risk subjects and drug-free, first-episode patients are crucial to further understand whether entorhinal cortex shrinkage is already present at the onset of the illness or appears as a consequence of the illness.

A TWIN STUDY OF THE COMMON VULNERABILITY BETWEEN HEIGHTENED SENSITIVITY TO HYPERCAPNIA AND PANIC DISORDER

American Journal of Medical Genetics Part B - Neuropsychiatric Genetics 2008;147B(5):587-593

Battaglia M, Pesenti-Gritti P, Spatola CAM, Ogliari A, Tambs K.

I.F. 2007: 4,224

For unknown reasons the inhalation of CO(2)-enriched air mixtures evokes acute panic-like symptoms in people with panic disorder and in their unaffected relatives. This study was set to determine whether, and to what extent, CO(2)-induced acute anxiety and panic disorder share the same genetic and environmental determinants. Cholesky structural equation models were used to decompose into genetic and environmental elements the correlation between self-assessed anxiety post-35%CO(2)-65%O(2) inhalation and interview-based DSM-IV lifetime diagnoses of panic disorder in 346 young adult twin pairs of the Norwegian Institute of Health Panel, 12% of whom had been invited to take part into the CO(2) study on the basis of self-reported symptoms of anxiety gathered 4-7 years before the provocation challenge. A full model corrected for the partially selective ascertainment showed that the phenotypic correlation between post-CO(2) anxiety and DSM-IV panic was largely due to additive genetic influences, while shared and unique environmental agents concurred to explain a relatively minor proportion of the correlation between these two traits. According to the best-fitting model the genetic correlation between post-CO(2) anxiety and panic was 0.81 (0.50-0.98); a common genetic factor was sufficient to explain the traits' covariation and a further, specific genetic factor was necessary to

account for the residual phenotypic variance. The genetic determinants that lead to overreact to a hypercapnic stimulus coincide at a considerable extent with those that influence liability to naturally occurring panic. Environmental factors provide a modest--or no--contribution to the covariation of CO(2)-provoked anxiety with naturally occurring panic. Copyright 2007 Wiley-Liss, Inc.

GENE-ENVIRONMENT INTERACTION AND BEHAVIORAL DISORDERS: A DEVELOPMENTAL PERSPECTIVE BASED ON ENDOPHENOTYPES

Novartis Foundation Symposium 2008;293:31-41; discussion 41-47, 68-70

Battaglia M, Marino C, Maziade M, Molteni M, D'Amato F.

I.F. 2007: 0,000

Abstract non disponibile.

THREE-DIMENSIONAL MAPPING OF HIPPOCAMPAL ANATOMY IN ADOLESCENTS WITH BIPOLAR DISORDER

Journal of the American Academy of Child and Adolescent Psychiatry 2008;47(5):515-525

Bearden Carrie E, Soares Jair C, Klunder AD, Nicoletti MA, Dierschke N, Hayashi Kiralee M, Narr KL, Brambilla P, Sassi RB, Axelson D, Ryan N, Birmaher B, Thompson PM.

I.F. 2007: 4,665

OBJECTIVE: Early-onset bipolar disorder is thought to be a particularly severe variant of the illness. Continuity with the adult form of illness remains unresolved, but preliminary evidence suggests similar biological underpinnings. Recently, we observed localized hippocampal decreases in unmedicated adults with bipolar disorder that were not detectable with conventional volumetric measures. Using the same three-dimensional mapping methods, we sought to investigate whether a similar pattern exists in adolescents with bipolar disorder. METHOD: High-resolution brain magnetic resonance images were acquired from 16 adolescents meeting DSM-IV criteria for bipolar disorder (mean age 15.5 +/- 3.4 years, 50% female) and 20 demographically matched, typically developing control subjects. Three-dimensional parametric mesh models of the hippocampus were created from manual tracings of the hippocampal formation. RESULTS: Controlling for total brain volume, total hippocampal volume was significantly smaller in adolescent patients with bipolar disorder relative to controls (by 9.2%). Statistical mapping results, confirmed by permutation testing, revealed significant localized deformations in the head and tail of the left hippocampus in adolescents with bipolar disorder, relative to normal controls. In addition, there was a significant positive correlation between hippocampal size and age in patients with bipolar disorder, whereas healthy controls showed an inverse relation. DISCUSSION: Localized hippocampal deficits in adolescent patients with bipolar disorder suggest a possible neural correlate for memory deficits observed in this illness. Moreover, age-related increases in hippocampal size in patients with bipolar disorder, not observed in healthy controls, may reflect abnormal developmental mechanisms in bipolar disorder. This possibility must be confirmed by longitudinal studies.

THREE-DIMENSIONAL MAPPING OF HIPPOCAMPAL ANATOMY IN UNMEDICATED AND LITHIUM-TREATED PATIENTS WITH BIPOLAR DISORDER

Neuropsychopharmacology 2008;33(6):1229-1238

Bearden CE, Thompson PM, Dutton RA, Frey Benicio N, Peluso MAM, Nicoletti MA, Dierschke N, Hayashi KM, Klunder AD, Glahn DC, Brambilla P, Sassi RB, Mallinger AG, Soares JC.

I.F. 2007: 6,157

Declarative memory impairments are common in patients with bipolar illness, suggesting underlying hippocampal pathology. However, hippocampal volume deficits are rarely observed in bipolar disorder. Here we used surface-based anatomic mapping to examine hippocampal anatomy in bipolar patients treated with lithium relative to matched control subjects and unmedicated patients with bipolar disorder. High-resolution brain magnetic resonance images were acquired from 33 patients with bipolar disorder (21 treated with lithium and 12 unmedicated), and 62 demographically matched healthy control subjects. Three-dimensional parametric mesh models were created from manual tracings of the hippocampal formation. Total hippocampal volume was significantly larger in lithium-treated bipolar patients compared with healthy controls (by 10.3%; p=0.001) and unmedicated bipolar patients (by 13.9%; p=0.003). Statistical mapping results, confirmed by permutation testing, revealed localized deficits in the

right hippocampus, in regions corresponding primarily to cornu ammonis 1 subfields, in unmedicated bipolar patients, as compared to both normal controls (p=0.01), and in lithium-treated bipolar patients (p=0.03). These findings demonstrate the sensitivity of these anatomic mapping methods for detecting subtle alterations in hippocampal structure in bipolar disorder. The observed reduction in subregions of the hippocampus in unmedicated bipolar patients suggests a possible neural correlate for memory deficits frequently reported in this illness. Moreover, increased hippocampal volume in lithium-treated bipolar patients may reflect postulated neurotrophic effects of this agent, a possibility warranting further study in longitudinal investigations.

DETAILED PHENOTYPE-GENOTYPE STUDY IN FIVE PATIENTS WITH CHROMOSOME 6Q16 DELETION: NARROWING THE CRITICAL REGION FOR PRADER-WILLI-LIKE PHENOTYPE

European Journal of Human Genetics 2008;16(12):1443-1449

Bonaglia MC, Ciccone R, Gimelli G, Gimelli S, Marelli S, Verheij J, Giorda R, Grasso R, Borgatti R, Pagone F, Rodriguez L, Martinez-Frias ML, Van Ravenswaaij C, Zuffardi O.

I.F. 2007: 4,003

Most patients with an interstitial deletion of 6q16 have Prader-Willi-like phenotype, featuring obesity, hypotonia, short hands and feet, and developmental delay. In all reported studies, the chromosome rearrangement was detected by karyotype analysis, which provides an overview of the entire genome but has limited resolution. Here we describe a detailed clinical presentation of five patients, two of whom were previously reported, with overlapping interstitial 6q16 deletions and Prader-Willi-like phenotype. Our patients share the following main features with previously reported cases: global developmental delay, hypotonia, obesity, hyperphagia, and eye/vision anomalies. All rearrangement breakpoints have been accurately defined through array-CGH at about 100 Kb resolution. We were able to narrow the shortest region of deletion overlap for the presumed gene(s) involved in the Prader-Willi-like syndrome to 4.1 Mb located at 6q16.1q16.2. Our results support the evidence that haploinsufficiency of the SIM1 gene is responsible for obesity in these patients. A possible involvement of the GRIK2 gene in autistic-like behaviour, of POPDC3 in heart development, and of MCHR2 in the control of feeding behaviour and energy metabolism is also hypothesized.

A FAMILIAL INVERTED DUPLICATION/DELETION OF 2P25.1 PROVIDES NEW CLUES ON THE GENESIS OF INVERTED DUPLICATIONS

European Journal of Human Genetics 2008;in press

Bonaglia MC*, Giorda R*, Massagli A, Galluzzi R, Ciccone R, Zuffardi O.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2007: 4,003

Abstract non disponibile.

CONCURRENT TRANSPOSITION OF DISTAL 6P AND 20 Q TELOMERE: A RECURRENT BENIGN CHROMOSOMAL VARIANT

European Journal of Medical Genetics 2008;51(2):148-155 – Short Report

Bonaglia MC, Giorda R, Beri S, Peters GB, Kirk EP, Hung D, Ciccone R, Gottardi G, Zuffardi O.

I.F. 2007: 1,857

We report the second instance of a complex unbalanced rearrangement consisting of distal trisomy 6p and 20q due to the concurrent transposition of distal 6p and 20q to the 22q telomere, previously described as a benign familial chromosomal variant. In the previous case, the nonpathogenicity of the rearrangement was based on the absence of genotypic differences between the affected proband and his normal father, and on the absence of imprinted genes in the unbalanced region. We now describe the same variant in an unrelated affected subject, in whom testing confirmed the diagnosis of Angelman syndrome, and in his healthy father. Molecular investigations confirmed that the two families have an identical subtelomeric rearrangement. However, genotyping of the flanking sequences on 22q showed a completely different pattern in the two families, demonstrating that they are indeed unrelated. Array-CGH analysis with a resolution of approximately 20 kb (Kit 244A, Agilent) defined a deletion size of 5.9 Mb on 15q11.2. No other imbalances were visible at subtelomeric regions. Further Array-CGH analysis using DNA of the proband (as test) and his mother (as reference) did not detect

any duplication at the 6p and 20q subtelomeric regions. The proband and his father appear to have a copy number of the transposed regions equal to that of individuals with a normal repartition of the subtelomeric regions. This is not suggestive of a trisomy but rather of CNV regions. This type of rearrangement could define a new class of polymorphic variants, i.e. positional variants, as observed for pericentromeric heterochromatin.

MOSAIC 22Q13 DELETIONS: EVIDENCE FOR CONCURRENT MOSAIC SEGMENTAL ISODISOMY AND GENE CONVERSION

European Journal of Human Genetics 2008;in press

Bonaglia MC*, Giorda R*, Beri S, Bigoni A, Sensi A, Baroncini A, Capucci A, De Agostini C, Gwilliam R, Deloukas P, Dunham I, Zuffardi O.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2007: 4,003

Abstract non disponibile.

LYMPHOMONOCYTE ALPHA-SYNUCLEIN LEVELS IN AGING AND IN PARKINSON DISEASE

Neurobiology of Aging 2008;in press

Brighina L, Prigione A, Begni B, Galbussera A, Andreoni S, Piolti R, Ferrarese C.

I.F. 2007: 5,607

Abstract non disponibile.

THE FIRST ITALIAN FAMILY WITH EVIDENCE OF PYRAMIDAL IMPAIRMENT AS PHENOTYPIC MANIFESTATION OF SILVER SYNDROME BSCL2 GENE MUTATION

Neurological Sciences 2008;29(3):189-191 – Brief Communication

Cafforio G, Calabrese R, Morelli N, Mancuso M, Piazza S, Martinuzzi A, Bassi MT, Crippa F, Siciliano G.

I.F. 2007: 1,006

Silver syndrome (SPG17) is a rare form of hereditary spastic paraparesis. Its relationship to distal hereditary motor neuropathy (dHMN) type V is underlined by the recent discovery of causative mutation in BSCL2 gene coding for a protein termed seipin, an integral membrane protein of endoplasmic reticulum, with unknown function. Here we report the third Italian family with dHMN and SPG17 in which two affected members harbor the heterozygous N88S mutation in the BSCL2 gene. The proband developed a severe paraparetic spastic gait, while, in the other Italian families reported so far, no signs of upper motor neuron involvement were observed. This family confirms the clinical heterogeneity associated with this specific mutation. Moreover, this is the first report in which neuroimaging seems to confirm the pyramidal alterations in dHMN associated to SPG17.

THE SIGNATURE OF LONG-STANDING BALANCING SELECTION AT THE HUMAN DEFENSIN BETA-1 PROMOTER

Genome Biology 2008;9(9):R143

Cagliani R, Fumagalli M, Riva S, Pozzoli U, Comi GP, Menozzi G, Bresolin N, Sironi M.

I.F. 2007: 6,589

BACKGROUND: Defensins, small endogenous peptides with antimicrobial activity, are pivotal components of the innate immune response. A large cluster of defensin genes is located on human chromosome 8p; among them the beta defensin 1 (DEFB1) promoterhas been extensively studied since discovery that specific polymorphisms and haplotypes associate with asthma and atopy, susceptibility to severe sepsis, as well as HIV and Candida infection predisposition. RESULTS: Here, we characterize the sequence variation and haplotype structure of the DEFB1 promoter region in six human populations. In all of them, we observed high levels of nucleotide variation, an excess of intermediate-frequency alleles, reduced population differentiation and a genealogy with common haplotypes separated by deep branches. Indeed, a significant departure from the expectation of evolutionary neutrality was observed in all populations and the possibility that this is due to demographic history alone was ruled out. Also, we verified that the selection signature is restricted to the promoter region and not due to a linked balanced polymorphism. A phylogeny-based estimation indicated that the two major haplotype clades separated around 4.5 million years ago, approximately the time when the human and chimpanzee lineages split. CONCLUSION: Altogether, these features represent strong molecular signatures of long-term balancing selection, a process that is thought to be extremely rare outside major histocompatibility complex genes. Our data indicate that the DEFB1 promoter region carries functional variants and

support previous hypotheses whereby alleles predisposing to atopic disorders are widespread in modern societies because they conferred resistance to pathogens in ancient settings.

VIRTUAL LESION OF VENTRAL PREMOTOR CORTEX IMPAIRS VISUAL PERCEPTION OF BIOMECHANICALLY POSSIBILE BUT NOT IMPOSSIBLE ACTIONS

Social Neuroscience 2008;3(3-4):388-400

Candidi M, Urgesi C, Ionta S, Aglioti S.

I.F. 2007: 4,750

Single-pulse transcranial magnetic stimulation (TMS) studies show that action observation facilitates the onlooker's cortico-spinal system supporting the notion of motor mirroring. Repetitive transcranial magnetic stimulation (rTMS) over ventral premotor cortex (vPMc) impairs visual discrimination of body actions. Although studies suggest that the action observation-execution matching system may map only actions that belong to the observer's motor repertoire, we demonstrated comparable motor and premotor facilitation during observation of biomechanically possible as well as impossible actions. It has also been shown that seeing impossible body movements activates the extrastriate body area (EBA). Using event-related rTMS, we sought to determine whether vPMc and EBA are actively involved in the visual discrimination of actions performed through biomechanically possible or impossible kinematics and of their biomechanical plausibility. Stimulation of vPMc impaired discrimination of possible actions while leaving intact the discrimination of biomechanically impossible actions and of biomechanical plausibility. No effect of EBA rTMS on any type of action processing was found. Thus, vPMc is crucial for discrimination of the goal of actions that can be actually performed suggesting that this area is involved in the visual processing of goal-directed actions.

ENHANCED FOLATE BINDING OF CULTURED FIBROBLASTS FROM ALZHEIMER'S DISEASE PATIENTS

Neuroscience Letters 2008;436(3):317-320

Cazzaniga E, Bulbarelli A, Lonati E, Re F, Galimberti G, Gatti E, Pitto M, Ferrarese C, Masserini M.

I.F. 2007: 2,085

We compared the levels of serum folate from Alzheimer's disease (AD) patients and from age-matched healthy subjects and used primary cultures of fibroblasts, obtained from the two groups, to assess possible differences in their ability to bind folate. The results show that the levels of circulating folate are significantly ($p<0.01$; $n=30$) lower in AD patients than in controls (4.91+/-2.44 and 7.56+/-2.5 ng/mL, respectively). Moreover, the folate binding of AD fibroblasts is significantly ($p<0.01$; $n=8$) higher (2-4-fold) with respect to controls. RT-PCR experiments suggest that the higher folate binding could be due to an enhanced expression in AD fibroblasts of folate receptor alpha.

THE IMMUNE SYSTEM FACING INJURED TISSUES AND STEM CELLS: MORE OF A HEALER OR A FIGHTER?

Pharmacological Research 2008;58(2):87

Clementi E, Manfredi AA.

I.F. 2007: 1,895

Abstract non disponibile.

HDAC2 BLOCKADE BY NITRIC OXIDE AND HISTONE DEACETYLASE INHIBITORS REVEALS A COMMON TARGET IN DUCHENNE MUSCULAR DYSTROPHY TREATMENT

Proceedings of the National Academy of Sciences of the United States of America (PNAS), 2008;105(49):19183-19187

Colussi C, Mozzetta C, Gurtner A, Illi B, Rosati J, Straino S, Ragone G, Pescatori M, Zaccagnini G, Antonini A, Minetti G, Martelli F, Piaggio G, Gallinari P, Steinkulher C, Clementi E, Dell'Aversana C, Altucci L, Mai A, Capogrossi MC, Puri PL, Gaetano C.

I.F. 2007: 9,598

The overlapping histological and biochemical features underlying the beneficial effect of deacetylase inhibitors and NO donors in dystrophic muscles suggest an unanticipated molecular link among dystrophin, NO signaling, and the histone deacetylases (HDACs). Higher global deacetylase activity and selective increased expression of the class I histone deacetylase HDAC2 were detected in muscles of dystrophin-deficient MDX mice. In vitro and in vivo siRNA-mediated down-regulation of HDAC2 in dystrophic muscles was sufficient to replicate the morphological and functional benefits observed with deacetylase inhibitors and NO donors. We found that restoration of NO signaling in vivo, by adenoviral-mediated expression of a constitutively

active endothelial NOS mutant in MDX muscles, and in vitro, by exposing MDX-derived satellite cells to NO donors, resulted in HDAC2 blockade by cysteine S-nitrosylation. These data reveal a special contribution of HDAC2 in the pathogenesis of Duchenne muscular dystrophy and indicate that HDAC2 inhibition by NO-dependent S-nitrosylation is important for the therapeutic response to NO donors in MDX mice. They also define a common target for independent pharmacological interventions in the treatment of Duchenne muscular dystrophy.

NEURAL STEM CELL TRANSPLANTATION CAN AMELIORATE THE PHENOTYPE OF A MOUSE MODEL OF SPINAL MUSCULAR ATROPHY

Journal of Clinical Investigation (The) 2008;118(10):3316-3330

Corti S, Nizzardo M, Nardini M, Donadoni C, Salani S, Ronchi D, Saladino F, Bordoni A, Fortunato F, Del Bo R, Papadimitriou D, Locatelli F, Menozzi G, Strazzer S, Bresolin N, Comi GP.

I.F. 2007: 16,915

Spinal muscular atrophy (SMA), a motor neuron disease (MND) and one of the most common genetic causes of infant mortality, currently has no cure. Patients with SMA exhibit muscle weakness and hypotonia. Stem cell transplantation is a potential therapeutic strategy for SMA and other MNDs. In this study, we isolated spinal cord neural stem cells (NSCs) from mice expressing green fluorescent protein only in motor neurons and assessed their therapeutic effects on the phenotype of SMA mice. Intrathecally grafted NSCs migrated into the parenchyma and generated a small proportion of motor neurons. Treated SMA mice exhibited improved neuromuscular function, increased life span, and improved motor unit pathology. Global gene expression analysis of laser-capture-microdissected motor neurons from treated mice showed that the major effect of NSC transplantation was modification of the SMA phenotype toward the wild-type pattern, including changes in RNA metabolism proteins, cell cycle proteins, and actin-binding proteins. NSC transplantation positively affected the SMA disease phenotype, indicating that transplantation of NSCs may be a possible treatment for SMA.

CLINICAL FEATURES AND NEW MOLECULAR FINDINGS IN CARNITINE PALMITOYLTRANSFERASE II (CPT II) DEFICIENCY

Journal of the Neurological Sciences 2008;266(1-2):97-103

Corti S, Bordoni A, Ronchi D, Musumeci O, Aguennouz M, Toscano A, Lamperti C, Bresolin N, Comi GP.

I.F. 2007: 2,312

Carnitine palmitoyltransferase II (CPT II) deficiency is the most common inherited disorder of lipid metabolism characterized in its adult form by attacks of myalgia and myoglobinuria. We analyzed a cohort of 22 CPT II-deficient patients (representing 20 independent probands) to correlate clinical presentation and molecular data. The common p.Ser113Leu mutation was detected with an allelic frequency of 67.5% (27/40), in association with mild adult-onset phenotype. In addition to the p.Ser113Leu mutation, other 10 disease-causing mutations were identified, 5 of which were novel. They are a micro-insertion within exon 5, three aminoacid substitutions within the coding region, namely p.Arg151Trp, p.Asp576Gly, p.Arg247Trp and a truncating stop codon mutation (p.Arg554Ter). Our data expand the spectrum of CPT II mutations and help to evaluate possible correlations between genotypes and phenotypes.

ENDOTHELIAL NITRIC OXIDE SYNTHASE OVEREXPRESSION BY NEURONAL CELLS IN NEURODEGENERATION: A LINK BETWEEN INFLAMMATION AND NEUROPROTECTION

Journal of Neurochemistry 2008;106(1):193-204

De Palma C, Falcone S, Panzeri C, Radice S, Bassi MT, Clementi E.

I.F. 2007: 4,451

The roles of neuronal and inducible nitric oxide synthases in neurones have been extensively investigated; by contrast, the biological significance of endothelial nitric oxide synthase (eNOS) overexpression that occurs in several pathological conditions has not yet been studied. We have started addressing this issue in a cell model of neurodegeneration, i.e. human SKNBE neuroblastoma cells transfected with a mutant form of alsin, a protein causing an early-onset type of amyotrophic lateral sclerosis, ALS2. We found that eNOS, which is endogenously expressed by these cells, was activated by tumour necrosis factor-alpha (TNF-alpha), a proinflammatory cytokine that plays important roles in ALS2 and several neurodegenerative diseases. The TNF-alpha-dependent eNOS activation occurred through generation, by sphingosine-kinase-1, of sphingosine-1-phosphate,

stimulation of its membrane receptors and activation of Akt, as determined using small interference RNA and dominant negative constructs specific for the enzymes and receptors. eNOS activation by TNF-alpha conferred cytoprotection from excitotoxicity and neurotoxic cues such as reactive oxygen species, endoplasmic reticulum stress, DNA damage, and mutated alsin itself. Our results suggest that overexpression of eNOS by neurones is a broad-range protective mechanism activated during damage and establish a link of pathophysiological relevance between this enzyme and inflammation accompanying neurodegenerative diseases. These findings also question the concept that high NO output in the presence of oxidative stress leads always to peroxynitrite formation contributing to neurodegeneration.

ROLE OF VEGF GENE VARIABILITY IN LONGEVITY: A LESSON FROM THE ITALIAN POPULATION

Neurobiology of Aging 2008;29(12):1917-1922

Del Bo R, Ghezzi S, Scarlato M, Albani D, Galimberti D, Lucca U, Tettamanti M, Scarpini E, Forloni G, Bresolin N, Comi GP.

I.F. 2007: 5,607

Vascular endothelial growth factor (VEGF) gene polymorphisms have been associated with an increased risk of developing a wide variety of disorders from diabetes to neurodegenerative diseases suggesting functions not confined to its vascular effects originally described. Based on the VEGF protective roles undisclosed in pathological conditions, we evaluate whether VEGF variability might be a determinant also for longevity. Four polymorphisms (-2578C/A, -1190G/A, -1154G/A and -634G/C) within the VEGF gene promoter region in 490 unrelated Italian healthy subjects have been analysed. Significant changes of allele, genotype (-2578/AA versus -2578/CC: OR=2.08, p=0.007; -1190/AA versus -1190/GG: OR=2.01, p=0.011) and haplotype (AAGG: 10.4% versus 14.9%, p=0.03) frequency distributions were observed between young/elderly (25-84 years old) and long-lived (85-99 years old) subjects. These results suggest that VEGF gene variability can be inserted among the genetic factors influencing the lifespan.

MELAS MITOCHONDRIAL DNA MUTATION A3243G REDUCES GLUTAMATE TRANSPORT IN CYBRIDS CELL LINES

Experimental Neurology 2008;212(1):152-156

Di Francesco J, Cooper JM, Lam A, Hart PE, Tremolizzo L, Ferrarese C, Schapira AHV.

I.F. 2007: 3,982

MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes) is commonly associated with the A3243G mitochondrial DNA (mtDNA) mutation encoding the transfer RNA of leucine (UUR) (tRNA (Leu(UUR))). The pathogenetic mechanisms of this mutation are not completely understood. Neuronal functions are particularly vulnerable to alterations in oxidative phosphorylation, which may affect the function of the neurotransmitter glutamate, leading to excitotoxicity. In order to investigate the possible effects of A3243G upon glutamate homeostasis, we assessed glutamate uptake in osteosarcoma-derived cytoplasmic hybrids (cybrids) expressing high levels of this mutation. High-affinity Na(+)-dependent glutamate uptake was assessed as radioactive [(3)H]-glutamate influx mediated by specific excitatory amino acid transporters (EAATs). The maximal rate (V(max)) of Na(+)-dependent glutamate uptake was significantly reduced in all the mutant clones. Although the defect did not relate to either the mutant load or magnitude of oxidative phosphorylation defect, we found an inverse relationship between A3243G mutation load and mitochondrial ATP synthesis, without any evidence of increased cellular or mitochondrial free radical production in these A3243G clones. These data suggest that a defect of glutamate transport in MELAS neurons may be due to decreased energy production and might be involved in mediating the pathogenic effects of the A3243G mtDNA mutation.

MULTI-SITE TRIAL ON EFFICACY OF CONSTRAINT INDUCED MOVEMENT THERAPY IN CHILDREN WITH HEMIPLEGIA: STUDY DESIGN AND METHODOLOGY

American Journal of Physical Medicine and Rehabilitation 2008;in press

Facchin P, Rizzotto MR, Turconi AC, Pagliano E, Fazzi E, Stortini M, Fedrizzi E, GIPCI Study Group (Cazzagon M, Germinasi C, Martinuzzi A, Megliani C, Trabacca A).

I.F. 2007: 1,557

Abstract non disponibile.

SLUGGISH ENGAGEMENT AND DISENGAGEMENT OF NON-SPATIAL ATTENTION IN DYSLEXIC CHILDREN

Cortex 2008;44(9):1221-1233 – Research Report

Facoetti A, Ruffino M, Peru A, Paganoni P,

Chelazzi L.

I.F. 2007: 3,123

Although the dominant view posits that developmental dyslexia arises from a deficit in phonological processing and memory, efficient phonological decoding requires precise visual selection of graphemes. Therefore, visual engagement and disengagement of non-spatial attention were studied in 13 dyslexic children and 13 chronological age and intelligence quotient (IQ) matched normally reading children by measuring "attentional masking" (AM) and "attentional blink" (AB) effects. AM refers to an impaired identification of the first (T1) of two rapidly sequential targets (i.e., attentional engagement). In contrast, AB refers to an impaired identification of the second target in the sequence (T2; i.e., attentional disengagement). The results revealed a specific temporal deficit of AM as well as of AB in dyslexic children. Our results showed that the abnormality in AM and AB is rather widespread, since 77% and 54% of dyslexic children deviated at least 1 standard deviation (SD) from the mean of the controls, respectively, for the two deficits. We further showed that individual differences in non-spatial attention were specifically related to nonword reading ability. These results suggest that non-spatial attention deficits (possibly related to a parietal cortex dysfunction) may selectively impair the reading development via sublexical mechanisms.

SENSITIVITY TO OBJECT VIEWPOINT AND ACTION INSTRUCTION DURING SEARCH FOR TARGETS IN THE LOWER VISUAL FIELD

Psychological Science 2008;19(1):42-48

Forti S, Humphreys GW.

I.F. 2007: 4,251

We provide evidence for long-term priming based on view-specific representations of neglected stimuli. A patient with visual neglect, M.P., was asked to search for a target presented amongst other objects on a table. Subsequently recognition memory was tested for items that were identified and for items missed in search. Items that were missed were rejected more slowly than novel items in the recognition memory task, providing evidence for implicit processing (Experiment 1). Implicit memory for missed items was both item-specific (Experiment 2) and view-specific (Experiment 3), and it was eliminated when there were intervening activities lasting about 1 hour (Experiment 4). There was also an implicit memory for distractors in the search task, which was item- but not view-specific (Experiments 2 and 3) and it lasted for at least an hour, even with other intervening activities (Experiment 4). The data suggest that the representations of neglected stimuli may differ qualitatively from those of nonneglected items, with representations of neglected objects being both view-specific and vulnerable across extended retention intervals. The results support the argument that attention is needed in order to encode object representations that are robust to view transformations and temporal decay or interference.

ILLNESS DURATION AND TOTAL BRAIN GRAY MATTER IN BIPOLAR DISORDER: EVIDENCE FOR NEURODEGENERATION?

European Neuropsychopharmacology 2008;18(10):717-722

Frey BN, Zunta-Soares GB, Caetano SC, Nicoletti MA, Hatch JP, Brambilla P, Mallinger AG, Soares JC.

I.F. 2007: 4,430

Previous studies have suggested that bipolar disorder (BD) is associated with alterations in neuronal plasticity, but the effects of the progression of illness on brain anatomy have been poorly investigated. We studied the correlation between length of illness, age, age at onset, and the number of previous episodes and total brain, total gray, and total white matter volumes in BD, unipolar (UP) and healthy control (HC) subjects. Thirty-six BD, 31 UP and 55 HCs underwent a 1.5 T brain magnetic resonance imaging scan, and gray and white matter volumes were manually traced blinded to the subjects' diagnosis. Partial correlation analysis showed that length of illness was inversely correlated with total gray matter volume after adjusting for total intracranial volume in BD ($r(p) = -0.51$; $p = 0.003$) but not in UP subjects ($r(p) = -0.23$; $p = 0.21$). Age at illness onset and the number of previous episodes were not significantly correlated with gray matter volumes in BD or UP subjects. No significant correlation with total white matter volume was observed. These results suggest that the progression of illness may be associated with abnormal cellular plasticity. Prospective longitudinal studies are necessary to elucidate the long-term effects of illness progression on brain structure in major mood disorders.

PREVALENCE AND CORRELATES OF MENTAL DISORDERS AMONG ADOLESCENTS IN ITALY: THE PRISMA STUDY

European Child & Adolescent Psychiatry 2008;in press

Frigerio A, Rucci P, Goodman R, Ammaniti M, Carlet O, Cavolina P, De Girolamo G, Lenti C, Lucarelli L, Mani E, Martinuzzi A, Micali N, Milone A, Morosini P, Muratori F, Nardocci F, Pastore V, Polidori G, Tullini A, Vanzin L, Villa L, Walder M, Zuddas A, Molteni M.

I.F. 2007: 1,992

Abstract non disponibile.

WIDESPREAD BALANCING SELECTION AND PATHOGEN-DRIVEN SELECTION AT BLOOD GROUP ANTIGEN GENES

Genome Research 2008;in press

Fumagalli M, Cagliani R, Pozzoli U, Riva S, Comi GP, Menozzi G, Bresolin N, Sironi M.

I.F. 2007: 11,224

Historically, allelic variations in blood group antigen (BGA) genes have been regarded as possible susceptibility factors for infectious diseases. Since host-pathogen interactions are major determinants in evolution, BGAs can be thought of as selection targets. In order to verify this hypothesis, we obtained an estimate of pathogen richness for geographic locations corresponding to 52 populations distributed worldwide; after correction for multiple tests and for variables different from selective forces, significant correlations with pathogen richness were obtained for multiple variants at 11 BGA loci out of 26. In line with this finding, we demonstrate that 3 BGA genes, namely CD55, CD151, and SLC14A1 have been subjected to balancing selection, a process, rare outside MHC genes, which maintains variability at a locus. Moreover, we identified a gene region immediately upstream the transcription start site of FUT2 which has undergone non-neutral evolution independently from the coding region. Finally, in the case of BSG, we describe the presence of a highly divergent haplotype clade and the possible reasons for its maintenance, including frequency-dependent balancing selection, are discussed. These data indicate that BGAs have been playing a central role in the host-pathogen arms race during human evolutionary history and no other gene category shows similar levels of widespread selection, with the only exception of loci involved in antigen recognition.

THE EFFECT OF FREQUENCY OF CEREBRAL PALSY TREATMENT: A MATCHED-PAIR PILOT STUDY

Pediatric Neurology 2008;39(5):335-340

Gagliardi C, Maghini C, Germiniasi C, Stefanoni G, Molteni F, Burt MD, Turconi AC.

I.F. 2007: 1,375

The feasibility and effectiveness of a year-long integrated rehabilitation program for young children (less than 6 years old) with cerebral palsy was evaluated, and efficacy of different treatment schedules was compared. A sample of 40 children (20 male; mean age, 3 years +/-1.22) took part: 20 presented with tetraparesis, 12 with diparesis, and 8 with hemiparesis. Participants' motor abilities were classified according to the Gross Motor Function Measure classification system at baseline and after 1 year of treatment. For half of the participants, treatment consisted of continuous integrated intervention twice a week; for the other half, treatment was the 3i intervention (Intermittent, Intensive, Integrated), in which a month of intensive, twice-a-day treatment was followed by a continuous, twice-a-week phase, lasting 5 months. Overall, there was an improvement in gross motor function, with 37% of children improving and no children showing lowered function. Neither baseline general cognitive abilities nor age had a significant effect on the level of improvement, although initial gross motor function did. Children undergoing the intensive intermittent intervention showed the greatest motor function improvement. Results support the effectiveness of the integrated intervention and of periods of higher frequency intervention in young children.

POST-METHIONINE LOAD TEST: A MORE SENSITIVE TOOL TO REVEAL HYPERHOMOCYSTEINEMIA IN ALZHEIMER PATIENTS?

Clinical Biochemistry 2008;41(10-11): 914-916

Galimberti G, Conti E, Zini M, Piazza F, Fenaroli F, Isella V, Facheris M, Perlangeli V, Antolini L, De Filippi F, Ferrarese C.

I.F. 2007: 2,072

OBJECTIVE: To identify the real number of hyperhomocysteinemic Alzheimer's patients who may benefit from homocysteine-lowering therapy. METHODS: Basal and post-methionine load homocysteine levels were assessed by rp-HPLC system. RESULTS: PML test revealed twice as many hyperhomocysteinemic AD subjects with respect

to the fasting analysis. CONCLUSION: PML test resulted useful in detecting higher number of hyperhomocysteinemic AD patients who may have the chance of an early folate treatment.

A NOVEL DE NOVO NONSENSE MUTATION IN ATP1A2 ASSOCIATED WITH SPORADIC HEMIPLEGIC MIGRAINE AND EPILEPTIC SEIZURES

Journal of the Neurological Sciences 2008;273(1-2):123-126

Gallanti A*, Tonelli A*, Cardin V, Bussone G, Bresolin N, Bassi MT.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2007: 2,312

Familial hemiplegic migraine (FHM) is a severe dominant form of migraine with aura associated with transient hemiparesis. Several other neurological signs and symptoms can be associated with FHM such as cerebellar abnormalities, cerebral edema and coma after minor head trauma, epileptic seizures and mental retardation. The sporadic form of hemiplegic migraine named SHM, presents with identical clinical symptoms. Here we report a case of a young hemiplegic migraine patient, 11 years old, who had the first hemiplegic attack at the age of 10 years. This patient has a clinical history of epileptic seizures in the childhood successfully controlled with drug therapy. No familiarity for any type of migraine or seizures can be observed within the paternal or maternal line. The patient who can therefore be considered a sporadic case, carries a novel de novo nonsense mutation p.Tyr1009X in the ATP1A2 gene (FHM2), leading to a truncated alpha-2 subunit of the Na+/K+-ATPase pump thus lacking the last 11 amino acids. The novel mutation identified confirms the role of FHM2 gene in forms of hemiplegic migraine associated with epilepsy with both familial and sporadic occurrence, and expands the spectrum of mutations related to these forms of the disease.

HYPERFRACTIONATED ACCELERATED RADIOTHERAPY AFTER INTENSIVE NEOADJUVANT CHEMOTHERAPY IN THE "MILAN" STRATEGY FOR METASTATIC MEDULLOBLASTOMA

Journal of Clinical Oncology 2008;in press

Gandola L, Massimino M, Cefalo G, Solero CL, Spreafico F, Pecori E, Riva D, Collini P, Pignoli E, Giangaspero F, Luksch R, Berretta S, Poggi G, Biassoni V, Ferrari A, Pollo B, Favre C, Sardi I, Terenziani M, Fossati-Bellani F.

I.F. 2007: 13,598

PURPOSE: With a view to improving the prognosis for patients with metastatic medulloblastoma, we tested the efficacy and toxicity of a hyperfractionated accelerated radiotherapy (HART) regimen delivered after intensive sequential chemotherapy. PATIENTS AND METHODS: Between 1998 and 2007, 33 consecutive patients received postoperative methotrexate (8 g/m(2)), etoposide (2.4 g/m(2)), cyclophosphamide (4 g/m(2)), and carboplatin (0.8 g/m(2)) in a 2-month schedule, then HART with a maximal dose to the neuraxis of 39 Gy (1.3 Gy/fraction, 2 fractions/d) and a posterior fossa boost up to 60 Gy (1.5 Gy/fraction,2 fractions/d). Patients with persistent disseminated disease before HART were consolidated with two myeloablative courses and circulating progenitor cell rescue. RESULTS: Patients were classified as having M1 (n = 9), M2 (n = 6), M3 (n = 17), and M4 (n = 1) disease. Seven patients younger than 10 years old who achieved complete response after chemotherapy received a lower dose to the neuraxis (31.2 Gy). Twenty-two of the 32 assessable patients responded to chemotherapy; disease was stable in five patients and progressed in five patients. One septic death occurred before radiotherapy. Eight patients experienced relapse after a median of 12 months. Fourteen of the 33 patients underwent consolidation therapy after HART. With a median 82-month survivor follow-up, the 5-year event-free, progression-free, and overall survival rates were 70%, 72%, and 73%, respectively. No severe clinical complications of HART have emerged so far. CONCLUSION: HART after intensive postoperative chemotherapy, followed by myeloablative chemotherapy in selected cases, proved feasible in children with metastatic medulloblastoma. The results of our treatment compare favorably with other series treated using conventional therapies.

WIDE AND DIFFUSE PERCEPTUAL MODES CHARACTERIZES DYSLEXICS IN VISION AND AUDITION

Perception 2008;in press

Geiger G, Cattaneo C, Galli R, Pozzoli U, Lorusso ML, Facoetti A, Molteni M.

I.F. 2007: 1,617

Abstract non disponibile.

PROTECTION AGAINST OXIDANT-INDUCED APOPTOSIS BY EXOGENOUS GLUTATHIONE IN LEBER HEREDITARY OPTIC NEUROPATHY CYBRIDS

Investigative Ophthalmology and Visual Science 2008;49(2):671-676

Ghelli A, Porcelli AM, Zanna C, Martinuzzi A, Carelli V, Rugolo M.

I.F. 2007: 3,528

PURPOSE: To use different paradigms of oxidative and metabolic stress in a cellular model of Leber hereditary optic neuropathy (LHON), with the aim of evaluating the efficacy of potentially therapeutic molecules for the treatment of this disease. METHODS: Cybrids bearing one of the three most common LHON pathogenic mutations (11778/ND4, 3460/ND1, 14484/ND6) were incubated with two compounds known to induce oxidative injury, tert-butyl hydroperoxide (t-BH) and rotenone. To mimic metabolic stress, cells were incubated in a glucose-free medium containing galactose. Cell viability was determined using the MTT assay. To identify the apoptotic type of cell death, nuclear morphology was examined after cell loading with Hoechst. Cellular glutathione (GSH), and oxidized glutathione (GSSG) levels were measured enzymatically. RESULTS: Incubation with t-BH caused apoptotic cell death of control and LHON cybrids, whereas only LHON cybrids were damaged by rotenone concentrations up to 2.5 muM. Both types of stress caused a marked imbalance in the glutathione levels, but an increase in the GSSG/GSH+GSSG ratio was detected only after rotenone treatment. The efficacy of several antioxidant and antiapoptotic compounds was then assessed in cells exposed to these two oxidative paradigms. Only exogenous GSH remarkably protected the t-BH- and rotenone-treated cybrids from cell death. In contrast, GSH was unable to increase the viability of cybrids exposed to metabolic stress. CONCLUSIONS: These results suggest that GSH is an effective antioxidant compound to be tested as a potential treatment for LHON.

MOLECULAR AND CYTOGENETIC ANALYSIS OF THE SPREADING OF X INACTIVATION IN A GIRL WITH MICRODEPHALY, MILD DYSMORPHIC FEATURES AND T(X;5)(Q22.1;Q31.1)

European Journal of Human Genetics 2008;16(8):897-905

Giorda R, Bonaglia MC, Milani G, Baroncini A, Spada F, Beri S, Menozzi G, Rusconi M, Zuffardi O.

I.F. 2007: 4,003

X chromosome inactivation involves initiation, propagation, and maintenance of gene inactivation. Studies of replication pattern and timing in X;autosome translocations have suggested that X inactivation may spread to autosomal DNA. To examine this phenomenon at the molecular level, we have tested the transcriptional activity of a number of chromosome 5 loci in a female subject with microcephaly, mild dysmorphic features and 46,X,der(X)t(X;5)(q22.1;q31.1) karyotype. RT-PCR analysis of 20 transcribed sequences spanning 5q31.1-qter revealed that nine of them were not expressed in somatic cell hybrid clones carrying the translocated chromosome. However, eight genes were expressed and therefore escaped inactivation. This direct expression test demonstrates that spreading of inactivation from the X chromosome to the adjoining autosomal DNA was incomplete and 'patchy'. Inactivation was associated in most instances to methylation of the CpG sequences in genes containing CpG islands, but was also present in CpG islandless genes. These results agree with those obtained for other X;autosome translocations and demonstrate that autosomes are partially resistant to Xist-mediated spreading and/or maintenance of inactivation. Repeat distribution analysis does not suggest an association between L1 and LINE repeat density on chromosome 5 and gene inactivation. The expression data may also explain why the proband manifests an attenuated clinical phenotype compared to subjects with partial chromosome 5 trisomy.

CLINICAL, MOLECULAR, AND PROTEIN CORRELATIONS IN A LARGE SAMPLE OF GENETICALLY DIAGNOSED ITALIAN LIMB GIRDLE MUSCULAR DYSTROPHY PATIENTS

Human Mutation 2008;29(2):258-266

Guglieri M, Magri F, D'Angelo MG, Prelle A, Morandi L, Rodolico C, Cagliani R, Mora M, Fortunato F, Bordoni A, Del Bo R, Ghezzi S, Pagliarani S, Lucchiari S, Salani S, Zecca C, Lamperti C, Ronchi D, Aguennouz M, Ciscato P, Di Blasi C, Ruggieri A, Moroni I, Turconi AC, Toscano A, Moggio M, Bresolin N, Comi GP.

I.F. 2007: 6,273

Limb girdle muscular dystrophies (LGMD) are characterized by genetic and clinical heterogeneity: seven autosomal dominant and 12 autosomal recessive loci have so far been identified. Aims of this

study were to evaluate the relative proportion of the different types of LGMD in 181 predominantly Italian LGMD patients (representing 155 independent families), to describe the clinical pattern of the different forms, and to identify possible correlations between genotype, phenotype, and protein expression levels, as prognostic factors. Based on protein data, the majority of probands (n=72) presented calpain-3 deficiency; other defects were as follows: dysferlin (n=31), sarcoglycans (n=32), alpha-dystroglycan (n=4), and caveolin-3 (n=2). Genetic analysis identified 111 different mutations, including 47 novel ones. LGMD relative frequency was as follows: LGMD1C (caveolin-3) 1.3%; LGMD2A (calpain-3) 28.4%; LGMD2B (dysferlin) 18.7%; LGMD2C (gamma-sarcoglycan) 4.5%; LGMD2D (alpha-sarcoglycan) 8.4%; LGMD2E (beta-sarcoglycan) 4.5%; LGMD2F (delta-sarcoglycan) 0.7%; LGMD2I (Fukutin-related protein) 6.4%; and undetermined 27.1%. Compared to Northern European populations, Italian patients are less likely to be affected with LGMD2I. The order of decreasing clinical severity was: sarcoglycanopathy, calpainopathy, dysferlinopathy, and caveolinopathy. LGMD2I patients showed both infantile noncongenital and mild late-onset presentations. Age at disease onset correlated with variability of genotype and protein levels in LGMD2B. Truncating mutations determined earlier onset than missense substitutions (20+/-5.1 years vs. 36.7+/-11.1 years; P=0.0037). Similarly, dysferlin absence was associated with an earlier onset when compared to partial deficiency (20.2+/-standard deviation [SD] 5.2 years vs. 28.4+/-SD 11.2 years; P=0.014). (c) 2007 Wiley-Liss, Inc.

CYTOSOLIC PH BUFFERING DURING EXERCISE AND RECOVERY IN SKELETAL MUSCLE OF PATIENTS WITH MCARDLE'S DISEASE

European Journal of Applied Physiology 2008;in press

Kemp GJ, Tonon C, Malucelli E, Testa C, Liava A, Manners D, Trevisi E, Martinuzzi A, Barbiroli B, Lodi R.

I.F. 2007: 1,752

Cellular pH control is important in muscle physiology, and for interpretation of (31)P magnetic resonance spectroscopy (MRS) data. Cellular acidification in exercise results from coupled glycolytic ATP production mitigated by cytosolic buffering, 'consumption' of H(+) by phosphocreatine (PCr) breakdown, and membrane transport processes. Ex vivo methods for cytosolic buffer capacity are vulnerable to artefact, and MRS methods often require assumptions. (31)P MRS of early exercise, when pH increases unopposed by glycolysis, is conceptually simple, but limited in normal muscle by time resolution and signal-to-noise. A therapeutic trial (Martinuzzi A et al. Musc Nerve 37: 350-357, 2007) in McArdle's disease (glycogen phosphorylase deficiency), where pH does not decrease with exercise, offered the opportunity to test (31)P MRS data obtained throughout incremental plantar flexion exercise and recovery in ten McArdle's patients against the simple model of cellular pH control. Changes in pH, [Pi] and [PCr] throughout exercise and recovery were quantitatively consistent with mean +/- SEM buffer capacity of 10 +/- 1 mM/(pH unit), which was not significantly different from the control subjects under the initial-exercise conditions where the comparison could be made. The simple model of cellular acid-base balance therefore gives an adequate account of cellular pH changes during both exercise and recovery in McArdle's disease.

COGNITIVE-BEHAVIOURAL STIMULATION PROTOCOL FOR SEVERELY BRAIN-DAMAGED PATIENTS IN THE POST-ACUTE STAGE IN DEVELOPMENTAL AGE

Disability and Rehabilitation 2008;30(4):275-285

Liscio M, Adduci A, Galbiati S, Poggi G, Sacchi D, Strazzer S, Castelli E, Flannery J.

I.F. 2007: 1,414

PURPOSE: To present a cognitive-behavioural stimulation (CBS) protocol designed to help severely damaged patients in the early post-acute stage by describing the underlying methodology and assessing its efficacy compared to traditional rehabilitation methods. This protocol combines multisensory stimulation and cognitive-behavioural techniques to elicit and intensify the occurrence of adaptive responses and reduce maladaptive behavioural patterns. METHODS: A control group and an experimental group--both evaluated with the Levels of Cognitive Functioning Assessment Scale (LOCFAS)--were compared at the beginning of the rehabilitation programme and at the end of it. The control group consisting of patients assessed and treated before receiving the CBS protocol was enrolled in a traditional rehabilitation programme (only physical therapy and speech therapy). Besides the traditional therapy, the experimental group also received the CBS protocol. RESULTS: Patients on the CBS proto-

col show a greater improvement and are therefore more responsive than the control group after the 16-week remediation programme. The mean LOCFAS improvement of the experimental group is more marked during the first month of rehabilitation and is associated to the entry LOCFAS level, while in the control group the improvement on LOCFAS is considered to be 'spontaneous' and is associated to the aetiology of the brain damage. CONCLUSIONS: Our results show a better initial outcome for patients receiving the CBS protocol.

STEM CELL THERAPY IN STROKE

Cellular and Molecular Life Sciences 2008;in press

Locatelli F, Bersano A, Ballabio E, Lanfranconi S, Papadimitriou D, Strazzer S, Bresolin N, Comi GP, Corti S.

I.F. 2007: 5,239

Recent work has focused on cell transplantation as a therapeutic option following ischemic stroke, based on animal studies showing that cells transplanted to the brain not only survive, but also lead to functional improvement. Neural degeneration after ischemia is not selective but involves different neuronal populations, as well as glial and endothelial cell types. In models of stroke, the principal mechanism by which any improvement has been observed, has been attributed to the release of trophic factors, possibly promoting endogenous repair mechanisms, reducing cell death and stimulating neurogenesis and angiogenesis. Initial human studies indicate that stem cell therapy may be technically feasible in stroke patients, however, issues still need to be addressed for use in human subjects.

ENDOSCOPIC ANATOMY OF THE FOURTH VENTRICLE

Journal of Neurosurgery 2008;109(3):530-535

Longatti P, Fiorindi A, Feletti A, D'Avella D, Martinuzzi A.

I.F. 2007: 1,990

OBJECT: Microsurgical anatomy of the fourth ventricle has been comprehensively addressed by masterly reports providing classic descriptions of this complex region. Neuroendoscopy could offer a new, somewhat different perspective of the "inside" view of the fourth ventricle. The purpose of this study was to examine from the anatomical point of view the access to the fourth ventricle achieved by the endoscopic transaqueductal approach, to enumerate and describe the anatomically identifiable landmarks, and to compare them with those described during microsurgery. METHODS: The video recordings of 52 of 75 endoscopic explorations of the fourth ventricle performed at the authors' institution for different pathological conditions were reviewed and evaluated to identify and describe every anatomical landmark. According to the microsurgical anatomy, at least 23 superficial structures are clearly identifiable in the fourth ventricle, and they represent the comparative basis of parallel endoscopic anatomy of the structures found during the fourth ventricle navigation. RESULTS: The following anatomical structures were identified in all cases: median sulcus, superior and inferior vela medullare, choroid plexus, inferior fovea, hypoglossal and vagal triangles, area postrema, obex, canalis medullaris, lateral recess, and the foramina of Luschka and Magendie. The median eminence, facial colliculus, striae medullaris, auditory tubercle, and inferior fovea were seen in the majority of cases. The locus caeruleus could never be seen. CONCLUSIONS: On the whole, 20 anatomical structures could consistently be identified by exploring the fourth ventricle with a fiberscope. Neuroendoscopy offers a quite different outlook on the anatomy of the fourth ventricle, and compared with the microsurgical descriptions it seems to provide a superior and detailed visualization, particularly of the structures located in the inferior triangle.

CHARCOT-MARIE-TOOTH TYPE 1A IN A CHILD WITH LONG QT SYNDROME

European Journal of Pediatric Neurology 2008;in press

Losito L, De Rinaldis M, Gennaro L, Priori SG, Bloise R, Bassi MT, Bresolin N, Trabacca A.

I.F. 2007: 0,861

Charcot-Marie-Tooth disease (CMTD) is a hereditary demyelinating peripheral neuropathy clinically presenting with sensory and motor defects, but rarely affecting cardiac function. Long QT syndrome (LQTS) is a congenital or acquired cardiovascular disorder characterized by ventricular depolarization defect. No studies reported CMTD in association with LQTS. We describe a child and his family who had both CMT1A and LQTS.

COLOCALIZATION OF RIBONUCLEAR INCLUSIONS WITH MUSCLE BLIND LIKE-PROTEINS IN A FAMILY WITH MYOTONIC

DYSTROPHY TYPE 2 ASSOCIATED WITH A SHORT CCTG EXPANSION

Journal of the Neurological Sciences 2008;275(1-2):159-163

Lucchiari S, Pagliarani S, Corti S, Mancinelli E, Servida M, Fruguglietti E, Sansone V, Moggio M, Bresolin N, Comi GP, Meola G.

I.F. 2007: 2,312

Myotonic dystrophy type 2 (DM2) is an autosomal dominant multisystemic disorder caused by a CCTG repeat expansion in intron 1 of the zinc finger protein 9 (ZNF9) gene. We present a three first-degree relative Italian family (proband, his mother and his sister) with a mild DM2 phenotype associated with a short (CCTG)(100) expansion as far as regards the proband and his mother, while his sister shows larger expansion correlated to a more severe phenotype. FISH analysis with (CAGG)(5) probe demonstrated that nuclear foci of mutant RNA were present in the proband muscle and co-localized with muscleblind-like proteins, determining their sequestration in the nucleus. This is one of the smallest expansion reported and the shortest with the evidence of nuclear foci. These data contribute to the clinical and molecular correlation of ZNF9 gene short expansion.

CORRELATION OF CIRCULATING CD133+ PROGENITOR SUBCLASSES WITH A MILD PHENOTYPE IN DUCHENNE MUSCULAR DYSTROPHY PATIENTS

Plos One 2008;3(5):E2218

Marchesi C, Belicchi M, Meregalli M, Farini A, Cattaneo A, Parolini D, Gavina M, Porretti L, D'Angelo MG, Bresolin N, Cossu G, Torrente Y.

I.F. 2007: 0,000

BACKGROUND: Various prognostic serum and cellular markers have been identified for many diseases, such as cardiovascular diseases and tumor pathologies. Here we assessed whether the levels of certain stem cells may predict the progression of Duchenne muscular dystrophy (DMD). METHODS AND FINDINGS: The levels of several subpopulations of circulating stem cells expressing the CD133 antigen were determined by flow cytometry in 70 DMD patients. The correlation between the levels and clinical status was assessed by statistical analysis. The median (+/-SD) age of the population was 10.66+/-3.81 (range 3 to 20 years). The levels of CD133+CXCR4+CD34- stem cells were significantly higher in DMD patients compared to healthy controls (mean+/-standard deviation: 17.38+/-1.38 vs. 11.0+/-1.70; P = 0.03) with a tendency towards decreased levels in older patients. Moreover, the levels of this subpopulation of cells correlated with the clinical condition. In a subgroup of 19 DMD patients after 24 months of follow-up, increased levels of CD133+CXCR4+CD34- cells was shown to be associated with a phenotype characterised by slower disease progression. The circulating CD133+CXCR4+CD34- cells in patients from different ages did not exhibit significant differences in their myogenic and endothelial in vitro differentiation capacity. CONCLUSIONS: Our results suggest that levels of CD133+CXCR4+CD34- could function as a new prognostic clinical marker for the progression of DMD.

ASSESSMENT OF LINGUISTIC ABILITIES IN ITALIAN CHILDREN WITH SPECIFIC LANGUAGE IMPAIRMENT

Neuropsychologia 2008;46(11):2816-2823

Marini A, Tavano A, Fabbro F.

I.F. 2007: 3,630

This study aims to describe in detail the linguistic skills of a large group of SLI participants. Particular attention is paid to the analysis of age-related effects on their linguistic performance and to whether a linguistic assessment of a narrative task can capture language impairments that might not be adequately pointed out by standardized neuropsychological tests assessing linguistic functions. The narratives produced by 62 children diagnosed with SLI with mixed expressive-receptive disorders were compared to those provided by a group of 195 children with Typical Language Development matched for chronological age and level of formal education. Furthermore, an age-related groups' performance analysis has been performed in order to determine possible correlations between patients' ages and types of language impairment. The SLI participants produced an amount of words comparable to that produced by the control group, albeit in a simpler fashion, as their narratives were teeming with omissions and/or substitutions of bound and free morphemes. These data suggest that the domains of morphosyntax and syntax were particularly impaired.

DISSEMINATING THE WHO INTERNATIONAL CLASSIFICATION OF FUNCTIONING HEALTH AND DISABILITY (ICF) IN THE VENETO REGION OF ITALY

Disability and Rehabilitation 2008;30(1):71-80

Martinuzzi A, Frare M, Pradal M, Mion M, Dugone

S, Durante M, Corò A, Francescutti C, Leonardi M.

I.F. 2007: 1,414

PURPOSE: To show the feasibility and effect of a large formation effort focused on the International Classification of Functioning, Disability and Health (ICF), which may introduce a revolutionary new conceptual framework for people involved in rehabilitation services. METHODS: We here describe the large information/formation project launched by the Regional Direction for Social Services of the Veneto region (Italy). Here we describe the first of the two steps of the project, aimed to reach 900 health professionals throughout the whole region. They were exposed to a structured modular course consisting of a mix of frontal lectures and workshop sessions. During the workshop sessions the participants were confronted with questions referring to the actual application of ICF in their services. RESULTS: The results show that the attendance (90%) was very high. The workshop sessions provided interesting indications on the possible applications of ICF in the clinical settings, as well as points of strength and potential problems that the implementation of ICF may have in the Regional Health Service. CONCLUSIONS: To our knowledge this is the largest alphabetization effort on ICF attempted in a public health system, and it indicates a possible effective approach to its controlled diffusion and future implementation.

RANDOMIZED PLACEBO-CONTROLLED DOUBLE-MIND PILOT TRIAL OF RAMIPRIL IN MCARDLE'S DISEASE

Muscle & Nerve 2008;37(3):350-357

Martinuzzi A, Liava A, Trevisi E, Frare M, Tonon C, Malucelli E, Manners D, Kemp G, Testa C, Barbiroli B, Lodi R.

I.F. 2007: 2,424

McArdle's disease causes limitation in exercise capacity as well as disability, the severity of which has been associated with the angiotensin-converting enzyme (ACE) insertion (I)/deletion (D) haplotype-patients with the genotype associated with higher ACE activity show the most severe phenotype. Modulation of ACE activity through the use of inhibitors may thus positively affect disease expression. In a double-blind, randomized, placebo-controlled trial, we assessed the efficacy of an ACE inhibitor (2.5 mg ramipril) in 8 patients with McArdle's disease. End-points were changes in parameters of exercise physiology (cycloergometer and muscle 31P-magnetic resonance spectroscopy), quality of life (QoL) according to the Short Form 36 (SF-36), and disability according to the World Health Organization-Disability Assessment Scale II (WHO-DAS II). Patients had lower QoL and higher disability than controls. Measures of exercise physiology were not changed by ramipril in the whole group, but treatment induced higher peak VO2 ($P = 0.017$) in ACE D/D patients, yet not in I/D patients. Treatment significantly improved disability ($P < 0.05$). McArdle's disease is a disabling condition affecting patients' QoL. Treatment with ramipril improves disability and modifies exercise physiology only in D/D patients, raising the possibility of a differential haplotype-linked sensitivity to the treatment.

DIFFUSE PONTINE GLIOMAS IN CHILDREN: CHANGING STRATEGIES, CHANGING RESULTS? A MONO-INSTITUTIONAL 20-YEAR EXPERIENCE

Journal of Neuro-Oncology 2008;87(3):355-361

Massimino M, Spreafico F, Biassoni V, Simonetti F, Riva D, Trecate G, Giombini S, Poggi G, Pecori E, Pignoli E, Casanova M, Ferrari A, Meazza C, Luksch R, Terenziani M, Cefalo G, Podda M, Polastri D, Clerici CA, Fossati-Bellani F, Gandola M.

I.F. 2007: 1,856

Patients with diffuse pontine gliomas have a median survival of less than one year and represent a challenge for pediatric oncologists, prompting them to attempt experimental therapies. From 1987 to 2005, 62 children with diffuse pontine glioma, not amenable to curative surgery, were treated according to four successive pilot protocols: (1) concomitant chemo-radiotherapy (etoposide, cytarabine, ifosfamide, cisplatin, and dactinomycin); (2) intensive high-dose courses chemotherapy (cisplatin/etoposide, cyclophosphamide/vincristine/methotrexate) and a subsequent course of myeloablative thiotepa followed by radiation and maintenance chemotherapy; (3) cisplatin/etoposide followed by isotretinoin before, during and after focal irradiation; and (4) iv vinorelbine before, during, and after irradiation. Considering all patients, 77% experienced a transient response to treatment, always detectable after radiotherapy. The progression-free survival (PFS) rate was 25 +/- 6% at one year, median PFS was seven months; overall survival (OS) was 45 +/- 6%, median OS was eleven months: no statistical differences in the four studies in terms of outcome were detected. Despite improved diagnostic, therapeutic, and supportive tools in pediatric neuro-oncology, little has been achieved for patients with diffuse pontine tumors.

NO SALVAGE USING HIGH-DOSE CHEMOTHERAPY PLUS/MINUS RE-IRRADIATION FOR RELAPSING, PREVIOUSLY IRRADIATED MEDULLOBLASTOMA

International Journal of Radiation Oncology Biology Physics 2008;in press

Massimino M, Gandola L, Spreafico F, Biassoni V, Luksch R, Collini P, Solero CL, Simonetti F, Pignoli E, Cefalo G, Poggi G, Modena P, Mariani L, Potepan P, Podda M, Casanova M, Pecori E, Acerno S, Ferrari A, Terenziani M, Meazza C, Polastri D, Ravagnani F, Fossati-Bellani F.

I.F. 2007: 4,290

PURPOSE: Myeloablative regimens were frequently used for medulloblastoma relapsing after craniospinal irradiation (CSI): in 1997-2002, we used repeated surgery, standard-dose and myeloablative chemotherapy, and reirradiation. METHODS AND MATERIALS: In 10 patients, reinduction included sequential high-dose etoposide, high-dose cyclophosphamide/vincristine, and high-dose carboplatin/vincristine, then two myeloablative courses with high-dose thiotepa (+/- carboplatin); 6 other patients received two of four courses of cisplatin/etoposide. Hematopoietic precursor mobilization followed high-dose etoposide or high-dose cyclophosphamide or cisplatin/etoposide therapy. After the overall chemotherapy program, reirradiation was prescribed when possible. RESULTS: Seventeen patients were treated: previous treatment included CSI of 19.5-36 Gy with posterior fossa/tumor boost and chemotherapy in 16 patients. Fifteen patients were in their first and 2 in their second and third relapses, respectively. First progression-free survival had lasted a median of 26 months. Relapse sites included leptomeninges in 9 patients, spine in 4 patients, posterior fossa in 3 patients, and brain in 1 patient. Three patients underwent complete resection of recurrence, and 10 underwent reirradiation. Twelve of 14 patients with assessable tumor had an objective response after reinduction; 2 experienced progression and were not given the myeloablative courses. Remission lasted a median of 16 months. Additional relapses appeared in 13 patients continuing the treatment. Fifteen patients died of progression and 1 died of pneumonia 13 months after relapse. The only survivor at 93 months had a single spinal metastasis that was excised and irradiated. Survival for the series as a whole was 11-93 months, with a median of 41 months. CONCLUSIONS: Despite responses being obtained and ample use of surgery and reirradiation, second-line therapy with myeloablative schedules was not curative, barring a few exceptions. A salvage therapy for medulloblastoma after CSI still needs to be sought.

SHARED NEUROCOGNITIVE DYSFUNCTIONS IN YOUNG OFFSPRINGS AT EXTREME RISK FOR SCHIZOPHRENIA OR BIPOLAR DISORDER IN EASTERN QUEBEC MULTIGENERATIONAL FAMILIES

Schizophrenia Bulletin 2008;in press

Maziade M, Rouleau N, Gingras N, Boutin P, Paradis ME, Jomphe V, Letourneau K, Gilbert E, Lefebvre AA, Dorè MC, Marino C, Battaglia M, Merette C, Roy MA.

I.F. 2007: 5,843

BACKGROUND: Adult patients having schizophrenia (SZ) or bipolar disorder (BP) may have in common neurocognitive deficits. Former evidence suggests impairments in several neuropsychological functions in young offspring at genetic risk for SZ or BP. Moreover, a dose-response relation may exist between the degree of familial loading and cognitive impairments. This study examines the cognitive functioning of high-risk (HR) offspring of parents having schizophrenia (HRSZ) and high-risk offspring of parents having bipolar disorder (HRBP) descending from densely affected kindreds. METHODS: The sample consisted of 45 young offspring (mean age of 17.3 years) born to a parent having SZ or BP descending from large multigenerational families of Eastern Québec that are densely affected by SZ or BP and followed up since 1989. The offspring were administered a lifetime best-estimate diagnostic procedure (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV]) and an extensive standard neuropsychological battery. Raw scores were compared with age- and gender-matched controls. RESULTS: The offspring displayed differences in memory and executive functions when compared with controls. Moderate to large effect sizes (Cohen d) ranging from 0.65 to 1.25 (for IQ and memory) were observed. Several of the cognitive dysfunctions were present in both HRSZ and HRBP, even when considering DSM-IV clinical status. CONCLUSIONS: HRSZ and HRBP shared several aspects of their cognitive impairment. Our data suggest that the extremely high genetic and familial loading of these HRs may have contributed to a quantitatively increased magnitude of the cognitive impairments in both HR

subgroups, especially in memory. These offspring at heightened risk present difficulties in processing information that warrant preventive research.

COMBINED BEHAVIORAL AND EEG POWER ANALYSIS IN DAI IMPROVE ACCURANCY IN THE ASSESSMENT OF SUSTAINED ATTENTION DEFICIT

Annals of Biomedical Engineering 2008;36(7):1216-1227

Molteni E, Bianchi AM, Butti M, Reni G, Zucca C.

I.F. 2007: 2,346

In clinical routine, the evaluation of sustained attention is often performed by analyzing the behavioral data collected during specific tests. Such analyses are rarely accompanied by a detailed examination of the subject's simultaneous electroencephalographic (EEG) activity, and particularly its frequency content. In this study, a group of healthy volunteers and a group of patients affected by diffuse axonal injury (DAI) were tested while performing a modified version of the Conners' continuous performance test. A comparative study was carried out between the behavioral and neuropsychological data obtained during the task, to investigate neural activation. Spectral power was calculated for each of the recorded EEG signals, taking account of the frequency bands traditionally considered in literature. Then a compressed spectral array sequence of spectra was plotted to put into evidence the temporal modifications in the signal power spectral density, and, finally, the analysis of the rhythm variability was carried out. Evaluation of the results thus obtained shows that the two groups registered very different cerebral activation dynamics during the ongoing attentional task. Moreover, DAI patients showed mild cortical activation in the prefrontal region, spread equally throughout both brain hemispheres, while controls showed strong predominant activation of the right prefrontal area. Our findings encourage further investigations of the combined employment of tests and EEG recordings during the clinical assessment of sustained attention performance.

MRI STUDY OF THE CEREBELLUM IN YOUNG BIPOLAR PATIENTS

Progress in Neuro-Psychopharmacology and Biological Psychiatry 2008;32(3):613-619

Monkul ES, Hatch JP, Sassi RB, Axelson D, Brambilla P, Nicoletti MA, Keshavan Matcheri S, Ryan N, Birmaher B, Soares JC.

I.F. 2007: 2,802

Prior studies demonstrate structural abnormalities of cerebellar vermis in adult bipolar patients. Cerebella of 16 young bipolar patients (mean age+/-S.D.=15.5+/-3.4) and 21 healthy controls (mean age+/-S.D.=16.9+/-3.8) were examined using magnetic resonance imaging. The volumes of right, left and total cerebellum, vermis, and areas of vermal regions V1 (lobules I-V), V2 (lobules VI-VII), and V3 (lobules VIII-X) were measured. Analysis of covariance, with age, gender, and intra-cranial brain volume as covariates, revealed no significant differences in cerebellum or vermis measures between patients and controls; however, there was a trend to smaller vermis V2 areas in patients (p=0.06). The number of previous affective episodes and vermis area V2 were inversely correlated (partial correlation coefficient=-0.97, P=0.001) in the male bipolar patient group. Our results are preliminary, but consistent with the findings from studies in adult bipolar patients suggesting the involvement of structural changes in cerebellar vermis in the pathophysiology of bipolar disorder.

THE DEVELOPMENT OF DYNAMIC FACIAL EXPRESSION RECOGNITION AT DIFFERENT INTENSITIES IN 4- TO 18-YEAR-OLDS

Social Development 2008;in press

Montirosso R, Peverelli M, Frigerio E, Crespi M, Borgatti R.

I.F. 2007: 0,986

Abstract non disponibile.

THE NEURAL BASIS OF BODY FORM AND BODY ACTION AGNOSIA

Neuron 2008;60(2):235-246

Moro V, Urgesi C, Pernigo S, Lanteri P, Pazzaglia M, Aglioti S.

I.F. 2007: 13,894

Visual analysis of faces and nonfacial body stimuli brings about neural activity in different cortical areas. Moreover, processing body form and body action relies on distinct neural substrates. Although brain lesion studies show specific face processing deficits, neuropsychological evidence for defective recognition of nonfacial body parts is lacking. By combining psychophysics studies with lesion-mapping techniques, we found that lesions of ventromedial, occipitotemporal areas induce face and body recognition deficits while lesions involving extrastriate body area

seem causatively associated with impaired recognition of body but not of face and object stimuli. We also found that body form and body action recognition deficits can be double dissociated and are causatively associated with lesions to extrastriate body area and ventral premotor cortex, respectively. Our study reports two category-specific visual deficits, called body form and body action agnosia, and highlights their neural underpinnings.

FINGER RECOGNITION AND GESTURE IMITATION IN GERSTMANN'S SYNDROME

Neurocase 2008;in press

Moro V, Pernigo S, Urgesi C, Zapparoli P, Aglioti S.

I.F. 2007: 1,505

We report the association between finger agnosia and gesture imitation deficits in a right-handed, right-hemisphere damaged patient with Gerstmann's syndrome (GS), a neuropsychological syndrome characterized by finger and toe agnosia, left-right disorientation and dyscalculia. No language deficits were found. The patient showed a gestural imitation deficit that specifically involved finger movements and postures. The association between finger recognition and imitation deficits suggests that both static and dynamic aspects of finger representations are impaired in GS. We suggest that GS is a disorder of body representation that involves hands and fingers, that is, the non-facial body parts most involved in social interactions.

HIPPOCAMPAL REMODELLING AFTER MDMA NEUROTOXICITY: A SINGLE CASE STUDY

World Journal of Biological Psychiatry (The) 2008;Case Report in press

Nifosi F, Martinuzzi A, Toffanin T, Costanzo R, Vestri A, Battaglia MA, Bertagnoni GE, Lupi A, Amistà P, Carollo C, Perini G.

I.F. 2007: 1,691

Acute ingestion of MDMA (ecstasy) causes a transient marked increase in serotonin and dopamine at central synapses. Recent studies demonstrated that MDMA induces damage of serotonergic nerve terminals and alters hippocampal processing. Pronounced cognitive deficits in MDMA users affect learning and memory abilities. This pattern of predominant and long-lasting memory dysfunction suggests that the functioning of the hippocampus might be affected by the neurotoxic effects of MDMA. We present the case of a 16-year-old girl who developed an acute organic and psychotic syndrome caused by occasional use of low to moderate dose of MDMA. Serial neuroimaging ((18)F-FDG-PET and brain MRI) were correlated with her neurocognitive performance and clinical evolution. The structural and metabolic changes correlated with a severe cognitive impairment. After 16 months of intensive neuropsychological rehabilitation she showed significant improvement in hippocampal-related memory cognitive functions, which correlated with normalization of her (18)F-FDG-PET and remarkable hippocampal remodelling. This case report indicates that even non-chronic MDMA use may cause subacute toxic encephalopathy in which the clinical evolution is paralleled by neuroimaging changes in specific cerebral areas. The most relevant aspect is the reversibility of the volumetric changes, which may be the structural correlate of an ongoing hippocampal remodelling.

THE INFLUENCE OF FAMILY STRUCTURE, THE TPH2 G-703T AND THE 5-HTTLPR SEROTONERGIC GENES UPON AFFECTIVE PROBLEMS IN CHILDREN AGED 10-14 YEARS

Journal of Child Psychology and Psychiatry 2008;in press

Nobile M, Rusconi M, Bellina M, Marino C, Giorda R, Carlet O, Vanzin L, Molteni M, Battaglia M.

I.F. 2007: 4,432

Abstract non disponibile.

MITOCHONDRIAL DNA BACKGROUND MODULATES THE ASSEMBLY KINETICS OF OXPHOS COMPLEXES IN A CELLULAR MODEL OF MITOCHONDRIAL DISEASE

Human Molecular Genetics 2008;17(24):4001-4011

Pello R, Martin MA, Carelli V, Nijtmans LG, Achilli A, Pala M, Torroni A, Gómez-Durán A, Ruiz-Pesini E, Martinuzzi A, Smeitink Jan A, Arenas J, Ugalde C.

I.F. 2007: 7,806

Leber's hereditary optic neuropathy (LHON), the most frequent mitochondrial disorder, is mostly due to three mitochondrial DNA (mtDNA) mutations in respiratory chain complex I subunit genes: 3460/ND1, 11778/ND4 and 14484/ND6. Despite considerable clinical evidences, a genetic modifying role of the mtDNA haplogroup background in the clinical expression of LHON remains experimentally unproven. We investigated the effect of mtDNA haplo-

groups on the assembly of oxidative phosphorylation (OXPHOS) complexes in transmitochondrial hybrids (cybrids) harboring the three common LHON mutations. The steady-state levels of respiratory chain complexes appeared normal in mutant cybrids. However, an accumulation of low molecular weight subcomplexes suggested a complex I assembly/stability defect, which was further demonstrated by reversibly inhibiting mitochondrial protein translation with doxycycline. Our results showed differentially delayed assembly rates of respiratory chain complexes I, III and IV amongst mutants belonging to different mtDNA haplogroups, revealing that specific mtDNA polymorphisms may modify the pathogenic potential of LHON mutations by affecting the overall assembly kinetics of OXPHOS complexes.

NITRIC OXIDE AND SPHINGOLIPIDS: MECHANISMS OF INTERACTION AND ROLE IN CELLULAR PATHOPHISIOLOGY

Biological Chemistry 2008;389(11):1391-1397

Perrotta C, De Palma C, Clementi E.

I.F. 2007: 2,840

Nitric oxide is a short-lived messenger with pleiotropic roles in the regulation of cell patho-physiological processes, including survival, death, proliferation and differentiation. Increasing evidence over the last few years has shown that nitric oxide effects in apoptosis, growth and differentiation originate in significant part from its interplay with signalling members of the sphingolipid family. In many cell types belonging to different lineages, nitric oxide and sphingolipids interact in two-way pathways leading to regulation of the activity and expression of enzymes involved in each other's signalling events. These crosstalk signalling events involve various sphingolipids, with key roles for ceramide and sphingosine-1-phosphate, and signal transduction molecules downstream of nitric oxide, with cyclic GMP as a main player. The biological implications of some of these interactions are now being understood. The best-characterised so far, the mutual regulation of sphingomyelinases and endothelial nitric oxide synthase, acts as a tuning system in crucial patho-physiological processes such as inflammation, proliferation and cell death.

THE CO-OCCURRENCE BETWEEN INTERNALIZING AND EXTERNALIZING BEHAVIORS

European Child and Adolescent Psychiatry 2008;17(2):82-92

Pesenti-Gritti P, Spatola CAM, Fagnani C, Ogliari A, Patriarca V, Stazi MA, Battaglia M.

I.F. 2007: 1,992

Although Internalized and Externalized problem behaviors are described as separate phenomena at the psychometric and clinical levels, they frequently co-occur. Only few studies, however, have investigated the causes of such covariation. In a sample of 398 twin pairs aged 8-17 drawn from the general population-based Italian Twin Registry, we applied bivariate genetic analyses to parent-rated CBCL/6-18 Internalization and Externalization scores. Covariation of Internalizing and Externalizing problem behaviors was best explained by genetic and common environmental factors, while the influence of unique environmental factors upon covariance appeared negligible. Odds ratio values showed that a borderline/clinical level of Externalization is a robust predictor of co-existing Internalizing problems in the same child, or within a sibship. Our findings help to approximate individual risks (e.g., in clinical practice, predicting the presence of Internalization in an externalizing child, and vice-versa), and to recognize that several shared environmental and genetic factors can simultaneously affect a child's proneness to suffer from both types of problem behaviors.

ACADEMIC PERFORMANCE IN CHILDREN WITH ROLANDIC EPILEPSY

Developmental Medicine and Child Neurology 2008;50(5):353-356

Piccinelli P, Borgatti R, Aldini A, Bindelli D, Ferri M, Perna S, Pitillo G, Termine C, Zambonin F, Balottin U.

I.F. 2007: 2,433

The aim of this study was to investigate the frequency of reading, writing, and calculation disabilities in children with typical rolandic epilepsy (RE) and healthy control children. We also aimed to define the possible electroclinical markers of specific cognitive dysfunctions in RE. School abilities were evaluated and compared in 20 children (eight males, 12 females; mean age 10y 3mo [SD 1y 7mo]; range 7y 9mo-12y 9mo) consecutively diagnosed with typical RE, and a group of 21 healthy controls (nine males, 12 females; mean age 10y 4mo [SD 1y 8mo]; range 7y 6mo-13y 3mo). All the children received standardized neuropsychological tests. For each patient an exhaustive seizure diary was kept and all the sleep electroencephalogram (EEG) recordings were reviewed. Specific difficulties with

reading, writing, and calculation (diagnosed according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition) were found in nine out of 20 children with RE and two out of 21 healthy controls (chi2=0.01). The specific learning disabilities in the RE group were correlated with a marked increase in epileptiform discharges during sleep (chi2=0.02) and an early onset of epilepsy (chi2=0.02). Our findings suggest that seizure onset before age 8 years and epileptiform discharges (more than 50% of the sleep EEG recording) in several tracings over more than a year are relevant markers for identifying patients at risk of developing academic difficulties.

PSYCHOLOGICAL INTERVENTION IN YOUNG BRAIN TUMOR SURVIVORS: THE EFFICACY OF THE COGNITIVE BEHAVIOURAL APPROACH

Disability and Rehabilitation 2008;in press

Poggi G, Liscio M, Pastore V, Adduci A, Galbiati S, Spreafico F, Gandola L, Massimino M.

I.F. 2007: 1,414

Abstract non disponibile.

RESPIRATORY COMPLEX I DYSFUNTION DUE TO MITOCHONDRIAL DNA MUTATIONS SHIFTS THE VOLTAGE THRESHOLD FOR OPENING OF THE PERMEABILITY TRANSITION PORE TOWARD RESTING LEVELS

Journal of Biological Chemistry 2008;in press

Porcelli AM, Angelin A, Ghelli A, Mariani E, Martinuzzi A, Carelli V, Petronilli V, Bernardi P, Rugolo M.

I.F. 2007: 5,581

We have studied mitochondrial bioenergetics in HL180 cells (a cybrid line harboring the T14484C/ND6 and G14279A/ND6 mtDNA mutations of Leber hereditary optic neuropathy, leading to an about 50% decrease of ATP synthesis) and XTC.UC1 cells (derived from a thyroid oncocytoma bearing a disruptive frameshift mutation in the MT-ND1 gene, which impairs complex I assembly). Addition of rotenone to HL180 cells and of antimycin A to XTC.UC1 cells caused fast mitochondrial membrane depolarization that was prevented by treatment with cyclosporin A, intracellular Ca2+ chelators, and antioxidant. Both cell lines also displayed an anomalous response to oligomycin, with rapid onset of depolarization that was prevented by cyclosporin A and by overexpression of Bcl-2. These findings indicate that depolarization by respiratory chain inhibitors and oligomycin was due to opening of the mitochondrial permeability transition pore (PTP). A shift of the threshold voltage for PTP opening close to the resting potential may therefore be the underlying cause facilitating cell death in diseases affecting complex I activity. This study provides a unifying reading frame for previous observations on mitochondrial dysfunction, bioenergetic defects and Ca2+ deregulation in mitochondrial diseases. Therapeutic strategies aimed at normalizing the PTP voltage threshold may be instrumental in ameliorating the course of complex I-dependent mitochondrial diseases.

BOTH SELECTIVE AND NEUTRAL PROCESSES DRIVE GC CONTENT EVOLUTION IN THE HUMAN GENOME

BMC Evolutionary Biology 2008;8:99

Pozzoli U, Menozzi G, Fumagalli M, Cereda M, Comi GP, Cagliani R, Bresolin N, Sironi M.

I.F. 2007: 4,091

BACKGROUND: Mammalian genomes consist of regions differing in GC content, referred to as isochores or GC-content domains. The scientific debate is still open as to whether such compositional heterogeneity is a selected or neutral trait. RESULTS: Here we analyze SNP allele frequencies, retrotransposon insertion polymorphisms (RIPs), as well as fixed substitutions accumulated in the human lineage since its divergence from chimpanzee to indicate that biased gene conversion (BGC) has been playing a role in within-genome GC content variation. Yet, a distinct contribution to GC content evolution is accounted for by a selective process. Accordingly, we searched for independent evidences that GC content distribution does not conform to neutral expectations. Indeed, after correcting for possible biases, we show that intron GC content and size display isochore-specific correlations. CONCLUSION: We consider that the more parsimonious explanation for our results is that GC content is subjected to the action of both weak selection and BGC in the human genome with features such as nucleosome positioning or chromatin conformation possibly representing the final target of selective processes. This view might reconcile previous contrasting findings and add some theoretical background to recent evidences suggesting that GC content domains display diffe-

rent behaviors with respect to highly regulated biological processes such as developmentally-stage related gene expression and programmed replication timing during neural stem cell differentiation.

PHARMACOLOGICAL AND NUTRITIONAL TREATMENT FOR McARDLE DISEASE (GLYCOGEN STORAGE DISEASE TYPE V)

Cochrane Database of Systematic Reviews 2008;2(CD003458) – Review

Quinlivan R, Beynon RJ, Martinuzzi A.

I.F. 2007: 4,654

BACKGROUND: McArdle disease (Glycogen Storage Disease type V) is caused by the absence of the glycolytic enzyme, muscle phosphorylase. People present with exercise-induced pain, cramps, fatigue, and myoglobinuria, which can result in acute renal failure if it is severe. OBJECTIVES: To systematically review the evidence from randomised controlled trials of pharmacological or nutritional treatments in improving exercise performance and quality of life in McArdle disease. SEARCH STRATEGY: We updated the review by searching the Cochrane Neuromuscular Disease Group Trials Register (November 2007), MEDLINE (January 1966 to November 2007) and EMBASE (January 1980 to November 2007) using the search terms 'McArdle disease' and its synonym 'Glycogen Storage Disease type V'. SELECTION CRITERIA: We included randomised controlled trials (including crossover studies) and quasi-randomised trials. Open trials and individual patient studies with no participant or observer blinding were included in the discussion. Types of interventions included any pharmacological agent or micronutrient or macronutrient supplementation. Primary outcome measures included any objective assessment of exercise endurance (for example aerobic capacity (VO(2)) max, walking speed, muscle force or power and improvement in fatiguability). Secondary outcome measures included metabolic changes (such as reduced plasma creatine kinase activity and a reduction in the frequency of myoglobinuria), subjective measures (including quality of life scores and indices of disability) and serious adverse events. DATA COLLECTION AND ANALYSIS: Three review authors checked the titles and abstracts identified by the search and reviewed the manuscripts. Two review authors (RQ and RB) independently assessed methodological quality of the full text of potentially relevant studies and extracted data onto a specially designed form. MAIN RESULTS: We reviewed 24 studies. Twelve trials fulfilled the criteria for inclusion, with two being first identified in this update. The 12 excluded trials are included in the discussion. The largest treatment trial included 19 cases. The other trials included fewer than 12 cases. As there were only single trials for a given intervention we were unable to undertake a meta-analysis. AUTHORS' CONCLUSIONS: There is no evidence of significant benefit from any specific nutritional or pharmacological treatment in McArdle disease. In one small trial low dose creatine produced slight benefit but high dose creatine caused myalgia. Ingestion of oral sucrose immediately before exercise reduced perceived ratings of exertion and heart rate and improved exercise tolerance. This treatment will not influence sustained or unexpected exercise and may cause significant weight gain. A carbohydrate rich diet did benefit patients. Because of the rarity of McArdle disease, there is a need to develop international multicentre collaboration and standardised assessment protocols for future treatment trials.

DISSOCIATED EFFECTS OF QUIET STANCE ON STANDARD AND HIGH-FREQUENCY (600 HZ) LOWER LIMB SOMATOSENSORY EVOKED POTENTIALS

Clinical Neurophysiology 2008;119(6):1408-1418

Restuccia D, Micoli B, Cazzagon M, Fantinel R, Del Piero I, Della Marca G.

I.F. 2007: 2,468

OBJECTIVE: To verify whether standing can modulate somatosensory input from lower limb to the cortex. Somatosensory afferents have been evaluated not only by means of somatosensory evoked potentials recorded by means of classical wide-bandpass filtering (standard SEPs), but also by high-frequency somatosensory evoked potentials (HF-SEPs), which probably play a role in the processing of rapid adaptive changes. METHODS: Eight healthy subjects underwent right posterior tibial nerve (PTN) stimulation in two different conditions (standing and lying supine). Standard SEPs reflecting the activity of both subcortical and cortical generators further underwent digital filtering (300-800 Hz), in order to enhance HF-SEP components. RESULTS: Stance significantly reduces the P40 cortical component of standard SEPs. By contrast, HF-SEPs did not show any significant change between the two conditions. CONCLUSIONS: The lack of any gating effect on HF-SEPs lends further substance to the hypothesis that HF-SEPs play a

pivotal role in the processing of somatosensory inputs related to rapid adaptive changes. SIGNIFICANCE: Our data confirm that standard and HF-SEPs reflect two distinct mechanisms with strongly different functional significance. Further studies are needed to definitively establish whether this dissociation is merely caused by the activation of anatomically different neuronal pools, or by the involvement of distinct functional mechanisms.

MUTATIONS IN CNGA3 IMPAIR TRAFFICKING OR FUNCTION OF CONE CYCLIC NUCLEOTIDE-GATED CHANNELS, RESULTING IN ACHROMATOPSIA

Human Mutation 2008;29(10):1228-1236

Reuter P, Koeppen K, Ladewig T, Kohl S, Baumann B, Achromatopsia Clinical Study Group (Giorda R), Wissinger B.

I.F. 2007: 6,273

CNGA3 encodes the A-subunit of the cone photoreceptor cyclic nucleotide-gated (CNG) channel, which is a crucial component of the phototransduction cascade in cone outer segments. Mutations in the CNGA3 gene have been associated with complete and incomplete forms of achromatopsia (ACHR), a congenital, autosomal recessively inherited retinal disorder characterized by lack of color discrimination, reduced visual acuity, nystagmus, and photophobia. Here we report the identification of three novel CNGA3 missense mutations in ACHR patients: c.682G>A (p.E228 K), c.1315C>T (p.R439W), and c.1405G>A (p.A469 T), and the detailed functional analyses of these new as well as five previously reported mutations (R283Q, T291R, F547L, G557R, and E590 K), in conjunction with clinical data of patients carrying these mutations, to establish genotype-phenotype correlations. The functional characterization of mutant CNGA3 channels was performed with calcium imaging and patch clamp recordings in a heterologous HEK293 cell expression system. Results were corroborated by immunostaining and colocalization experiments of the channel protein with the plasma membrane. Several mutations evoked pronounced alterations of the apparent cGMP sensitivity of mutant channels. These functional defects were fully or partially compensated by coexpressing the mutant CNGA3 subunit with the wild-type CNGB3 subunit for channels with the mutations R439W, A469 T, F547L, and E590 K. We could show that several mutant channels with agonist dose-response relationships similar to the wild-type exhibited severely impaired membrane targeting. In addition, this study presents the positive effect of reduced cell culture temperature on surface expression and functional performance of mutant CNG channels with protein folding or trafficking defects.

CORNELIA DE LANGE SYNDROME MUTATIONS IN SMC1A OR SMC3 AFFECT BINDING TO DNA

Human Molecular Genetics 2008;18, in press

Revenkova E, Focarelli ML, Susani L, Paulis M, Bassi MT, Mannini L, Frattini A, Delia D, Krantz I, Vezzoni P, Jessberger R, Musio A.

I.F. 2007: 7,806

Cornelia de Lange syndrome (CdLS) is a clinically heterogeneous developmental disorder characterized by facial dysmorphia, upper-limb malformations, growth and cognitive retardation. Mutations in the sister chromatid cohesion factor genes NIPBL, SMC1A and SMC3 are present in about 65% of CdLS patients. In addition to their canonical roles in chromosome segregation, the cohesin proteins are involved in other biological processes such as regulation of gene expression, DNA repair and maintenance of genome stability. To gain insights into the molecular basis of CdLS, we analysed the affinity of mutated SMC1A and SMC3 hinge domains for DNA. Mutated hinge dimers bind DNA with higher affinity than wild type proteins. SMC1A- and SMC3-mutated CdLS cell lines display genomic instability and sensitivity to ionizing radiation and interstrand crosslinking agents. We propose that SMC1A and SMC3 CdLS mutations affect the dynamic association between SMC proteins and DNA, providing new clues to the underlying molecular cause of CdLS.

BEHAVIORAL AND EMOTIONAL PROBLEMS AMONG ITALIAN INTERNATIONAL ADOPTEES AND NON-ADOPTED CHILDREN: FATHER'S AND MOTHER'S REPORTS

Journal of Family Psychology 2008;22(3):541-549

Rosnati R, Montirosso R, Barni D.

I.F. 2007: 1,728

This study intends to fill the gap in empirical research carried out in Italy regarding international adoptees' behavioral and emotional problems. Assuming a multi-informant approach, it aims to compare parents' reports of behavioral problems of adopted and non-adopted children and to exa-

mine parental agreement. The sample was composed of 186 adoptive couples and 195 biological couples with the target child between ages 7 and 11 years. The mother and father filled in the Child Behavior Checklist (CBCL) separately. Analysis of the CBCL revealed that adopted children are perceived by their parents as having more Total and Externalizing Problems than are their non-adopted counterparts. Moreover, they are more likely to demonstrate attention difficulties and aggressive behavior. The agreement between parents turned out to be moderate for adoptive parents and slightly lower for the biological ones. Consistent with most adoption research, the results confirm the higher risk of behavioral problems among adopted children. They also shed light on the significant perceptual discrepancy between mothers and fathers, underlining the importance of considering both parents' reports in the study of adopted children's adjustment.

A 12 MB DELETION AT 7Q33-Q35 ASSOCIATED WITH AUTISM SPECTRUM DISORDERS AND PRIMARY AMENORRHEA

European Journal of Medical Genetics 2008;51(6):631-638

Rossi E, Verri AP, Patricelli MG, Destefani V, Ricca I, Vetro A, Ciccone R, Giorda R, Toniolo D, Maraschio P, Zuffardi O.

I.F. 2007: 1,857

An interstitial deletion of about 12Mb at 7q33-q36 was found in an adult female affected by autism and primary amenorrhea. Two genes, CNTNAP2 and NOBOX, both contained within the deletion region, have been recently associated with autism susceptibility and premature ovarian failure, respectively. Our findings reinforce the hypothesis that haploinsufficiency of both these genes is sufficient for autism development and occurrence of primary amenorrhea, confirming a previous case in which CNTNAP2 had been disrupted by a chromosome inversion and possibly enlarging the phenotype of ovarian function disturbances already demonstrated for NOBOX mutations.

CELL DEATH: TIPPING THE BALANCE OF AUTOIMMUNITY AND TISSUE REPAIR

Current Pharmaceutical Design 2008;14(3):269-277 – Review

Rovere-Querini P, Brunelli S, Clementi E, Manfredi AA.

I.F. 2007: 4,868

Inflammation is a key homeostatic process elicited by microbial components and by tissue damage. Increasing evidence indicates that the outcomes either tissue repair or persistent inflammatory damage and degeneration tightly depend on the pattern of cell death in situ and on infiltrating leukocytes and antigen presenting cells. Defects in the initiation and execution steps of programmed cell death such as in the clearance of cell debris are indeed often associated to inflammation defective repair and autoimmunity. Here we report recent developments on the control of apoptosis induction and execution discussing how cell death may be exploited for therapeutic purposes and the links between cell death persisting inflammation and stem cell recruitment and activation in experimental models of complex human diseases such as muscular dystrophy and cancer.

LACK OF EVIDENCE FOR OXIDATIVE STRESS IN SPORADIC AMYOTROPHIC LATERAL SCLEROSIS FIBROBLASTS

Neurodegenerative Diseases 2008;6(1-2):9-15

Sala G, Trombin F, Mattavelli L, Beretta S, Tremolizzo L, Andreoni S, Calabrese E, Sanvito L, Ferrarese C.

I.F. 2007: 0,000

BACKGROUND: It is conceivable that an early therapeutic intervention in amyotrophic lateral sclerosis (ALS) would lead to better results in terms of disease progression for these patients. One possible strategy to increase the sensitivity of the diagnosis is represented by the use of biological parameters reflecting, for example, oxidative stress alterations associated with ALS. Such biomarkers would be valuable tools both for a better diagnostic evaluation and for studying the impact of therapeutic interventions on the disease course. A special category of experimental models is represented by peripheral cells obtained directly from patients (ex vivo). OBJECTIVE: In this study, primary fibroblasts obtained from 10 sporadic ALS (SALS) patients and 10 healthy matched controls were used to investigate a panel of parameters related to the oxidative status. METHODS: Reactive oxygen species production, protein carbonylation and nitration, susceptibility to hydrogen peroxide exposure, p38-mitogen-activated protein kinase activation and adenosine triphosphate intracellular content were evaluated. RESULTS: No significant difference was observed in all investigated parameters between patient and control cells, and no correlation with

the disease severity was found. CONCLUSION: Collectively, our data show no major alterations of the oxidative and bioenergetic status in SALS cultured fibroblasts, suggesting that these cells do not represent a useful model to study the oxidative dysfunction associated with SALS. Copyright 2008 S. Karger AG, Basel.

ANTIOXIDANTS PARTIALLY RESTORE GLUTAMATE TRANSPORT DEFECT IN LEBER HEREDITARY OPTIC NEUROPATHY CYBRIDS

Journal of Neuroscience Research 2008;86(15):3331-3337

Sala G, Trombin F, Beretta S, Tremolizzo L, Presutto P, Montopoli M, Fantin M, Martinuzzi A, Carelli V, Ferrarese C.

I.F. 2007: 3,268

Leber hereditary optic neuropathy (LHON) is a mitochondrial disease characterized by visual loss resulting from retinal ganglion cell degeneration. Despite the important role of respiratory chain deficiency and oxidative stress induced by mtDNA point mutations affecting complex I, excitotoxic injury has been postulated as a concurrent pathogenic factor. We used transmitochondrial cybrid cell lines constructed using enucleated fibroblasts from three LHON probands carrying the most severe 3460/ND1 mutation and three controls as mitochondria donors, and the osteosarcoma-derived mtDNA-less cells, to study the possible efficacy of two selected antioxidant compounds in preventing glutamate uptake reduction previously observed in LHON cybrids. We demonstrated that two antioxidants, Trolox and decylubiquinone, partially restore glutamate transport impairment occurring in LHON cybrids. Rotenone, a classic complex I inhibitor, did not worsen the glutamate uptake defect present in LHON cybrids under basal conditions but significantly reduced glutamate transport in control cybrids. Furthermore, we observed that LHON cybrids showed an increased protein carbonylation under basal conditions, not further affected by rotenone and partially counteracted by antioxidants. Our findings strengthen the hypothesis that the complex I defect associated with LHON causes free radical overproduction, which is responsible for glutamate transport inhibition. We suggest that selected antioxidants may be clinically tested in LHON patients and relatives to restore glutamate uptake defect caused by LHON-associated free radical overproduction.

COGNITIVE MEMORY CONTROL IN BORDERLINE PERSONALITY DISORDER PATIENTS

Psychological Medicine 2008;in press

Sala M, Caverzasi E, Marraffini E, De Vidovich G, Lazzaretti M, D'Allio G, Isola M, Balestrieri M, D'Angelo E, Zappoli Thyrion F, Scagnelli P, Barale F, Brambilla P.

I.F. 2007: 4,212

BACKGROUND: It has been demonstrated that the mechanism of cognitive memory control in humans is sustained by the hippocampus and prefrontal cortices, which have been found to be structurally and functionally abnormal in borderline personality disorder (BPD). We investigated whether the memory control mechanism is affected in BPD. MethodNineteen Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV BPD patients and 19 matched healthy controls (HC) performed a specific think/no-think paradigm exploring the capacity of remembering and suppressing pair of words previously learned. After the think-no think phase, the second member of each word pair has to be remembered either when subjects are presented with the cue word showed at the beginning of the test (Same Probe Test; SPT) or when they are presented with an extra-list categorical word (Independent Probe Test; IPT). We evaluated the effect of suppression and of retrieval activity on later retention of words. RESULTS: Both on the SPT and on the IPT, HC showed the expected improvement of memory retrieval on to-be-remembered words, unlike BPD patients. On the SPT, HC, but not BPD patients, correctly recalled significantly more words among remembered words (RW) than among suppressed words (SW). Similarly to HC, subjects with BPD without a history of childhood abuse showed a significantly higher percentage of correctly recalled words among RW than among SW. CONCLUSIONS: The mechanism of active retrieval of memories and of improvement through repetition is impaired in BPD, particularly in those who experienced traumatic experiences. This impairment might play an important role, possibly resulting in the emergence of unwanted memories and dissociative symptoms.

BINDING OF SFRP-3 TO EGF IN THE EXTRA-CELLULAR SPACE AFFECTS PROLIFERATION, DIFFERENTIATION AND MORPHOGENETIC EVENTS REGULATED BY THE TWO MOLECULES

Plos One 2008;3(6):E2471

Scardigli R, Gargioli C, Tosoni D, Borello U,

Sampaolesi M, Sciorati C, Cannata S, Clementi E, Brunelli S, Cossu G.

I.F. 2007: 0,000

BACKGROUND: sFRP-3 is a soluble antagonist of Wnts, widely expressed in developing embryos. The Wnt gene family comprises cysteine-rich secreted ligands that regulate cell proliferation, differentiation, organogenesis and oncogenesis of different organisms ranging from worms to mammals. In the canonical signal transduction pathway Wnt proteins bind to the extracellular domain of Frizzled receptors and consequently recruit Dishevelled (Dsh) to the cell membrane. In addition to Wnt membrane receptors belonging to the Frizzled family, several other molecules have been described which share homology in the CRD domain and lack the putative trans-membrane domain, such as sFRP molecules (soluble Frizzled Related Protein). Among them, sFRP-3 was originally isolated from bovine articular cartilage and also as a component of the Spemann organizer. sFRP-3 blocks Wnt-8 induced axis duplication in Xenopus embryos and binds to the surface of cells expressing a membrane-anchored form of Wnt-1. Injection of sFRP-3 mRNA blocks expression of XMyoD mRNA and leads to embryos with enlarged heads and shortened trunks. METHODOLOGY/PRINCIPAL FINDINGS: Here we report that sFRP-3 specifically blocks EGF-induced fibroblast proliferation and foci formation. Over-expression of sFRP-3 reverts EGF-mediated inhibition of hair follicle development in the mouse ectoderm while its ablation in Xenopus maintains EGF-mediated inhibition of ectoderm differentiation. Conversely, over-expression of EGF reverts the inhibition of somitic myogenesis and axis truncation in Xenopus and mouse embryos caused by sFRP-3. In vitro experiments demonstrated a direct binding of EGF to sFRP-3 both on heparin and on the surface of CHO cells where the molecule had been membrane anchored. CONCLUSIONS/SIGNIFICANCE: sFRP-3 and EGF reciprocally inhibit their effects on cell proliferation, differentiation and morphogenesis and indeed are expressed in contiguous domains of the embryo, suggesting that in addition to their canonical ligands (Wnt and EGF receptor, respectively) these molecules bind to each other and regulate their activities during embryogenesis

BRAIN MAGNETIC RESONANCE IMAGING AFTER HIGH-DOSE CHEMOTHERAPY AND RADIOTHERAPY FOR CHILDHOOD BRAIN TUMORS

International Journal of Radiation Oncology Biology Physics 2008;70(4):1011-1019

Spreafico F, Gandola L, Marchianò A, Simonetti F, Poggi G, Adduci A, Clerici CA, Luksch R, Biassoni V, Meazza C, Catania S, Terenziani M, Musumeci R, Fossati-Bellani F, Massimino M.

I.F. 2007: 4,290

PURPOSE: Brain necrosis or other subacute iatrogenic reactions has been recognized as a potential complication of radiotherapy (RT), although the possible synergistic effects of high-dose chemotherapy and RT might have been underestimated. METHODS AND MATERIALS: We reviewed the clinical and radiologic data of 49 consecutive children with malignant brain tumors treated with high-dose thiotepa and autologous hematopoietic stem cell rescue, preceded or followed by RT. The patients were assessed for neurocognitive tests to identify any correlation with magnetic resonance imaging (MRI) anomalies. RESULTS: Of the 49 children, 18 (6 of 25 with high-grade gliomas and 12 of 24 with primitive neuroectodermal tumors) had abnormal brain MRI findings occurring a median of 8 months (range, 2-39 months) after RT and beginning to regress a median of 13 months (range, 2-26 months) after onset. The most common lesion pattern involved multiple pseudonodular, millimeter-size, T1-weighted unevenly enhancing, and T2-weighted hyperintense foci. Four patients with primitive neuroectodermal tumors also had subdural fluid leaks, with meningeal enhancement over the effusion. One-half of the patients had symptoms relating to the new radiographic findings. The MRI lesion-free survival rate was 74%+/-6% at 1 year and 57%+/-8% at 2 years. The number of marrow ablative courses correlated significantly to the incidence of radiographic anomalies. No significant difference was found in intelligent quotient scores between children with and without radiographic changes. CONCLUSION: Multiple enhancing cerebral lesions were frequently seen on MRI scans soon after high-dose chemotherapy and RT. Such findings pose a major diagnostic challenge in terms of their differential diagnosis vis-à-vis recurrent tumor. Their correlation with neurocognitive results deserves further investigation.

SPECIFIC LINGUISTIC AND PRAGMATIC DEFICITS IN ITALIAN PATIENTS WITH SCHIZOPHRENIA

Schizophrenia Research 2008;102(1-3):53-62

Tavano A, Sponda S, Fabbro F, Perlini C, Rambaldelli G, Ferro A, Cerruti S, Tansella M, Brambilla P.

I.F. 2007: 4,240

OBJECTIVE: Verbal communication impairments are prominent features of schizophrenia. The grammatical and pragmatic components of expressive and receptive verbal abilities were systematically examined, for the first time, in Italian patients with schizophrenia. Indeed, most of the language literature is composed of studies on English speaking people. METHOD: Elicited narrative production, and syntactic and pragmatic receptive abilities were analyzed in a cohort of 37 patients with schizophrenia and 37 healthy controls. Furthermore, a conversational speech production task was administered to an age- and gender-matched subset of this population. The level of significance was set at p<or=0.01. RESULTS: Participants with schizophrenia produced significantly less words on the narrative task and were less fluent on the conversational task than healthy controls. In both narrative and conversational speech they showed significantly poorer syntactic diversity skills. Errors at word level did not distinguish the two groups. At a receptive level, syntactic abilities were selectively impaired in patients with schizophrenia, who were also slower than controls in providing their answers. Metaphor and idiom explanations revealed consistent deficits in patients with respect to controls. CONCLUSIONS: Reduced syntactic diversity characterized expressive language skills in schizophrenia. Syntactic abilities were selectively impaired also at the receptive level, suggesting an underlying processing deficit. On the pragmatic test schizophrenia patients were significantly less able to produce appropriate interpretations, indicating the presence of abnormal pragmatic inferential abilities. These findings confirm that language impairment is a key feature of schizophrenia independent of mother language and suggest a possible deficit involving hemispheric lateralization processes.

ACTION VERBS AND THE PRIMARY MOTOR CORTEX: A COMPARATIVE TMS STUDY OF SILENT READING, FREQUENCY JUDGMENTS, AND MOTOR IMAGERY

Neuropsychologia 2008;46(7):1915-1926

Tomasino B, Fink Gereon R, Sparing R, Dafotakis M, Weiss PH.

I.F. 2007: 3,630

Single pulse transcranial magnetic stimulation (TMS) was applied to the hand area of the left primary motor cortex or, as a control, to the vertex (STIMULATION: TMS(M1) vs. TMS(vertex)) while right-handed volunteers silently read verbs related to hand actions. We examined three different tasks and time points for stimulation within the same experiment: subjects indicated with their left foot when they (i) had finished reading, (ii) had judged whether the corresponding movement involved a hand rotation after simulating the hand movement, and (iii) had judged whether they would frequently encounter the action verb in a newspaper (TASK: silent reading, motor imagery, and frequency judgment). Response times were compared between TMS(M1) and TMS(vertex), both applied at different time points after stimulus onset (DELAY: 150, 300, 450, 600, and 750 ms). TMS(M1) differentially modulated task performance: there was a significant facilitatory effect of TMS(M1) for the imagery task only (about 88 ms), with subjects responding about 10% faster (compared to TMS(vertex)). In contrast, response times for silent reading and frequency judgments were unaffected by TMS(M1). No differential effect of the time point of TMS(M1) was observed. The differential effect of TMS(M1) when subjects performed a motor imagery task (relative to performing silent reading or frequency judgments with the same set of verbs) suggests that the primary motor cortex is critically involved in processing action verbs only when subjects are simulating the corresponding movement. This task-dependent effect of hand motor cortex TMS on the processing of hand-related action verbs is discussed with respect to the notion of embodied cognition and the associationist theory.

DYSMORPHIC FEATURES, SIMPLIFIED GYRAL PATTERN AND 7Q11.23 DUPLICATION RECIPROCAL TO THE WILLIAMS-BEUREN DELETION

European Journal of Human Genetics 2008;16(8):880-887

Torniero C, Dalla Bernardina B, Novara F, Cerini R, Bonaglia MC, Pramparo T, Ciccone R, Guerrini R, Zuffardi O.

I.F. 2007: 4,003

We report a patient with mild pachygyria, ascertained during a screening of subjects with abnormal neuronal migration and/or epilepsy, having a 7q11.23 duplication reciprocal to the Williams-Beuren critical region (WBCR) deletion. He exhibited speech delay and mental retardation together to type II trigonocephaly and other abnormalities. The proband's mother carried the same imbalance, though her phenotype was milder and no abnormal conformation of the cranium was reported. She

had suffered a few seizures in infancy, as already described in other duplicated subjects. This genomic imbalance, now described in 17 subjects, including one parent for each of the four probands, is associated with a variable phenotype. Speech impairment is present in most cases; no distinctive facial gestalt is recognizable; seizures have been reported in four subjects and brain magnetic resonance, performed in eight cases, resulted abnormal in six, while detected abnormal neuronal migration in two. Although the clinical description of additional cases is needed to delineate a definite phenotypic core for WBCR duplications, trigonocephaly, also reported in another dup(7)(q11.23) patient, is possibly a trait that, together with speech impairment, may call for clinically oriented specific screening. Abnormal development of the cerebral cortex, reported also in the Williams-Beuren deletion, suggests that at least one gene is present in the critical region whose deletion/duplication impairs neuronal migration.

RAPIDLY CYCLING ENCEPHALOPATHY FROM AN ALMOST FORGOTTEN ENTITY

Neurological Sciences 2008;29(2):125-126

Tremolizzo L, Galbussera A, Frigo M, Apale P, Capra M, Appollonio I, Ferrarese C.

I.F. 2007: 1,006

Abstract non disponibile.

FLUENCY REMEDIATION IN DYSLEXIC CHILDREN: DOES AGE MAKE A DIFFERENCE?

Dyslexia 2008;14(2):142-152

Tressoldi PE, Lorusso ML, Brenbati F, Donini R.

I.F. 2007: 1,265

This study tested the hypothesis whether older dyslexic children may obtain fewer gains on fluency and accuracy with respect to their younger peers after specific remediation.Changes in accuracy and fluency of a group of children with a diagnosis of dyslexia attending third and fourth grades were compared with those obtained by a group of children attending the sixth, seventh or eighth grade in two different treatments, one based on the Balance model (Bakker) and the second based on the automatization of syllable recognition (sublexical).Among all comparisons between the gains in accuracy and fluency obtained by the two groups, only the younger group in the sublexical treatment obtained a statistically significant gain with respect to their older peers' accuracy in reading words. These outcomes suggest that, at least for the chronological ages and types of treatments considered in this study, older children with dyslexia may obtain comparable gains to their younger peers, suggesting that 'it is never too late' to remediate reading fluency and accuracy.

CLINICAL AND MOLECULAR CHARACTERISTICS FOR 1QTER SYNDROME: DELINEATING A CRITICAL REGION FOR CORPUS CALLOSUM AGENESIS/HYPOGENESIS

Journal of Medical Genetics 2008;45(6):346-354

van Bon BW, Koolen DA, Borgatti R, Magee A, Garcia-Minaur S, Rooms L, Reardon W, Zollino M, Bonaglia MC, De Gregori M, Novara F, Grasso R, Ciccone R, van Duyvenvoorde HA, Aalbers AM, Guerrini R, Fazzi E, Nillesen WM, McCullough S, Kant SG, Marcelis CL, Pfundt R, de Leeuw N, Smeets D, Sistermans EA, Wit JM, Hamel BC, Brunner HG, Kooy F, Zuffardi O, de Vries BB.

I.F. 2007: 5,535

BACKGROUND: Patients with a microscopically visible deletion of the distal part of the long arm of chromosome 1 have a recognisable phenotype, including mental retardation, microcephaly, growth retardation, a distinct facial appearance and various midline defects including corpus callosum abnormalities, cardiac, gastro-oesophageal and urogenital defects, as well as various central nervous system anomalies. Patients with a submicroscopic, subtelomeric 1qter deletion have a similar phenotype, suggesting that the main phenotype of these patients is caused by haploinsufficiency of genes in this region. OBJECTIVE: To describe the clinical presentation of 13 new patients with a submicroscopic deletion of 1q43q44, of which nine were interstitial, and to report on the molecular characterisation of the deletion size. Results and CONCLUSIONS: The clinical presentation of these patients has clear similarities with previously reported cases with a terminal 1q deletion. Corpus callosum abnormalities were present in 10 of our patients. The AKT3 gene has been reported as an important candidate gene causing this abnormality. However, through detailed molecular analysis of the deletion sizes in our patient cohort, we were able to delineate the critical region for corpus callosum abnormalities to a 360 kb genomic segment which contains four possible candidate genes, but excluding the AKT3 gene.

CRYPTOGENETIC EPILEPTIC SYNDROMES RELATED TO SCN1A: TWELVE NOVEL MUTATIONS IDENTIFIED

Archives of Neurology 2008;65(4):489-494

Zucca C, Redaelli F, Epifanio R, Zanotta N, Romeo A, Lodi M, Veggiotti P, Airoldi G, Panzeri C, Romaniello R, De Polo G, Bonanni P, Cardinali S, Baschirotto C, Martorell L, Borgatti R, Bresolin N, Bassi MT.

I.F. 2007: 5,783

BACKGROUND: Sodium channel alpha 1 subunit gene, SCN1A, is the gene encoding the neuronal voltage-gated sodium channel alpha 1 subunit (Na(v)1.1) and is mutated in different forms of epilepsy. Mutations in this gene were observed in more than 70% of patients with severe myoclonic epilepsy of infancy (SMEI) and were also found in different types of infantile epileptic encephalopathy. OBJECTIVE: To search for disease-causing mutations in SCN1A in patients with cryptogenic epileptic syndromes (ie, syndromes with an unknown cause). DESIGN: Clinical characterization and molecular genetic analysis of a cohort of patients. SETTING: University hospitals, rehabilitation centers, and molecular biology laboratories. PATIENTS: Sixty unrelated patients with cryptogenic epileptic syndromes. MAIN OUTCOME MEASURES: Samples of DNA were analyzed for mutations and for large heterozygous deletions encompassing the SCN1A gene. A search for microdeletions in the SCN1A gene was also performed in the subset of patients with SMEI/SMEI-borderland who had negative results at the point mutation screening. RESULTS: No large deletions at the SCN1A locus were found in any of the patients analyzed. In contrast, 13 different point mutations were identified in 12 patients: 10 with SMEI, 1 with generalized epilepsy with febrile seizures plus, and 1 with cryptogenic focal epilepsy. An additional search for SCN1A intragenic microdeletions in the remaining patients with SMEI/SMEI-borderland and no point mutations was also negative. CONCLUSIONS: These results confirm the role of the SCN1A gene in different types of epilepsy, including cryptogenic epileptic syndromes. However, large deletions encompassing SCN1A were not common disease-causing rearrangements in this group of epilepsies.

LETTERS TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE Anno 2007

DELETION OF A 760 KB REGION AT 4p16 DETERMINES THE PRENATAL AND POSTNATAL GROWTH RETARDATION CHARACTERISTIC OF WOLFHIRSCHHORN SYNDROME

Journal of Medical Genetics 2007;44(10):647-650 – Letter to the Editor

Concolino D*, Rossi E*, Strisciuglio P, Iembo MA, Giorda R, Ciccone R, Tenconi R, Zuffardi O.

* Autori che hanno contribuito in ugual misura al lavoro

I.F. 2006: 5,087

BACKGROUND: Recently the genotype/phenotype map of Wolf-Hirschhorn syndrome (WHS) has been refined, using small 4p deletions covering or flanking the critical region in patients showing only some of the WHS malformations. Accordingly, prenatal-onset growth retardation and failure to thrive have been found to result from haploinsufficiency for a 4p gene located between 0.4 and 1.3 Mb, whereas microcephaly results from haploinsufficiency of at least two different 4p regions, one of 2.2-2.38 Mb and a second one of 1.9-1.28 Mb. METHODS AND RESULTS: We defined the deletion size of a ring chromosome (r(4)) in a girl with prenatal onset growth retardation, severe failure to thrive and true microcephaly but without the WHS facial gestalt and mental retardation. A high-resolution comparative genome hybridisation array revealed a 760 kb 4p terminal deletion. CONCLUSIONS: This case, together with a familial 4p deletion involving the distal 400 kb reported in normal women, may narrow the critical region for short stature on 4p to 360-760 kb. This region is also likely to contain a gene for microcephaly. “In silico” analysis of all genes within the critical region failed to reveal any strikingly suggestive expression pattern; all genes remain candidates for short stature and microcephaly.

LETTERS TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE Anno 2008

LACK OF EVIDENCE FOR BORRELIA BURGDORFERI SEROPOSITIVITY IN ALZHEIMER DISEASE

Alzheimer Disease and Associated Disorders 2008;22(3):308 – Letter to the Editor

Galbussera A, Tremolizzo L, Isella V, Gelosa G, Vezzo R, Vigorè L, Brenna M, Ferrarese C, Appollonio I.

I.F. 2007: 2,244

Abstract non disponibile.

INCREASED OXIDATIVE STRESS IN LYMPHOCYTES FROM UNTREATED PARKINSON'S DISEASE PATIENTS

Parkinsonism and Related Disorders – Letter to the Editor 2008;in press

Prigione A, Isaias IU, Galbussera A, Brighina L, Begni B, Andreoni S, Pezzoli G, Antonini A, Ferrarese C.

I.F. 2007: 2,021

Abstract non disponibile.

A RECURRENT 15Q13.3 MICRODELETION SYNDROME ASSOCIATED WITH MENTAL RETARDATION AND SEIZURES

Nature Genetics 2008;40(3):322-328 – Letter to the Editor

Sharp AJ, Mefford HC, Li K, Baker C, Skinner C, Stevenson RE, Schroer RJ, Novara F, De Gregori M, Ciccone R, Broomer A, Casuga I, Wang Y, Xiao C, Barbacioru C, Gimelli G, Dalla Bernardina B, Torniero C, Giorda R, Regan R, Murday V, Mansour S, Fichera M, Castiglia L, Failla P, Ventura M, Jiang Z, Cooper GM, Knight SJL, Romano C, Zuffardi O, Chen C, Schwartz CE, Eichler EE.

I.F. 2007: 25,556

We report a recurrent microdeletion syndrome causing mental retardation, epilepsy and variable facial and digital dysmorphisms. We describe nine affected individuals, including six probands: two with de novo deletions, two who inherited the deletion from an affected parent and two with unknown inheritance. The proximal breakpoint of the largest deletion is contiguous with breakpoint 3 (BP3) of the Prader-Willi and Angelman syndrome region, extending 3.95 Mb distally to BP5. A smaller 1.5-Mb deletion has a proximal breakpoint within the larger deletion (BP4) and shares the same distal BP5. This recurrent 1.5-Mb deletion contains six genes, including a candidate gene for epilepsy (CHRNA7) that is probably responsible for the observed seizure phenotype. The BP4-BP5 region undergoes frequent inversion, suggesting a possible link between this inversion polymorphism and recurrent deletion. The frequency of these microdeletions in mental retardation cases is approximately 0.3% (6/2,082 tested), a prevalence comparable to that of Williams, Angelman and Prader-Willi syndromes.

FIRST CASE OF COMPOUND HETEROZYGOSITY IN ALS2 GENE IN INFANTILE-ONSET ASCENDING SPASTIC PARALYSIS WITH BULBAR INVOLVEMENT

Clinical Genetics 2008;73(6):591-593 – Letter to the Editor

Sztriha L, Panzeri C, Kalmanchey R, Szabo N, Endreffy E, Turi S, Baschirotto C, Bresolin N, Vekerdy Z, Bassi MT.

I.F. 2007: 3,181

Abstract non disponibile.

LAVORI PER ESTESO PUBBLICATI SU RIVISTE NON RECENSITE Anno 2007

QUALITÀ E VELOCITÀ DELLA PRODUZIONE GRAFICA: INFLUENZA DELLA POSTURA DEL CORPO, DELL'IMPUGNATURA E DEGLI ARREDI

Difficoltà di Apprendimento 2007;12(4):491-510

Bearzotti F, Tentori M, Del Torre E.

RITARDO MENTALE GRAVE: VOGLIAMO FINALMENTE ANDARE AVANTI?

Saggi – Child Development & Disabilities 2007;XXXIV(3):11-28

Cannao M.

LA QUALITÀ DI VITA IN BAMBINI CON PARALISI CEREBRALE INFANTILE

Giornale Italiano di Medicina Riabilitativa 2007;21(2):159-166

De Rinaldis M, Russo L, Cavallo FME, Gesualdi ME, Losito L, Mastronardi R, Trabacca A.

LA RICERCA EPIDEMIOLOGICA SUI DISTURBI MENTALI IN ETÀ EVOLUTIVA IN ITALIA: LO STUDIO PRISMA

NOOS - Aggiornamenti in psichiatria 2007;3:191-200

Frigerio A., Rucci P, De Girolamo G, Molteni M, I Ricercatori del Progetto Italiano Salute Mentale Infantile (PRISMA)

AUTONOMIA NEI CONTESTI DI VITA: IL RUOLO DEGLI AUSILI

Saggi – Child Development & Disabilities 2007;XXXV(4):39-54

Guerreschi M.

STIMOLAZIONE EMISFERO-SPECIFICA SECONDO IL METODO BAKKER PER IL TRATTAMENTO DELLA DISLESSIA EVOLUTIVA: RISULTATI E FOLLOW-UP

Saggi - Child Development & Disabilities 2007;XXXIII(1):41-52

Lorusso ML, Cattaneo C.

PSICO(PATO)LOGIA DEL RITARDO MENTALE

Saggi – Child Development & Disabilities 2007;XXXIV(3):77-88

Mansi G, Molteni M.

ICF E TERAPIA OCCUPAZIONALE

Saggi – Child Development & Disabilities 2007;XXXV(4):77-92

Martinuzzi A, Giurati R

IL TEMPO LIBERO E IL GIOCO: UN ESEMPIO PROGETTUALE

Saggi – Child Development & Disabilities 2007;XXXV(4):29-38

Martocchi V.

METODICHE E STRUMENTI NEUROPSICOLOGICI PER LA RIABILITAZIONE IN ETÀ EVOLUTIVA

Giornale di Neuropsichiatria dell'Età Evolutiva 2007;27: 253-263

Molteni M, Lorusso ML, Pellegri A.

REGOLAZIONE EMOZIONALE IN BAMBINI TRA I 3 E I 16 MESI: APPLICAZIONE DEL PARADIGMA STILL-FACE

Giornale Italiano di Psicologia 2007;1:193-222

Montirosso R, Premoli B, Cozzi P, Borgatti R, Tronick E.

COMPETENZA SOCIALE E PROFILO COMPORTAMENTALE IN GRUPPO DI BAMBINI IN ETÀ PRESCOLARE. UN CONTRIBUTO ALLA VALIDAZIONE ITALIANA DEL SOCIAL COMPETENCE AND BEHAVIOR EVALUATION (SCBE)

Psicologia Clinica dello Sviluppo 2007;XI,3:477-500

Montirosso R, Frigerio A, Molteni M, Cozzi P, Pastore V, Borgatti R, LaFreniere P.

EFFICACY OF ARIPIPRAZOLE ON BEHAVIOURAL SYMPTOMS IN A YOUNG PATIENT WITH SEVERE ACQUIRED BRAIN INJURY

Confinia Neuropsychiatrica 2007;2:105-108 – versione italiana 2:109-112

Piccoli S, Martinuzzi A, Perini G.

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TRIALS CLINICI REALIZZATI O IN CORSO DI REALIZZAZIONE NEGLI ANNI 2007 - 2008

OBSERVATIONAL STUDY TO EVACUATE THE THERAPEUTIC OPTIONS IN REFRACTORY EPILEPSY TO MONOTHERAPY (THEOREM)

Codice dello studio: /

Approvato dal Comitato Etico dell'Istituto

Casa farmaceutica coinvolta: Janssen-Cilag SpA

Polo Scientifico di Conegliano - Responsabile Dott. Andrea Martinuzzi

AN ITALIAN RANDOMISED, DOUBLE-BLIND PLACEBO CONTROLLED STUDY OF THE EFFICACY OF ATOMOXETINE HYDROCHLORIDE IN THE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBID OPPOSITIONAL DEFIANT DISORDER

Codice dello studio: B4Z-IT–LYCY

Approvato dal Comitato Etico dell'Istituto

Casa farmaceutica coinvolta: Ely Lilly – Italia

Polo Scientifico di San Vito al Tagliamento – Responsabile Dott. Amerigo Zanella

AN OPEN-LABEL STUDY OF THE EFFICACY OF ATOMOXETINE HYDROCHLORIDE ON QUALITY OF LIFE OF CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS WITH OR WITHOUT COMORBID CONDITIONS

Codice dello studio: B4Z-IT–LYDS

Approvato dal Comitato Etico dell'Istituto

Casa farmaceutica coinvolta: Ely Lilly – Italia

Polo Scientifico di Bosisio Parini – Responsabile Dott. Massimo Molteni

Polo Scientifico di Ostuni – Responsabile Dott. Angelo Massagli

"A RANDOMIZED, CONTROLLED, OPEN-LABEL STUDY OF THE LONG TERM IMPACT ON FUNCTIONING USING ATOMOXETINE HYDROCHLORIDE COMPARED TO OTHER EARLY STANDARD CARE IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN TREATMENT-NAÏVE CHILDREN AND ADOLESCENTS, (ADHD-LIFE STUDY)"

Codice dello studio: BZ4-EW-LYDY

Approvato dal Comitato Etico dell'Istituto

Casa farmaceutica coinvolta: Ely Lilly – Italia

Polo Scientifico di San Vito al Tagliamento - Responsabile Dott. Domenico Restuccia

COLLABORAZIONI INTERNAZIONALI E NAZIONALI

L'attività clinica, di ricerca e formativa del biennio ha portato a diverse collaborazioni con Istituti, Università ed Enti di ricerca internazionali e nazionali, di cui di seguito si riportano i più significativi:

Nazionale - Internazionale	Ente/Istituto/Università	Città	Stato
Internazionale	Brain Tumor Committee Working Group-SIOP		AUSTRALIA FRANCIA GERMANIA SPAGNA REGNO UNITO
Internazionale	Departement of Human Genetics, Radboud Univeristy Nijmegen medical Centre	Nijmegen	OLANDA
Internazionale	Department of Psychology Bowdoin College	Brunswik	STATI UNITI
Internazionale	Drexel University	Philadelphia	STATI UNITI
Internazionale	Gillette Children's Specially healthcare	ST Paul	STATI UNITI
Internazionale	Harvard Medical School	Boston	STATI UNITI
Internazionale	Hospital Nacional de Paraplejicos, FENNSI Group, SESCAM	Toledo	SPAGNA
Internazionale	Karolinska hospital, Clinical Genetic Unit, Departement of Molecular Medicine	Stockholm	SVEZIA
Internazionale	Laval University Department of psychiatry	Quebec city	CANADA
Internazionale	M.I.T.	Boston	STATI UNITI
Internazionale	Mount Sinai School of Medicine	New York	STATI UNITI
Internazionale	National Institute of Arthritis and Musculoskeletal and Skin Disease	Bethesda	STATI UNITI
Internazionale	Noldus Information Technology	Wageningen	OLANDA
Internazionale	Ospedale Pediatrico Necker	Parigi	FRANCIA
Internazionale	Psychology Departement University of Maine	Orono	STATI UNITI
Internazionale	Research Unit, School of Psychology	Reading	REGNO UNITO
Internazionale	Trinity College Dublin	Dublin	IRLANDA
Internazionale	Wadsworth Center, Center for Medical Sciences, Molecular Genetics Program	Albany, NY	STATI UNITI
Internazionale	Yale University School of Medicine	New Haven	STATI UNITI
Nazionale	AISEA (Associazione Italiana Sindrome Emiplegia Alternante)	(Sede legale) Verderio Superiore	ITALIA
Nazionale	Area Science Park – Trieste	Trieste	ITALIA
Nazionale	ARES Puglia	Bari	ITALIA
Nazionale	ASIPSE	Milano	ITALIA

Nazionale	Azienda Ospedaliera “Osp. di Circolo” Busto Arsizio	Busto Arsizio (Va)	ITALIA
Nazionale	Azienda Ospedaliera Regina Margherita S. Anna	Torino	ITALIA
Nazionale	Centro Milanese di Terapia della Famiglia	Milano	ITALIA
Nazionale	Centro Nazionale Ricerca sulla pratica psicomotoria (CNRP)	Milano	ITALIA
Nazionale	Centro Studi Terapia della Gestalt	Milano	ITALIA
Nazionale	Centro Terapia Cognitiva– COMO	Como	ITALIA
Nazionale	Clinica Universitaria Borgo Roma	Verona	ITALIA
Nazionale	CNR – IENI	Lecco	ITALIA
Nazionale	CNR –Tecnologie Biomediche	Milano	ITALIA
Nazionale	Federazione Italiana Medici Pediatri – FIMP	Roma	ITALIA
Nazionale	Fondazione “Città della Speranza”	Malo (VI)	ITALIA
Nazionale	Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, U.O. di Neurologia, U.O. di Terapia intensiva Neonatale, clinica Pediatrica, dipartimento di Neuroscienze	Milano	ITALIA
Nazionale	Fondazione Mariani	Milano	ITALIA
Nazionale	Fondazione Telethon	Roma	ITALIA
Nazionale	G.I.T.I.M. di Treviso (Gruppo Italiano per le tecniche psicoterapiche d’imagerie mentale)	Treviso	ITALIA
Nazionale	I.Co.S Punto Counselling	Milano	ITALIA
Nazionale	I.R.E.P. Scuola di specializzazione in Psicoterapia – Roma	Roma	ITALIA
Nazionale	IRCCS Istituto Nazionale Neurologico “Carlo Besta”	Milano	ITALIA
Nazionale	IRCCS Fondazione “Santa Lucia”	Roma	ITALIA
Nazionale	IRCCS Fondazione “Stella Maris”	Pisa	ITALIA
Nazionale	IRCCS Fondazione Centro San Raffaele Monte Tabor	Milano	ITALIA
Nazionale	IRCCS Fondazione Don Carlo Gnocchi	Milano	ITALIA
Nazionale	IRCCS Fondazione S. Maugeri - Clinica del Lavoro e Riabilitazione – Cassano delle Murge	Cassano delle Murge (Ba)	ITALIA
Nazionale	IRCCS Humanitas	Rozzano (Mi)	ITALIA
Nazionale	IRCCS INRCA - Istituto Nazionale Riposo e Cura per Anziani	Casatenovo (Lc)	ITALIA
Nazionale	IRCCS Istituto “Giannina Gaslini”	Genova	ITALIA
Nazionale	IRCCS Istituto di Ricerca Codivilla Putti - Istituti Ortopedici Rizzoli	Bologna	ITALIA

Nazionale	IRCCS Ospedale "Casa Sollievo della Sofferenza" – San Giovanni Rotondo	San Giovanni Rotondo (Fg)	ITALIA
Nazionale	IRCCS Ospedale Infantile e Pie Fondazioni Burlo Garofolo e de Manussi	Trieste	ITALIA
Nazionale	IRCCS Ospedale Pediatrico Bambin Gesù - Sede di Palidoro	Roma	ITALIA
Nazionale	IRCCS Policlinico San Matteo – Pavia	Pavia	ITALIA
Nazionale	ISFAR -Scuola di Psicomotricità Funzionale	Firenze	ITALIA
Nazionale	Istituto di Psicomotricità Anne-Marie Wille - Milano	Milano	ITALIA
Nazionale	Istituto Galeazzi	Milano	ITALIA
Nazionale	Istituto Multimedia Castellanza	Varese - Milano	ITALIA
Nazionale	Istituto Policlinico Clinica Neurologica - S. Donato	San Donato Milanese (Mi)	ITALIA
Nazionale	Istituto Superiore di Sanità	Roma	ITALIA
Nazionale	Ospedale Le Molinette	Torino	ITALIA
Nazionale	Ospedale Buzzi	Milano	ITALIA
Nazionale	Ospedale del Ponte, U.O. di Neuropsichiatria Infantile e dell'Adolescenza	Varese	ITALIA
Nazionale	Ospedale Manzoni, U.O. di Neonatologia e Terapia Intensiva Dipartimento Materno Infantile	Lecco	ITALIA
Nazionale	Ospedale Niguarda "Ca Granda"	Milano	ITALIA
Nazionale	Ospedale Oftalmico-Fatebenefratelli, Centro Regionale Epilessia Età evolutiva	Milano	ITALIA
Nazionale	Ospedale Sacra Famiglia, Fatebenefratelli, U.O. di Pediatria	Erba (Co)	ITALIA
Nazionale	Ospedale San Gerardo	Monza (Mi)	ITALIA
Nazionale	Ospedali Riuniti di Bergamo	Bergamo	ITALIA
Nazionale	Policlinico "Le Scotte" Università di Siena, Sezione di Genetica Medica	Siena	ITALIA
Nazionale	Polo Ospedaliero San Paolo Cattedra e U.O. di Chirurgia Maxillo-Facciale	Milano	ITALIA
Nazionale	Scuola Italiana di psicoterapia per le tecniche immaginative di analisi e ristrutturazione del profondo –ITP	Treviso	ITALIA
Nazionale	Scuola Superiore Internazionale di Scienze della Formazione – SISF – Facoltà di Scienze dell'Educazione Università Pontificia Salesiana di Roma	Roma	ITALIA
Nazionale	SSPC-IFREP Scuola in Psicologia Clinica di Roma	Roma	ITALIA

Nazionale	Tribunale Minorenni	Lecce	ITALIA
Nazionale	Università “Ca’ Foscari” di Venezia Corso di laurea in servizio sociale	Venezia	ITALIA
Nazionale	Università “ La Sapienza” di Roma Facoltà di psicologi	Roma	ITALIA
Nazionale	Università “Magna Graecia” Facoltà di Farmacia	Catanzaro	ITALIA
Nazionale	Università “Ca’ Foscari” Venezia, Corso di laurea in economia aziendale	Venezia	ITALIA
Nazionale	Università “Vita e Salute” – Facoltà di Psicologia	Milano	ITALIA
Nazionale	Università Bocconi	Milano	ITALIA
Nazionale	Università Cattolica del Sacro Cuore, Facoltà di Scienze della formazione	Brescia	ITALIA
Nazionale	Università Cattolica, Centro Studi sulla Famiglia e ricerca	Milano	ITALIA
Nazionale	Università degli Studi di c/o Ospedale Sacco, Scuola Specializzazione Oculistica	Milano	ITALIA
Nazionale	Università degli Studi di Milano, Scuola Specializzazione Medicina Fisica e Riabilitazione	Milano	ITALIA
Nazionale	Università degli Studi Milano, Scuola Specializzazione Neurologia	Milano	ITALIA
Nazionale	Università degli Studi Milano Bicocca, Scuola Specializzazione Neurologia	Monza (Mi)	ITALIA
Nazionale	Università degli Studi Bari, Facoltà di Scienze della Formazione	Bari	ITALIA
Nazionale	Università degli Studi Bari - Polo di Brindisi, Corso di Laurea in Fisioterapia	Brindisi	ITALIA
Nazionale	Università degli Studi Bari, Scuola di specializzazione in NPI	Bari	ITALIA
Nazionale	Università degli Studi di Milano, Scuola Specializzazione N.P.I.	Milano	ITALIA
Nazionale	Università degli Studi di Bari, Dipartimento di Biochimica	Bari	ITALIA
Nazionale	Università degli Studi di Cagliari, Facoltà di Psicologia	Cagliari	ITALIA
Nazionale	Università degli Studi di Pavia, Scuola Specializzazione N.P.I.	Pavia	ITALIA
Nazionale	Università degli studi di Udine, Facoltà di Medicina	Udine	ITALIA
Nazionale	Università degli Studi Trieste, Facoltà scienze formazione	Trieste	ITALIA
Nazionale	Università di Padova, Dipartimento di Scienze Neurologiche e Psichiatriche	Padova	ITALIA

Nazionale	Università di Bergamo	Bergamo	ITALIA
Nazionale	Università di Bologna, Dipartimento di Biologia Evoluzionistica Sperimentale	Bologna	ITALIA
Nazionale	Università di Brescia, Facoltà di Medicina	Brescia	ITALIA
Nazionale	Università Di Firenze, Facoltà di Biologia	Firenze	ITALIA
Nazionale	Università di Genova, Facoltà di Scienze della Formazione	Genova	ITALIA
Nazionale	Università di Lecce, Facoltà di Scienze della Formazione	Lecce	ITALIA
Nazionale	Università di Messina, Clinica Neurologica	Messina	ITALIA
Nazionale	Università di Milano, Dipartimento di Scienze precliniche LITA-Vialba	Milano	ITALIA
Nazionale	Università di Modena e Reggio Emilia	Reggio Emilia	ITALIA
Nazionale	Università di Padova, Facoltà di psicologa	Padova	ITALIA
Nazionale	Università di Padova, Scuola di specializzazione in NPI	Padova	ITALIA
Nazionale	Università di Padova, Corso di laurea in terapia occupazionale	Padova	ITALIA
Nazionale	Università di Padova, Dipartimento di Pediatria	Padova	ITALIA
Nazionale	Università di Padova, Corso di Laurea in fisioterapia	Padova	ITALIA
Nazionale	Università di Padova, Dipartimento di Farmacologia e Anestesiologia	Padova	ITALIA
Nazionale	Università Di Roma Tre, Facoltà di Biologia	Roma	ITALIA
Nazionale	Università di Trieste, Facoltà di Psicologia	Trieste	ITALIA
Nazionale	Università di Udine, Clinica di psichiatria	Udine	ITALIA
Nazionale	Università di Udine, Corso di laurea in Educazione professionale	Udine	ITALIA
Nazionale	Università di Urbino, Facoltà di Farmacia.	Urbino (Pu)	ITALIA
Nazionale	Università di Verona, Polo di Rovereto, Corsi di laurea delle professioni sanitarie	Verona	ITALIA
Nazionale	Università Trieste, Corso di laurea in Educazione professionale	Trieste	ITALIA
Nazionale	Università Trieste	Trieste	ITALIA
Nazionale	Università Trieste, Corso di Laurea in Servizio Sociale	Trieste	ITALIA
Nazionale	Università di Torino, Dipartimento di Neuroscienze	Torino	ITALIA

AFFILIAZIONI A SOCIETÀ SCIENTIFICHE

Società Scientifica	Acronimo	Cognome e nome	Polo Scientifico (*)
American Society for text Discourse	ASRD	Marini Andrea	SV
American Academy of Neurology	AAN	Martinuzzi Andrea (Corresponding Fellow)	CN
American Association for the Advancement of Science	AAAS	Martinuzzi Andrea	CN
American Neurological Association	ANA	Martinuzzi Andrea	CN
American Speech-Language-Hearing Association	ASLHA	Fabbro Franco	SV
Association of European Psychiatrists	AEP	Brambilla Paolo	SV
Associazione Italiana di Analisi e Modificazione del Comportamento e Terapia Comportamentale e Cognitiva	AIAMC	Aceti Giuseppe	BP
Associazione Italiana di Miologia	AIM	Trabacca Antonio	OS
Associazione Italiana di Psicologia e Psicoterapia Costruttivista	AIPPC	Grada Claudio	CN
Associazione Italiana Dislessia	AID	Fenu Luciana	OS
Associazione Italiana Dislessia	AID	Lorusso Maria Luisa	BP
Associazione Italiana Disturbi dell'Attenzione con Iperattività	AIDAI	Lorusso Maria Luisa	BP
Associazione Italiana Disturbi dell'Attenzione con Iperattività	AIDAI	Prete Florenza	OS
Associazione Italiana Famiglie ADHD	AIFA	Massagli Angelo	OS
Associazione Italiana Pedagogisti Clinici	ANPEC	Nadal Alessandra	CN
Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento	AIRIPA	Bortolot Sonia	CN
Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento	AIRIPA	Cattaneo Carmen	BP
Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento	AIRIPA	Gubernale Marco	CN
Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento	AIRIPA	Lorusso Maria Luisa	PB
Associazione Italiana per la Ricerca e l'Intervento nella Psicopatologia dell'Apprendimento	AIRIPA	Poli Cinzia	SV
Associazione Italiana Psicogeriatria	AIP	Piccoli Sara	CN
Associazione Italiana Psicologia - sezione sperimentale	AIP	Vestri Alec	CN
Associazione Microbiologi Clinici Italiani	AMCLI	Raggi Maria Elisabetta	BP
Associazione Nazionale dei Pedagogisti Italiani	ANPE	Bortolot Sonia	CN
Associazione Nazionale dei Pedagogisti Italiani	ANPE	Cerchier Giovanni	CN
Associazione Nazionale dei Pedagogisti Italiani	ANPE	Nadal Alessandra	CN
Behavior Genetics Association	BGA	Maria Nobile	BP
Bioinformatics ITalian Society	BITS	Pozzoli Uberto	BP

Bioinformatics ITalian Society	BITS	Sironi Manuela	BP
Centro Interdipartimentale di Ricerca sulla Famiglia	CIRF	Maino Eleonora	BP
Collegium Internationale Neuropsychopharmacologicum	CINP	Brambilla Paolo	SV
Disability Italian Network	DIN	Bortolot Sonia	CN
Disability Italian Network	DIN	De Polo Gianni	CN
Disability Italian Network	DIN	Frare Mara	CN
Disability Italian Network	DIN	Martinuzzi Andrea (Vicepresidente)	CN
Disability Italian Network	DIN	Russo Emanuela	CN
Dyslexia International Tools and Technology	DITT	Lorusso Maria Luisa	BP
European Association for Transactional Analysis	EATA	Frare Mara	CN
European Association for Transactional Analysis	EATA	Marchi Silvia	CN
European Brain Injury Society	EBIS	Strazzer Sandra	BP
European College of Neuropsychopharmachology	ECNP	Brambilla Paolo	SV
European Cytogeneticists Association	ECA	Bonaglia Maria Clara	BP
European Epilepsy Academy	EUREPA	Liava Alexandra	CN
European Epilepsy Academy	EUREPA	Trabacca Antonio	OS
European Ligand Assay Society	ELAS	Raggi Maria Elisabetta	BP
European Paediatric Neurology Society	EPNS	Liava Alexandra	CN
European Society of Human Genetics	ESGH	Bassi Maria Teresa	BP
Eye Movement Desensitization and Reprocessing	EMDR	Angarano Alberto	SV
GIPCI Gruppo Italiano Paralisi Cerebrali Infantili	GIPCI	Convertini Angela	OS
Gruppo di Lavoro Handicap	GLH	Fenu Luciana	OS
Gruppo di Lavoro Interregionale Centri Ausili elettronici ed informatici per disabili	GLIC	Castaldi Angelo	OS
Gruppo di Studio Paralisi Cerebrale Infantile	GIPCI	Cazzagon Monica	SV
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Marchi Silvia	CN
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Piccione Marta	CN
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Scemenzin Erica	CN
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Tonon Ezio	CN
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Verticilo Luca	CN
Gruppo Italiano di Riabilitazione in Neuropsicologia	GIRN	Vestri Alec	CN
Gruppo Italiano Paralisi Cerebrali Infantili	GIPCI	De Rinaldis Marta	OS
Gruppo Italiano Paralisi Cerebrali Infantili	GIPCI	Trabacca Antonio	OS
Gruppo Italiano Paralisi Cerebrali Infantili	GIPCI	Turconi Anna Carla	BP
Gruppo Italiano Paralisi Cerebrali Infantili	GIPCI	Vespino Teresa	OS

Infantile Seizure Society	ISS	Liava Alexandra	CN
Institute of Electrical and Electronics Engineers	IEEE	Reni Gianluigi	BP
International Association of Logopaedics and Phoniatrics	IALP	Fabbro Franco	SV
International Association of Logopaedics and Phoniatrics	IALP	Tavano Alessandro	SV
International Association of Physicians in Audiology	IAPA	Brambilla Daniele	BP
International Neuropsychological Society	INS	Lorusso Maria Luisa	BP
International Pragmatics Association	IPRA	Tavano Alessandro	SV
Istituto di Formazione e Ricerca per Educatori e Psicoterapeuti	IFREP	Poli Cinzia	SV
Istituto di Formazione e Ricerca per Educatori e Psicoterapeuti	IFREP	Venier Francesco	SV
Italian Society of Psychiatric Epidemiology	SIEP	Brambilla Paolo	SV
Lega Italiana Contro l'Epilessia	LICE	Bonanni Paolo	CN
Lega Italiana Contro l'Epilessia	LICE	De Polo Gianni	CN
Lega Italiana Contro l'Epilessia	LICE	Epifanio Roberta	BP
Lega Italiana Contro l'Epilessia	LICE	Gubernale Marco	CN
Lega Italiana Contro l'Epilessia	LICE	Liava Alexandra	CN
Lega Italiana Contro l'Epilessia	LICE	Zanotta Nicoletta	BP
Lega Italiana Contro l'Epilessia	LICE	Zucca Claudio	BP
Neuroimaging section of the Association of European Psychiatrists	AEP	Brambilla Paolo	SV
Schizophrenia International Research Society	SIRS	Brambilla Paolo	SV
Società degli Psicologi dell'Area Neuropsicologica	SPAN	Liso Mario	OS
Società Internazionale di Ricerca e Studio sul Rachide	SIRER	Salghetti Annamaria	CN
Società Italiana Biochimica e Biologia Molecolare Clinica	SIBIOC	Raggi Maria Elisabetta	BP
Società Italiana Chirurgia del Rachide	GIS	Scattin Luciana	CN
Società Italiana di Analisi del Movimento in Clinica	SIAMOC	Nogarol Anita	CN
Società Italiana di Analisi Transazionale	SIAT	Frare Mara	CN
Società Italiana di Analisi Transazionale	SIAT	Marchi Silvia	CN
Società Italiana di Audiologia	SIA	Brambilla Daniele	BP
Società Italiana di Foniatria e Logopedia	SIFEL	Amorelli Valeria	BP
Società Italiana di Genetica Umana	SIGU	Bonaglia Maria Clara	BP
Società Italiana di Genetica Umana	SIGU	Giorda Roberto	BP
Società Italiana di Genetica Umana	SIGU	Sironi Manuela	BP
Società Italiana di Medicina Funzionale	SIMF	Soi Daniela	BP
Società Italiana di Miologia		Martinuzzi Andrea (socio fondatore)	CN

Società Italiana di Neurofisiologia Clinica	SINC	Restuccia Domenico	SV
Società Italiana di Neurofisiologia Clinica	SINC	Zanotta Nicoletta	BP
Società Italiana di Neurologia	SIN	Losito Luciana	OS
Società Italiana di Neurologia	SIN	Martinuzzi Andrea	CN
Società Italiana di Neurologia	SIN	Trabacca Antonio	OS
Società Italiana di Neurologia Pediatrica	SINP	Battaglia Maria Amalia	CN
Società Italiana di Neurologia, sezione Triveneta		Martinuzzi Andrea (Segretario)	CN
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Carlet Ombretta	CN
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Corletto Enrica	CN
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	De Polo Gianni	CN
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Epifanio Roberta	BP
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Ancona Vitilde	OS
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Massagli Angelo	OS
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Pasca Maria Grazia	OS
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Bianchi Gaia	BP
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Mani Elisa	BP
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Trabattoni Sara	BP
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza	SINPIA	Poggi Geraldina	BP
Società Italiana di Neuropsicologia	SINP	Vestri Alec	CN
Società Italiana di Neuropsicologia	SINP	Zilli Tiziana	SV
Società Italiana di Oftalmologia Pediatrica	SIOP	Cordaro Claudia	SV
Società Italiana di Oftalmologia Pediatrica	SIOP	Massagli Angelo	OS
Società Italiana di Oftalmologia Pediatrica	SIOP	Mavilio Alberto	OS
Società Italiana di Oftalmologia Pediatrica	SIOP	Salati Roberto	BP
Società Italiana di Oftalmologia Pediatrica	SIOP	Scigliuzzo Giuseppe	OS
Società Italiana di Otorinolaringoiatria	SIO	Amorelli Valeria	BP
Società Italiana di Otorinolaringoiatria	SIO	Brambilla Daniele	BP
Società Italiana di Otorinolaringoiatria	SIO	Soi Daniela	BP

Società Italiana di Pediatria	SIP	Battaglia Maria Amalia	CN
Società Italiana di Perimentria	SIPE	Mavilio Alberto	OS
Società Italiana di Perimentria	SIPE	Scigliuzzo Giuseppe	OS
Società Italiana di Psichiatria	SIP	Mansi Gianluigi	BP
Società Italiana di Psichiatria Sezione Veneta	PSIVE	Piccoli Sara	CN
Società Italiana di Psico-Oncologia	SIPO	Poggi Geraldina	BP
Società Italiana di Riabilitazione Neurologica	SIRN	Martinuzzi Andrea	CN
Società Italiana di Terapia Comportamentale e Cognitiva	SITCC	Vestri Alec	CN
Società Italiana Medicina Fisica e Riabilitativa	SIMFER	Cavallo Francesco	OS
Società Italiana Medicina Fisica e Riabilitativa	SIMFER	Trabacca Antonio	OS
Società Italiana Medicina Fisica e Riabilitazione	SIMFER	Cazzagon Monica	SV
Società Italiana Medicina Fisica e Riabilitazione	SIMFER	Maghini Cristina	BP
Società Italiana Medicina Fisica e Riabilitazione	SIMFER	Nogarol Anita	CN
Società Italiana Medicina Fisica e Riabilitazione	SIMFER	Scattin Luciana	CN
Società Italiana Medicina Fisica e Riabilitazione	SIMFER	Turconi Anna Carla	BP
Società Italiana Neuroscienze	SINS	Tavano Alessandro	SV
Società Italiana per lo Studio delle Cefalee	SISC	Corletto Enrica	CN
Società Italiana di Terapia Comportamentale e Cognitiva	SITCC	Frigerio Alessandra	BP
Società Italiana di Terapia Comportamentale e Cognitiva	SITCC	Zaccaria Alessia	OS
Società Oftalmologica Italiana	SOI	Cordaro Claudia	SV
Società Oftalmologica Italiana	SOI	Mavilio Alberto	OS
Società Oftalmologica Lombarda	SOL	Salati Roberto	BP
Società Oftalmologica Italiana	SOI	Salati Roberto	BP
Società Triveneta Neurologia	SIN	Imelio Sergio	SV
Society of Neuroscience		Brambilla Paolo	SV
World Federation of Societies of Biological Psychiatry	WFSBP	Brambilla Paolo	SV
World Muscle Society	WMS	D'Angelo Mariagrazia	BP
World Muscle Society	WMS	Martinuzzi Andrea	CN
World Muscle Society	WMS	Turconi Anna Carla	BP

(*)
BP = IRCCS E. Medea - Polo Scientifico di Bosisio Parini
CN = IRCCS E. Medea - Polo Scientifico di Conegliano e Pieve di Soligo
SV = IRCCS E. Medea - Polo Scientifico di San Vito al Tagliamento e Pasian di Prato
OS = IRCCS E. Medea - Polo Scientifico di Ostuni