LAVORI PER ESTESO PUBBLICATI SU RIVISTE RECENSITE

ANNO 2011

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Avenanti Alessio, Urgesi Cosimo (2011); UNDERSTANDING "WHAT" OTHERS DO: MIRROR MECHANISMS PLAY A CRUCIAL ROLE IN ACTION PERCEPTION; Social Cognitive and Affective Neuroscience, 6(3):257-259

Doi: 10.1093/scan/nsr004 **PMID: 21653637**

I.F. 2010: 4,482

Neurophysiological and imaging studies suggest that the inferior frontal cortex (IFC) implements a mechanism that matches perceived actions to one's motor representation of similar actions (mirror mechanism) and recent lesion studies have also established that IFC is critical for action perception. However, to date causative evidence that action perception requires activation within the same populations of IFC neurons involved in action execution is lacking. In this issue, Cattaneo and colleagues provide the first direct evidence that mirror mechanisms in IFC influence action perception. We discuss the implications of these findings for the understanding of the functional role of mirror mechanisms.

Bellani Marcella, Dusi Nicola, Yeh Ping-Hong, Soares Jair C., Brambilla Paolo (2011); THE EFFECTS OF ANTIDEPRESSANTS ON HUMAN BRAIN AS DETECTED BY IMAGING STUDIES. FOCUS ON MAJOR DEPRESSION; Progress in Neuro-Psychopharmacology and Biological Psychiatry, 35(7):1544-1552

Doi: 10.1016/j.pnpbp.2010.11.040 **PMID: 21138750**

I.F. 2010: 2,877

Recent brain imaging studies have shed light on understanding the pathogenesis of mood disorders. Evidence of structural, chemical, and functional brain changes, particularly in prefrontal cortex, cingulate, and amygdala, has been revealed in major depressive disorder (MDD). Furthermore, imaging techniques have been applied to monitor the effects of antidepressants (ADs) both in the brains of healthy volunteers and MDD patients. Although with some discrepancies due to the differences in study designs and patient samples, imaging findings have shown that ADs, particularly those having effects on the serotonergic system, modulate the volumes, functions and

biochemistry of brain structures, i.e. dorsolateral prefrontal cortex, anterior cingulate and amygdala, which have been demonstrated abnormal in MDD by earlier imaging studies. This paper reviews imaging studies conducted in MDD patients and healthy controls treated with different ADs.

Bellani Marcella, Baiano Monica, Brambilla Paolo (2011); BRAIN ANATOMY OF MAJOR DEPRESSION II. FOCUS ON AMYGDALA; Epidemiology and Psychiatric Sciences, 20(1):33-36

Doi: 10.1017/S2045796011000096 PMID: 21657113

I.F. 2010: 2,032

Here, we briefly summarize the most consistent structural magnetic resonance imaging (MRI) studies on amygdala in major depression and debate the effects of clinical variables on amygdalar morphology.

Bellani Marcella, Peruzzo Denis, Isola Miriam, Rambaldelli Gianluca, Perlini Cinzia, Baiano Monica, Cerini Roberto, Andreone Nicola, Barillari Marco, Pozzi Mucelli Roberto, Balestrieri Matteo, Tansella Michele, Bertoldo Alessandra, Brambilla Paolo (2011); CEREBELLAR AND LOBAR BLOOD FLOW IN SCHIZOPHRENIA: A PERFUSION WEIGHTED IMAGING STUDY; Psychiatry Research: Neuroimaging, 193(1):46-52

Doi: 10.1016/j.pscychresns.2010.12.010 PMID: 21600740

I.F. 2010: 2,064

It is still not clear whether brain hemodynamics plays a role in the functional and structural alterations in schizophrenia, since prior imaging studies showed conflicting findings. In this study we non-invasively explored cerebral and cerebellar lobe perfusion in the largest population of participants with schizophrenia thus far studied with perfusion-weighted imaging (PWI). Forty-seven participants affected by schizophrenia and 29 normal controls were recruited. PWI images were acquired following the intravenous injection of a paramagnetic contrast agent. Regional cerebral blood volume (CBV), blood flow (rCBF), and mean transit time (MTT) were obtained with the block-Circulant Singular Value Decomposition (cSVD) for frontal, temporal, parietal, occipital, and cerebellar lobes, bilaterally. Perfusion parameters were separately obtained for both gray and white matter in each lobe. Subjects with schizophrenia showed no significant differences in perfusion parameters when compared with controls. Interestingly, inverse correlations between age at onset and occipital, frontal and cerebellar MTT and between length of illness and frontal CBV were found. Preserved cerebral and cerebellar perfusion in

our chronic population may in part be due to the effects of antipsychotic treatment which may have normalized blood volume and flow. Hypoperfusion in relation to chronicity, particularly in the frontal lobe, has been observed in accordance with earlier studies using positron emission tomography.

Bellani Marcella, Brambilla Paolo (2011); DIFFUSION IMAGING STUDIES OF WHITE MATTER INTEGRITY IN BIPOLAR DISORDER; Epidemiology and Psychiatric Sciences, 20(2):137-140

Doi: 10.1017/S2045796011000229 **PMID: 21714360**

I.F. 2010: 2,032

Diffusion tensor imaging (DTI) is a neuroimaging technique with a potential to elucidate white matter integrity. Recently, it has been used in the field of psychiatry to further understand the pathophysiology of major diseases, including bipolar disorder (BD). This review sought to focus on existing DTI findings on white matter organization in BD.

Bellani Marcella, Fornasari Livia, Chittaro L., Brambilla Paolo (2011); VIRTUAL REALITY IN AUTISM: STATE OF THE ART; Epidemiology and Psychiatric Sciences, 20(3):235-238

Doi: 10.1017/S2045796011000448 **PMID: 21922965**

I.F. 2010: 2,032

Autism spectrum disorders are characterized by core deficits with regard to three domains, i.e. social interaction, communication and repetitive or stereotypic behaviour. It is crucial to develop intervention strategies helping individuals with autism, their caregivers and educators in daily life. For this purpose, virtual reality (VR), i.e. a simulation of the real world based on computer graphics, can be useful as it allows instructors and therapists to offer a safe, repeatable and diversifiable environment during learning. This mini review examines studies that have investigated the use of VR in autism.

Bellani Marcella, Moretti Anna, Perlini Cinzia, Brambilla Paolo (2011); LANGUAGE DISTURBANCES IN ADHD; Epidemiology and Psychiatric Sciences, 20(4):311-315

Doi: 10.1017/S2045796011000527 **PMID: 22201208**

I.F. 2010: 2,032

This article aims to review the studies exploring language abilities in attention deficit hyperactivity disorder (ADHD; with or without comorbid language impairment) focusing on oral speech discrimination, listening comprehension, verbal and spatial working memory as well as on discourse analysis and

pragmatic aspects of communication and language comprehension.

Benedetti Francesco, Yeh Ping-Hong, Bellani Marcella, Radaelli Daniele, Nicoletti Mark A., Poletti Sara, Falini Andrea, Dallaspezia Sara, Colombo Cristina, Scotti Giuseppe, Smeraldi Enrico, Soares Jair C., Brambilla Paolo (2011); DISRUPTION OF WHITE MATTER INTEGRITY IN BIPOLAR DEPRESSION AS A POSSIBILE STRUCTURAL MARKER OF ILLNESS; Biological Psychiatry, 69(4):309-317

Doi: 10.1016/j.biopsych.2010.07.028 **PMID: 0926068**

I.F. 2010: 8,674

BACKGROUND: Diffusion tensor imaging allows the study of integrity of white matter (WM) tracts. Literature suggests that WM integrity could be altered in bipolar disorder. Heterogeneity of brain imaging methods, the studied samples, and drug treatments make localization, nature, and severity of the WM abnormalities unclear.
METHODS: We applied tract-based spatial statistics of diffusion tensor imaging measures to compare fractional anisotropy (FA), mean, and radial diffusivity of the WM skeleton in a group of 40 consecutively admitted inpatients affected by a major depressive episode without psychotic features with a diagnosis of bipolar disorder type I and 21 unrelated healthy volunteers from the general population.
RESULTS: Compared with control subjects, patients showed lower FA in the genu of the corpus callosum and in anterior and right superior-posterior corona radiata and higher values of radial diffusivity in WM tracts of splenium, genu and body of corpus callosum, right mid-dorsal part of the cingulum bundle, left anterior and bilateral superior and posterior corona radiata, bilateral superior longitudinal fasciculus, and right posterior thalamic radiation. Patients had no brain areas with higher FA or lower diffusivity values than control subjects.
CONCLUSIONS: Reduced FA with increased mean and radial diffusivity suggests significant demyelination and/or dysmyelination without axonal loss. Comparing our findings with other observations in homogeneous samples of euthymic and manic patients, it can be hypothesized that changes in measures of WM integrity might parallel illness phases of bipolar illness.

Bonaglia Maria Clara*, Giorda Roberto*, Beri Silvana, De Agostini Cristina, Novara Francesca, Fichera Marco, Grillo Lucia, Galesi Ornella, Vetro Annalisa, Ciccone Roberto, Bonati Maria Teresa, Giglio Sabrina, Guerrini Renzo, Osimani Sara, Marelli Susan, Zucca Claudio, Grasso Rita, Borgatti Renato, Mani Elisa, Motta Cristina,

Molteni Massimo, Romano Corrado, Greco Donatella, Reitano Santina, Baroncini Anna, Lapi Elisabetta, Cecconi Antonella, Arrigo Giulia, Patricelli Maria Grazia, Pantaleoni Chiara, D'Arrigo Stefano, Riva Daria, Sciacca Francesca, Dalla Bernardina Bernardo, Zoccante Leonardo, Darra Francesca, Termine Cristiano, Maserati Emanuela, Bigoni Stefania, Priolo Emanuela, Bottani Armand, Gimelli Stefania, Bena Frederique, Brusco Alfredo, Di Gregorio Eleonora, Bagnasco Irene, Giussani Ursula, Nitsch Lucio, Politi Pierluigi, Martinez-Frias Maria-Luisa, Martinez-Fernandez Maria Luisa, Martinez Guardia Nieves, Bremer Anna, Anderlid Brittmarie, Zuffardi Orsetta (2011); MOLECULAR MECHANISMS GENERATING AND STABILIZING TERMINAL 22Q13 DELETIONS IN 44 SUBJECTS WITH PHELAN/MC DERMID SYNDROME; Plos Genetics, 7(7):e1002173

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1371/journal.pgen.1002173 **PMID: 21779178**

I.F. 2010: 9,543

In this study, we used deletions at 22q13, which represent a substantial source of human pathology (Phelan/McDermid syndrome), as a model for investigating the molecular mechanisms of terminal deletions that are currently poorly understood. We characterized at the molecular level the genomic rearrangement in 44 unrelated patients with 22q13 monosomy resulting from simple terminal deletions (72%), ring chromosomes (14%), and unbalanced translocations (7%). We also discovered interstitial deletions between 17-74 kb in 9% of the patients. Haploinsufficiency of the SHANK3 gene, confirmed in all rearrangements, is very likely the cause of the major neurological features associated with PMS. SHANK3 mutations can also result in language and/or social interaction disabilities. We determined the breakpoint junctions in 29 cases, providing a realistic snapshot of the variety of mechanisms driving non-recurrent deletion and repair at chromosome ends. De novo telomere synthesis and telomere capture are used to repair terminal deletions; non-homologous end-joining or microhomology-mediated break-induced replication is probably involved in ring 22 formation and translocations; non-homologous end-joining and fork stalling and template switching prevail in cases with interstitial 22q13.3. For the first time, we also demonstrated that distinct stabilizing events of the same terminal deletion can occur in different early embryonic cells, proving that terminal deletions can be repaired by multistep healing events and supporting the recent hypothesis that rare pathogenic germline rearrangements may have mitotic origin. Finally, the progressive clinical deterioration observed throughout the longitudinal medical history of three subjects over forty years supports the hypothesis of

a role for SHANK3 haploinsufficiency in neurological deterioration, in addition to its involvement in the neurobehavioral phenotype of PMS.

Brambilla Paolo, Cerruti Stefania, Bellani Marcella, Perlini Cinzia, Ferro Adele, Marinelli Veronica, Giusto Daniele, Tomelleri Luisa, Rambaldelli Gianluca, Tansella Michele, Diwadkar Vaibhav A. (2011); SHARED IMPAIRMENT IN ASSOCIATIVE LEARNING IN SCHIZOPHRENIA AND BIPOLAR DISORDER; Progress in Neuro-Psychopharmacology and Biological Psychiatry, 35(4):1093-1099

Doi: 10.1016/j.pnpbp.2011.03.007 PMID: 21420463

I.F. 2010: 2,877

BACKGROUND: Schizophrenia (SCZ) and bipolar disorder (BD) share some cognitive commonalities. However, the role of associative learning, which is a cornerstone of human cognition mainly relying on hippocampus, has been under-investigated. We assessed behavioral performance during associative learning in a group of SCZ, BD and healthy controls (HC).
METHODS: Nineteen patients with SCZ (36 ± 8.1 years; 13 males, 6 females; all Caucasians), 14 patients with BD (41 ± 9.6 years; 5 males, 9 females; all Caucasians) and 45 HC (27.7 ± 6.9 years; 18 males, 27 females; all Caucasians) were studied. Learning was assessed using an established object-location paired-associative learning paradigm. Subjects learned associations between nine equi-familiar common objects and locations in a nine-location grid. Performance data were analyzed in a repeated measures analysis of variance with time (repeated) and group as factors.
RESULTS: Learning curves (performance = (1-e(-k x time)) fitted to average performance data in the three groups revealed lower learning rates in SCZ and BD ($k = 0.17$ and $k = 0.34$) than HC ($k = 0.78$). Significant effects of group ($F = 11.05$, $p < 0.001$) and time ($F = 122.06$, $p < 0.001$) on learning performance were observed.
CONCLUSIONS: Our study showed that associative learning is impaired in both SCZ and BD, being potentially not affected by medication. Future studies should investigate the neural substrates of learning deficits in SCZ and BD, particularly focusing on hippocampus function and glutamatergic transmission.

Brescianini Sonia, Volzone Anna, Fagnani Corrado, Patriarca Valeria, Grimaldi Valentina, Lanni Roberta, Serino Laura, Mastroiacovo Pierpaolo, Stazi Maria Antonietta (2011); GENETIC AND ENVIRONMENTAL FACTORS SHAPE INFANT SLEEP PATTERNS: A STUDY OF 18-MONTH-OLD TWINS; Pediatrics, 127(5):e1296-e1302

Doi: 10.1542/peds.2010-0858 **PMID: 21482604**

I.F. 2010: 5,391

OBJECTIVE: Between 25% and 30% of children and adolescents experience sleep disorders. These disorders are complex phenotypes that are regulated by many genes, the environment, and gene-environment interactions. The objective of this study was to evaluate the contribution of genetic and environmental factors to sleep behaviors in early childhood and to contribute to the knowledge on appropriate therapeutic approaches, using a twin design.

PATIENTS AND METHODS: Data on sleeping behavior were collected from 314 18-month-old twin pairs (127 monozygotic and 187 dizygotic) using a parent-rated questionnaire. We used structural equation modeling to estimate genetic and environmental variance components for different sleep behaviors (cosleeping, sleep duration, and night awakenings).

RESULTS: Shared environment explained almost all (98.3%) of the total variance in cosleeping. Sleep duration was substantially influenced by shared environmental factors (64.1% nocturnal sleep and 61.2% diurnal sleep), with a moderate contribution of additive genetic effects (30.8% and 36.3% for nocturnal and diurnal sleep, respectively). For nocturnal waking episodes, we found a shared environmental contribution of 63.2% and a heritability estimate of 35.3%.

CONCLUSIONS: Most sleep disturbances during early childhood are explained by common shared environmental factors, and behavioral interventions adopted by parents and focused on modifying sleep behavior could contribute to solving sleep disturbances in this age group. However, the influence of genetic factors should not be underestimated, and research in this area could clarify the physiologic architecture of sleeping and contribute to selecting appropriate personalized therapeutic approaches.

Briguglio Marilena, Pinelli Lorenzo, Giordano Lucio, Ferraris Alessandro, Germanò Eva, Micheletti Serena, Severino Mariasavina, Bernardini Laura, Loddo Sara, Tortorella Gaetano, Ormitti Francesca, Gasparotti Roberto, the CBCD Study Group (Borgatti Renato, Romaniello Romina, Arrigoni Filippo), Rossi Andrea, Valente Enza Maria (2011); PONTINE TEGMENTAL CAP DYSPLASIA: DEVELOPMENTAL AND COGNITIVE OUTCOME IN THREE ADOLESCENT PATIENTS; Orphanet Journal of Rare Diseases, 6(1):36

Doi: 10.1186/1750-1172-6-36 **PMID: 21651769**

I.F. 2010: 5,933

Pontine Tegmental Cap Dysplasia (PTCD) is a recently described, rare disorder characterized by a peculiar cerebellar and brainstem malformation. Nineteen patients have been reported to date, of which only one in the adolescent age, and data on the clinical, cognitive and behavioural outcome of this syndrome are scarce. Here we describe three adolescent patients with PTCD. All presented bilateral deafness and multiple cranial neuropathies, variably associated with skeletal, cardiac and gastro-intestinal malformations. Feeding and swallowing difficulties, that are often causative of recurrent aspiration pneumonias and death in the first years of life, completely resolved with age in all three patients. Neuropsychological assessment showed borderline to moderate cognitive impairment, with delay in adaptive functioning, visual-spatial and language deficits. Two of three patients also showed mild behavioural problems, although their overall socialization abilities were well preserved. Cochlear implantation in two patients significantly improved their relational and learning abilities. Fibre tractography confirmed the abnormal bundle of transversely oriented fibres forming the typical pontine "tegmental cap" and absence of decussation of the superior cerebellar peduncles, supporting the hypothesis that PTCD results from abnormal axonal guidance and/or migration. These data indicate that PTCD may have a favourable long-term outcome, with borderline cognitive deficit or even normal cognition and partially preserved speech.

Broli Marcella, Bisulli Francesca, Mastrangelo Massimo, Fontana Elena, Fiocchi Isabella, Zucca Claudio, Bonaglia Maria Clara, Buono Serafino, Musumeci Sebastiano, Romano Corrado, Reitano Santina, Savio Maria, Vitello Girolamo A., Bernardi Bruno, Cevolani Daniela, Agati Raffaele, Poda Roberto, Gallassi Roberto, Giorda Roberto, Zuffardi Orsetta, Dalla Bernardina Bernardo, Seri Marco, Tinuper Paolo (2011); DEFINITION OF THE NEUROLOGICAL PHENOTYPE ASSOCIATED WITH DUP (X)(P11.22-P11.23); Epileptic Disorders, 13(3):240-251

Doi: 10.1684/epd.2011.0462 **PMID: 21926047**

I.F. 2010: 1,092

The aim of this study was to describe in detail the neurological features of nine patients carrying the recently reported microduplication at Xp11.22-11.23. Clinical and neurological examination, brain magnetic resonance imaging (except for two patients), electroencephalography and a neuropsychological assessment specific for language disturbances were performed in nine patients with microduplication at Xp11.22-11.23, disclosed by comparative genomic hybridisation array. Six patients were familial cases belonging to

three unrelated pedigrees and three were sporadic cases. The patients had the following characteristics: mild dysmorphic facial features (except for two patients), mental retardation with moderate to severe global language deterioration, electroencephalographic epileptiform discharges during wakefulness and especially during sleep or electrical status epilepticus during slow sleep in younger cases, and negative brain magnetic resonance imaging. The main clinical features of this new microduplication syndrome were mild facial dysmorphisms, from increased electroencephalogram abnormalities during sleep to electrical status epilepticus during slow sleep, and mental retardation mainly involving language function in the absence of detectable brain lesions. In the absence of detectable brain lesions, speech delay may be associated with electrical status epilepticus during slow sleep or, alternatively, related to abnormal brain expression of a dosage-sensitive gene contained within the duplication region.

Brunetti-Pierri Nicola, Paciorkowski Alex R., Ciccone Roberto, Della Mina Erika, Bonaglia Maria Clara, Borgatti Renato, Schaaf Christian P., Sutton V. Reid, Xia Zhilian, Jelluma Naftha, Ruivenkkamp Claudia, Bertrand Mary, De Ravel Thomy JL, Jayakar Parul, Belli Serena, Rocchetti Katia, Pantaleoni Chiara, D'Arrigo Stefano, Hughes Jeff, Cheung Sau Wai, Zuffardi Orsetta, Stankiewicz Pawel (2011); DUPLICATIONS OF FOXG1 IN 14Q12 ARE ASSOCIATED WITH DEVELOPMENTAL EPILEPSY, MENTAL RETARDATION, AND SEVERE SPEECH IMPAIRMENT; European Journal of Human Genetics, 19(1):102-107

Doi: 10.1038/ejhg.2010.142 **PMID: 20736978**

I.F. 2010: 4,380

Genome-wide high-resolution array analysis is rapidly becoming a reliable method of diagnostic investigation in individuals with mental retardation and congenital anomalies, leading to the identification of several novel microdeletion and microduplication syndromes. We have identified seven individuals with duplication on chromosome 14q11.2q13.1, who exhibited idiopathic developmental delay and cognitive impairment, severe speech delay, and developmental epilepsy. Among these cases, the minimal common duplicated region on chromosome 14q11.2q13.1 includes only three genes, FOXG1, C14orf23, and PRKD1. We propose that increased dosage of Forkhead Box G1 (FOXG1) is the best candidate to explain the abnormal neurodevelopmental phenotypes observed in our patients. Deletions and inactivating mutations of FOXG1 have been associated with a Rett-like syndrome characterized by hypotonia, irritability, developmental delay, hand

stereotypies, and deceleration of head growth. FOXG1, encoding a brain-specific transcription factor, has an important role in the developing brain. In fact, in vivo studies in chicken brain demonstrated that overexpression of FOXG1 results in thickening of the neuroepithelium and outgrowth of the telencephalon and mesencephalum, secondary to a reduction in neuroepithelial cell apoptosis.

Cagliani Rachele, Fruguglietti Maria Elisa, Berardinelli A., D'Angelo Maria Grazia, Prelle Alessandro, Riva Stefania, Gorni K., Orcesi Simona, Lamperti Costanza, Pichiecchio A., Signaroldi E., Tupler Rossella, Magri Francesca, Govoni Alessandra, Corti Stefania, Bresolin Nereo, Moggio Maurizio, Comi Giacomo Pietro (2011); NEW MOLECULAR FINDINGS IN CONGENITAL MYOPATHIES DUE TO SELENOPROTEIN N GENE MUTATIONS; Journal of the Neurological Sciences, 300(1-2):107-113

Doi: 10.1016/j.jns.2010.09.011 PMID: 20937510

I.F. 2010: 2,167

Selenoprotein N-related myopathy (SEPN1-RM) is an early-onset muscle disorder that can manifest clinically as congenital muscular dystrophy with spinal rigidity and can result in specific pathological entities such as multiminicore disease, desmin-related myopathy with Mallory body-like inclusions, and congenital fiber-type disproportion. Here we describe the clinical, histopathological, muscle magnetic resonance imaging (MRI) and genetic findings of three Italian SEPN1-RM families. Proband 1 is a 31-year-old female who was floppy at birth and developed axial and mild lower limb-girdle weakness. The second proband is a 13-year-old boy with RSMD1. Probands 3 and 4 were brothers showing clinical phenotype of congenital myopathy. Muscle MRI demonstrated selective involvement of sartorius, gluteal muscles and distal gastrocnemius and sparing of rectus femoris and gracilis. Muscle histopathology showed in proband 1 myopathic changes with mild connective tissue increase and some fibres lacking the Z-line, while probands 2 and 3 had multiminicores. SEPN1 gene analysis revealed five mutations, three of which are novel. Proband 1 was a compound heterozygote for a 92-bp (exon 1) and a 1-bp deletion (exon 9); proband 2 had a 99-bp deletion and a 10-bp duplication in exon 1, and proband 3 presented a novel homozygous mutation in intron 10 acceptor splice site.

Cagliani Rachele, Riva Stefania, Pozzoli Uberto, Fumagalli Matteo, Comi Giacomo Pietro, Bresolin Nereo, Clerici Mario, Sironi Manuela (2011); BALANCING SELECTION IS COMMON IN THE EXTENDED

MHC REGION BUT MOST ALLELES WITH OPPOSITE RISK PROFILE FOR AUTOIMMUNE DISEASE ARE NEUTRALLY EVOLVING; BMC Evolutionary Biology, 11(1):171

Doi: 10.1186/1471-2148-11-171 **PMID: 21682861**

I.F. 2010: 3,702

BACKGROUND: Several susceptibility genetic variants for autoimmune diseases have been identified. A subset of these polymorphisms displays an opposite risk profile in different autoimmune conditions. This observation open interesting questions on the evolutionary forces shaping the frequency of these alleles in human populations. We aimed at testing the hypothesis whereby balancing selection has shaped the frequency of opposite risk alleles.

RESULTS: Since balancing selection signatures are expected to extend over short genomic portions, we focused our analyses on 11 regions carrying putative functional polymorphisms that may represent the disease variants (and the selection targets). No exceptional nucleotide diversity was observed for ZSCAN23, HLA-DMB, VARS2, PTPN22, BAT3, C6orf47, and IL10; summary statistics were consistent with evolutionary neutrality for these gene regions. Conversely, CDSN/PSORS1C1, TRIM10/TRIM40, BTNL2, and TAP2 showed extremely high nucleotide diversity and most tests rejected neutrality, suggesting the action of balancing selection. For TAP2 and BTNL2 these signatures are not secondary to linkage disequilibrium with HLA class II genes. Nonetheless, with the exception of variants in TRIM40 and CDSN, our data suggest that opposite risk SNPs are not selection targets but rather have accumulated as neutral variants.

CONCLUSION: Data herein indicate that balancing selection is common within the extended MHC region and involves several non-HLA loci. Yet, the evolutionary history of most SNPs with an opposite effect for autoimmune diseases is consistent with evolutionary neutrality. We suggest that variants with an opposite effect on autoimmune diseases should not be considered a distinct class of disease alleles from the evolutionary perspective and, in a few cases, the opposite effect on distinct diseases may derive from complex haplotype structures in regions with high genetic diversity.

Cagliani Rachele, Riva Stefania, Fumagalli Matteo, Biasin Mara, Lo Caputo Sergio, Mazzotta Francesco, Piacentini Luca, Pozzoli Uberto, Bresolin Nereo, Clerici Mario*, Sironi Manuela* (2011);

A POSITIVELY SELECTED APOBECHC3H HAPLOTYPE IS ASSOCIATED WITH NATURAL RESISTANCE TO HIV-1 INFECTION; Evolution, 65(11):3311-3322

**Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1111/j.1558-5646.2011.01368.x **PMID: 22023594**

I.F. 2010: 5,659

APOBEC3 genes encode cytidine deaminases endowed with the ability to inhibit retroviruses and retrotransposons. These genes have been targets of natural selection throughout primate evolutionary history. We analyzed their selection pattern in human populations observing that APOBEC3F and 3G are neutrally evolving. Conversely, nucleotide diversity was extremely high for APOBEC3H, and most tests rejected the hypothesis of selective neutrality in Eurasian populations. Haplotype analysis and the derived intraallelic nucleotide diversity test indicated that positive selection has driven the increase in frequency of one haplotype (Hap I) outside Africa. Consistently, population genetic differentiation between African and non-African populations was higher than expected under neutrality. A case-control association analysis indicated that Hap I is associated with protection from sexually transmitted HIV-1 infection. Hap I carries a protein-destabilizing variant and a residue conferring resistance to Vif-mediated degradation. Data herein suggest that lower protein stability might have been traded-off with a higher ability to circumvent Vif-mediated hijacking. Alternatively, transcription regulatory variants might represent the selection target. Our data represent an example of how the selective pressures exerted by extinct or unknown viral agents can be exploited to provide valuable information on the allelic determinants of susceptibility to modern infections.

Calciolari Guido, Montirosso Rosario (2011); THE SLEEP PROTECTION IN THE PRETERM INFANTS; The Journal of Maternal-Fetal and Neonatal Medicine, 24(S(1)):12-14

Doi: 10.3109/14767058.2011.607563 **PMID: 21942583**

I.F. 2010: 2,071

The importance of sleep in the development is only now beginning to be understood: sleep and established sleep cycles have an important role in the normal neurosensory and cortex development. The biological basis of sleep organization has been highlighted by several studies however environmental differences can affect the sleep patterns in preterm infants in the NICU. Sleep disorders are related to several physiological conditions but it is important to know the relationship between sleep organization and neurocognitive and socio-emotional outcomes. From the recent literature it is possible to find out potentially better practices that preserve and promote infant sleep in the NICU.

Carlomagno Sergio, Giannotti Sara, Vorano Lorenza, Marini Andrea (2011); DISCOURSE INFORMATION CONTENT IN NON-APHASIC ADULTS WITH BRAIN INJURY: A PILOT STUDY; Brain Injury, 25(10):1010-1018

Doi: 10.3109/02699052.2011.605097 **PMID: 21812587**

I.F. 2010: 1,75

BACKGROUND: The functional evaluation of discourse informativeness is widely used in both clinical practice and research, and impoverished and confused discourse has been described in individuals with traumatic brain injury (TBI). These symptoms have been related to language processing deficits at the macrolinguistic level. However, the functional counterpart of these deficits, i.e. poor informativeness in standardized analysis of elicited speech samples, has been less explored.
METHODS AND PROCEDURES: In this pilot study, samples of narrative discourse from 10 non-aphasic TBI adults and 28 healthy adults were examined to study the relationship between standardized measures of informativeness (i.e. Correct Information Unit analysis) and language processing errors at the macrolinguistic level and to compare performance of the two groups.
MAIN OUTCOMES AND RESULTS: The participants with TBI did not produce relevant within-sentence errors and information content of their narratives was not different from that of the healthy participants. However, their production of errors of cohesion, local coherence and global coherence was significantly greater. These macrolinguistic errors corresponded to reduced levels of information efficiency (% CIUs score).
CONCLUSIONS: Functional measures of speech informativeness such as the CIU scores may be useful for the clinical assessment of discourse processing deficits in TBI individuals without aphasic symptoms.

Castellani Umberto, Mirtuono Pasquale, Murino Vittorio, Bellani Marcella, Rambaldelli Gianluca, Tansella Michele, Brambilla Paolo (2011); A NEW SHAPE DIFFUSION DESCRIPTOR FOR BRAIN CLASSIFICATION; Medical Image Computing and Computer-Assisted Intervention: MICCAI... International Conference on Medical Image Computing and Computer-Assisted Intervention, 14(Pt 2):426-433

PMID: 21995057

I.F. 2010: 0,000

In this paper, we exploit spectral shape analysis techniques to detect brain

morphological abnormalities. We propose a new shape descriptor able to encode morphometric properties of a brain image or region using diffusion geometry techniques based on the local Heat Kernel. Using this approach, it is possible to design a versatile signature, employed in this case to classify between normal subjects and patients affected by schizophrenia. Several diffusion strategies are assessed to verify the robustness of the proposed descriptor under different deformation variations. A dataset consisting of MRI scans from 30 patients and 30 control subjects is utilized to test the proposed approach, which achieves promising classification accuracies, up to 83.33%. This constitutes a drastic improvement in comparison with other shape description techniques.

Cereda Matteo, Sironi Manuela, Cavalleri Matteo, Pozzoli Uberto (2011); GECO++: A CC++ LIBRARY FOR GENOMIC FEATURES COMPUTATION AND ANNOTATION IN THE PRESENCE OF VARIANTS; Bioinformatics, 27(9):1313-1315

Doi: 10.1093/bioinformatics/btr123 **PMID: 21398667**

I.F. 2010: 4,887

We propose a C++ class library developed to the purpose of making the implementation of sequence analysis algorithms easier and faster when genomic annotations and variations need to be considered. The library provides a class hierarchy to seamlessly bind together annotations of genomic elements to sequences and to algorithm results; it allows to evaluate the effect of mutations/variations in terms of both element position shifts and of algorithm results, limiting recalculation to the minimum. Particular care has been posed to keep memory and time overhead into acceptable limits. AVAILABILITY AND IMPLEMENTATION: A complete tutorial as well as a detailed doxygen generated documentation and source code is freely available at http://bioinformatics.emedea.it/geco, under the GPL license. The library was written in standard ISO C++, and does not depend on external libraries.

Cimolin Veronica, Piccinini Luigi, Portinaro Nicola, Turconi Anna Carla, Albonico Sonia, Crivellini Marcello, Galli Manuela (2011); THE EFFECTS OF FEMORAL DEROTATION OSTEOTOMY IN CEREBRAL PALSY: A KINEMATIC AND KINETIC STUDY; Hip International, 21(6):657-664

Doi: 10.5301/HIP.2011.8758 **PMID: 22038310**

I.F. 2010: 0,792

We attempted to quantify the effects of isolated femoral derotation osteotomies using clinical evaluation and gait analysis (kinematics and kinetics) in patients with cerebral palsy (CP). Twelve children with CP were evaluated before and 10 months after isolated femoral derotation osteotomy, and 15 healthy children were evaluated as controls. There were significant improvements on clinical examination. A better position of the hip and ankle in the transverse plane was evident and significant changes occurred in terms of hip and ankle kinetics after surgery. Improvements in kinematics and hip and ankle power are very important biomechanically. The correction of lever arm dysfunction and more physiological hip and ankle power generation result in an improvement in terms of energy consumption, leading to a more functional and economic gait pattern.

Corsi Fabio, Fiandra Luisa, De Palma Clara, Colombo Miriam, Mazzucchelli Serena, Verderio Paolo, Allevi Raffaele, Tosoni Antonella, Nebuloni Manuela, Clementi Emilio, Prosperi Davide (2011); HER2 EXPRESSION IN BREAST CANCER CELLS IS DOWNREGULATED UPON ACTIVE TARGETING BY ANTIBODY-ENGINEERED MULTIFUNCTIONAL NANOPARTICLES IN MICE; ACS Nano, 5(8):6383-6393

Doi: 10.1021/nn201570n PMID: 21790185

I.F. 2010: 9,865

Subcellular destiny of targeted nanoparticles in cancer cells within living organisms is still an open matter of debate. By in vivo and ex vivo experiments on tumor-bearing mice treated with antibody-engineered magnetofluorescent nanocrystals, in which we combined fluorescence imaging, magnetic relaxation, and trasmission electron microscopy approaches, we provide evidence that nanoparticles are effectively delivered to the tumor by active targeting. These nanocrystals were demonstrated to enable contrast enhancement of the tumor in magnetic resonance imaging. In addition, we were able to discriminate between the fate of the organic corona and the metallic core upon cell internalization. Accurate immunohistochemical analysis confirmed that hybrid nanoparticle endocytosis is mediated by the complex formation with HER2 receptor, leading to a substantial downregulation of HER2 protein expression on the cell surface. These results provide a direct insight into the pathway of internalization and degradation of targeted hybrid nanoparticles in cancer cells in vivo and suggest a potential application of this immunotheranostic nanoagent in neoadjuvant therapy of cancer.

Costantini Marcello, Urgesi Cosimo, Galati Gaspare, Romani

Gian Luca, Aglioti Salvatore (2011); HAPTIC PERCEPTION AND BODY REPRESENTATION IN LATERAL AND MEDIAL OCCIPITO-TEMPORAL CORTICES; Neuropsychologia, 49(5):821-829

Doi: 10.1016/j.neuropsychologia.2011.01.034 PMID: 21316376

I.F. 2010: 3,949

Although vision is the primary sensory modality that humans and other primates use to identify objects in the environment, we can recognize crucial object features (e.g., shape, size) using the somatic modality. Previous studies have shown that the occipito-temporal areas dedicated to the visual processing of object forms, faces and bodies also show category-selective responses when the preferred stimuli are haptically explored out of view. Visual processing of human bodies engages specific areas in lateral (extrastriate body area, EBA) and medial (fusiform body area, FBA) occipito-temporal cortex. This study aimed at exploring the relative involvement of EBA and FBA in the haptic exploration of body parts. During fMRI scanning, participants were asked to haptically explore either real-size fake body parts or objects. We found a selective activation of right and left EBA, but not of right FBA, while participants haptically explored body parts as compared to real objects. This suggests that EBA may integrate visual body representations with somatosensory information regarding body parts and form a multimodal representation of the body. Furthermore, both left and right EBA showed a comparable level of body selectivity during haptic perception and visual imagery. However, right but not left EBA was more activated during haptic exploration than visual imagery of body parts, ruling out that the response to haptic body exploration was entirely due to the use of visual imagery. Overall, the results point to the existence of different multimodal body representations in the occipito-temporal cortex which are activated during perception and imagery of human body parts.

Crimella Claudia, Cantoni Orazio, Guidarelli Andrea, Vantaggiato Chiara, Martinuzzi Andrea, Fiorani Mara, Azzolini Catia, Orso Genny, Bresolin Nereo, Bassi Maria Teresa (2011); A NOVEL NONSENSE MUTATION IN THE APTX GENE ASSOCIATED WITH DELAYED DNA SINGLE-STRANDS BREAK REMOVAL FAILS TO ENHANCE SENSITIVITY TO DIFFERENT GENOTOXIC AGENTS; Human Mutation, 32(4):E2118-E2133

Doi: 10.1022/humu.21464 PMID: 21412945

I.F. 2010: 5,956

APTX is the gene involved in ataxia with oculomotor apraxia type 1 (AOA1),

a recessive disorder with early-onset cerebellar ataxia, oculomotor apraxia and peripheral neuropathy. The encoded protein, aprataxin, is a DNA repair protein processing the products of abortive ligations, 5'-adenylated DNA. We describe a novel nonsense mutation in APTX, c.892C>T (p.Gln298X), segregating in two AOA1 patients and leading to the loss of aprataxin protein in patient's cells. These cells, while exhibiting reduced catalase activity, are not hypersensitive to toxicity elicited by H(2)O(2) exposure at either physiologic or ice-bath temperature. On the other hand, the rate of repair of DNA single-strand-breaks (SSBs) induced in both conditions is always significantly slower in AOA1 cells. By using the alkylating agent methyl methane sulphonate (MMS) we confirmed the association of the APTX mutation with a DNA repair defect in the absence of detectable changes in susceptibility to toxicity. These results, while consistent with a role of aprataxin in the repair of SSBs induced by H(2)O(2), or MMS, demonstrate that other mechanisms may be recruited in AOA1 cells to complete the repair process, although at a slower rate. Lack of hypersensitivity to the oxidant, or MMS, also implies that delayed repair is not per se a lethal event.

Curran Sarah, Bolton Patrick, Rozsnyai Kinga, Chiocchetti Andreas, Klauck Sabine M., Duketis Eftichia, Poustka Fritz, Schlitt Sabine, Freitag Christine M., Lee Irene, Muglia Pierandrea, ITAN, the Italian Autism Network (Molteni Massimo), Poot Martin, Staal Wouter, De Jonge Maretha V., Ophoff Roel A., Lewis Cathryn, Skuse David, Mandy Will, Vassos Evangelos, Fossdal Ragnheidur, Magnusson Pall, Hreidarsson Stefan, Saemundsen Evald, Stefansson Hreinn, Stefansson Kari, Collier David (2011); NO ASSOCIATION BETWEEN A COMMON SINGLE NUCLEOTIDE POLYMORPHISM, RS4141463, IN THE MACROD2 GENE AND AUTISM SPECTRUM DISORDER; American Journal of Medical Genetics Part B - Neuropsychiatric Genetics, 156B(6):633-639

Doi: 10.1002/ajmg.b.31201 **PMID: 21656903**

I.F. 2010: 4,156

The Autism Genome Project (AGP) Consortium recently reported genome-wide significant association between autism and an intronic single nucleotide polymorphism marker, rs4141463, within the MACROD2 gene. In the present study we attempted to replicate this finding using an independent case-control design of 1,170 cases with autism spectrum disorder (ASD) (874 of which fulfilled narrow criteria for Autism (A)) from five centers within Europe (UK, Germany, the Netherlands, Italy, and Iceland), and 35,307 controls. The combined sample size gave us a non-centrality parameter (NCP) of 11.9,

with 93% power to detect allelic association of rs4141463 at an alpha of 0.05 with odds ratio of 0.84 (the best odds ratio estimate of the AGP Consortium data), and for the narrow diagnosis of autism, an NCP of 8.9 and power of 85%. Our case-control data were analyzed for association, stratified by each center, and the summary statistics were combined using the meta-analysis program, GWAMA. This resulted in an odds ratio (OR) of 1.03 (95% CI 0.944-1.133), with a P-value of 0.5 for ASD and OR of 0.99 (95% CI 0.88-1.11) with P-value = 0.85 for the Autism (A) sub-group. Therefore, this study does not provide support for the reported association between rs4141463 and autism.

D'Angelo Maria Grazia*, Romei Marianna*, Lo Mauro Antonella, Marchi Eraldo, Gandossini Sandra, Bonato Sara, Comi Giacomo Pietro, Magri Francesca, Turconi Anna Carla, Pedotti Antonio, Bresolin Nereo, Aliverti Andrea (2011); RESPIRATORY PATTERN IN AN ADULT POPULATION OF DYSTROPHIC PATIENTS; Journal of the Neurological Sciences, 306(1-2):54-61

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.jns.2011.03.045 **PMID: 21529845**

I.F. 2010: 2,167

We studied respiratory function and Chest Wall kinematics in a large population of adult patients affected by slow course muscular dystrophies such as Limb-Girdle Muscular Dystrophy (LGMD, n=38), Becker Muscular Dystrophy (BMD, n=20) and Facio-Scapulo Humeral Dystrophy (FSHD, n=30), through standard spirometry and through the Optoelectronic Plethysmography, to measure the thoraco-abdominal motion during Quiet Breathing and Slow Vital Capacity maneuvers. Within the restrictive pulmonary syndrome characterizing LGMD and FSHD, several different thoraco-abdominal patterns compared to those of healthy subjects were present in the more advanced stages of the disease. These differences were present in the seated position, during the execution of a maximal maneuver such as Slow Vital Capacity. A global respiratory (both inspiratory and expiratory) muscle involvement was more pronounced in the LGMD and FSHD than in the BMD patients, and a significant reduction of abdominal contribution in wheelchair bound patients was observed. In conclusion, OEP technique is able to reveal mild initial modifications in the respiratory muscles in FSHD and LGMD patients, which could be helpful for functional and new therapeutic strategy evaluation.

D'Angelo Maria Grazia, Lorusso Maria Luisa, Civati Federica, Comi Giacomo Pietro, Magri Francesca, Del Bo Roberto, Guglieri Michela, Molteni Massimo, Turconi Anna Carla, Bresolin Nereo

(2011); NEUROCOGNITIVE PROFILES IN DUCHENNE MUSCULAR DYSTROPHY AND GENE MUTATION; Pediatric Neurology, 45(5):292-299

Doi: 10.1016/j.pediatrneurol.2011.08.003 **PMID: 22000308**

I.F. 2010: 1,513

The presence of nonprogressive cognitive impairment is recognized as a common feature in a substantial proportion of patients with Duchenne muscular dystrophy. To investigate the possible role of mutations along the dystrophin gene affecting different brain dystrophin isoforms and specific cognitive profiles, 42 school-age children affected with Duchenne muscular dystrophy, subdivided according to sites of mutations along the dystrophin gene, underwent a battery of tests tapping a wide range of intellectual, linguistic, and neuropsychologic functions. Full-scale intelligence quotient was approximately 1 S.D. below the population average in the whole group of dystrophic children. Patients with Duchenne muscular dystrophy and mutations located in the distal portion of the dystrophin gene (involving the 140-kDa brain protein isoform, called Dp140) were generally more severely affected and expressed different patterns of strengths and impairments, compared with patients with Duchenne muscular dystrophy and mutations located in the proximal portion of the dystrophin gene (not involving Dp140). Patients with Duchenne muscular dystrophy and distal mutations demonstrated specific impairments in visuospatial functions and visual memory (which seemed intact in proximally mutated patients) and greater impairment in syntactic processing.

De Marco Patrizia*, Raso Alessandro*, Beri Silvana*, Gimelli Stefania*, Merello Elisa*, Mascelli Samantha*, Baldi Maurizia*, Baffico Ave Maria*, Pavanello Marco*, Cama Armando*, Capra Valeria*, Giorda Roberto*, Gimelli Giorgio* (2011); A DE NOVO BALANCED TRANSLOCATION T(7;12)(p21.2;p12.3) IN A PATIENT WITH SAETHRE-CHOTZEN-LIKE PHENOTYPE DOWNREGULATES TWIST AND AN OSTEOCLASTIC PROTEIN-TYROSINE PHOSPHATASE, PTC-OC; European Journal of Medical Genetics, 54(5):e478-e483

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.ejmg.2011.05.007 **PMID: 21708297**

I.F. 2010: 2,335

Saethre-Chotzen syndrome (SCS) is an autosomal dominant craniosynostosis syndrome with variable expression. Here we report on a female infant with a

de novo balanced translocation 46, XX, t(7;12)(p21.2;p12.3) and presenting at birth brachycephaly, antimongolic palpebral fissures, ocular hypertelorism, broad nose with low nasal bridge and low-set ears. This phenotype is suggestive of a subtle form of SCS, given the absence of limbs anomalies. Cloning of both breakpoints revealed that the translocation does not interrupt the TWIST1 coding region, on 7p21, known to be causative for SCS, but downregulates TWIST1 expression due to a position effect. On chromosome 12, the breakpoint translocates a shorter transcript of PTPRO gene, the osteoclastic protein-tyrosine phosphatase, PTP-oc, near to regulatory region of 7p leading to down-regulation of PTP-oc in the proband's fibroblasts. This is a confirmatory case report providing further evidence for TWIST1 haploinsufficiency in SCS, although a possible role of PTP-oc as genetic factor underlying or at least influencing the development of craniosynostosis could not be a priori excluded.

Didoni Anna, Sequi Marco, Panei Pietro, Bonati Maurizio, Lombardy ADHD Registry Group (Bertella Silvana, Molteni Massimo, Simone Daniela) (2011); ONE-YEAR PROSPECTIVE FOLLOW-UP OF PHARMACOLOGICAL TREATMENT IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER; European Journal of Clinical Pharmacology, 67(10):1061-1067

Doi: 10.1007/s00228-011-1050-3 PMID: 21538145

I.F. 2010: 3,032

OBJECTIVES: To delineate the safety and tolerability profile of methylphenidate and atomoxetine in children and adolescents with attention deficit hyperactivity disorder (ADHD) monitored for more than 1 year.
DESIGN: A cohort study analyzing data from the national ADHD register on patients from the Lombardy Region treated with MPH or atomoxetine.
PARTICIPANTS: A total of 229 children (median age 11 years, range 6-17), enrolled in 15 regional centers between June 2007 and May 2010.
RESULTS: The prevalence rate of pharmacological treatment for ADHD was 0.23%, whereas the estimated ADHD prevalence in the population was 0.95%. In total, 73.8% of patients had been treated with atomoxetine (10-90 mg daily) or MPH (10-75 mg daily); 22% of patients also received an additional psychotropic drug. Of the treated children, 26.9% discontinued the drug prior to 1 year of treatment, mostly because of adverse effects (28.6%). No new or unexpected adverse events (rate 39.2%) were encountered. Decreased appetite, headache, and unstable mood were the leading events. The most severe events occurred in two boys: one experienced absence seizures for the first time with MPH, the other experienced hallucinations with

atomoxetine. Therapy was discontinued in ten male patients (7.7%) because of adverse events. All patients with adverse effects recovered well.
CONCLUSIONS: A very low rate of ADHD prevalence was estimated in Italian children compared to that reported in other countries. Although the medications for ADHD are generally well tolerated, with only mild or minor adverse effects in most cases, their rational use can only be guaranteed by disseminating and monitoring evidence-based practices and by monitoring the safety and efficacy of treatments in both the short and long terms with appropriate tools and approaches.

Facchin Paola, Rizzotto Melissa Rosa, Visonà Dalla Pozza L., Turconi Anna Carla, Pagliano Emanuela, Signorini Sabrina, Tornetta Lorella, Trabacca Antonio, Fedrizzi Ermellina, Gipci Study Group (Germiniasi Chiara, Magagnin Bertilla, Martinuzzi Andrea, Megliani Chiara, Molteni Francesca, Stefanoni Giuseppe, Vespino Teresa) (2011); MULTISITE TRIAL COMPARING THE EFFICACY OF CONSTRAINT-INDUCED MOVEMENT THERAPY WITH THAT OF BIMANUAL INTENSIVE TRAINING IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY; American Journal of Physical Medicine and Rehabilitation, 90(7):539-553

Doi: 10.1097/PHM.0b013e3182247076 PMID: 21765273

I.F. 2010: 1,762

OBJECTIVE: The aim of this study was to compare the effects of modified constraint-induced movement therapy (mCIMT; restraint of unaffected limb combined with unimanual intensive rehabilitation) with those of a bimanual intensive rehabilitation treatment (IRP) in children with hemiplegic cerebral palsy after a 10-wk practice vs. standard treatment (ST).
DESIGN: This study is a multicenter, cluster-randomized controlled clinical trial of tested groups of children with hemiplegic cerebral palsy treated using mCIMT, IRP, or ST. For 10 wks, in mCIMT and IRP, the intensive practice lasted 3 hrs/day, 7 days/wk; in ST, 1-hr sessions twice a week were provided. The primary outcomes are upper limb/hand function (Quality of Upper Extremity Skills Test) and activities of daily living (Besta Scale), which are assessed before and after treatment. One hundred five patients were recruited, 39 to the mCIMT group, 33 to the IRP group, and 33 to the ST group.
RESULTS: IRP and mCIMT significantly improved paretic hand function both in the Quality of Upper Extremity Skills Test and in the Besta Scale, whereas ST did not. mCIMT improved grasp more than IRP did ($P < 0.01$), whereas bimanual spontaneous use in play increased more with IRP ($P = 0.0005$). Activities of daily living in 2- to 6-yr-olds improved more with IRP ($P < 0.0001$)

than with mCIMT (P = 0.011). Unaffected limb improved more from bimanual practice (IRP; P = 0.02).
CONCLUSIONS: More advantages resulted from intensive practice than in the standard one, in mCIMT for grasp and in IRP for bimanual spontaneous use and activities of daily living in younger children.

Fagnani Corrado, Bellani Marcella, Tansella Michele, Balestrieri Matteo, Toccaceli Virgilia, Patriarca Valeria, Stazi Maria Antonietta, Brambilla Paolo (2011); INVESTIGATION OF SHARED GENETIC EFFECT FOR PSYCHOTIC AND OBSESSIVE SYMPTOMS IN YOUNG ADULT TWINS; Psychiatry Research, 188(2):276-282

Doi: 10.1016/j.psychres.2010.12.002 PMID: 21215460

I.F. 2010: 2,803

Genetic and environmental architecture of psychotic and obsessive symptoms are not completely elucidated. This study estimated for these symptoms (i) the genetic and environmental components, (ii) the within-individual association, and (iii) the extent to which this association originates from common genetic and environmental factors. Young adult twins (N=701) from the population-based Italian Twin Register were assessed for psychotic and obsessive-compulsive symptoms by using the Symptom Check List (SCL-90). Multivariate Cholesky models were fitted by the Mx statistical program. No previous study used this design to examine the same dimensions. The best-fitting model included additive genetic and nonshared environmental components, each accounting for about half of total variance in the symptoms. Genetic influences on the different symptoms overlapped considerably (r(g)=0.81 to 0.99). Phenotypic correlations of psychotic symptoms and of psychotic with obsessive symptoms were high (r=0.61 to 0.76), with 53% to 69% explained by shared genetic effects. This study shows substantial genetic influence on psychotic and obsessive symptoms, and indicates that their co-occurrence may be due to genetic factors to a greater extent than to environmental effects. These results encourage the search for genetic and environmental factors underlying the covariance between different psychotic traits as well as between psychotic and obsessive traits.

Forti Sara, Valli Angela, Perego Paolo, Nobile Maria, Crippa Alessandro, Molteni Massimo (2011); MOTOR PLANNING AND CONTROL IN AUTISM. A KINEMATIC ANALYSIS OF PRESCHOOL CHILDREN; Research in Autism Spectrum Disorders, 5(2):834-842

Doi: 10.1016/j.rasd.2010.09.013

I.F. 2010: 1,586

Kinematic recordings in a reach and drop task were compared between 12 preschool children with autism without mental retardation and 12 gender and age-matched normally developing children. Our aim was to investigate whether motor anomalies in autism may depend more on a planning ability dysfunction or on a motor control deficit. Planning and control processes were separately investigated by examining kinematic recordings divided into primary movement- (planning-based) and corrective submovement-(control-based) phases.
Despite longer movement durations, participants with autism were as accurate in their movements as normally developing children were and showed a preserved movement structure. No differences were observed for the initial movement phases for hand velocity, accuracy and inter-trial variability.
Our main finding was that of a group difference in proximity of the target, at transition from planning-based to control-based movement guidance. At primary movement conclusion, the normally developing children had already reduced velocity and begun orienting their hands for ball drop. Also, they tended to terminate movements within the same movement unit that had transported the hand into the target box. Compared to this group, participants with autism reached this stage with less preparation: their speed was significantly higher, wrist inclination reduced and they showed further movement units after entering the box over the vast majority of trials. These additional movement units were presumed to represent late control-based spatial adjustments. Hence, our data support the hypothesis that children with autism have a greater need for corrective submovements.
We provide evidence that motor anomalies in autism might be determined either by a disruption in planning-control integration, or by a limited planning process capacity, as participants with autism might have been able to plan only the very beginning of the movement, leaving its final phases to further planning on the fly, with important consequences on movement time optimization.

Fumagalli Matteo, Sironi Manuela, Pozzoli Uberto, Ferrer-Admettla Anna, Pattini Linda, Nielsen Rasmus (2011); SIGNATURES OF ENVIRONMENTAL GENETIC ADAPTATION PINPOINT PATHOGENS AS THE MAIN SELECTIVE PRESSURE THROUGH HUMAN EVOLUTION; Plos Genetics, 7(11):e1002355

Doi: 10.1371/journal.pgen.1002355 **PMID: 22072984**

I.F. 2010: 9,543

Previous genome-wide scans of positive natural selection in humans have identified a number of non-neutrally evolving genes that play important roles

in skin pigmentation, metabolism, or immune function. Recent studies have also shown that a genome-wide pattern of local adaptation can be detected by identifying correlations between patterns of allele frequencies and environmental variables. Despite these observations, the degree to which natural selection is primarily driven by adaptation to local environments, and the role of pathogens or other ecological factors as selective agents, is still under debate. To address this issue, we correlated the spatial allele frequency distribution of a large sample of SNPs from 55 distinct human populations to a set of environmental factors that describe local geographical features such as climate, diet regimes, and pathogen loads. In concordance with previous studies, we detected a significant enrichment of genic SNPs, and particularly non-synonymous SNPs associated with local adaptation. Furthermore, we show that the diversity of the local pathogenic environment is the predominant driver of local adaptation, and that climate, at least as measured here, only plays a relatively minor role. While background demography by far makes the strongest contribution in explaining the genetic variance among populations, we detected about 100 genes which show an unexpectedly strong correlation between allele frequencies and pathogenic environment, after correcting for demography. Conversely, for diet regimes and climatic conditions, no genes show a similar correlation between the environmental factor and allele frequencies. This result is validated using low-coverage sequencing data for multiple populations. Among the loci targeted by pathogen-driven selection, we found an enrichment of genes associated to autoimmune diseases, such as celiac disease, type 1 diabetes, and multiples sclerosis, which lends credence to the hypothesis that some susceptibility alleles for autoimmune diseases may be maintained in human population due to past selective processes.

Gagliardi Chiara, Martelli Sara, Tavano Alessandro, Borgatti Renato (2011); BEHAVIOURAL FEATURES OF ITALIAN INFANTS AND YOUNG ADULTS WITH WILLIAMS-BEUREN SYNDROME; Journal of Intellectual Disability Research, 55(Part. 2):121-131

Doi: 10.1111/J.1365-2788.2010.01376.X PMID: 21205040

I.F. 2010: 1,596

BACKGROUND: The increased interest in social interaction in Williams-Beuren syndrome (WBS) is evident from infancy onwards, together not only with increased empathy, positive interpersonal bias, but also with social disinhibition. Previous studies have described behavioural and emotional problems as being widely represented in WBS. There is limited scope for comparisons between literature data because of the variety of instruments

used to assess behaviour.
METHOD: Forty-one children and young adults with WBS were enrolled and underwent general cognitive assessment. In order to compare our data with the literature, we used standardised questionnaires used in previous studies (Developmental Behaviour Checklist: DBC-P). General cognitive abilities, gender and age were included in the analysis.
RESULTS: Behavioural problems were more relevant than expected according to intellectual impairment. Some features were present at any age: inattention, anxiety, disruptive behaviours. Antisocial conduct was almost absent; perseverative conduct, a poor sense of danger and, more generally, self-absorbed behaviours tended to diminish along with age and to be linked to more pronounced cognitive impairment.
CONCLUSION: As previously described for other countries, behaviour disturbances occur frequently in the Italian WBS population. Our data could support the existence of some 'intrinsic' behavioural characteristics in WBS such as inattention and anxiety, which are detectable and important at any age; both learning and social exposure to a structured context such as school could help diminish self-absorbed behaviour.

Gagliardi Chiara, Tavano Alessandro, Turconi Anna Carla, Pozzoli Uberto, Borgatti Renato (2011); SEQUENCE LEARNING IN CEREBRAL PALSY; Pediatric Neurology, 44(3):207-213

Doi: 10.1016/j.pediatrneurol.2010.10.004 PMID: 21310337

I.F. 2010: 1,513

We investigated sequence-learning skills in 64 children with cerebral palsy (aged 4.01-14.7 years; 49 with bilateral, two with dystonic, and 13 with unilateral cerebral palsy), compared with a matched control group of typically developing children. Participants' motor and handling abilities were classified according to the Gross Motor Function Classification System and the Manual Ability Classification System. General cognitive, visuoperceptual, and constructive abilities were assessed. Participants performed an experimental computerized version of Corsi Span, followed by a normalized Supraspan sequence. Controls outperformed cerebral palsy participants in visual memory and accuracy. Participants with cerebral palsy were likelier to fail the test (cerebral palsy, 37.5%; control subjects, 5%) and obtain overall lower scores. Sequence learning skills were not related to motor and handling impairments. Failure to learn sequences resulted in an overall lower functioning profile regarding visuoperceptual, verbal, and performance abilities. The ability to fix sequences seemed to split the cerebral palsy group into an overall high-functioning group (successful in sequence learning) and

low-functioning (failing) group. Results are discussed in light of a specific implicit memory impairment and the abnormal development of white matter frontostriatal and parietal connections.

Gallanti Andrea, Cardin Veronica, Tonelli Alessandra, Bussone Gennaro, Bresolin Nereo, Mariani Claudio, Bassi Maria Teresa (2011); THE GENETIC FEATURES OF 24 PATIENTS AFFECTED BY FAMILIAL AND SPORADIC HEMIPLEGIC MIGRAINE; Neurological Sciences, 32(Suppl. 1):S141-S142 – Brief Communication

Doi: 10.1007/s10072-011-0517-4 PMID: 21533730

I.F. 2010: 1,220

Familial hemiplegic migraine (FHM) is the only migraine subtype for which a monogenic mode of inheritance, autosomal dominant has been clearly established. It is genetically heterogeneous and at least three different genes exist (CACNA1A, ATP1A2, and SCN1A), the so-called FHM1, FHM2, and FHM3 genes, respectively. Sporadic hemiplegic migraine (SHM) is a disorder, in which some patients may have their pathophysiology identical to FHM, but others, possibly the majority, may have different pathophysiology, probably related to the mechanisms of typical migraine with aura. In our study, we have screened the DNA of 24 patients affected by FHM and SHM. Only in three patients, 2 sporadic and 1 familial cases, we have described genetic mutations, all of them in the ATP1A2 gene. In our opinion, these results demonstrate a more frequent involvement of the ATP1A2 gene not only in the sporadic form, but probably also in the Italian FHM patients without permanent cerebellar signs. Moreover, the absence of CACNA1A, ATP1A2 and SCN1A mutations in the other 12 familial cases suggests the involvement of still unknown genes.

Giorda Roberto, Beri Silvana, Bonaglia Maria Clara, Spaccini Luigina, Scelsa Barbara, Manolakos Emmanouil, Della Mina Erika, Ciccone Roberto, Zuffardi Orsetta (2011); COMMON STRUCTURAL FEATURES CHARACTERIZE INTERSTITIAL INTRACHROMOSOMAL XP AND 18Q TRIPLICATIONS; American Journal of Medical Genetics Part A, 155(11):2681-2687

Doi: 10.1002/ajmg.a.34248 PMID: 21965167

I.F 2010: 2,505

Rare intrachromosomal triplications producing partial tetrasomies have been reported for a number of chromosomes. A detailed molecular characterization, necessary to define the mechanism of their formation, has so far been

lacking. We report on the detailed clinical, cytogenetic, and molecular characterization of two triplications, one de novo involving chromosome 18q, the other familial on chromosome Xp. The clinical phenotype of the patient with 18q triplication, very likely due to overexpression of one or more of the genes in the region, consists mainly of facial dysmorphisms and developmental delay. The familial Xp triplication does not cause an increase in the number of copies of any gene and is almost certainly a polymorphism. The rearrangements are actually complex duplications/triplications. In both patients, their proximal breakpoints are located within complex segmental duplications, one containing the VCX gene cluster on chromosome Xp, the other the TCEB3 genes on chromosome 18q. A proximal duplicated region is also present in both patients. All junctions we analyzed were formed by non-homologous end joining (NHEJ). The structural features shared between our patients suggest the involvement of a common mechanism in the genesis of interstitial intrachromosomal triplications.

Giordano Carla*, Montopoli Monica*, Perli Elena, Orlandi Maurizia, Fantin Marianna, Ross-Cisneros Fred N., Caparrotta Laura, Martinuzzi Andrea, Ragazzi Eugenio, Ghelli Anna, Sadun A. Alfredo, D'Amati Giulia, Carelli Valerio (2011); OESTROGENS AMELIORATE MITOCHONDRIAL DYSFUNCTION IN LEBER'S HEREDITARY OPTIC NEUROPATHY; Brain, 134(Pt 1):220-234

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1093/brain/awq276 **PMID: 20943885**

I.F. 2010: 9,232

Leber's hereditary optic neuropathy, the most frequent mitochondrial disease due to mitochondrial DNA point mutations in complex I, is characterized by the selective degeneration of retinal ganglion cells, leading to optic atrophy and loss of central vision prevalently in young males. The current study investigated the reasons for the higher prevalence of Leber's hereditary optic neuropathy in males, exploring the potential compensatory effects of oestrogens on mutant cell metabolism. Control and Leber's hereditary optic neuropathy osteosarcoma-derived cybrids (11778/ND4, 3460/ND1 and 14484/ND6) were grown in glucose or glucose-free, galactose-supplemented medium. After having shown the nuclear and mitochondrial localization of oestrogen receptors in cybrids, experiments were carried out by adding 100 nM of 17β-oestradiol. In a set of experiments, cells were pre-incubated with the oestrogen receptor antagonist ICI 182780. Leber's hereditary optic neuropathy cybrids in galactose medium presented overproduction of reactive oxygen species, which led to decrease in mitochondrial membrane

potential, increased apoptotic rate, loss of cell viability and hyper-fragmented mitochondrial morphology compared with control cybrids. Treatment with 17β-oestradiol significantly rescued these pathological features and led to the activation of the antioxidant enzyme superoxide dismutase 2. In addition, 17β-oestradiol induced a general activation of mitochondrial biogenesis and a small although significant improvement in energetic competence. All these effects were oestrogen receptor mediated. Finally, we showed that the oestrogen receptor β localizes to the mitochondrial network of human retinal ganglion cells. Our results strongly support a metabolic basis for the unexplained male prevalence in Leber's hereditary optic neuropathy and hold promises for a therapeutic use for oestrogen-like molecules.

Gori Simone, Giora Enrico, Yazdanbakhsh Arash, Mingolla Ennio (2011); A NEW MOTION ILLUSION BASED ON COMPETITION BETWEEN TWO KINDS OF MOTION PROCESSING UNITS: THE ACCORDION GRATING; Neural Networks, 24(10):1082-1092

Doi: 10.1016/j.neunet.2011.06.017 PMID: 21784613

I.F. 2010: 1,972

Parametric psychophysical investigations are reported for two related illusory effects that occur when viewing an elementary square-wave grating while making "back and forth" head movements along the projection line. Observers report a non-rigid distortion of the pattern, including: (i) an expansion in a direction perpendicular to the stripes, and (ii) a perceived curvature of the stripes. We investigated these two phenomena independently. The first depends on the classical physiological aperture problem that confronts early cells in the vision system. Interactions between ambiguous and unambiguous motion signals, generated at line interiors and line ends, respectively, can explain why the perceived expansion occurs only in directions perpendicular to the stripes. A simple model is presented and successfully tested by a nulling psychophysical experiment with four subjects. The experiment varies key stimulus attributes that generate ambiguous and unambiguous motion signals. Regarding the illusory curvature, a differential geometry model of the optics of our display, which identifies a non-classical three-dimensional (3D) aperture problem, is proposed (Yazdanbakhsh & Gori, 2011). We tested that model by implementing its closed form prediction of distortion to design displays for a second psychophysical experiment that also uses a nulling technique. Results from four subjects allow the quantification of the degree of perceived curvature as a function of speed, distance and stimulus type (blurred vs. unblurred grating) and are compatible with the predictions of the model.

Hallahan Brian, Newell John, Soares Jair C., Brambilla Paolo, Strakowski Stephen M., Fleck David E., Kieseppa Tuula, Altshuler Lori L., Fornito Alex, Malhi Gin S., McIntosh Andrew M., Yurgelun-Todd Deborah A., Labar Kevin S., Sharma Verinder, MacQueen Glenda M., Murray Robin M., McDonald Colm (2009); STRUCTURAL MAGNETIC RESONANCE IMAGING IN BIPOLAR DISORDER: AN INTERNATIONAL COLLABORATIVE MEGA-ANALYSIS OF INDIVIDUAL ADULT PATIENT DATA; Biological Psychiatry, 69(4):326-335

Doi: 10.106/J.BIOPSYCH.2010.08.029 PMID: 21030008

I.F. 2010: 8,674

BACKGROUND: There is substantial inconsistency in results of brain structural magnetic resonance imaging studies in adult bipolar disorder. This is likely consequent upon limited statistical power of studies together with their clinical and methodological heterogeneity. The current study was undertaken to perform an international collaborative mega-analysis of regional volumetric measurements of individual patient and healthy subject data, to optimize statistical power, detect case-control differences, assess the association of psychotropic medication usage with brain structural variation, and detect other possible sources of heterogeneity.
METHODS: Eleven international research groups contributed published and unpublished data on 321 individuals with bipolar disorder I and 442 healthy subjects. We used linear mixed effects regression models to evaluate differences in brain structure between patient groups.
RESULTS: Individuals with bipolar disorder had increased right lateral ventricular, left temporal lobe, and right putamen volumes. Bipolar patients taking lithium displayed significantly increased hippocampal and amygdala volume compared with patients not treated with lithium and healthy comparison subjects. Cerebral volume reduction was significantly associated with illness duration in bipolar individuals.
CONCLUSIONS: The application of mega-analysis to bipolar disorder imaging identified lithium use and illness duration as substantial and consistent sources of heterogeneity, with lithium use associated with regionally specific increased brain volume.

Lanfranconi Silvia, Locatelli Federica, Corti Stefania, Candelise Livia, Comi Giacomo Pietro, Baron Pierluigi, Strazzer Sandra, Bresolin Nereo, Bersano Anna (2011); GROWTH FACTORS IN ISCHEMIC STROKE; Journal of Cellular and Molecular Medicine,

15(8):1645-1687

Doi: 10.1111/j.1582-4934.2009.00987.x PMID: 20015202

I.F. 2010: 4,608

Data from pre-clinical and clinical studies provide evidence that colony-stimulating factors (CSFs) and other growth factors (GFs) can improve stroke outcome by reducing stroke damage through their anti-apoptotic and anti-inflammatory effects, and by promoting angiogenesis and neurogenesis. This review provides a critical and up-to-date literature review on CSF use in stroke. We searched for experimental and clinical studies on haemopoietic GFs such as granulocyte CSF, erythropoietin, granulocyte-macrophage colony-stimulating factor, stem cell factor (SCF), vascular endothelial GF, stromal cell-derived factor-1α and SCF in ischemic stroke. We also considered studies on insulin-like growth factor-1 and neurotrophins. Despite promising results from animal models, the lack of data in human beings hampers efficacy assessments of GFs on stroke outcome. We provide a comprehensive and critical view of the present knowledge about GFs and stroke, and an overview of ongoing and future prospects.

Lorusso Maria Luisa, Facoetti Andrea, Bakker Dirk J. (2011); NEUROPSYCHOLOGICAL TREATMENT OF DYSLEXIA: DOES TYPE OF TREATMENT MATTER?; Journal of Learning Disabilities, 44(2):136-149

Doi: 10.1177/0022219410391186 PMID: 21383106

I.F. 2010: 2,240

In this study, 123 children with a diagnosis of developmental dyslexia were assigned to different treatment groups, either variations of Bakker's intervention program based on the balance model or a control, a specific reading training group. Thorough cognitive and neuropsychological assessment allowed determination of the subtype of dyslexia according to the balance model and the neuropsychological profile with respect to reading and spelling abilities, verbal memory, and phonemic awareness. Characteristics of hemisphere-specific stimulation were systematically manipulated in an effort to shed light on the bases and mechanisms of reading improvement. It was shown that the effects of treatment vary according to type of dyslexia and that the different intervention programs have differential effects on reading-related neuropsychological functions. Since opposite effects can be produced by the same type of treatment in different dyslexia subtypes, the results of the study suggest that accurate classification of subtype on the base of reading and reading-related variables is advantageous for an optimal planning of the

therapy.

Magri Francesca, Govoni Alessandra, D'Angelo Maria Grazia, Del Bo Roberto, Ghezzi Serena, Gandossini Sandra, Turconi Anna Carla, Sciacco Monica, Ciscato Patrizia, Bordoni Andreina, Tedeschi Silvana, Fortunato Francesco, Lucchini Valeria, Bonato Sara, Lamperti Costanza, Coviello Domenico, Torrente Yvan, Corti Stefania, Moggio Maurizio, Bresolin Nereo (2011); GENOTYPE AND PHENOTYPE CHARACTERIZATION IN A LARGE DYSTROPHINOPATHIC COHORT WITH EXTENDED FOLLOW-UP; Journal of Neurology, 258(9):1610-1623

Doi: 10.1007/s00415-011-5979-z PMID: 21399986

I.F. 2010: 3,853

Duchenne and Becker muscular dystrophy (DMD and BMD, respectively) are allelic disorders with different clinical presentations and severity determined by mutations in the gene DMD, which encodes the sarcolemmal protein dystrophin. Diagnosis is based on clinical aspects and muscle protein analysis, followed by molecular confirmation. We revised the main aspects of the natural history of dystrophinopathies to define genotype-phenotype correlations in large patient cohorts with extended follow-up. We also specifically explored subjects carrying nucleotide substitutions in the DMD gene, a comparatively less investigated DMD/BMD subgroup. We studied 320 dystrophinopathic patients (205 DMD and 115 BMD), defining muscular, cardiac, respiratory, and cognitive involvement. We also subdivided patients according to the kind of molecular defect (deletions, duplications, nucleotide substitutions or other microrearrangements) and the mutation sites (proximal/distal to exon 45), studying phenotype-genotype correlations for each group. In DMD, mutation type did not influence clinical evolution; mutations located in distal regions (irrespective of their nature) are more likely to be associated with lower IQ levels ($p = 0.005$). BMD carrying proximal deletions showed a higher degree of cardiac impairment than BMD with distal deletions ($p = 0.0046$). In the BMD population, there was a strong correlation between the entity of muscle dystrophin deficiency and clinical course ($p = 0.002$). An accurate knowledge of natural history may help in the clinical management of patients. Furthermore, several clinical trials are ongoing or are currently planned, some of which aim to target specific DMD mutations: a robust natural history is therefore essential to correctly design these experimental trials.

Magri Francesca, Del Bo Roberto, D'Angelo Maria Grazia, Govoni

Alessandra, Ghezzi Serena, Gandossini Sandra, Sciacco Monica, Ciscato Patrizia, Bordoni Andreina, Tedeschi Silvana, Fortunato Francesco, Lucchini Valeria, Cereda Matteo, Corti Stefania, Moggio Maurizio, Bresolin Nereo, Comi Giacomo Pietro (2011); CLINICAL AND MOLECULAR CHARACTERIZATION OF A COHORT OF PATIENTS WITH NOVEL NUCLEOTIDE ALTERATIONS OF THE DYSTROPHIN GENE DETECTED BY DIRECT SEQUENCING; BMC Medical Genetics, 12:37

Doi: 10.1186/1471-2350-12-37 **PMID: 21396098**

I.F. 2010: 2,439

BACKGROUND: Duchenne and Becker Muscular dystrophies (DMD/BMD) are allelic disorders caused by mutations in the dystrophin gene, which encodes a sarcolemmal protein responsible for muscle integrity. Deletions and duplications account for approximately 75% of mutations in DMD and 85% in BMD. The implementation of techniques allowing complete gene sequencing has focused attention on small point mutations and other mechanisms underlying complex rearrangements.

METHODS: We selected 47 patients (41 families; 35 DMD, 6 BMD) without deletions and duplications in DMD gene (excluded by multiplex ligation-dependent probe amplification and multiplex polymerase chain reaction analysis). This cohort was investigated by systematic direct sequence analysis to study sequence variation. We focused our attention on rare mutational events which were further studied through transcript analysis.

RESULTS: We identified 40 different nucleotide alterations in DMD gene and their clinical correlates; altogether, 16 mutations were novel. DMD probands carried 9 microinsertions/microdeletions, 19 nonsense mutations, and 7 splice-site mutations. BMD patients carried 2 nonsense mutations, 2 splice-site mutations, 1 missense substitution, and 1 single base insertion. The most frequent stop codon was TGA (n=10 patients), followed by TAG (n=7) and TAA (n=4). We also analyzed the molecular mechanisms of five rare mutational events. They are two frame-shifting mutations in the DMD gene 3'end in BMD and three novel splicing defects: IVS42: c.6118-3C>A, which causes a leaky splice-site; c.9560A>G, which determines a cryptic splice-site activation and c.9564-426 T>G, which creates pseudoexon retention within IVS65.

CONCLUSION: The analysis of our patients' sample, carrying point mutations or complex rearrangements in DMD gene, contributes to the knowledge on phenotypic correlations in dystrophinopatic patients and can provide a better understanding of pre-mRNA maturation defects and dystrophin functional domains. These data can have a prognostic relevance and can be useful in

directing new therapeutic approaches, which rely on a precise definition of the genetic defects as well as their molecular consequences.

Malucelli Emil, Iotti Stefano, Manners David, Testa Claudia, Martinuzzi Andrea, Barbiroli Bruno, Lodi Raffaele (2011); THE ROLE OF PH ON THE THERMODYNAMICS AND KINETICS OF MUSCLE BIOCHEMISTRY: AN IN VIVO STUDY BY P-MRS IN PATIENTS WITH MYO-PHOSPHORYLASE DEFICIENCY; Biochimica et Biophysica Acta-Bioenergetics, 1807(9):1244-1249

Doi: 10.106/J.BBABIO.2011.06.013 **PMID: 21722623**

I.F. 2010: 5,132

In this study we assessed ΔG'(ATP) hydrolysis, cytosolic [ADP], and the rate of phosphocreatine recovery using Phosphorus Magnetic Resonance Spectroscopy in the calf muscle of a group of patients affected by glycogen myo-phosphorylase deficiency (McArdle disease). The goal was to ascertain whether and to what extent the deficit of the glycogenolytic pathway would affect the muscle energy balance. A typical feature of this pathology is the lack of intracellular acidosis. Therefore we posed the question of whether, in the absence of pH decrease, the rate of phosphocreatine recovery depends on the amount of phosphocreatine consumed during exercise. Results showed that at the end of exercise both [ADP] and ΔG'(ATP) of patients were significantly higher than those of matched control groups reaching comparable levels of phosphocreatine concentration. Furthermore, in these patients we found that the rate of phosphocreatine recovery is not influenced by the amount of phosphocreatine consumed during exercise. These outcomes provide experimental evidence that: i) the intracellular acidification occurring in exercising skeletal muscle is a protective factor for the energy consumption; and ii) the influence of pH on the phosphocreatine recovery rate is at least in part related to the kinetic mechanisms of mitochondrial creatine kinase enzyme.

Manna Ida, Gambardella Antonio, Bianchi Amedeo, Striano Pasquale, Tozzi Rossana, Aguglia Umberto, Beccaria Francesca, Benna Paolo, Campostrini Roberto, Canevini Maria Paola, Condino Francesca, Durisotti Christine, Elia Maurizio, Giallonardo Anna T., Iudice Alfonso, Labate Angelo, La Neve Angela, Michelucci Roberto, Muscas Gian C., Paravidino Roberta, Zaccara Gaetano, Zucca Claudio, Zara Federico, Perucca Emilio (2011); A FUNCTIONAL POLYMORPHISM IN THE SCNIA GENE DOES NOT INFLUENCE ANTIEPILEPTIC DRUG RESPONSIVENESS IN ITALIAN PATIENTS

WITH FOCAL EPILEPSY; Epilepsia, 52(5):E40-E44 – Brief Communication

Doi: 10.1111/j.1528-1167.2011.03097.x PMID: 21561445

I.F. 2010: 3,955

A splice site variation (c.603-91G>A or rs3812718) in the SCN1A gene has been claimed to influence efficacy and dose requirements of carbamazepine and phenytoin. We investigated the relationship between c.603-91G>A polymorphism and response to antiepileptic drugs (AEDs) in 482 patients with drug-resistant and 401 patients with drug-responsive focal epilepsy. Most commonly used AEDs were carbamazepine and oxcarbazepine. The distribution of c.603-91G>A genotypes was similar among drug-resistant and drug-responsive subjects, both in the entire population and in the groups treated with carbamazepine or oxcarbazepine. There was no association between the c.603-91G>A genotype and dosages of carbamazepine or oxcarbazepine. These findings rule out a major role of the SCN1A polymorphism as a determinant of AED response.

Manry Jérèmy, Laval Guillaume, Patin Etienne, Fornarino Simona, Itan Yuval, Fumagalli Matteo, Sironi Manuela, Tichit Magali, Bouchier Christiane, Casanova Jean-Laurent, Barreiro Luis B., Quintana-Murci Lluis (2011); EVOLUTIONARY GENETIC DISSECTION OF HUMAN INTERFERONS; Journal of Experimental Medicine (The), 208(13):2747-2759

Doi: 10.1084/jem.20111680 PMID: 22162829

I.F. 2010: 14,776

Interferons (IFNs) are cytokines that play a key role in innate and adaptive immune responses. Despite the large number of immunological studies of these molecules, the relative contributions of the numerous IFNs to human survival remain largely unknown. Here, we evaluated the extent to which natural selection has targeted the human IFNs and their receptors, to provide insight into the mechanisms that govern host defense in the natural setting. We found that some IFN-α subtypes, such as IFN-α6, IFN-α8, IFN-α13, and IFN-α14, as well as the type II IFN-γ, have evolved under strong purifying selection, attesting to their essential and nonredundant function in immunity to infection. Conversely, selective constraints have been relaxed for other type I IFNs, particularly for IFN-α10 and IFN-ε, which have accumulated missense or nonsense mutations at high frequencies within the population, suggesting redundancy in host defense. Finally, type III IFNs display geographically restricted signatures of positive selection in European and Asian populations,

indicating that genetic variation at these genes has conferred a selective advantage to the host, most likely by increasing resistance to viral infection. Our population genetic analyses show that IFNs differ widely in their biological relevance, and highlight evolutionarily important determinants of host immune responsiveness.

Marangi Giuseppe, Ricciardi Stefania, Orteschi Daniela, Lattante Serena, Murdolo Marina, Dallapiccola Bruno, Biscione Chiara, Lecce Rosetta, Chiurazzi Pietro, Romano Corrado, Greco Donatella, Pettinato Rosa, Sorge Giovanni, Pantaleoni Chiara, Alfei Enrico, Toldo Irene, Magnani Cinzia, Bonanni Paolo, Martinez Federica, Serra Gigliola, Battaglia Domenica, Lettori Donatella, Vasco Gessica, Baroncini Anna, Daolio Cecilia, Zollino Marcella (2011); THE PITT-HOPKINS SYNDROME: REPORT OF 16 NEW PATIENTS AND CLINICAL DIAGNOSTIC CRITERIA; American Journal of Medical Genetics Part A, 155(7):1536-1545

Doi: 10.1002/ajmg.a.34070 **PMID: 21671391**

I.F. 2010: 2,505

Pitt-Hopkins syndrome (PTHS) is characterized by severe intellectual disability, typical facial gestalt and additional features, such as breathing anomalies. Following the discovery of the causative haploinsufficiency of transcription factor 4 (TCF4), about 60 patients have been reported. We looked for TCF4 mutations in 63 patients with a suspected PTHS. Haploinsufficiency of TCF4 was identified in 14 patients, as a consequence of large 18q21.2 chromosome deletions involving TCF4 (2 patients), gene mutations (11 patients) and a t(14q;18q) balanced translocation disrupting TCF4 (one patient). By evaluating the clinical features of these patients, along with literature data, we noticed that, in addition to the typical facial gestalt, the PTHS phenotype results from the various combinations of the following characteristics: intellectual disability with severe speech impairment, normal growth parameters at birth, postnatal microcephaly, breathing anomalies, motor incoordination, ocular anomalies, constipation, seizures, typical behavior and subtle brain abnormalities. Although PTHS is currently considered to be involved in differential diagnosis with Angelman and Rett syndromes, we found that combining the facial characteristics with a detailed analysis of both the physical and the neurological phenotype, made molecular testing for PTHS the first choice. Based on striking clinical criteria, a diagnosis of PTHS was made clinically in two patients who had normal TCF4. This report deals with the first series of PTHS patients of Italian origin.

Marcon Gabriella, Rossi Giacomina, Giaccone Giorgio, Giovagnoli Anna Rita, Piccoli Elena, Zanini Sergio, Geatti Onelio, Toso Vito, Grisoli Marina, Tagliavini Fabrizio (2011); VARIABILITY OF THE CLINICAL PHENOTYPE IN AN ITALIAN FAMILY WITH DEMENTIA ASSOCIATED WITH AN INTRONIC DELETION IN THE GRN GENE; Journal of Alzheimer's Disease, 26(3):583-590

Doi: 10.3233/JAD-2011-110332 PMID: 21677378

I.F. 2010: 4,261

Mutations in the progranulin gene (GRN) were recently identified as an important cause of familial frontotemporal dementia (FTD). More than 60 pathogenic mutations have been reported up to now and prominent phenotypic variability within and among affected kindreds has been described. We have studied an Italian family with clinical evidence of dementia, and here we report detailed clinical records, imaging, sequential neurological examinations, cognitive assessments, and genetic analysis of three affected members of the same generation. Genetic analysis revealed the presence of the null mutation IVS6 + 5_8delGTGA in GRN, leading to haploinsufficiency, as documented by mRNA analysis. The mutation is associated with wide variation of the clinical phenotype, ranging from FTD to Alzheimer's disease and to a rapidly-progressive dementia. In summary, the patients of this kindred showed highly variable clinical features that do not have a close correspondence with the pattern of the cerebral atrophy. Our data extend the phenotypic spectrum and the complexity of neurodegenerative diseases linked to GRN mutations.

Marini Andrea, Galetto Valentina, Zampieri Elisa, Vorano Lorenza, Zettin Marina, Carlomagno Sergio (2011); NARRATIVE LANGUAGE IN TRAUMATIC BRAIN INJURY; Neuropsychologia, 49(10):2904-2910

Doi: 10.1016/j.neuropsychologia.2011.06.017 PMID: 21723304

I.F. 2010: 3,949

Persons with traumatic brain injury (TBI) often show impaired linguistic and/or narrative abilities. The present study aimed to document the features of narrative discourse impairment in a group of adults with TBI. 14 severe TBI non-aphasic speakers (GCS<8) in the phase of neurological stability and 14 neurologically intact participants were recruited for the experiment. Their cognitive, linguistic and narrative skills were thoroughly assessed. The group of non-aphasic individuals with TBI had normal lexical and grammatical skills. However, they produced narratives with increased errors of cohesion and coherence due to the frequent interruption of ongoing utterances, derailments

and extraneous utterances that made their discourse vague and ambiguous. They produced a normal amount of thematic units (i.e. concepts) in their narratives. However, this information was not correctly organized at micro- and macrolinguistic levels of processing. A Principal Component Analysis showed that a single factor accounted for the production of global coherence errors, and the reduction of both propositional density at the utterance level and proportion of words that conveyed information. It is hypothesized that the linguistic deficits observed in the participants with TBI may reflect a deficit at the interface between cognitive and linguistic processing rather than a specific linguistic disturbance.

Marini Andrea, Andreetta Sara, Del Tin Silvana, Carlomagno Sergio (2011); A MULTI-LEVEL APPROACH TO THE ANALYSIS OF NARRATIVE LANGUAGE IN APHASIA; Aphasiology, 25(11):1372-1392

Doi: 10.1080/02687038.2011.584690

I.F. 2010: 0,974

Background: Several studies have shown that traditional standardised aphasia tests may not be sensitive enough to adequately assess linguistic deficits and recovery patterns in persons with aphasia. As a result, both functional and structural methods for the analysis of connected language samples from people with aphasia have been devised (see Armstrong, 2000; Prins & Bastiaanse, 2004).

Aims: The present article focuses on our attempt to provide a comprehensive, multi-level procedure for both structural and functional analysis of narrative discourse produced by speakers with brain damage. Accordingly, we will describe a method for analysis of connected language samples elicited on single picture and cartoon story description tasks. This method has proven sensitive in the assessment of language deficits in many neurogenic populations.

Methods & Procedures: A comprehensive description of the language production system, a thorough discussion of the different approaches to discourse analysis in persons with aphasia, and the procedure for the analysis of narrative discourse are detailed. The characteristics of the eliciting stimuli, the procedures for their administration and the transcription of the language samples are carefully explained. The analysis focuses on four main aspects of linguistic processing: productivity, lexical and grammatical processing, narrative organisation, and informativeness. To further illustrate the analytic procedure, two case reports and an appendix with the analysis of a narrative sample are provided.

Outcomes & Results: We will provide direct evidence of the usefulness of the multi-level procedure for discourse analysis for assessing changes in discourse performance of two persons with fluent aphasia, with different aetiologies, that were not captured by traditional standardised aphasia tests. Conclusions: The method of analysis presented in this paper has strong grounds in linguistic and psychological theories of linguistic structure and functioning. It also has the advantage of being both quantitative and functional as it captures selective aspects of linguistic processing, and can provide relevant information about the person's communicative and informative skills.

Marino Cecilia, Mascheretti Sara, Riva Valentina, Cattaneo Francesca, Rigoletto Catia, Rusconi Marianna, Gruen Jeffrey R., Giorda Roberto, Lazazzera Claudio, Molteni Massimo (2011); PLEIOROPIC EFFECTS OF DCDC2 AND DYX1C1 GENES ON LANGUAGE AND MATHEMATICS TRAITS IN NUCLEAR FAMILIES OF DEVELOPMENTAL DYSLEXIA; Behavior Genetics, 41(1):67-76

Doi: 10.1007/S10519-010-9412-7 PMID: 21046216

I.F. 2010: 3,000

Converging evidence indicates that developmental problems in oral language and mathematics can predate or co-occur with developmental dyslexia (DD). Substantial genetic correlations have been found between language, mathematics and reading traits, independent of the method of sampling. We tested for association of variants of two DD susceptibility genes, DCDC2 and DYX1C1, in nuclear families ascertained through a proband with DD using concurrent measurements of language and mathematics in both probands and siblings by the Quantitative Transmission Disequilibrium Test. Evidence for significant associations was found between DCDC2 and 'Numerical Facts' (p value = 0.02, with 85 informative families, genetic effect = 0.57) and between 'Mental Calculation' and DYX1C1 markers -3GA (p value = 0.05, with 40 informative families, genetic effect = -0.67) and 1249GT (p value = 0.02, with 49 informative families, genetic effect = -0.65). No statistically significant associations were found between DCDC2 or DYX1C1 and language phenotypes. Both DCDC2 and DYX1C1 DD susceptibility genes appear to have a pleiotropic role on mathematics but not language phenotypes.

Massimino Maura, Giangaspero Felice, Garré Maria Luisa, Gandola Lorenza, Poggi Geraldina, Biassoni Veronica, Gatta Gemma, Rutkowski Stefan (2011); CHILDHOOD MEDULLOBLASTOMA; Critical Reviews in Oncology/Hematology, 79(1):65-83

Doi: 10.106/j.critrevonc.2010.07.010 **PMID: 21129995**

I.F. 2010: 4,689

Among all the childhood central nervous system tumours, medulloblastoma and other neuroectodermal tumours account for 16–25% of cases. The causative factors of medulloblastoma/PNET have not been well established. It is more frequent in boys than in girl and in children than in adults. There was a significant improvement of survival for children diagnosed in 2000–2002 compared to those diagnosed in 1995–1999. The risk of dying was reduced by 30%. Patients are generally divided into risk-stratified schemes on the basis of age, the extent of residual disease, and dissemination. Sixty to 70% of patients older than 3 years are assigned to the average-risk group. High-risk patients include those in the disseminated category, and in North American trials those that have less than a gross or near-total resection, which is arbitrarily defined as 1.5 cm2 of post-operative residual disease. Current and currently planned clinical trials will:
(1) evaluate the feasibility of reducing both the dose of craniospinal irradiation and the volume of the posterior fossa radiotherapy boost by the modest intensification of chemotherapy in standard-risk patients;
(2) determine whether intensification of chemotherapy or irradiation can improve outcome in patients with high-risk disease;
define molecular and biological markers that improve outcome prediction in patients with medulloblastoma and which can be incorporated for front-line stratification of newly defined risk subgroups.

Maziade Michel, Rouleau Nancie, Merette Chantal, Cellard Caroline, Battaglia Marco, Marino Cecilia, Jomphe Valerie, Gilbert Elsa, Achim Amelie, Bouchard Roch-Hugo, Paccalet Thomas, Paradis Marie-Eve, Roy Marc-Andrè (2011); VERBAL AND VISUAL MEMORY IMPAIRMENTS AMONGST YOUNG OFFSPRING AND HEALTHY ADULT RELATIVES OF PATIENTS WITH SCHIZOPHRENIA AND BIPOLAR-DISORDER: SELECTIVE GENERATIONAL PATTERNS INDICATE DIFFERENT DEVELOPMENTAL TRAJECTORIES; Schizophrenia Bulletin, 37(6):1218-1228

Doi: 10.1093/schbul/sbq026 **PMID: 20410238**

I.F. 2010: 8,273

OBJECTIVE: Memory deficits have been shown in patients affected by schizophrenia (SZ) and bipolar (BP)/mood disorder. We recently reported that young high-risk offspring of an affected parent were impaired in both verbal episodic memory (VEM) and visual episodic memory (VisEM). Understanding better the trajectory of memory impairments from childhood to adult clinical

status in risk populations is crucial for early detection and prevention. In multigenerational families densely affected by SZ or BP, our aim was to compare the memory impairments observed in young nonaffected offspring with memory functioning in nonaffected adult relatives and patients.
METHODS: For 20 years, we followed up numerous kindreds in the Eastern Québec population. After having characterized the Diagnostic and Statistical Manual of Mental Disorders phenotypes, we assessed cognition (N = 381) in 3 subsamples in these kindreds and in controls: 60 young offspring of a parent affected by SZ or BP, and in the adult generations, 92 nonaffected adult relatives and 40 patients affected by SZ or BP. VEM was assessed with the California Verbal Learning Test and VisEM with the Rey figures. RESULTS: The VEM deficits observed in the offspring were also found in adult relatives and patients. In contrast, the VisEM impairments observed in the young offspring were present only in patients, not in the adult relatives.
CONCLUSION: Implications for prevention and genetic mechanisms can be drawn from the observation that VEM and VisEM would show distinct generational trajectories and that the trajectory associated with VisEM may offer a better potential than VEM to predict future risk of developing the disease.

Maziade Michel, Rouleau Nancie, Cellard Caroline, Battaglia Marco, Paccalet Thomas, Moreau Isabel, Gagnon Valerie, Gingras Nathalie, Marino Cecilia, Gilbert Elsa, Roy Marc-André (2011); YOUNG OFFSPRING AT GENETIC RISK OF ADULT PSYCHOSES: THE FORM OF THE TRAJECTORY OF IQ OR MEMORY MAY ORIENT TO THE RIGHT DYSFUNCTION AT THE RIGHT TIME; Plos One, 6(4):E19153

Doi: 10.1371/journal.pone.0019153 **PMID: 21559460**

I.F. 2010: 4,411

OBJECTIVE: Neurocognitive dysfunctions analogous to those of adult patients have been detected in children at risk of schizophrenia and bipolar disorder. This led to the following developmental question: Do IQ and memory impairments exhibit different developmental courses from childhood to young adulthood in terms of stability or fluctuations?
METHODS: In a high risk sample, we used a step by step sampling approach to narrow-down the early disease mechanisms. Upstream, we started with a 20-year follow-up of 48 densely affected multigenerational kindreds, including 1500 clinically characterized adult members. We then identified 400 adult members affected by a DSM-IV schizophrenia or bipolar disorder. Downstream, we finally focused on 65 offspring (of an affected parent) aged 7 to 22, who were administered a neuropsychological battery. We then

constructed cross-sectional trajectories that were compared to those of controls.
RESULTS: The childhood IQ deficit displayed a stability until young adulthood. The delay in visual memory exhibited a non-linear two-stage trajectory: a lagging period during childhood followed by a recuperation period from adolescence until adulthood, as supported by a significant Group x Age Periods interaction. No data suggested deterioration between 7 and 22.
CONCLUSION: In these offspring at genetic risk, the developmental trajectory of global IQ impairment may not apply to specific domains of cognition such as episodic memory. Different cognitive dysfunctions would mark different developmental courses. The shape of the trajectories might itself have a meaning and provide empirical leads for targeting the right dysfunction at the right time in future prevention research.

Mengotti Paola, D'Agostini Serena, Terlevic Robert, De Colle Cristina, Biasizzo Elsa, Londero Danielle, Ferro Adele, Rambaldelli Gianluca, Balestrieri Matteo, Zanini Sergio, Fabbro Franco, Molteni Massimo, Brambilla Paolo (2011); ALTERED WHITE MATTER INTEGRITY AND DEVELOPMENT IN CHILDREN WITH AUTISM: A COMBINED VOXEL-BASED MORPHOMETRY AND DIFFUSION IMAGING STUDY; Brain Research Bulletin, 84(2):189-195

Doi: 10.1016/j.brainresbull.2010.12.002 PMID: 21146593

I.F. 2010: 2,498

BACKGROUND: A combined protocol of voxel-based morphometry (VBM) and diffusion-weighted imaging (DWI) was applied to investigate the neurodevelopment of gray and white matter in autism.
METHODS: Twenty children with autism (mean age= 7 ± 2.75 years old; age range: 4-14; 2 girls) and 22 matched normally developing children (mean age = 7.68 ± 2.03 years old; age range: 4-11; 2 girls) underwent magnetic resonance imaging (MRI). VBM was employed by applying the Template-o-Matic toolbox (TOM), a new approach which constructs the age-matched customized template for tissue segmentation. Also, the apparent diffusion coefficients (ADC) of water molecules were obtained from the analysis of DWI. Regions of interests (ROIs), standardized at 5 pixels, were placed in cortical lobes and corpus callosum on the non-diffusion weighted echo-planar images (b = 0) and were then automatically transferred to the corresponding maps to obtain the ADC values.
RESULTS: Compared to normal children, individuals with autism had significantly: (1) increased white matter volumes in the right inferior frontal gyrus, the right fusiform gyrus, the left precentral and supplementary

motor area and the left hippocampus, (2) increased gray matter volumes in the inferior temporal gyri bilaterally, the right inferior parietal cortex, the right superior occipital lobe and the left superior parietal lobule, and (3) decreased gray matter volumes in the right inferior frontal gyrus and the left supplementary motor area. Abnormally increased ADC values in the bilateral frontal cortex and in the left side of the genu of the corpus callosum were also reported in autism. Finally, age correlated negatively with lobar and callosal ADC measurements in individuals with autism, but not in children with normal development.
CONCLUSIONS: These findings suggest cerebral dysconnectivity in the early phases of autism coupled with an altered white matter maturation trajectory during childhood potentially taking place in the frontal and parietal lobes, which may represent a neurodevelopmental marker of the disorder, possibly accounting for the cognitive and social deficits.

Michieletto Paola, Bonanni Paolo, Pensiero Stefano (2011); OPHTHALMIC FINDINGS IN ANGELMAN SYNDROME; Journal of AAPOS, 15(2):158-161

Doi: 10.1016/j.jaapos.2010.12.013 PMID: 21596294

I.F. 2010: 1,062

PURPOSE: To provide detailed information about opthalmological findings in a group of patients with Angelman syndrome (AS).
METHODS: Consecutive patients with a genetically confirmed diagnosis of AS were submitted to ophthalmic and orthoptic examinations. Strabismus, visual acuity, cycloplegic refraction, and iris and fundus pigmentation were evaluated. Parents were also examined to compare the extent of fundus pigmentation.
RESULTS: A total of 34 patients were identified, representing 3 genetic classes: deletion, uniparental disomy, and mutation. Ametropia >1 D was present in 97% of cases: myopia in 9%, hyperopia in 76%, and astigmatism in 94%. Myopia and anisometropia were found only in the genetic deletion group. Strabismus, most frequently exotropia, was found in 24 patients (75%). Ocular hypopigmentation was observed in 18 subjects (53%), with choroidal involvement in 3 cases and isolated iris involvement in 4. Hypopigmentation was observed in all of the 3 genetic classes.
CONCLUSIONS: Ophthalmic alterations in AS were observed more frequently than has been previously reported, except for ocular hypopigmentation, which was observed less frequently.

Molteni Massimo, Clementi Emilio, Zuccotti Gian Vincenzo (2011);

INTRODUCTION TO THE NEW "PERSPECTIVES IN PAEDIATRIC PHARMACOLOGY" SERIES; Pharmacological Research, 63(5):361

Doi: 10.1016/j.phrs.2011.01.008 **PMID: 21256963**

I.F. 2010: 3,612

Abstract non disponibile

Montirosso Rosario, Cozzi Patrizia, Putnam Samuel P., Gartstein Maria A., Borgatti Renato (2011); STUDYING CROSS-CULTURAL DIFFERENCES IN TEMPERAMENT IN THE FIRST YEAR OF LIFE: UNITED STATES OF AMERICA (US) AND ITALY; International Journal of Behavioral Development, 35(1):27-37

Doi: 10.1177/0165025410368944

I.F. 2010: 1,304

An Italian translation of the Infant Behavior Questionnaire-Revised (IBQ-R) was developed and evaluated with 110 infants, demonstrating satisfactory internal consistency, discriminant validity, and construct validity in the form of gender and age differences, as well as factorial integrity. Cross-cultural differences were subsequently evaluated for matched samples of Italian and United States (US) (N ¼ 110) 3–12-month-olds. Across infancy, parents of US infants reported higher levels of activity, high and low intensity pleasure, and vocal reactivity, whereas Italian infants, particularly males, were rated higher on cuddliness. In early infancy only, US infants were viewed a higher on high intensity pleasure and perceptual sensitivity.

Moss Tyler J., Daga Andrea, McNew James A. (2011); FUSING A LASTING RELATIONSHIP BETWEEN ER TUBULES; Trends in Cell Biology, Review 21(7):416-423

Doi: 10.1016/j.tbc.2011.03.009 **PMID: 21550242**

I.F. 2010: 12,140

Atlastin is an integral membrane GTPase localized to the endoplasmic reticulum (ER). In vitro and in vivo analyses indicate that atlastin is a membrane fusogen capable of driving membrane fusion, suggesting a role in ER structure and maintenance. Interestingly, mutations in the human atlastin-1 gene, SPG3A, cause a form of autosomal dominant hereditary spastic paraplegia (HSP). The etiology of HSP is unclear, but two predominant forms of the disorder are caused by mutant proteins that affect ER structure, formation and maintenance in motor neurons. In this review, we describe the current knowledge about the molecular mechanism of atlastin function and its potential role in HSP. Greater understanding of the function of atlastin

and associated proteins should provide important insight into normal ER biogenesis and maintenance, as well as the pathology of disease.

Moss Tyler J., Andreazza Camilla, Verma Avani, Daga Andrea, McNew James A. (2011); MEMBRANE FUSION BY THE GPTASE ATLASTIN REQUIRES A CONSERVED C-TERMINAL CYTOPLASMIC TAIL AND DIMERIZATION THROUGH THE MIDDLE DOMAIN; Proceedings of the National Academy of Sciences of the United States of America (PNAS), 108(27):11133-11138

Doi: 10.1073/pnas.110556108/-/DCSupplemental PMID: 21690399

I.F. 2010: 9,771

The biogenesis and maintenance of the endoplasmic reticulum (ER) requires membrane fusion. ER homotypic fusion is driven by the large GTPase atlastin. Domain analysis of atlastin shows that a conserved region of the C-terminal cytoplasmic tail is absolutely required for fusion activity. Atlastin in adjacent membranes must associate to bring the ER membranes into molecular contact. Drosophila atlastin dimerizes in the presence of GTPγS but is monomeric with GDP or without nucleotide. Oligomerization requires the juxtamembrane middle domain three-helix bundle, as does efficient GTPase activity. A soluble version of the N-terminal cytoplasmic domain that contains the GTPase domain and the middle domain three-helix bundle serves as a potent, concentration-dependent inhibitor of membrane fusion both in vitro and in vivo. However, atlastin domains lacking the middle domain are without effect. GTP-dependent dimerization of atlastin generates an enzymatically active protein that drives membrane fusion after nucleotide hydrolysis and conformational reorganization.

Musumeci Olimpia, Bassi Maria Teresa, Mazzeo Anna, Grandis Marina, Crimella Claudia, Martinuzzi Andrea, Toscano Antonio (2011); A NOVEL MUTATION IN KIF5A GENE CAUSING HEREDITARY SPASTIC PARAPLEGIA WITH AXONAL NEUROPATHY; Neurological Sciences, 32(4):665-668

Doi: 10.1007/s10072-010-0445-8 PMID: 21107874

I.F. 2010: 1,220

Hereditary spastic paraplegias (HSPs) include a group of neurodegenerative diseases, and so far 46 SPG loci have been mapped and 17 genes isolated. Among the autosomal dominant HSPs (AD-HSPs), SPG10 is a rare form due to mutations in KIF5A gene (locus 12q13.3). We describe the clinical, neurophysiological, morphological and genetic study of an Italian family with

AD-HSP. The proband presented with an adult onset spastic paraparesis and diffuse paresthesias where neurophysiological and nerve biopsy morphological studies revealed an axonal neuropathy. Molecular genetic analysis identified a new missense mutation (c.608C>G) of KIF5A gene resulting in a serine to cysteine substitution, S203C, located in a highly conserved domain of the protein. This pedigree confirms the occurrence of an axonal peripheral neuropathy in SPG10.

Najt Pablo, Fusar-Poly Paolo, Brambilla Paolo (2011); CO-OCCURRING MENTAL AND SUBSTANCE ABUSE DISORDERS: A REVIEW ON THE POTENTIAL PREDICTORS AND CLINICAL OUTCOMES; Psychiatry Research, 186(2-3):159-164

Doi: 10.1016/j.psychres.2010.07.042 PMID: 20728943

I.F. 2010: 2,803

This article reviews the literature on co-occurring mental disorders and substance use disorders. The co-occurrence of mental disorders with substance use disorders presents a major challenge to those who provide psychiatric services. Despite the clinical and social burdens caused by this complex problem, research in this area is still insufficient. We found 18 studies showing potential predictors of co-occurring disorders (COD). Poor outcomes have been associated with: (i) COD compared to single disorders and (ii) COD with prior mental disorder compared to COD with prior substance use disorders. Poorer outcomes were reported for substance use disorder patients with comorbid major depressive disorder, and patients with substance use disorder and post-traumatic stress disorder. Furthermore, more negative outcomes were related to COD patients with temporally prior onset of mood disorders. Comorbidity between major depressive disorder or post-traumatic stress disorder and substance use disorder is suggested in the literature as a potential predictor of COD problems.

Nizzardo Monica, Nardini Martina, Ronchi Dario, Salani Sabrina, Donadoni Chiara, Fortunato Francesco, Colciago Giorgia, Falcone Marianna, Simone Chiara, Riboldi Giulietta, Govoni Alessandra, Bresolin Nereo, Comi Giacomo Pietro, Corti Stefania (2011); BETA-LACTAM ANTIBIOTIC OFFERS NEUROPROTECTION IN A SPINAL MUSCULAR ATROPHY MODEL BY MULTIPLE MECHANISMS; Experimental Neurology, 229(2):214-225

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.expneurol.2011.01.017 PMID: 21295027

I.F. 2010: 4,436

Spinal muscular atrophy (SMA) is a devastating genetic motoneuron disease leading to infant death. No effective therapy is currently available. It has been suggested that β-lactam antibiotics such as ceftriaxone may offer neuroprotection in motoneuron diseases. Here, we investigate the therapeutic effect of ceftriaxone in a murine model of SMA. Treated animals present a modest, but significant ameliorated neuromuscular phenotype and increased survival, which correlate with protection of neuromuscular units. Whole gene expression profiling in treated mice demonstrates modifications in several genes including those involved in RNA metabolism toward wild-type. The neuroprotective effect seems to be mediated by multiple mechanisms that encompass the increase of the glutamate transporter Glt1, the transcription factor Nrf2, as well as SMN protein. This study provides the first evidence of a potential positive effect of this class of molecules in SMA. Further investigation of analogs with increased and more specific therapeutic effects warrants the development of useful therapies for SMA.

Nobile Maria, Perego Paolo, Piccinini Luigi, Mani Elisa, Rossi Agnese, Bellina Monica, Molteni Massimo (2011); FURTHER EVIDENCE OF COMPLEX MOTOR DYSFUNCTION IN DRUG NAIVE CHILDREN WITH AUTISM USING AUTOMATIC MOTION ANALYSIS OF GAIT; Autism, 15(3):263-283

Doi: 10.1007/s00702-010-0548-7 PMID: 21203783

I.F. 2010: 2,606

In order to increase the knowledge of locomotor disturbances in children with autism, and of the mechanism underlying them, the objective of this exploratory study was to reliably and quantitatively evaluate linear gait parameters (spatio-temporal and kinematic parameters), upper body kinematic parameters, walk orientation and smoothness using an automatic motion analyser (ELITE systems) in drug naïve children with Autistic Disorder (AD) and healthy controls. The children with AD showed a stiffer gait in which the usual fluidity of walking was lost, trunk postural abnormalities, highly significant difficulties to maintain a straight line and a marked loss of smoothness (increase of jerk index), compared to the healthy controls. As a whole, these data suggest a complex motor dysfunction involving both the cortical and the subcortical area or, maybe, a possible deficit in the integration of sensory-motor information within motor networks (i.e., anomalous connections within the fronto-cerebello-thalamo-frontal network). Although the underlying neural structures involved remain to be better defined, these data may contribute to highlighting the central role of motor impairment in

autism and suggest the usefulness of taking into account motor difficulties when developing new diagnostic and rehabilitation programs.

Paglialonga Alessia, Barozzi Stefania, Brambilla Daniele, Soi Daniela, Cesarani Antonio, Gagliardi Chiara, Comiotto Elisabetta, Spreafico Emanuela, Tognola Gabriella (2011); COCHLEAR ACTIVE MECHANISMS IN YOUNG NORMAL-HEARING SUBJECTS AFFECTED BY WILLIAMS SYNDROME: TIME-FREQUENCY ANALYSIS OF OTOACOUSTIC EMISSIONS; Hearing Research, 272(1-2):157-167

Doi: 10.1016/j.heares.2010.10.004 **PMID: 20969939**

I.F. 2010: 2,428

The aim of this study was to investigate the functionality of cochlear active mechanisms in normal-hearing subjects affected by Williams syndrome (WS). Transient evoked otoacoustic emissions (TEOAEs) were recorded in a group of young WS subjects and a group of typically developing control subjects, all having normal-hearing thresholds and normal middle-ear functionality. We also analysed the narrow-band frequency components of TEOAEs, extracted from the broad-band TEOAE recordings by using a time-frequency analysis algorithm based on the Wavelet transform. We observed that TEOAEs and the frequency components extracted from TEOAEs measured in WS subjects had significantly lower energy compared to the controls. Also, the narrow-band frequency components of TEOAEs measured in WS subjects had slightly increased latency compared to the controls. Overall, results would suggest a subtle (i.e., sub-clinical) dysfunction of the cochlear active mechanisms in WS subjects with otherwise normal hearing. Also, results point out the relevance of using otoacoustic emissions in the audiological evaluation and monitoring of WS subjects to early identify possible subtle auditory dysfunctions, before the onset of mild or moderate hearing loss that could exacerbate language or cognitive impairments associated with WS.

Pagnamenta Alistair T., Khan Hameed, Walker Susan, Gerrelli Dianne, Wing Kirsty, Bonaglia Maria Clara, Giorda Roberto, Berney Tom, Mani Elisa, Molteni Massimo, Pinto Dalila, Le Couteur Ann, Hallmayer Joachim, Sutcliffe James S., Szatmari Peter, Paterson Andrew D., Scherer Stephen W., Vieland Veronica J., Monaco Anthony P. (2011); RARE FAMILIAL 16Q21 MICRODELETIONS UNDER A LINKAGE PEAK IMPLICATE CADHERIN 8 (CDH8) IN SUSCEPTIBILITY TO AUTISM AND LEARNING DISABILITY; Journal of Medical Genetics, 48(1):48-54

Doi: 10.1136/jmg.2010.079426 **PMID: 20972252**

I.F. 2010: 7,037

BACKGROUND: Autism spectrum disorder (ASD) is characterised by impairments in social communication and by a pattern of repetitive behaviours, with learning disability (LD) typically seen in up to 70% of cases. A recent study using the PPL statistical framework identified a novel region of genetic linkage on chromosome 16q21 that is limited to ASD families with LD.
METHODS: In this study, two families with autism and/or LD are described which harbour rare >1.6 Mb microdeletions located within this linkage region. The deletion breakpoints are mapped at base-pair resolution and segregation analysis is performed using a combination of 1M single nucleotide polymorphism (SNP) technology, array comparative genomic hybridisation (CGH), long-range PCR, and Sanger sequencing. The frequency of similar genomic variants in control subjects is determined through analysis of published SNP array data. Expression of CDH8, the only gene disrupted by these microdeletions, is assessed using reverse transcriptase PCR and in situ hybridisation analysis of 9 week human embryos.
RESULTS: The deletion of chr16: 60 025 584-61 667 839 was transmitted to three of three boys with autism and LD and none of four unaffected siblings, from their unaffected mother. In a second family, an overlapping deletion of chr16: 58 724 527-60 547 472 was transmitted to an individual with severe LD from his father with moderate LD. No copy number variations (CNVs) disrupting CDH8 were observed in 5023 controls. Expression analysis indicates that the two CDH8 isoforms are present in the developing human cortex.
CONCLUSION: Rare familial 16q21 microdeletions and expression analysis implicate CDH8 in susceptibility to autism and LD.

Pastore Valentina, Colombo Katia, Liscio Mariarosaria, Galbiati Susanna, Adduci Annarita, Villa Federica, Strazzer Sandra (2011); EFFICACY OF COGNITIVE BEHAVIOURAL THERAPY FOR CHILDREN AND ADOLESCENTS WITH TRAUMATIC BRAIN INJURY; Disability and Rehabilitation, 33(8):675-683

Doi: 10.3109/09638288.2010.506239 **PMID: 20695794**

I.F. 2010: 1,489

PURPOSE: Behavioural and psychological disorders after traumatic brain injury (TBI) are very common. The purposes of this study were to estimate the frequency of these problems in our sample, to evaluate the effectiveness of cognitive behavioural therapy (CBT) and to assess the predictive value of important clinical variables for the treatment outcome.

METHOD: Forty patients aged 4-18 years were included in this study. Twenty-eight patients received CBT at our Institute (clinical group), while 12 patients did not receive any treatment at all (control group). The CBCL/4-18 and the VABS were administered to parents at the beginning of the study and after 12 months.
RESULTS: A high frequency of psychological and behavioural problems was found in both groups of patients. After CBT, the clinical group showed a significant advantage on several CBCL scales and a greater increase in adaptive behaviour on the VABS Socialisation domain. The Glasgow Coma Scale score, days of unconsciousness and age at injury were not predictors of the severity of psychological problems at the follow-up for the patients of the clinical group.
CONCLUSIONS: Our results suggest that CBT is an effective intervention for young patients with psychological problems after TBI.

Pendin Diana, McNew James A., Daga Andrea (2011); BALANCING ER DYNAMICS: SHAPING, BENDING, SEVERING, AND MENDING MEMBRANES; Current Opinion in Cell Biology, 23(4):435-442

Doi: 10.1016/j.ceb.2011.04.007 PMID: 21641197

I.F. 2010: 13,540

The endoplasmic reticulum is a multifunctional organelle composed of functionally and morphologically distinct domains. These include the relatively planar nuclear envelope and the peripheral ER, a network of sheet-like cisternae interconnected with tubules that spread throughout the cytoplasm. The ER is highly dynamic and the shape of its domains as well as their relative content are in constant flux. The multiple forces driving these morphological changes depend on the interaction between the ER and microtubules, membrane fusion and fission events and the action of proteins capable of actively shaping membranes. The interplay between these forces is ultimately responsible for the dynamic morphology of the ER, which in turn is crucial for properly executing the varied functions of this organelle.

Pendin Diana*, Tosetto Jessica*, Moss Tyler J., Andreazza Camilla, Moro Stefano, McNew James A., Daga Andrea (2011); GTP-DEPENDENT PACKING OF A THREE-HELIX BUNDLE IS REQUIRED FOR ATLASTIN-MEDIATED FUSION; Proceedings of the National Academy of Sciences of the United States of America (PNAS), 108(39):16283-16288

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1073/pnas.1106421108/-/CDSupplemental PMID: 21930898

I.F. 2010: 9,771

The mechanisms governing atlastin-mediated membrane fusion are unknown. Here we demonstrate that a three-helix bundle (3HB) within the middle domain is required for oligomerization. Mutation of core hydrophobic residues within these helices inactivates atlastin function by preventing membrane tethering and the subsequent fusion. GTP binding induces a conformational change that reorients the GTPase domain relative to the 3HB to permit self-association, but the ability to hydrolyze GTP is required for full fusion, indicating that nucleotide binding and hydrolysis play distinct roles. Oligomerization of atlastin stimulates its ability to hydrolyze GTP, and the energy released drives lipid bilayer merger. Mutations that prevent atlastin self-association also abolish oligomerization-dependent stimulation of GTPase activity. Furthermore, increasing the distance of atlastin complex formation from the membrane inhibits fusion, suggesting that this distance is crucial for atlastin to promote fusion.

Pensiero Stefano, Cecchini Paolo, Michieletto Paola, Pelizzo Gloria, Madonia Maurizio, Parentin Fulvio (2011); CONGENITAL APLASIA OF THE OPTIC CHIASM AND ESOPHAGEAL ATRESIA: A CASE REPORT; Journal of Medical Case Reports, 5(1):335

Doi: 10.1186/1752-1947-5-335 PMID: 21806818

I.F. 2010: 0,000

INTRODUCTION: The complete absence of the chiasm (chiasmal aplasia) is a rare clinical condition. Hypoplasia of the optic nerve and congenital nystagmus are almost invariably associated characteristics. Microphthalmos or anophthalmos are common features in chiasmal aplasia, while central nervous system abnormalities are less frequent. Esophageal atresia can be isolated or syndromic. In syndromic cases, it is frequently associated with cardiac, limb, renal or vertebral malformations and anal atresia. More rarely, esophageal atresia can be part of anophthalmia-esophageal-genital syndrome, which comprises anophthalmia or microphthalmia, genital abnormalities, vertebral defects and cerebral malformations. Here, a previously unreported case of chiasmal aplasia presenting without microphthalmos and associated with esophageal atresia is described.

CASE PRESENTATION: Aplasia of the optic chiasm was identified in a Caucasian Italian 8-month-old boy with esophageal atresia. An ultrasound examination carried out at 21 weeks' gestation revealed polyhydramnios. Intrauterine growth retardation, esophageal atresia and a small atrial-septal defect were subsequently detected at 28 weeks' gestation. Repair of the esophageal atresia was carried out shortly after birth. A jejunostomy

was carried out at four months to facilitate enteral feeding. The child was subsequently noted to be visually inattentive and to be neurodevelopmentally delayed. Magnetic resonance imaging revealed chiasmal aplasia. No other midline brain defects were found. His karyotype was normal.
CONCLUSION: If achiasmia is a spectrum, our patient seems to depict the most severe form, since he appears to have an extremely severe visual impairment. This is in contrast to most of the cases described in the literature, where patients maintain good--or at least useful-- visual function. To the best of our knowledge, the association of optic nerve hypoplasia, complete chiasmal aplasia, esophageal atresia and atrial-septal defect, choanal atresia, hypertelorism and psychomotor retardation has never been described before.

Perego Paolo, Turconi Anna Carla, Andreoni Giuseppe, Maggi Luca, Beretta Elena, Parini Sergio, Gagliardi Chiara (2011); COGNITIVE ABILITY ASSESSMENT BY BRAIN-COMPUTER INTERFACE VALIDATION OF A NEW ASSESSMENT METHOD FOR COGNITIVE ABILITIES; Journal of Neuroscience Methods, 201(1):239-250

Doi: 10.1016/j.jneumeth.2011.06.025 PMID: 21816172

I.F. 2010: 2,1

Brain-Computer Interfaces (BCIs) are systems which can provide communication and environmental control to people with severe neuromuscular diseases. The current study proposes a new BCI-based method for psychometric assessment when traditional or computerized testing cannot be used owing to the subject's output impairment. This administration protocol was based on, and validated against, a widely used clinical test (Raven Colored Progressive Matrix) in order to verify whether BCI affects the brain in terms of cognitive resource with a misstatement result. The operating protocol was structured into two phases: phase 1 was aimed at configuring the BCI system on the subject's features and train him/her to use it; during phase 2 the BCI system was reconfigured and the test performed. A step-by-step checking procedure was adopted to verify progressive inclusion/exclusion criteria and the underpinning variables. The protocol was validated on 19 healthy subjects and the BCI-based administration was compared with a paper-based administration. The results obtained by both methods were correlated as known for traditional assessment of a similarly culture free and reasoning based test. Although our findings need to be validated on pathological participants, in our healthy population the BCI-based administration did not affect performance and added a further control of the response due to the several variables included and analyzed by the

computerized task.

Peruzzo Denis, Rambaldelli Gianluca, Bertoldo Alessandra, Bellani Marcella, Cerini Roberto, Marini Silvia, Pozzi Mucelli Roberto, Tansella Michele, Brambilla Paolo (2011); THE IMPACT OF SCHIZOPHRENIA ON FRONTAL PERFUSION PARAMETERS: A DSC-MR STUDY; Journal of Neural Transmission, 118(4):563-570

Doi: 10.007/s00702-010-0548-7 PMID: 21203783

I.F. 2010: 2,597

We performed a dynamic susceptibility contrast magnetic resonance imaging (DSC-MRI) analysis to study the role of the demographic/clinical information on perfusion parameters between patients with schizophrenia and normal control subjects. 39 schizophrenia patients and 27 normal controls were studied with a Siemens 1.5T magnet. PWI images were obtained following intravenous injection of paramagnetic contrast agent (gadolinium-DTPA). For each perfusion parameter, i.e. relative cerebral blood flow (rCBF), relative cerebral blood volume (rCBV), mean transit time (MTT) and time-to-peak (TTP), the best predictor model was computed in left and right frontal cortex following a stepwise strategy. First of all, a linear model, including all the sociodemographic information and clinical variables as predictors was computed. At each step, the least significant predictor was excluded and a new linear model was evaluated until all predictors were excluded. Then, the best predictor model was selected based on the F statistic value and on the p value. The models for the rCBF and the rCBV both in the left and right frontal cortex were estimated independently from each other, and the best models contained the same predictors, i.e. clinical state, age, and length of illness. No significant models were obtained for the MTT and the TTP. This study showed a decrease in rCBF and rCBV frontal cortex values in subject affected by schizophrenia. Future DSC-MRI studies should further investigate the role of cerebral perfusion for the pathophysiology of the disease by recruiting first-episode patients and by considering cerebellar, parietal and temporal regions.

Piccinini Luigi, Cimolin Veronica, D'Angelo Maria Grazia, Turconi Anna Carla, Crivellini Marcello, Galli Manuela (2011); 3D GAIT ANALYSIS IN PATIENTS WITH HEREDITARY SPASTIC PARAPARESIS AND SPASTIC DIPLEGIA: A KINEMATIC, KINETIC AND EMG COMPARISON; European Journal of Paediatric Neurology, 15(2):138-145

Doi: 10.1016/j.ejpn.2010.07.009 PMID: 20829081

I.F. 2010: 1,994

The predominant clinical feature of patients with Hereditary Spastic Paraparesis (HSP) is gait disturbance owing to spasticity and weakness of the lower limbs; the spasticity in early-onset disease (infancy or childhood) often cannot be distinguished from mild form of spastic diplegia (SD). The aim of this study was to quantify the gait strategy in HSP and SD children, focusing on the differences between groups as concerns functional limitation during gait. 9 HSP and 16 SD children were evaluated using Gait Analysis; kinematic and kinetic parameters and EMG pattern during walking were identified and calculated to compare the two gait strategies. The results revealed that these two pathologies are characterised by different gait strategies. In particular we found that knee joint, in terms of kinematics and kinetics, and rectus femoris pattern represent discriminatory aspects in order to compare and differentiate gait patterns of HSP and SD children. The findings strongly support the issue that HSP and SD patients need individualised therapeutical program, either neurosurgical or pharmacological treatment, based on the quantification of gait deficiencies and in order to address the peculiarity of their motor limitations and to prevent the onset of compensatory strategies.

Pietroboni Anna M., Fumagalli Giorgio G., Ghezzi Laura, Fenoglio Chiara, Cortini Francesca, Serpente Maria, Cantoni Claudia, Rotondo Emanuela, Corti Priscilla, Carecchio Miryam, Bassi Maria Teresa, Bresolin Nereo, Galbiati Domenico, Galimberti Daniela, Scarpini Elio (2011); PHENOTYPIC HETEROGENEITY OF THE GRN ASP22FS MUTATION IN A LARGE ITALIAN KINDRED; Journal of Alzheimer's Disease, 24(2):253-259

Doi: 10.3233/JAD-2011-101704 PMID: 21258152

I.F. 2010: 4,261

The Asp22fs(g.63_64insC) mutation in progranulin gene (GRN) has been so far reported in one patient who developed frontotemporal dementia (FTD) at the age of 65. Here, we describe the clinical heterogeneity associated with the GRN Asp22fs mutation in a large Italian family. Clinical and instrumental workup of two symptomatic carriers in two generations has been carried out, together with genetic analysis of probands and of nine asymptomatic family members. The first proband was a 47-year old male clinically diagnosed with FTD. Family history was positive and suggestive of an autosomal dominant pattern of inheritance. Evaluation of plasma GRN levels was consistent with the presence of a mutation in its encoding gene, that was demonstrated by sequencing [Asp22fs(g.63_64insC)]. Brain MRI showed multiple T2 and FLAIR hyperintense areas in the frontal lobe white matter and right hemisphere

cortical atrophy. The second proband was his 79 year old uncle, presenting with mild cognitive impairment. Brain MRI showed small T2 hyperintense lesions and widespread cortical atrophy. Cerebrospinal fluid amyloid-β, tau, and phosphotau protein levels were in both cases in the range of normality. Additional nine asymptomatic family members were studied. This family's description expands the spectrum of clinical presentations of frontotemporal lobar degeneration caused by GRN mutations, suggesting that the diagnosis could be missed in some individuals with an atypical presentation, and points up the importance of GRN plasma level evaluation.

Rescorla Leslie A., Achenbach Thomas M., Ivanova Masha Y., Harder Valerie S., Otten Laura, Bilenberg Niels, Bjarnadottir Gudrun, Capron Christiane, De Pauw Sarah S.W., Dias Pedro, Dobrean Anca, Dopfner Manfred, Duyme Michel, Eapen Valsamma, Erol Nese, Esmaeili Elaheh Mohammad, Ezpeleta Lourdes, Frigerio Alessandra, Fung Daniel S.S., Goncalves Miguel, Gudmundsson Halldor S., Jeng Suh-Fang, Jusiene Roma, Kim Young-Ah, Kristensen Solvejg, Liu Jianghong, Lecannelier Felipe, Leung Patrick, Machado Barbara Cesar, Montirosso Rosario, Oh Kyung-Ja, Ooi Yoon Phaik, Plueck Julia, Pomalima Rolando, Pranvera Jetishi, Shahini Mimoza, Silva Jaime R., Simsek Zeynep, Sourander Andre, Valverde Jose, Van Der Ende Jan, Van Leeuwen Karla G., Wu Yen-Tzu, Yurdusen Sema, Zubrick Stephen R., Verhulst Frank (2011); INTERNATIONAL COMPARISONS OF BEHAVIORAL AND EMOTIONAL PROBLEMS IN PRESCHOOL CHILDREN: PARENTS? REPORTS FROM 24 SOCIETIES; Journal of Clinical Child & Adolescent Psychology, 40(3):456-467

Doi: 10.1080/15374416.2011.563472 PMID: 21534056

I.F. 2010: 3,440

International comparisons were conducted of preschool children's behavioral and emotional problems as reported on the Child Behavior Checklist for Ages 1½-5 by parents in 24 societies (N = 19,850). Item ratings were aggregated into scores on syndromes; Diagnostic and Statistical Manual of Mental Disorders-oriented scales; a Stress Problems scale; and Internalizing, Externalizing, and Total Problems scales. Effect sizes for scale score differences among the 24 societies ranged from small to medium (3-12%). Although societies differed greatly in language, culture, and other characteristics, Total Problems scores for 18 of the 24 societies were within 7.1 points of the omnicultural mean of 33.3 (on a scale of 0-198). Gender and age differences, as well as gender and age interactions with society, were all very small (effect sizes <

1%). Across all pairs of societies, correlations between mean item ratings averaged .78, and correlations between internal consistency alphas for the scales averaged .92, indicating that the rank orders of mean item ratings and internal consistencies of scales were very similar across diverse societies.

Restuccia Domenico, Del Piero Ivana, Martucci Lucia, Zanini Sergio (2011); HIGH-FREQUENCY OSCILLATIONS AFTER MEDIAN-NERVE STIMULATION DO NOT UNDERGO HABITUATION: A NEW INSIGHT ON THEIR FUNCTIONAL MEANING?; Clinical Neurophysiology, 122(1):148-152

Doi: 10.1016/j.clinoh.2010.06.08 **PMID: 20619726**

I.F. 2010: 2,786

OBJECTIVE: Amplitude decrease of cortical responses after repeated stimuli ('habituation') is a well-known phenomenon, the functional meaning of which is to prevent sensory overflow and to save resources for meaningful and novel stimuli. It is known that the primary low-frequency N20 somatosensory evoked potential (SEP) undergoes habituation in healthy subjects. By contrast, the presence of this phenomenon has never been tested in High Frequency Oscillations (HFOs), which probably reflect the activity of a somatosensory arousal system.
METHODS: We recorded SEPs after right median nerve stimulation in 19 healthy volunteers. Six consecutive series of 500 sweeps were collected and averaged at a repetition rate of 5 Hz. SEPs were recorded by means of Erb'point-to-Fz, Cv6-to-AC and P3-to-F3 arrays. P3-to-F3 recording further underwent narrow-bandpass (400-800 Hz) digital filtering to selectively analyse high-frequency components.
RESULTS: Statistical analysis revealed a significant amplitude decrease of the primary N20 LF-SEP between the first and sixth block of stimuli. By contrast, HFO amplitudes remained substantially unchanged throughout the whole procedure.
CONCLUSIONS: Differently from the N20 LF-SEP, scalp-recorded HFOs do not undergo habituation.
SIGNIFICANCE: Our findings reinforce the view that HFOs reflect the activity of an arousal somatosensory system, which is able to signal novel stimuli, the relevance of which points out high synaptic efficacy.

Ronchi Dario*, Fassone Elisa*, Bordoni Andreina, Sciacco Monica, Lucchini Valeria, Di Fonzo Alessio, Rizzuti Mafalda, Colombo Irene, Napoli Laura, Ciscato Patrizia, Moggio Maurizio, Cosi Alessandra, Collotta Martina, Corti Stefania, Bresolin Nereo, Comi Giacomo

Pietro (2011); TWO NOVEL MUTATIONS IN PEO1 (TWINKLE) GENE ASSOCIATED WITH CHRONIC EXTERNAL OPHTHALMOPLEGIA; Journal of the Neurological Sciences, 308(1-2):173-176

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/J.JNS.2011.05.042 **PMID: 21689831**

I.F. 2010: 2,167

Maintenance and replication of mitochondrial DNA require the concerted action of several factors encoded by nuclear genome. The mitochondrial helicase Twinkle is a key player of replisome machinery. Heterozygous mutations in its coding gene, PEO1, are associated with progressive external ophthalmoplegia (PEO) characterised by ptosis and ophthalmoparesis, with cytochrome c oxidase (COX)-deficient fibres, ragged-red fibres (RRF) and multiple mtDNA deletions in muscle. Here we describe clinical, histological and molecular features of two patients presenting with mitochondrial myopathy associated with PEO. PEO1 sequencing disclosed two novel mutations in exons 1 and 4 of the gene, respectively. Although mutations in PEO1 exon 1 have already been described, this is the first report of mutation occurring in exon 4.

Ronchi Dario, Bordoni Andreina, Cosi Alessandra, Rizzuti Mafalda, Fassone Elisa, Di Fonzo Alessio, Servida Maura, Sciacco Monica, Collotta Martina, Ronzoni Marco, Lucchini Valeria, Mattioli Marco, Moggio Maurizio, Bresolin Nereo, Corti Stefania, Comi Giacomo Pietro (2011), UNUSUAL ADULT-ONSET LEIGH SYNDROME PRESENTATION DUE TO THE MITOCHONDRIAL M.9176T>C MUTATION; Biochemical and Biophysical Research Communications, 412(2):245-248

Doi: 10.1016/j.bbrc.2011.07.076 **PMID: 21819970**

I.F. 2010: 2,595

Leigh syndrome (LS) is an incurable, nearly always fatal, neurodegenerative, pediatric disorder that results from respiratory chain failure. The most common mitochondrial DNA (mtDNA) mutations that result in LS are m.8993T⇢C/G and m.9176T⇢C/G, which were previously found in several patients with early-onset Leigh syndrome. Here, we describe clinical and molecular features of a novel pedigree, where LS developed in two siblings. The proband was a young woman with an unusual adult-onset LS. She harbored a homoplasmic m.9176T⇢C mutation, based on analysis of a muscle biopsy. In contrast, the brother died at a young age. This novel case report and literature review highlights the variability of phenotypic expression

of the m.9176T⇢C mutation.

Rossetto Maria Giovanna*, Zanarella Erica*, Orso Genny, Scorzeto Michele, Megighian Aram, Kumar Vimlesh, Delgado-Escueta Antonio V., Daga Andrea (2011); DEFHC1.1, A HOMOLOGUE OF THE JUVENILE MYOCLONIC GENE EFHC1, MODULATES ARCHITECTURE AND BASAL ACTIVITY OF THE NEUROMUSCULAR JUNCTION IN DROSOPHILA; Human Molecular Genetics, 20(21):4248-4257

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1093/hmg/ddr352 PMID: 21835885

I.F. 2010: 8,058

Mutations in the EFHC1 gene have been linked to juvenile myoclonic epilepsy. To understand EFHC1 function in vivo, we generated knockout Drosophila for the fly homolog Defhc1.1. We found that the neuromuscular junction synapse of Defhc1.1 mutants displays an increased number of satellite boutons resulting in increased spontaneous neurotransmitter release. Defhc1.1 binds to microtubules in vitro and overlaps in vivo with axonal and synaptic microtubules. Elimination of Defhc1.1 from synaptic terminals reduces the number of microtubule loops, suggesting that Defhc1.1 is a negative regulator of microtubule dynamics. In fact, pharmacological treatment of Defhc1.1 mutants with vinblastine, an inhibitor of microtubule dynamics, suppresses the satellite bouton phenotype. Furthermore, Defhc1.1 mutants display overgrowth of the dendritic arbor and Defhc1.1 overexpression reduces dendrite elaboration. These results suggest that Defhc1.1 functions as an inhibitor of neurite growth by finely tuning the microtubule cytoskeleton dynamics and that EFHC1-dependent juvenile myoclonic epilepsy may result from augmented spontaneous neurotransmitter release due to overgrowth of neuronal processes.

Ruzzoli Manuela*, Gori Simone*, Pavan Andrea, Pirulli Cornelia, Marzi Carlo Alberto, Miniussi Carlo (2011); THE NEURAL BASIS OF THE ENIGMA ILLUSION: A TRANSCRANIAL MAGNETIC STIMULATION STUDY; Neuropsychologia, 49(13):3648-3655

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.neuropsychologia.2011.09.020 PMID: 21952193

I.F. 2010: 3,949

The aim of this study was to test the role of the visual primary (V1) and the middle temporal area (V5/MT) in the illusory motion perception evoked

by the Enigma figure. The Enigma figure induces a visual illusion that is characterized by apparent rotatory motion in the presence of a static figure. By means of repetitive transcranial magnetic stimulation (rTMS) we show that V5/MT is causally linked to the illusory perception of motion. When rTMS was applied bilaterally over V5/MT just prior to presentation of the Enigma figure, the perception of illusory motion was disrupted for approximately 400 ms resulting in a delayed illusion onset. In contrast, rTMS applied over V1 did not have any effect on the illusory perception of motion. These results show that V5/MT, a visual cortical area associated with real motion perception, is also important for the perception of illusory motion, while V1 appears not to be functionally involved in illusory motion perception.

Sala Michela, Caverzasi Edgardo, Lazzaretti Matteo, Morandotti N., De Vidovich Giulia, Marraffini E., Gambini F., Isola Miriam, De Bona M., Rambaldelli Gianluca, D'Allio Giorgio, Barale Francesco, Zappoli Thyrion F., Brambilla Paolo (2011); DORSOLATERAL PREFRONTAL CORTEX AND HIPPOCAMPUS SUSTAIN IMPULSIVITY AND AGGRESSIVENESS IN BORDERLINE PERSONALITY DISORDER; Journal of Affective Disorders, 131(1-3):417-421

Doi: 10.1016/j.jad.2010.11.036 PMID: 21211852

I.F. 2010: 3,740

BACKGROUND: Borderline Personality Disorder (BPD) patients are characterized by increased levels of aggressivity and reduction of impulse control, which are behavioural dimensions mainly sustained by hippocampus and dorsolateral prefrontal cortex (DLPFC). In this study we aimed at investigating whether hippocampus and DLPFC anatomy may sustain impulsive and aggressive behaviours in BPD.
METHODS: Fifteen DSM-IV BPD patients (11 females, 4 males) and fifteen 1:1 matched healthy controls (11 females, 4 males) were studied with a 1.5T magnetic resonance imaging (MRI) and underwent a psychopathological assessment in order to measure the severity of aggressive and impulsive traits.
RESULTS: Right hippocampal volumes were significantly reduced in BPD patients compared to healthy subjects ($p=0.027$), particularly in those with a history of childhood abuse ($p=0.01$). Moreover, in patients but not in controls, right hippocampal volumes significantly inversely correlated with aggressiveness and DLPFC grey matter volumes significantly inversely associated with impulsiveness ($p<0.05$).
CONCLUSIONS: Our results provide evidence that hippocampus and DLPFC play a separate and unique role in sustaining the control of impulse

and aggressive behaviours in BPD patients.

Sciorati Clara, Miglietta Daniela, Buono Roberta, Pisa Viviana, Cattaneo Dario, Azzoni Emanuele, Brunelli Silvia, Clementi Emilio (2011); A DUAL ACTING COMPOUND RELEASING NITRIC OXIDE (NO) AND IBUPROFEN, NCX 320, SHOWS SIGNIFICANT THERAPEUTIC EFFECTS IN A MOUSE MODEL OF MUSCULAR DYSTROPHY; Pharmacological Research, 64(3):210-217

Doi: 10.1016/j.phrs.2011.05.003 PMID: 21609764

I.F. 2010: 3,612

A resolutive therapy for muscular dystrophies, a heterogeneous group of genetic diseases leading to muscular degeneration and in the severe forms to death, is still lacking. Since inflammation and defects in nitric oxide generation are recognized key pathogenic events in muscular dystrophy, we have analysed the effects of a derivative of ibuprofen, NCX 320, belonging to the class of cyclooxygenase inhibiting nitric oxide donator (CINOD), in the α-sarcoglycan null mice, a severe mouse model of dystrophy. NCX 320 was administered daily in the diet for 8months starting 1month from weaning. Muscle functional recovery was evaluated by free wheel and treadmill tests at 8months. Serum creatine kinase activity, as well as the number of diaphragm inflammatory infiltrates and necrotic fibres, was measured as indexes of skeletal muscle damage. Muscle regeneration was evaluated in diaphragm and tibialis anterior muscles, measuring the numbers of centronucleated fibres and of myogenic precursor cells. NCX 320 mitigated muscle damage, reducing significantly serum creatine kinase activity, the number of necrotic fibres and inflammatory infiltrates. Moreover, NCX 320 stimulated muscle regeneration increasing significantly the number of myogenic precursor cells and regenerating fibres. All these effects concurred in inducing a significant improvement of muscle function, as assessed by both free wheel and treadmill tests. These results describe the properties of a new compound incorporating nitric oxide donation together with anti-inflammatory properties, showing that it is effective in slowing muscle dystrophy progression long term. Of importance, this new compound deserves specific attention for its potential in the therapy of muscular dystrophy given that ibuprofen is well tolerated in paediatric patients and with a profile of safety that makes it suitable for chronic treatment such as the one required in muscular dystrophies.

Sironi Manuela*, Guerini Franca Rosa*, Agliardi Cristina, Biasin Mara, Cagliani Rachele, Fumagalli Matteo, Caputo Domenico, Cassinotti Andrea, Ardizzone Sandro, Zanzottera Milena,

Bolognesi Elisabetta, Riva Stefania, Kanari Yasuyoshi, Miyazawa Masaaki, Clerici Mario (2011); AN EVOLUTIONARY ANALYSIS OF RAC2 IDENTIFIES HAPLOTYPES ASSOCIATED WITH HUMAN AUTOIMMUNE DISEASES; Molecular Biology and Evolution, 28(12):3319-3329

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1093/molbev/msr164 **PMID: 21680873**

I.F. 2010: 5,510

The human RAC2 gene encodes a small GTP-binding protein with a pivotal role in immune activation and in the induction of peripheral immune tolerance through restimulation-induced cell death (RICD). Different human pathogens target the protein product of RAC2, suggesting that the gene may be subject to natural selection, and that variants in RAC2 may affect immunological phenotypes in humans. We scanned the genomic region encompassing the entire transcription unit for the presence of putative noncoding regulatory elements conserved across mammals. This information was used to select two RAC2 gene regions and analyze their intraspecific genetic diversity. Results suggest that a region covering the 3' untranslated region has been a target of multiallelic balancing selection (or diversifying selection), and three major RAC2 haplogroups occur in human populations. Haplotypes belonging to one of these clades are associated with increased susceptibility to multiple sclerosis ($P = 0.022$) and earlier onset of disease symptoms ($P = 0.025$). This same haplogroup is significantly more common in patients with Crohn's disease compared with healthy controls ($P = 0.048$). These data reinforce recent evidences that susceptibility alleles/haplotypes are shared among multiple autoimmune disorders and support a causal "role for RAC2" variants in the pathogenesis of autoimmune diseases. Other genes with a role in RICD have previously been associated with autoimmunity in humans, suggesting that this pathway and RAC2 may represent novel therapeutic targets in autoimmune disorders.

Tollervey James R., Curk Tomaz, Rogelj Boris, Briese Michael, Cereda Matteo, Kayikci Melis, Konig Julian, Hortobagyi Tibor, Nishimura Agnes L., Zupunski Vera, Patani Rickie, Chandran Siddharthan, Rot Gregor, Zupan Blaz, Shaw Christopher E., Ule Jernej (2011); CHARACTERIZING THE RNA TARGETS AND POSITION-DEPENDENT SPLICING REGULATION BY TDP-43; Nature Neuroscience, 14(4):452-458

Doi: 10.1038/nn.2778 **PMID: 21358640**

I.F. 2010: 14,191

TDP-43 is a predominantly nuclear RNA-binding protein that forms inclusion bodies in frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). The mRNA targets of TDP-43 in the human brain and its role in RNA processing are largely unknown. Using individual nucleotide-resolution ultraviolet cross-linking and immunoprecipitation (iCLIP), we found that TDP-43 preferentially bound long clusters of UG-rich sequences in vivo. Analysis of RNA binding by TDP-43 in brains from subjects with FTLD revealed that the greatest increases in binding were to the MALAT1 and NEAT1 noncoding RNAs. We also found that binding of TDP-43 to pre-mRNAs influenced alternative splicing in a similar position-dependent manner to Nova proteins. In addition, we identified unusually long clusters of TDP-43 binding at deep intronic positions downstream of silenced exons. A substantial proportion of alternative mRNA isoforms regulated by TDP-43 encode proteins that regulate neuronal development or have been implicated in neurological diseases, highlighting the importance of TDP-43 for the regulation of splicing in the brain.

Tomasino Barbara, Skrap Miran, Rumiati Raffaella Ida (2011); CAUSAL ROLE OF THE SENSORIMOTOR CORTEX IN ACTION SIMULATION: NEUROPSYCHOLOGICAL EVIDENCE; Journal of Cognitive Neuroscience, 23(8):2068-2078

Doi: 10.1162/jocn.2010.21577 PMID: 20849231

I.F. 2010: 5,357

Interest in sensorimotor cortex involvement in higher cognitive functions has recently been revived, although whether the cortex actually contributes to the simulation of body part movements has not yet been established. Neurosurgical patients with selective lesions to the hand sensorimotor representation offer a unique opportunity to demonstrate that the sensorimotor cortex plays a causal role in hand action simulations. Patients with damage to hand representation showed a selective deficit in simulating hand movements compared with object movements (Experiment 1). This deficit extended to objects when the patients imagined moving them with their own hands while maintaining the ability to visualize them rotating in space (Experiment 2). The data provide conclusive evidence for a causal role of the sensorimotor cortex in the continuous update of sensorimotor representations while individuals mentally simulate motor acts.

Tomasino Barbara, Bellani Marcella, Perlini Cinzia, Rambaldelli Gianluca, Cerini Roberto, Isola Miriam, Balestrieri Matteo, Calì S.,

Versace Amelia, Pozzi Mucelli Roberto, Gasparini Anna, Tansella Michele, Brambilla Paolo (2011); ALTERED MICROSTRUCTURE INTEGRITY OF THE AMYGDALA IN SCHIZOPHRENIA: A BIMODAL MRI AND DWI STUDY; Psychological Medicine, 41(2):301-311

Doi: 10.1017/S0033291710000875 PMID: 20459886

I.F. 2010: 5,200

BACKGROUND: The amygdala plays a central role in the fronto-limbic network involved in the processing of emotions. Structural and functional abnormalities of the amygdala have recently been found in schizophrenia, although there are still contradictory results about its reduced or preserved volumes.
METHOD: In order to address these contradictory findings and to further elucidate the possibly underlying pathophysiological process of the amygdala, we employed structural magnetic resonance imaging (MRI) and diffusion weighted imaging (DWI), exploring amygdalar volume and microstructural changes in 69 patients with schizophrenia and 72 matched healthy subjects, relating these indices to psychopathological measures.
RESULTS: Measuring water diffusivity, the apparent diffusion coefficients (ADCs) for the right amygdala were found to be significantly greater in patients with schizophrenia compared with healthy controls, with a trend for abnormally reduced volumes. Also, significant correlations between mood symptoms and amygdalar volumes were found in schizophrenia.
CONCLUSIONS: We therefore provide evidence that schizophrenia is associated with disrupted tissue organization of the right amygdala, despite partially preserved size, which may ultimately lead to abnormal emotional processing in schizophrenia. This result confirms the major role of the amygdala in the pathophysiology of schizophrenia and is discussed with respect to amygdalar structural and functional abnormalities found in patients suffering from this illness.

Trabacca Antonio, Losito Luciana, De Rinaldis Marta, Gennaro Leonarda (2011); CONGENITAL HYPOTONIA IN A CHILD WITH A DE NOVO 22Q13 MONOSOMY AND 2PTER DUPLICATION: A CLINICAL AND MOLECULAR GENETIC STUDY; Journal of Child Neurology, 26(2):235-238

Doi: 10.1177/088307381444 PMID: 20921566

I.F. 2010: 1,668

The authors describe a 5-year-old girl with a neurological phenotype of 22q13 deletion syndrome (neonatal and persisting hypotonia, developmental

delay, absence of language, decreased perception of pain) and minor dysmorphisms. Subtelomeric fluorescent in situ hybridization tests revealed de novo 22q13 monosomy and 2pter duplication. Numerous genetic and neurologic disorders of childhood are characterized by congenital hypotonia. This muscle tone disorder is often one of the symptoms that a neurologist is asked to evaluate. Recent advances in genetic testing can help provide a specific diagnosis for children with this symptom. Subtelomeric deletions are a category of disorders of which hypotonia can be a prominent feature. Deletions of chromosome 22q13 are some of the most commonly observed terminal deletions in humans, whereas duplications of chromosome 2p25.2 are very rare, and little is known about the phenotypic effect of these duplications. To the best of the authors' knowledge, this association has never been described before.

Trabacca Antonio, Dicuonzo Franca, Gennaro Leonarda, Palma Michele, Cacudi Marilena, Losito Luciana, De Rinaldis Marta (2011); OS ODONTOIDEUM AS A RARE BUT POSSIBLE COMPLICATION IN CHILDREN WITH DYSKINETIC CEREBRAL PALSY: A CLINICAL AND NEURORADIOLOGIC STUDY; Journal of Child Neurology, 26(8):1021-1025

Doi: 10.1177/0883073810397835 PMID: 21616925

I.F. 2010: 1,668

The authors describe a 12-year-old boy with dyskinetic (athetoid-dystonic subtype) cerebral palsy and os odontoideum. Dystonic and choreoathetotic components in cerebral palsy are movement disorders that are difficult to treat and cause major disability. Dystonic posturing causes excessive flexion, extension, and rotation of the neck. Repetitive abnormal movements in patients with this type of cerebral palsy give rise to a higher incidence of pathologic conditions affecting the craniovertebral junction. Os odontoideum is one of these pathologies, and it represents a rare anomaly of the odontoid process. There are only a few reports describing os odontoideum in children with dyskinetic cerebral palsy. This clinical and neuroradiologic study focuses on the problem of atlantoaxial instability and os odontoideum in these forms of cerebral palsy, which is too often underestimated.

Turati Chiara, Montirosso Rosario, Brenna Viola, Ferrara Veronica, Borgatti Renato (2011); A SMILE ENHANCES 3-MONTH-OLDS' RECOGNITION OF AN INDIVIDUAL FACE; Infancy, 16(3):306-317

Doi: 10.1111/j.1532-7078.2010.00047.x

I.F. 2010: 1,507

Recent studies demonstrated that in adults and children recognition of face identity and facial expression mutually interact (Bate, Haslam, & Hodgson, 2009; Spangler, Schwarzer, Korell, & Maier-Karius, 2010). Here, using a familiarization paradigm, we explored the relation between these processes in early infancy, investigating whether 3-month-old infants' ability to recognize an individual face is affected by the positive (happiness) or neutral emotional expression displayed. Results indicated that infants' face recognition appears enhanced when faces display a happy emotional expression, suggesting the presence of a mutual interaction between face identity and emotion recognition as early as 3 months of age.

Ulas Aydin, Duin Robert P.W., Castellani Umberto, Loog Marco, Mirtuono Pasquale, Bicego Manuele, Murino Vittorio, Bellani Marcella, Cerruti Stefania, Tansella Michele, Brambilla Paolo (2011); DISSIMILARITY-BASED DETECTION OF SCHIZOPRENIA; International Journal of Imaging Systems and Technology, 21(2;S1):179-192

Doi: 10.1002/ima.20279

I.F. 2010: 0,684

In this article, a novel approach to schizophrenia classification using magnetic resonance images (MRI) is proposed. The presented method is based on dissimilarity-based classification techniques applied to morphological MRIs and diffusion-weighted images (DWI). Instead of working with features directly, pairwise dissimilarities between expert delineated regions of interest (ROIs) are considered as representations based on which learning and classification can be performed. Experiments are carried out on a set of 59 patients and 55 controls and several pairwise dissimilarity measurements are analyzed. We demonstrate that significant improvements can be obtained when combining over different ROIs and different dissimilarity measures. We show that combining ROIs using the dissimilaritybased representation, we achieve higher accuracies. The dissimilarity-based representation outperforms the feature-based representation
in all cases. Best results are obtained by combining the two modalities. In summary, our contribution is threefold: (i) We introduce the usage of dissimilarity-based classification to schizophrenia detection and show that dissimilarity-based classification achieves better results than normal features, (ii) We use dissimilarity combination to achieve better accuracies when carefully selected ROIs and dissimilarity measures are considered, and (iii) We show that by combining multiple modalities we can achieve even better results.

Urgesi Cosimo, Fornasari Livia, De Faccio Sara, Perini Laura, Mattiussi Elisa, Ciano Rossana, Balestrieri Matteo, Fabbro Franco, Brambilla Paolo (2011); BODY SCHEMA AND SELF-REPRESENTATION IN PATIENTS WITH BULIMIA NERVOSA; International Journal of Eating Disorders, 44(3):238-248

Doi: 10.1002/eat.20816 PMID: 20186715

I.F. 2010: 2,278

OBJECTIVE: Neuroimaging evidences in eating disorder (ED) patients document dysfunctional neural activity of the posterior parietal cortex, which is engaged in the representation of body schema. Yet a full neuropsychological investigation of body schema representation in ED patients is lacking. We examined mental imagery and body schema representation in patients with bulimia nervosa (BN) and binge eating disorder (BED).
METHOD: Consecutive samples of 15 BN patients and 15 BED patients were compared with two groups of 15 age-matched controls in tasks requiring body or object mental transformation.
RESULTS: BN, but not BED patients, were selectively impaired in the mental transformation of their own body, although this deficit was not correlated with measures of body dissatisfaction. In contrast, no patient group was impaired in the mental transformation of external objects.
DISCUSSION: Results showed altered self-body representation in BN, but not BED patients, as the neuropsychological consequences of posterior parietal cortex dysfunctions.

Urgesi Cosimo, Avenanti Alessio (2011); FUNCTIONAL AND EPIPHENOMENAL MODULATION OF NEURAL ACTIVITY IN BODY-SELECTIVE VISUAL AREAS; Cognitive Neuroscience, 2(3-4):212-214

Doi: 10.1080/17588928.2011.604725

I.F. 2010: 0,000

Although attention may play a major role in explaining EBA/FBA activation during high-order, bodyrelated tasks, it is important to establish the functional significance of top-down modulation in different tasks. While neuroimaging studies documented the functional and anatomical specificity of EBA/FBA activation during body form perception, repetitive transcranial magnetic stimulation (rTMS) and brain-lesion studies provided causative evidence that activity in EBA is essential for processing morphological details of body parts. Local processing of body shapes in EBA might contribute to the representation of high-order body attributes, including person identity and

body esthetics, which probably rely on a widespread network of different interconnected areas.

Vantaggiato Chiara, Bondioni Sara, Airoldi Giovanni, Bozzato Andrea, Borsani Giuseppe, Rugarli Elena I., Bresolin Nereo, Clementi Emilio*, Bassi Maria Teresa* (2011); SENATAXIN MODULATES NEURITE GROWTH THROUGH FIBROBLAST GROWTH FACTOR 8 SIGNALLING; Brain, 134(Pt 6):1808-1828

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1093/brain/awr084 **PMID: 21576111**

I.F. 2010: 9,232

Senataxin is encoded by the SETX gene and is mainly involved in two different neurodegenerative diseases, the dominant juvenile form of amyotrophic lateral sclerosis type 4 and a recessive form of ataxia with oculomotor apraxia type 2. Based on protein homology, senataxin is predicted to be a putative DNA/RNA helicase, while senataxin interactors from patients' lymphoblast cell lines suggest a possible involvement of the protein in different aspects of RNA metabolism. Except for an increased sensitivity to oxidative DNA damaging agents shown by some ataxia with neuropathy patients' cell lines, no data are available about possible functional consequences of dominant SETX mutations and no studies address the function of senataxin in neurons. To start elucidating the physiological role of senataxin in neurons and how disease-causing mutations in this protein lead to neurodegeneration, we analysed the effect of senataxin on neuronal differentiation in primary hippocampal neurons and retinoic acid-treated P19 cells by modulating the expression levels of wild-type senataxin and three different dominant mutant forms of the protein. Wild-type senataxin overexpression was required and sufficient to trigger neuritogenesis and protect cells from apoptosis during differentiation. These actions were reversed by silencing of senataxin. In contrast, overexpression of the dominant mutant forms did not affect the regular differentiation process in primary hippocampal neurons. Analysis of the cellular pathways leading to neuritogenesis and cytoprotection revealed a role of senataxin in modulating the expression levels and signalling activity of fibroblast growth factor 8. Silencing of senataxin reduced, while overexpression enhanced, fibroblast growth factor 8 expression levels and the phosphorylation of related target kinases and effector proteins. The effects of senataxin overexpression were prevented when fibroblast growth factor 8 signalling was inhibited, while exogenous fibroblast growth factor 8 reversed the effects of senataxin silencing. Overall, these results reveal a key role of senataxin in neuronal differentiation through the fibroblast growth factor 8

signalling and provide initial molecular bases to explain the neurodegeneration associated with loss-of-function mutations in senataxin found in recessive ataxia. The lack of effect on neuritogenesis observed with the overexpression of the dominant mutant forms of senataxin apparently excludes a dominant negative effect of these mutants while favouring haploinsufficiency as the pathogenic mechanism implicated in the amyotrophic lateral sclerosis 4-related degenerative condition. Alternatively, a different protein function, other than the one involved in neuritogenesis, may be implicated in these dominant degenerative processes.

Vetro Annalisa, Ciccone Roberto, Giorda Roberto, Patricelli Maria Grazia, Della Mina Erika, Forlino Antonella, Zuffardi Orsetta (2011); XX MALES SRY NEGATIVE: A CONFIRMED CAUSE OF INFERTILITY; Journal of Medical Genetics, 48(10):710-712

Doi: 10.1136/jmedgenet-2011-100036 PMID: 21653197

I.F. 2010: 7,037

BACKGROUND: SOX9 is a widely expressed transcription factor playing several relevant functions during development and essential for testes differentiation. It is considered to be the direct target gene of the protein encoded by SRY and its overexpression in an XX murine gonad can lead to male development in the absence of Sry. Recently, a family was reported with a 178 kb duplication in the gene desert region ending about 500 kb upstream of SOX9 in which 46,XY duplicated persons were completely normal and fertile whereas the 46,XX ones were males who came to clinical attention because of infertility.
METHODS AND RESULTS: We report a family with two azoospermic brothers, both 46,XX, SRY negative, having a 96 kb triplication 500 kb upstream of SOX9. Both subjects have been analyzed trough oligonucleotide array-CGH and the triplication was confirmed and characterised through qPCR, defining the minimal region of amplification upstream of SOX9 associated with 46,XX infertile males, SRY negative.
CONCLUSIONS: Our results confirm that even in absence of SRY, complete male differentiation may occur, possibly driven by overexpression of SOX9 in the gonadal ridge, as a consequence of the amplification of a gene desert region. We hypothesize that this region contains gonadal specific long-range regulation elements whose alteration may impair the normal sex development. Our data show that normal XX males, with alteration in copy number or, possibly, in the critical sequence upstream to SOX9 are a new category of infertility inherited in a dominant way with expression limited to the XX background.

Wischmeijer A.*, Magini Pamela*, Giorda Roberto*, Gnoli M., Ciccone Roberto, Cecconi I., Franzoni E., Mazzanti L., Romeo Giovanni, Zuffardi Orsetta, Seri Marco (2011); OLFACTORY RECEPTOR-RELATED DUPLICONS MEDIATE A MICRODELETION AT 11Q13.2Q13.4 ASSOCIATED WITH A SYNDROMIC PHENOTYPE; Molecular Syndromology, 1(4):176-184

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1159/000322054 PMID: 21373257

By array-CGH, we identified a cryptic deletion of about 3.4 Mb involving the chromosomal region 11q13.2q13.4 in a child with speech and developmental delay. Highly homologous segmental duplications related to the well-known olfactory receptor (OR)-containing clusters at 8p and 4p are located at the breakpoints of the imbalance and may be involved in its occurrence. Although these structural features are known to promote recurrent chromosomal rearrangements and previous studies had included the 11q13.2q13.4 deletion region among those considered potentially more unstable, neither deletions nor duplications of this region had been reported until now. Among the deleted genes, SHANK2 might play a role in the phenotype of the patient since it encodes a postsynaptic scaffolding protein similar to SHANK3, whose haploinsufficiency is a well-known cause of severe speech delay and autistic-like behavior, and recently deletions and mutations of SHANK2 have been described in patients with an autistic spectrum disorder or mental retardation.

Wissinger Bernd, Schaich Simone, Baumann Britta, Bonin Michael, Jägle Herbert, Friedburg Christoph, Varsànyi Balàzs, Hoyng Carel B., Dollfus Hélène, Heckenlively John R., Rosenberg Thomas, Rudolph Günter, Kellner Ulrich, Salati Roberto, Plomp Astrid, De Baere Elfride, Andrassi-Darida Monika, Sauer Alexandra, Wolf Christiane, Zobor Ditta, Bernd Antje, Leroy Bart P., Enyedi Péter, Cremers Frans P.M., Lorenz Birgit, Zrenner Eberhart, Kohl Susanne (2011); LARGE DELETIONS OF THE KCNV2 GENE ARE COMMON IN PATIENTS WITH CONE DYSTROPHY WITH SUPERNORMAL ROD RESPONSE; Human Mutation, 32(12):1398-1406

Doi: 10.1002/humu.21580 PMID: 21882291

I.F. 2010: 5,956

Cone dystrophy with supernormal rod response (CDSRR) is considered to be a very rare autosomal recessive retinal disorder. CDSRR is associated with mutations in KCNV2, a gene that encodes a modulatory subunit (Kv8.2)

of a voltage-gated potassium channel. In this study, we found that KCNV2 mutations are present in a substantial fraction (2.2-4.3%) of a sample of 367 independent patients with a variety of initial clinical diagnoses of cone malfunction, indicating that CDSRR is underdiagnosed and more common than previously thought. In total, we identified 20 different KCNV2 mutations; 15 of them are novel. A new finding of this study is the substantial proportion of large deletions at the KCNV2 locus that accounts for 15.5% of the mutant alleles in our sample. We determined the breakpoints and size of all five different deletions, which ranged between 10.9 and 236.8 kb. Two deletions encompass the entire KCNV2 gene and one also includes the adjacent VLDLR gene. Furthermore, we investigated N-terminal amino acid substitution mutations for its effect on interaction with Kv2.1 using yeast two-hybrid technology. We found that these mutations dramatically reduce or abolish this interaction suggesting a lack of assembly of heteromeric Kv channels as one underlying pathomechanism of CDSRR.

Yazdanbakhsh Arash, Gori Simone (2011); MATHEMATICAL ANALYSIS OF THE ACCORDION GRATING ILLUSION: A DIFFERENTIAL GEOMETRY APPROACH TO INTRODUCE THE 3D APERTURE PROBLEM; Neural Networks, 24(10):1093-1101

Doi: 10.1016/j.neunet.2011.06.016 PMID: 21782387

I.F. 2010: 1,972

When an observer moves towards a square-wave grating display, a non-rigid distortion of the pattern occurs in which the stripes bulge and expand perpendicularly to their orientation; these effects reverse when the observer moves away. Such distortions present a new problem beyond the classical aperture problem faced by visual motion detectors, one we describe as a 3D aperture problem as it incorporates depth signals. We applied differential geometry to obtain a closed form solution to characterize the fluid distortion of the stripes. Our solution replicates the perceptual distortions and enabled us to design a nulling experiment to distinguish our 3D aperture solution from other candidate mechanisms (see Gori et al. (in this issue)). We suggest that our approach may generalize to other motion illusions visible in 2D displays.

Zanini Sergio, Angeli Valentina, Tavano Alessandro (2011); PRIMARY PROGRESSIVE APHASIA IN A BILINGUAL SPEAKER: A SINGLE-CASE STUDY; Clinical Linguistics & Phonetics, 25(6-7):553-564

Doi: 10.3109/02699206.2011.566464 PMID: 21631307

I.F. 2010: 0,574

We report on the case of an elderly bilingual woman presenting with a diagnosis of primary progressive aphasia. The participant's native language was Friulian (L1), a predominantly oral Romance language, and her second language was Italian (L2), formally learned at primary school in oral and written forms. We investigated her linguistic abilities by means of the Bilingual Aphasia Test (Paradis, M., & Libben, G. (1987). The assessment of bilingual aphasia. Hillsdale, NJ: Lawrence Erlbaum Associates), which is specifically devised for studying language levels and skills in bilingual/polyglot individuals with aphasia. Specifically, we focused on different tasks extracted from the Bilingual Aphasia Test, targeting phonology, morphology, syntax and lexical semantics. Results show that both languages were affected to a clinically significant degree, but with different profiles in terms of linguistic levels, suggesting the presence of greater phonological, morphological, grammatical and syntactic impairments in L2. Results are discussed in terms of possible dissociations both within the language system of each language and between languages, within the Procedural/Declarative theoretical framework of language acquisition in bilinguals.

Zuliani Riccardo, Moorhead T. William J., Bastin Mark E., Johnstone Eve C., Lawrie Stephen M., Brambilla Paolo, O'Donovan Michael C., Owen Michael J., Hall Jeremy, McIntosh Andrew M. (2011); GENETIC VARIANTS IN THE ERBB4 GENE ARE ASSOCIATED WITH WHITE MATTER INTEGRITY; Psychiatry Research, 191(2):133-137

Doi: 10.1016/j.pscychresns.2010.11.001 PMID: 21232925

I.F. 2010: 2,803

Variations in the signalling NRG1-ErbB4 pathway have been associated with genetic susceptibility for both bipolar disorder and schizophrenia, although the underlying neural mechanisms are still uncertain. Reduced integrity of the anterior limb of the internal capsule (ALIC) has been found in association with risk-associated genetic variation in the 5' region of the NRG1 gene. We hypothesised that variation in the gene encoding the NRG1 receptor, ErbB4, would also be associated with reduced ALIC integrity and with cognitive impairments characteristic of individuals with bipolar disorder and schizophrenia. Using diffusion tensor imaging (DTI), we examined the white matter integrity associations of the ErbB4 polymorphism rs4673628, which resides within intron 12 of the gene encoding ErbB4, in 36 healthy individuals. We also sought to clarify the cognitive effects of any findings. We found that genetic variation at the rs4673628 locus in the ErbB4 gene was significantly associated with ALIC white matter integrity which was also significantly and positively associated with mnemonic function. These findings

provide further evidence to support a key role of NRG1-ErbB4 signalling in the pathophysiology of major mental disorders.

LAVORI PER ESTESO PUBBLICATI SU RIVISTE RECENSITE

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Abreu Ana Maria, Macaluso E., Azevedo R.T., Cesari Paola, Urgesi Cosimo, Aglioti Salvatore (2012); ACTION ANTICIPATION BEYOND THE ACTION OBSERVATION NETWORK: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY IN EXPERT BASKETBALL PLAYERS; European Journal of Neuroscience, 35(10):1646-1654

Doi: 10.1111/j.1460-9568.2012.08104.x PMID: 22541026

I.F. 2011: 3,631

The ability to predict the actions of others is quintessential for effective social interactions, particularly in competitive contexts (e.g. in sport) when knowledge about upcoming movements allows anticipating rather than reacting to opponents. Studies suggest that we predict what others are doing by using our own motor system as an internal forward model and that the fronto-parietal action observation network (AON) is fundamental for this ability. However, multiple-duty cells dealing with action perception and execution have been found in a variety of cortical regions. Here we used functional magnetic resonance imaging to explore, in expert basketball athletes and novices, whether the ability to make early predictions about the fate of sport-specific actions (i.e. free throws) is underpinned by neural regions beyond the classical AON. We found that, although involved in action prediction, the fronto-parietal AON was similarly activated in novices and experts. Importantly, athletes exhibited relatively greater activity in the extrastriate body area during the prediction task, probably due to their expert reading of the observed action kinematics. Moreover, experts exhibited higher activation in the bilateral inferior frontal gyrus and in the right anterior insular cortex when producing errors, suggesting that they might become aware of their own errors. Correct action prediction induced higher posterior insular cortex activity in experts and higher orbito-frontal activity in novices, suggesting that body awareness is important for performance monitoring in experts, whereas novices rely more on higher-order decision-making strategies. This functional reorganization highlights the tight relationship between action anticipation, error awareness and motor expertise leading to body-related processing and differences in decision-making processes.

Adduci Annarita, Jankovic Momcilo, Strazzer Sandra, Massimino

Maura, Clerici Carlo Alfredo, Poggi Geraldina (2012); PARENT-CHILD COMMUNICATION AND PSYCHOLOGICAL ADJUSTEMENT IN CHILDREN WITH A BRAIN TUMOR; Pediatric Blood & Cancer, 59(2):290-294

Doi: 10.1002/pbc.24165 **PMID: 22492656**

I.F. 2011: 1,891

BACKGROUND: Internalizing problems, anxiety, depression, withdrawal, and consequent social problems are frequently observed in children with brain tumors. The objective of this work is to describe the relationship between these psychological problems and the type of parent-child communication established about the disease.
PROCEDURES: A group of 64 children surviving a brain tumor (aged 4-18 years) underwent psychological assessment by means of parent reports on the Child Behavior Checklist (CBCL) and the Vineland Adaptive Behavior Scales (VABS). A semi-structured interview with each child and their parents enabled us to classify the method of communication regarding the disease as "avoidance," "ineffective," and "effective." Demographic, clinical, and functional data relating to the disease were also collected.
RESULTS: A significant relationship between the onset of Internalizing problems, withdrawal, anxiety-depression, and social problems and the presence of avoidance or ineffective communication about the disease was observed ($P = 0.001$, $P = 0.001$, $P = 0.001$, and $P = 0.01$, respectively). These psychological problems did not prove to be associated to demographic or clinical variables; however, they were found to be related to the children's residual functional problems. By contrast, the method of communication proved to be unrelated to clinical or functional variables, but it was associated to demographic variables such as sex and age at assessment.
CONCLUSIONS: Effective (complete, truthful, consistent, comprehensible, gradual and continuous, and tailored) communication to the child about his/her condition proved to be associated with a better psychological outcome.

Andreetta Sara, Cantagallo Anna, Marini Andrea (2012); NARRATIVE DISCOURSE IN ANOMIC APHASIA; Neuropsychologia, 50(8):1787-1793

I.F. 2011: 3,636

Doi: 10.1016/j.neuropsychologia.2012.04.003 **PMID: 22564448**

Anomic aphasia is a disturbance affecting lexical retrieval. Nonetheless, persons with this disorder may also experience difficulties in the construction of coherent narratives. Whether this symptom is a sign of a macrolinguistic

difficulty per se or reflects the lexical disorder is still an open debate. In order to analyze the effect of the lexical impairment on macrolinguistic processing, we compared the narrative skills of a group of ten participants with chronic anomic aphasia with those of ten healthy control individuals matched for age and educational level. The anomic participants produced narratives with lowered speech rate, reduced mean length of utterance, fewer grammatically well-formed sentences, more semantic paraphasias. The macrolinguistic analysis showed that they also produced more errors of cohesion and global coherence and fewer lexical information units. Interestingly, their levels of thematic selection were normal. A bivariate correlational analysis showed a strong correlation between the production of errors of cohesion and production of complete sentences, and between production of errors of global coherence and lexical information units. These correlations showed that aspects related to lexical retrieval may affect macrolinguistic processing during the construction of a narrative. Indeed, it is suggested that lexical deficits lead to two main consequences: First, patients with anomia frequently interrupt the utterances they are producing and this reduces the levels of sentence completeness and the overall degree of cohesion across the utterances; Second, they use strategies to cope with the lexical impairment and produce a quantity of lexical fillers and repetitions that, clustered in utterances, reduce the levels of global coherence.

Antoniazzi Stefania, Cattaneo Dario, Perrone Valentina, Carnovale Carla, Cherubini Simonetta, Mugolino Maria Carmela, Clementi Francesco, Zuccotti Gian Vincenzo, Clementi Emilio, Radice Sonia (2012); INFLAMMATION AND NEUROLOGICAL ADVERSE DRUGS REACTIONS: A CASE OF LONG LASTING IMPAIRED CONSCIOUSNESS AFTER OXATOMIDE ADMINISTRATION IN A PATIENT WITH GASTROENTERITIS; Italian Journal of Pediatrics, 38(1):11

Doi: 10.1186/1824-7288-38-11 **PMID: 22464080**

I.F. 2011: 0,791

Oxatomide at therapeutic doses generates occasionally drowsiness in children. When administered at toxic doses, however oxatomide may induce long lasting impaired consciousness. We now report a case of severe long lasting impaired consciousness induced by therapeutic doses of oxatomide occurring in a child affected by acute gastroenteritis. The clinical symptoms, the pharmacogenetic tests of polymorphisms in cytochrome P450 metabolizing enzymes (CYPs) and the clinical and laboratory analyses indicate that the enhanced drug sedative effect is likely due to an acute, yet mild, inflammatory

state of the patient. These findings highlight the importance of assessing common, not serious inflammatory states when oxatomide is prescribed in paediatric patients.

Antonucci Flavia, Turola Elena, Riganti Loredana, Caleo Matteo, Gabrielli Martina, Perrotta Cristiana, Novellino Luisa, Clementi Emilio, Giussani Paola, Viani Paola, Matteoli Michela, Verderio Claudia (2012); MICROVESICLES RELEASED FROM MICROGLIA STIMULATE SYNAPTIC ACTIVITY VIA ENHANCED SPHINGOLIPID METABOLISM; The EMBO Journal, 31(5):1231-1240

Doi: 10.1038/EMBOJ.2011.489 PMID: 22246184

I.F. 2011: 9,205

Microvesicles (MVs) released into the brain microenvironment are emerging as a novel way of cell-to-cell communication. We have recently shown that microglia, the immune cells of the brain, shed MVs upon activation but their possible role in microglia-to-neuron communication has never been explored. To investigate whether MVs affect neurotransmission, we analysed spontaneous release of glutamate in neurons exposed to MVs and found a dose-dependent increase in miniature excitatory postsynaptic current (mEPSC) frequency without changes in mEPSC amplitude. Paired-pulse recording analysis of evoked neurotransmission showed that MVs mainly act at the presynaptic site, by increasing release probability. In line with the enhancement of excitatory transmission in vitro, injection of MVs into the rat visual cortex caused an acute increase in the amplitude of field potentials evoked by visual stimuli. Stimulation of synaptic activity occurred via enhanced sphingolipid metabolism. Indeed, MVs promoted ceramide and sphingosine production in neurons, while the increase of excitatory transmission induced by MVs was prevented by pharmacological or genetic inhibition of sphingosine synthesis. These data identify microglia-derived MVs as a new mechanism by which microglia influence synaptic activity and highlight the involvement of neuronal sphingosine in this microglia-to-neuron signalling pathway.

Arnoldi Alessia, Crimella Claudia, Tenderini Erika, Martinuzzi Andrea, D'Angelo Maria Grazia, Musumeci Olimpia, Toscano Antonio, Scarlato Marina, Fantin Marianna, Bresolin Nereo, Bassi Maria Teresa (2012); CLINICAL PHENOTYPE VARIABILITY IN PATIENTS WITH HEREDITARY SPASTIC PARAPLEGIA TYPE 5 ASSOCIATED WITH CYP7B1 MUTATIONS; Clinical Genetics, 81(2):150-157

Doi: 10.1111/j.1399-0004.2011.01624.x PMID: 21214876

I.F. 2011: 3,128

Spastic paraplegia type 5 (SPG5) is caused by mutations in CYP7B1, a gene encoding the cytochrome P-450 oxysterol 7-α-hydroxylase, CYP7B1, an enzyme implicated in the cholesterol metabolism. Mutations in CYP7B1 were found in both pure and complicated forms of the disease with a mutation frequency of 7.7% in pure recessive cases. The mutation frequency in complex forms, approximately 6.6%, is more controversial and needs to be refined. We studied in more detail the SPG5-related spectrum of complex phenotypes by screening CYPB1 for mutations in a large cohort of 105 Italian hereditary spastic paraplegias (HSPs) index patients including 50 patients with a complicated HSP (cHSP) phenotype overlapping the SPG11- and the SPG15-related forms except for the lack of thin corpus callosum and 55 pure patients. Five CYP7B1 mutations, three of which are novel, were identified in four patients, two with a complex form of the disease and two with a pure phenotype. The CYP7B1 mutation frequencies obtained in both complicated and pure familial cases are comparable to the known ones. These results obtained extend the range of SPG5-related phenotypes and reveal variability in clinical presentation, disease course and functional profile in the SPG5-related patients while providing with some clues for molecular diagnosis in cHSP.

Avenanti Alessio, Annella Laura, Candidi Matteo, Urgesi Cosimo, Aglioti Salvatore (2012); COMPENSATORY PLASTICITY IN THE ACTION OBSERVATION NETWORK: VIRTUAL LESIONS OF STS ENHANCE ANTICIPATORY SIMULATION OF SEEN ACTIONS; Cerebral Cortex, in press

Doi: 10.1093/cercor/bhs040 **PMID: 22426335**

I.F. 2011: 6,544

Observation of snapshots depicting ongoing motor acts increases cortico-spinal motor excitability. Such motor facilitation indexes the anticipatory simulation of observed (implied) actions and likely reflects computations occurring in the parietofrontal nodes of a cortical network subserving action perception (action observation network, AON). However, direct evidence for the active role of AON in simulating the future of seen actions is lacking. Using a perturb-and-measure transcranial magnetic stimulation (TMS) approach, we show that off-line TMS disruption of regions within (inferior frontal cortex, IFC) and upstream (superior temporal sulcus, STS) the parietofrontal AON transiently abolishes and enhances the motor facilitation to observed implied actions, respectively. Our findings highlight the critical role of IFC in anticipatory motor simulation. More importantly, they show that disruption of

STS calls into play compensatory motor simulation activity, fundamental for counteracting the noisy visual processing induced by TMS. Thus, short-term plastic changes in the AON allow motor simulation to deal with any gap or ambiguity of ever-changing perceptual worlds. These findings support the active, compensatory, and predictive role of frontoparietal nodes of the AON in the perception and anticipatory simulation of implied actions.

Barozzi Stefania, Soi Daniela, Comiotto Elisabetta, Borghi Anna, Gavioli Chiara, Spreafico Emanuela, Gagliardi Chiara, Selicorni Angelo, Forti Stella, Ambrosetti Umberto, Cesarani Antonio, Brambilla Daniele (2012); AUDIOLOGICAL FINDINGS IN WILLIAMS SYNDROME: A STUDY OF 69 PATIENTS; American Journal of Medical Genetics Part A, 158A(4):759-771

Doi: 10.1002/ajmg.a.35241 **PMID: 22411878**

I.F. 2011: 2,391

The aim of this study was to investigate, in a clinical setting, the auditory function of a group of individuals affected by Williams syndrome (WS). Sixty-nine patients with WS, aged 2-30, underwent comprehensive audiological testing including air/bone conduction behavioral audiometry, speech audiometry, tympanometry and measurement of the acoustic reflex, transient evoked otoacoustic emissions and brainstem auditory evoked responses. Hearing loss, defined by a pure-tone average above 15 dB HL, affected 22.6% of the patients studied with traditional audiometry and was mostly slight in severity. Hearing loss was conductive in 9.4% of patients, mainly children with otitis media with effusion, and sensorineural in 13.2% of patients. However, 30% of the ears studied had a hearing impairment in the high frequency range (high-frequency pure-tone audiometry above 15 dB HL), higher in participants above 15 years (46.15%) than in the younger ones (23.45%). Contralateral stapedial reflexes were present in all patients with A-type tympanograms. Transient otoacoustic emissions were absent in 44% of the ears of patients with normal hearing. Brainstem auditory evoked responses fell within normal ranges thus confirming the absence of retrocochlear dysfunction. Although hearing loss does not seem to be frequent, a cochlear fragility, especially in the high frequency range, related to outer hair cells is characteristic of WS. Therefore we strongly recommend monitoring patients affected by WS using annual audiometric tests and performing otoacoustic emissions in order to identify a subclinical cochlear dysfunction which might benefit from an audiological follow up before the possible onset of hearing loss.

Barry Johanna G., Harbodt Silke, Cantiani Chiara, Sabisch Beate,

Zobay Oliver (2012); SENSITIVITY TO LEXICAL STRESS IN DYSLEXIA: A CASE OF COGNITIVE NOT PERCEPTUAL STRESS; Dyslexia, 18(3):139-165

Doi: 10.1002/dys.1440 **PMID: 22589197**

I.F. 2011: 1,116

Sensitivity to lexical stress in adult German-speaking students with reading difficulty was investigated using minimal pair prepositional verbs whose meaning and syntax depend on the location of the stressed syllable. Two tests of stress perception were used: (i) a stress location task, where listeners indicated the location of the perceptually most prominent syllable, and (ii) a stress pattern identification task, where listeners indicated if the stress pattern was appropriate for its semantic frame. The students with reading difficulties performed worse than the normally reading students on both tasks. Their poorer performance did not reflect the lack of a percept for lexical stress rather patterns of performance across the two tasks suggested that each loaded onto different underlying cognitive abilities. Deficits in these, rather than perceptual difficulties, explained observed group differences. Students with reading difficulties have a normal implicit knowledge of lexical stress usage but lack the necessary cognitive resources for developing an explicit metalinguistic awareness of it. Deficits in these skills not deficiencies in lexical stress perception are implicated in their reading difficulties.

Battaglia Marco, Zanoni Annalisa, Taddei Matilde, Giorda Roberto, Bertoletti Eleonora, Lampis Valentina, Scaini Simona, Cappa Stefano, Tettamanti Marco (2012); CEREBRAL RESPONSES TO EMOTIONAL EXPRESSIONS AND THE DEVELOPMENT OF SOCIAL ANXIETY DISORDER: A PRELIMINARY LONGITUDINAL STUDY; Depression and Anxiety, 29(1):54-61

Doi: 10.1002/da.20896 **PMID: 21898716**

I.F. 2011: 4,184

BACKGROUND: Cross-sectional studies report biased reactivity to facial expressions among shy children, anxious adolescents, and adults with social anxiety disorder (SAD). It remains unknown whether cerebral reactivity to facial expressions can predict longitudinally the development of SAD in adolescence and characterize the degree of social anxiety among the general population of adolescents.
METHODS: In a longitudinal study of 21 general population volunteers characterized for behavioral and genetic variables, N400 event-related potentials, and 3-Tesla fMRI activations in response to happy/neutral/angry expres-

sions were acquired at age 8-9 and 14-15, respectively.
RESULTS: By stepwise regression, N400 amplitudes acquired at age 8-9 predicted the number of DSM-IV SAD symptoms at age 14-15, with the sole, significant (P = .018) contribution of the "anger" condition. Factorial ANOVA revealed increased (Voxel-Level P((FWE)) range: .02-.0001) bilateral fMRI activations of several brain areas, including the amygdala, in response to facial expressions compared to a fixation cross. The number of symptoms of DSM-IV SAD was positively correlated with left amygdala response to angry (P((FWE)) = .036) and neutral (P((FWE)) = .025) facial expressions. Factorial ANOVA revealed that the 5-HTTLPR -S allele was associated with heightened left amygdala response to anger (P((FWE)) = .05).
CONCLUSION: Cerebral reactivity to facial expressions, anger especially, measured at different developmental stages by different techniques is associated with adolescence SAD. The 5-HTTLPR genotype affects the neural processing of interpersonal affective stimuli during development.

Bellani Marcella, Hatch John P., Nicoletti Mark A., Ertola Astrid E., Zunta-Soares Giovana B., Brambilla Paolo, Soares Jair C. (2012); DOES ANXIETY INCREASE IMPULSIVITY IN PATIENTS WITH BIPOLAR DISORDER OR MAJOR DEPRESSIVE DISORDER?; Journal of Psychiatric Research, 46(5):616-621

Doi: 10.1016/j.jpsychires.2012.01.016 PMID: 22326294

I.F. 2011: 4,664

The objective of this study was to examine whether anxiety increases impulsivity among patients with bipolar disorder (BPD) and major depressive disorder (MDD). Subjects comprised 205 BPD (mean age ± SD 36.6 ± 11.5 y; 29.3% males) and 105 with MDD (mean age ± SD 38 ± 13.1 y; 29.5% males) diagnosed using the DSM-IV-SCID. Impulsivity was assessed with the Barratt Impulsivity Scale and anxiety with the Hamilton Anxiety Rating Scale. Comorbid anxiety disorders were present in 58.9% of the BPD and 29.1% of MDD. BPD were significantly more impulsive than MDD ($p < 0.001$), and both BPD and MDD subjects showed significantly higher impulsivity when anxiety was present either as a comorbidity ($p = 0.010$) or as a symptom ($p = 0.011$). Impulsivity rose more rapidly with increasing anxiety symptoms in MDD than in BPD. The presence of anxiety, either as a comorbid disorder or as current anxiety symptoms, is associated with higher impulsivity in subjects with either BPD or MDD.

Bellani Marcella, Garzitto Marco, Brambilla Paolo (2012); FUNCTIONAL MRI STUDIES IN DISRUPTIVE BEHAVIOUR

DISORDERS; Epidemiology and Psychiatric Sciences, 21(1):31-33

Doi: 10.1017/S2045796011000692 **PMID: 22670410**

I.F. 2011: 0,000

Aggressive or antisocial behaviours with violations of social rules are the main features of disruptive behaviour disorders (DBDs), which are developmental diseases and include conduct disorder and oppositional defiant disorder. In the last decade, several efforts have been made to shed light on the biological underpinnings of DBDs. In this context, the main findings of functional magnetic resonance imaging studies in DBD are reported here. There are indications of neural dysfunctions in response to affective stimuli, especially regarding medial and orbitofrontal prefrontal cortex and connected subcortical structures.

Bellani Marcella, Negri Gioia Anna Laura, Brambilla Paolo (2012); THE DYSREGULATION PROFILE IN CHILDREN AND ADOLESCENTS: A POTENTIAL INDEX FOR MAJOR PSYCHOPATHOLOGY?; Epidemiology and Psychiatric Sciences, 21(2):155-159

Doi: 10.1017/ S2045796011000849 **PMID: 22789163**

I.F. 2011: 0,000

We here review the literature on Child Behaviour Checklist-Dysregulation Profile (CBCL-DP) index, which potentially represents a developmental profile of major psychopathology in early adulthood. The understanding of the neural underpinnings of children and adolescents with altered regulation of affect and behaviour may ultimately help in planning strategies to prevent psychiatric syndromes during development.

Bellani Marcella, Bonivento Carolina, Brambilla Paolo (2012); INTERACTION BETWEEN COGNITION AND EMOTION IN DEVELOPMENTAL PSYCHOPATHOLOGY: THE ROLE OF LINGUISTIC STIMULI; Epidemiology and Psychiatric Sciences, in press

Doi: 10.1017/S2045796012000273 **PMID: 22794034**

I.F. 2011: 0,000

Investigations on emotional words demonstrated that processing emotional information in child patients with anxiety disorders diagnosed for anxiety (generalized anxiety disorder and post-traumatic stress disorder) or depression is biased towards pathology-related stimuli. Also, neuroimaging studies showed a failure of prefrontal areas in inhibiting the emotional reaction in children with bipolar disorder. Finally, despite several studies investigated memory and attention using emotional words, little is known about the development of

emotional lexicon in both healthy and psychopathological children.

Bellani Marcella, Perlini Cinzia, Ferro Adele, Cerruti Stefania, Rambaldelli Gianluca, Isola Miriam, Cerini Roberto, Dusi Nicola, Andreone Nicola, Balestrieri Matteo, Pozzi Mucelli Roberto, Tansella Michele, Brambilla Paolo (2012); WHITE MATTER MISCROSTRUCTURE ALTERATIONS IN BIPOLAR DISORDER; Functional Neurology, 27(1):29-34

PMID: 22687164

I.F. 2011: 1,518

Genetic, neuropathological and magnetic resonance imaging findings support the presence of diffuse white matter cytoarchitectural disruption in bipolar disorder.
In this study, diffusion-weighted imaging (DWI) was applied to study cortical white matter microstructure organisation in 24 patients with DSM-IV bipolar disorder and 35 matched normal controls.
DWI images were obtained using a 1.5 Tesla scanner and apparent diffusion coefficient (ADC) values were determined over regions of interest placed, bilaterally, in the frontal, temporal, parietal, and occipital white matter.
Significantly increased ADC values were found in bipolar patients with respect to normal controls in the right temporal lobe, left parietal lobe and bilateral occipital lobes. ADC values did not associate significantly with age or with clinical variables ($p>0.05$).
Diffuse cortical white matter alterations on DWI in bipolar disorder denote widespread disruption of white matter integrity and may be due to altered myelination and/or axonal integrity.

Bertoletti Eleonora, Zanoni Annalisa, Giorda Roberto, Battaglia Marco (2012); INFLUENCE OF THE OPRM1 GENE POLYMORPHISMS UPON CHILDREN'S DEGREE OF WITHDRAWAL AND BRAIN ACTIVATION IN RESPONSE TO FACIAL EXPRESSIONS; Developmental Cognitive Neuroscience, 2(1):103-109

Doi: 10.1016/j.dcn.2011.05.001 PMID: 22682732

I.F. 2011: 0,000

Genetic variation of the A118G polymorphism of the μ-opioid receptor gene (OPRM1) predicts individual sensitivity to social rejection and fMRI activation during simulated social rejection in adults, while data on these relationships during childhood are lacking. We investigated whether this polymorphism predicts childhood withdrawal - a predictor of sensitivity to social rejection

-, and the face-specific N170 event-related waveform in response to facial expressions. Among facial expressions, 'anger' was expected to be particularly evocative, as it communicates social rejection. Forty-nine children aged 8-10 years were characterised for their OPRM1 genotype, their score at the Withdrawn Scale of the Child Behavior Checklist (CBCL), and for N170 latencies and amplitudes recorded during a task of implicit processing of happy, neutral, and angry expressions of other children. Children carrying the OPRM1-G allele had higher CBCL Withdrawn scores and enhanced N170 amplitudes in response to facial expressions. Multiple linear regressions showed that the Withdrawn scale score predicts larger N170 amplitudes at the Pz and C4 electrodes, only for the anger expression. Children who carry one or two copies of the OPRM1 G-allele are more likely to manifest withdrawn behaviours, and differ for electrophysiological responses to the early phases of processing affective stimuli.

Bonanni Paolo, Gubernale Marco, Martinez Federica, Randazzo Giovanna, Milantoni Luca, Martinuzzi Andrea, Boniver Clementina, Vecchi Marilena, Scarpa Maurizio (2012); NON-CONVULSIVE STATUS EPILEPTICUS OF FRONTAL ORIGIN IN MUCOPOLYSACCHARIDOSIS TYPE II SUCCESSFULLY TREATED WITH ETHOSUXIMIDE; Developmental Medicine and Child Neurology, in press

Doi: 10.1111/j.1469-8749.2012.04228x PMID: 22414067

I.F. 2011: 2,918

At 7 years of age, a female with mucopolysaccharidosis type II (MPS II) showed a sudden deterioration in neurological function, a sleep disorder, and progressive behavioural impairment. Electroencephalography was performed 1year and 8 months after the onset of the neurological regression and revealed continuous ictal activity in the frontal regions. The female was diagnosed as having frontal non-convulsive status epilepticus. After 5 weeks of therapy with ethosuximide, the ictal electroencephalographic activity disappeared. At the same time, her sleep and cognitive and behavioural functions were observed to improve. This is the first case of MPS type II reported in an individual with non-convulsive status epilepticus. Two main forms of MPS II can be recognized: attenuated and severe. Severe MPS II is characterized by neurodegeneration. No study has explored the relationship between epilepsy and neurological deterioration in MPS II. Our observation shows that epilepsy may be a treatable cause of neurological regression in individuals with MPS II.

Bosurgi Lidia, Corna Gianfranca, Vezzoli Michela, Touvier Thierry, Cossu Giulio, Manfredi Angelo A., Brunelli Silvia, Rovere-Querini Patrizia (2012); TRANSPLANTED MESOANGIOBLASTS REQUIRE MACROPHAGE IL-10 FOR SURVIVAL IN A MOUSE MODEL OF MUSCLE INJURY; The Journal of Immunology, 188(12):6267-6277

Doi: 10.4049/jimmunol.1102680 **PMID: 22573810**

I.F. 2011: 5,788

The aim of this study was to verify whether macrophages influence the fate of transplanted mesoangioblasts-vessel-associated myogenic precursors-in a model of sterile toxin-induced skeletal muscle injury. We have observed that in the absence of macrophages, transplanted mesoangioblasts do not yield novel fibers. Macrophages retrieved from skeletal muscles at various times after injury display features that resemble those of immunoregulatory macrophages. Indeed, they secrete IL-10 and express CD206 and CD163 membrane receptors and high amounts of arginase I. We have reconstituted the muscle-associated macrophage population by injecting polarized macrophages before mesoangioblast injection: alternatively activated, immunoregulatory macrophages only support mesoangioblast survival and function. This action depends on the secretion of IL-10 in the tissue. Our results reveal an unanticipated role for tissue macrophages in mesoangioblast function. Consequently, the treatment of muscle disorders with mesoangioblasts should take into consideration coexisting inflammatory pathways, whose activation may prove crucial for its success.

Brambilla Paolo, Como G., Isola Miriam, Taboga F., Zuliani Riccardo, Goljevscek S., Ragogna M., Brondani G., Baiano Monica, Perini Laura, Ferro Adele, Bazzocchi M., Zuiani C., Balestrieri Matteo (2012); WHITE-MATTER ABNORMALITIES IN THE RIGHT POSTERIOR HEMISPHERE IN GENERALIZED ANXIETY DISORDER: A DIFFUSION IMAGING STUDY; Psychological Medicine, 42(2):427-434

Doi: 10.1017/S0033291711001255 **PMID: 21781374**

I.F. 2011: 6,159

BACKGROUND: Prior imaging studies have shown structural, functional and biochemical impairments in patients with generalized anxiety disorder (GAD), particularly in the right hemisphere. In this study we investigated, for the first time to the best of our knowledge, the white-matter microstructure organization in GAD.MethodA total of 12 patients with DSM-IV GAD and 15 matched healthy controls underwent a magnetic resonance imaging session of diffu-

sion weighted imaging, exploring white-matter water molecules by the means of apparent diffusion coefficients (ADCs). Regions of interests were placed in the frontal, parietal, temporal and occipital lobes and in the splenium and genu of the corpus callosum, bilaterally.
RESULTS: ADC measures were significantly greater in patients with GAD in the right splenium and right parietal cortex compared with healthy controls ($p \leqslant 0.002$). No significant correlations between ADCs and age or clinical variables were found.
CONCLUSIONS: We provide evidence that GAD is associated with disrupted white-matter coherence of posterior right hemisphere regions, which may partly sustain the impaired cognitive regulation of anxiety. Future diffusion imaging investigations are expected to better elucidate the communication between the parietal cortex and other right hemisphere regions in sustaining the cognitive processing of social and emotional stimuli in patients with GAD.

Brambilla Paolo, Perlini Cinzia, Bellani Marcella, Tomelleri Luisa, Ferro Adele, Cerruti Stefania, Marinelli Veronica, Rambaldelli Gianluca, Christodoulou T., Jogia Jigar, Dima D., Tansella Michele, Balestrieri Matteo, Frangou Sophia (2012); INCREASED SALIENCE OF GAINS VERSUS DECREASED ASSOCIATIVE LEARNING DIFFERENTIATE BIPOLAR DISORDER FROM SCHIZOPHRENIA DURING INCENTIVE DECISON MAKING; Psychological Medicine, in press

Doi: 10.1017/S0033291712001304 **PMID: 22687364**

I.F. 2011: 6,159

BACKGROUND: Abnormalities in incentive decision making, typically assessed using the Iowa Gambling Task (IGT), have been reported in both schizophrenia (SZ) and bipolar disorder (BD). We applied the Expectancy-Valence (E-V) model to determine whether motivational, cognitive and response selection component processes of IGT performance are differentially affected in SZ and BD.MethodPerformance on the IGT was assessed in 280 individuals comprising 70 remitted patients with SZ, 70 remitted patients with BD and 140 age-, sex- and IQ-matched healthy individuals. Based on the E-V model, we extracted three parameters, ‘attention to gains or loses’, ‘expectancy learning’ and ‘response consistency’, that respectively reflect motivational, cognitive and response selection influences on IGT performance.
RESULTS: Both patient groups underperformed in the IGT compared to healthy individuals. However, the source of these deficits was diagnosis specific. Associative learning underlying the representation of expectancies was

disrupted in SZ whereas BD was associated with increased incentive salience of gains. These findings were not attributable to non-specific effects of sex, IQ, psychopathology or medication.
CONCLUSIONS: Our results point to dissociable processes underlying abnormal incentive decision making in BD and SZ that could potentially be mapped to different neural circuits.

Buono Roberta, Vantaggiato Chiara, Pisa Viviana, Azzoni Emanuele, Bassi Maria Teresa, Brunelli Silvia, Sciorati Clara, Clementi Emilio (2012); NITRIC OXIDE SUSTAINS LONG TERM SKELETAL MUSCLE REGENERATION BY REGULATING SATELLITE CELLS FATE VIA SIGNALLING PATHWAYS REQUIRING VANGL12 AND CYCLIC GMP; Stem Cells (Alphamed Press), 30(2):197-209

Doi: 10.1002/stem.783 **PMID: 22084027**

I.F. 2011: 7,781

Satellite cells are myogenic precursors that proliferate, activate, and differentiate on muscle injury to sustain the regenerative capacity of adult skeletal muscle; in this process, they self-renew through the return to quiescence of the cycling progeny. This mechanism, while efficient in physiological conditions does not prevent exhaustion of satellite cells in pathologies such as muscular dystrophy where numerous rounds of damage occur. Here, we describe a key role of nitric oxide, an important signaling molecule in adult skeletal muscle, on satellite cells maintenance, studied ex vivo on isolated myofibers and in vivo using the α-sarcoglycan null mouse model of dystrophy and a cardiotoxin-induced model of repetitive damage. Nitric oxide stimulated satellite cells proliferation in a pathway dependent on cGMP generation. Furthermore, it increased the number of Pax7(+)/Myf5(-) cells in a cGMP-independent pathway requiring enhanced expression of Vangl2, a member of the planar cell polarity pathway involved in the Wnt noncanonical pathway. The enhanced self-renewal ability of satellite cells induced by nitric oxide is sufficient to delay the reduction of the satellite cell pool during repetitive acute and chronic damages, favoring muscle regeneration; in the α-sarcoglycan null dystrophic mouse, it also slowed disease progression persistently. These results identify nitric oxide as a key messenger in satellite cells maintenance, expand the significance of the Vangl2-dependent Wnt noncanonical pathway in myogenesis, and indicate novel strategies to optimize nitric oxide-based therapies for muscular dystrophy.

Cagliani Rachele, Fumagalli Matteo, Guerini Franca Rosa, Riva Stefania, Galimberti Daniela, Comi Giacomo Pietro, Agliardi Cristina,

Scarpini Elio, Pozzoli Uberto, Forni Diego, Caputo Domenico, Asselta Rosanna, Biasin Mara, Paraboschi Elvezia M., Bresolin Nereo, Clerici Mario, Sironi Manuela (2012); IDENTIFICATION OF A NEW SUSCEPTIBILITY VARIANT FOR MULTIPLE SCLEROSIS IN OAS1 BY POPULATION GENETICS ANALYSIS; Human Genetics, 131(1):87-97

Doi: 10.1007/s00439-011-1053-2 **PMID: 21735172**

I.F. 2011: 5,069

Contrasting results have been reported concerning the association of a splice-site polymorphism (rs10774671) in OAS1 with multiple sclerosis (MS). We analysed two OAS1 regions encompassing alternatively spliced exons. While the region carrying the splice-site variant is neutrally evolving, a signature of long-standing balancing selection was observed across an alternative exon 7. Analysis of variants in this exon identified an insertion/deletion polymorphism (rs11352835, A/-) that originates predicted products with distinct C termini. This variant is located along the major branch of the haplotype genealogy, suggesting that it may represent the selection target. A case/control study for MS indicated that rs11352835 is associated with disease susceptibility (for an allelic model with the deleted allele predisposing to MS, OR 1.27, 95% CI 1.072-1.513, p = 0.010). No association was found between rs10774671 and MS. As the two SNPs are in linkage disequilibrium in Europeans, the previously reported association between rs10774671 and MS susceptibility might be driven by rs11352835, possibly explaining the contrasting results previously observed for the splice-site polymorphism. Thus, we describe a novel susceptibility variant for MS in OAS1 and show that population genetic analyses can be instrumental to the identification of selection targets and, consequently, of functional polymorphisms with an effect on phenotypic traits.

Cagliani Rachele, Riva Stefania, Marino Cecilia, Fumagalli Matteo, D'Angelo Maria Grazia, Riva Valentina, Comi Giacomo Pietro, Pozzoli Uberto, Forni Diego, Cáceres Mario, Bresolin Nereo, Clerici Mario, Sironi Manuela (2012); VARIANTS IN SNAP25 ARE TARGETS OF NATURAL SELECTION AND INFLUENCE VERBAL PERFORMANCE IN WOMEN; Cellular and Molecular Life Sciences, 69(10):1705-1715

Doi: 10.1007/s00018-011-0896-y **PMID: 22193912**

I.F. 2011: 6,570

Descriptions of genes that are adaptively evolving in humans and that carry polymorphisms with an effect on cognitive performances have been virtually absent. SNAP25 encodes a presynaptic protein with a role in regulation

of neurotransmitter release. We analysed the intra-specific diversity along SNAP25 and identified a region in intron 1 that shows signatures of balancing selection in humans. The estimated TMRCA (time to the most recent common ancestor) of the SNAP25 haplotype phylogeny amounted to 2.08 million years. The balancing selection signature is not secondary to demographic events or to biased gene conversion, and encompasses rs363039. This SNP has previously been associated to cognitive performances with contrasting results in different populations. We analysed this variant in two Italian cohorts in different age ranges and observed a significant genotype effect for rs363039 on verbal performances in females alone. Post hoc analysis revealed that the effect is driven by differences between heterozygotes and both homozygous genotypes. Thus, heterozygote females for rs363039 display higher verbal performances compared to both homozygotes. This finding was replicated in a cohort of Italian subjects suffering from neuromuscular diseases that do not affect cognition. Heterozygote advantage is one of the possible reasons underlying the maintenance of genetic diversity in natural populations. The observation that heterozygotes for rs363039 display higher verbal abilities compared to homozygotes perfectly fits the underlying balancing selection model. Although caution should be used in inferring selective pressures from observed signatures, SNAP25 might represent the first description of an adaptively evolving gene with a role in cognition.

Cagliani Rachele, Guerini Franca Rosa, Fumagalli Matteo, Riva Stefania, Agliardi Cristina, Galimberti Daniela, Pozzoli Uberto, Goris A., Dubois B., Fenoglio Chiara, Forni Diego, Sanna S., Zara I., Pitzalis M., Zoledziewska M., Cucca F., Marini Federico, Comi Giacomo Pietro, Scarpini Elio, Bresolin Nereo, Clerici Mario, Sironi Manuela (2012); A TRANS-SPECIFIC POLYMORPHISM IN ZC3HAV1 IS MAINTAINED BY LONG-STANDING BALANCING SELECTION AND MAY CONFER SUSCEPTIBILITY TO MULTIPLE SCLEROSIS; Molecular Biology and Evolution, 29(6):1599-1613

Doi: 10.1093/molbev/mss002 **PMID: 22319148**

I.F. 2011: 5,550

The human ZC3HAV1 gene encodes an antiviral protein. The longest splicing isoform of ZC3HAV1 contains a C-terminal PARP-like domain, which has evolved under positive selection in primates. We analyzed the evolutionary history of this same domain in humans and in Pan troglodytes. We identified two variants that segregate in both humans and chimpanzees; one of them (rs3735007) does not occur at a hypermutable site and accounts for a non-synonymous substitution (Thr851Ile). The probability that the two trans-spe-

cific polymorphisms have occurred independently in the two lineages was estimated to be low (P = 0.0054), suggesting that at least one of them has arisen before speciation and has been maintained by selection. Population genetic analyses in humans indicated that the region surrounding the shared variants displays strong evidences of long-standing balancing selection. Selection signatures were also observed in a chimpanzee population sample. Inspection of 1000 Genomes data confirmed these findings but indicated that search for selection signatures using low-coverage whole-genome data may need masking of repetitive sequences. A case-control study of more than 1,000 individuals from mainland Italy indicated that the Thr851Ile SNP is significantly associated with susceptibility to multiple sclerosis (MS) (odds ratio [OR] = 1.47, 95% confidence intervals [CI]: 1.08-1.99, P = 0.011). This finding was confirmed in a larger sample of 4,416 Sardinians cases/controls (OR = 1.18, 95% CI: 1.037-1.344, P = 0.011), but not in a population from Belgium. We provide one of the first instances of human/chimpanzee trans-specific coding variant located outside the major histocompatibility complex region. The selective pressure is likely to be virus driven; in modern populations, this variant associates with susceptibility to MS, possibly via the interaction with environmental factors.

Cantiani Chiara, Lorusso Maria Luisa, Perego Paolo, Molteni Massimo, Guasti Maria Teresa (2012); ERPS REVEAL ANOMALOUS MORPHOSYNTATIC PROCESSING IN DEVELOPMENTAL DYSLEXIA; Applied Psycholinguistics, in press

I.F. 2011: 0,950

Abstrat non disponibile

Castellani Umberto, Rossato E., Murino Vittorio, Bellani Marcella, Rambaldelli Gianluca, Perlini Cinzia, Tomelleri Luisa, Tansella Michele, Brambilla Paolo (2012); CLASSIFICATION OF SCHIZOPHRENIA USING FEATURE-BASED MORPHOMETRY; Journal of Neural Transmission, 119(3):395-404

Doi: 10.1007/s00702-011-0693-7 PMID: 21904897

I.F. 2011: 2,730

The objective of this study was to use a combined local descriptor, namely scale invariance feature transform (SIFT), and a non linear support vector machine (SVM) technique to automatically classify patients with schizophrenia. The dorsolateral prefrontal cortex (DLPFC), considered a reliable neuroanatomical marker of the disease, was chosen as region of interest (ROI). Fifty-four schizophrenia patients and 54 age- and gender-matched normal

controls were studied with a 1.5T MRI (slice thickness 1.25 mm). Three steps were conducted: (1) landmark detection and description of the DLPFC, (2) feature vocabulary construction and Bag-of-Words (BoW) computation for brain representation, (3) SVM classification which adopted the local kernel to implicitly implement the feature matching. Moreover, a new weighting approach was proposed to take into account the discriminant relevance of the detected groups of features. Substantial results were obtained for the classification of the whole dataset (left side 75%, right side 66.38%). The performances were higher when females (left side 84.09%, right side 77.27%) and seniors (left side 81.25%, right side 70.83%) were considered separately. In general, the supervised weighed functions increased the efficacy in all the analyses. No effects of age, gender, antipsychotic treatment and chronicity were shown on DLPFC volumes. This integrated innovative ROI-SVM approach allows to reliably detect subjects with schizophrenia, based on a structural brain marker for the disease such as the DLPFC. Such classification should be performed in first-episode patients in future studies, by considering males and females separately.

Cattaneo Dario, Meraviglia Paola, Cozzi Valeria, Baldelli Sara, Milani Greta, Clementi Emilio (2012); ATYPICAL PHARMACOKINETICS OF ATAZANAVIR IN AN HIV-1-INFECTED PATIENT; Fundamental & Clinical Pharmacology, 26(2):204-206

Doi: 10.1111/j.1472-8206.2010.00905.x PMID: 21210843

I.F. 2011: 1,799

An HIV-infected patient with very low atazanavir (ATV) plasma trough concentrations despite clinical signs of poor drug tolerability was described. By therapeutic drug monitoring (TDM), the authors found that the patient had an atypical ATV pharmacokinetics characterized by rapid drug absorption followed by very fast drug clearance probably attributable to his genetic background. This case underlines the importance of traditional and pharmacogenetic-based TDM for the individualization of ATV therapy in HIV-1 patients.

Cattaneo Dario, Ripamonti Diego, Gervasoni Cristina, Landonio Simona, Meraviglia Paola, Baldelli Sara, Cozzi Valeria, Fucile Serena, Clementi Emilio (2012); LIMITED SAMPLING STRATEGIES FOR THE ESTIMATION OF RALTEGRAVIR DAILY EXPOSURE IN HIV-INFECTED PATIENTS; Journal of Clinical Pharmacology, 52(3):440-445

Doi: 10.1177/0091270010395939 PMID: 21383337

I.F. 2011: 2,911

Stepwise multiple regression analyses were applied to 50 raltegravir pharmacokinetic profiles from 50 HIV patients with the goal to identify limited sampling strategies for the prediction of drug area under the time-concentration curve (AUC(0-12)). Raltegravir single sampling point-based equations failed to reliably predict daily drug exposure. Conversely, different algorithms based on few samples and associated with good correlation, acceptable bias, and imprecision with the measured raltegravir AUC(0-12) were identified. These models could used to predict raltegravir exposure for clinic or research purposes.

Cattaneo Dario, Gervasoni Cristina, Cozzi Valeria, Baldelli Sara, Fucile Serena, Meraviglia Paola, Landonio Simona, Boreggio Simona, Rizzardini Giuliano, Clementi Emilio (2012); CO-ADMINISTRATION OF RALTEGRAVIR REDUCES DAILY DARUNAVIR EXPOSURE IN HIV-1 INFECTED PATIENTS; Pharmacological Research, 65(2):198-203

Doi: 10.1016/j.phrs.2011.09.006 **PMID: 21958880**

I.F. 2011: 4,436

The potential drug-to-drug interaction between darunavir and raltegravir in the setting of HIV infection is a highly debated issue still unresolved. In the present study we have evaluated the pharmacokinetics of darunavir and ritonavir in 53 HIV-1 infected patients with or without concomitant raltegravir administration. The assessment of trough plasma drug concentrations was carried out in all subjects and the potential influence of raltegravir on darunavir and ritonavir disposition, assessed by specific pharmacokinetic evaluations in a subgroup of 25 patients. No significant differences on darunavir and ritonavir plasma trough levels were observed between patients receiving or not raltegravir. Co-administration of raltegravir was, however, associated with a 40% reduction in darunavir C(max) and estimated AUC(0-24), as well a 60% increase in the estimated darunavir clearance compared with values measured in patients not given raltegravir. Notably, this interaction was independent of the dosage of darunavir and not due to effects of raltegravir on the pharmacokinetics of ritonavir. These results should be taken into account when darunavir-based regimens are implemented in the setting of HIV, especially considering that this drug is usually administered at fixed daily dose and no therapeutic drug monitoring is performed in most centres.

Cattaneo Dario, Ripamonti Diego, Baldelli Sara, Cozzi Valeria, Fucile Serena, Clementi Emilio (2012); LIMITED SAMPLING STRATEGIES FOR THE ESTIMATION OF ATAZANAVIR DAILY EXPOSURE IN HIV-

INFECTED PATIENTS; Fundamental & Clinical Pharmacology, in press

Doi: 10.1111/j.1472-8206.2011.01005.x PMID: 22044510

I.F. 2011: 1,799

Stepwise multiple regression analyses were applied to 44 atazanavir pharmacokinetic profiles from 44 HIV-1 infected patients concomitantly treated with raltegravir with the goal of identifying limited sampling strategies for the prediction of drug AUC(0-12) . Atazanavir trough-based equations failed to reliably predict daily drug exposure in patients with low drug bioavailability. Conversely, different algorithms based on few samples and associated with good correlation, acceptable bias and imprecision with the measured atazanavir AUC(0-12) were identified. These models could be used to predict atazanavir exposure for clinic or research purposes.

Cattaneo Dario*, Gervasoni Cristina*, Meraviglia Paola, Landonio Simona, Fucile Serena, Cozzi Valeria, Baldelli Sara, Pellegrini Michela, Galli Massimo, Clementi Emilio (2012); INTER- AND INTRA-PATIENT VARIABILITY OF RALTEGRAVIR PHARMACOKINETICS IN HIV-1-INFECTED SUBJECTS; Journal of Antimicrobial Chemotherapy, 67(2):460-464

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1093/jac/dk498 PMID: 22127581

I.F. 2011: 5,068

OBJECTIVES: Limited studies in healthy volunteers and in HIV-1-infected patients have shown that raltegravir pharmacokinetics are characterized by high inter-patient variability. Only scanty data are, however, available on intra-patient raltegravir variability. The present study was designed to evaluate in parallel the inter- and intra-patient variability of raltegravir pharmacokinetics in HIV-1-infected patients during routine therapeutic drug monitoring (TDM). METHODS: Fifteen HIV-infected patients treated with highly active antiretroviral therapy containing 400 mg of raltegravir twice daily were included in the study. Pharmacokinetic evaluations were performed during two consecutive visits. Only patients given raltegravir for at least 1 month and with no changes in antiretroviral and concomitant therapy between the two pharmacokinetic evaluations were considered. Raltegravir plasma concentrations were determined by a validated HPLC method. Blood samples were collected at 0, 1, 2, 3 and 4 h after the morning drug dose. Raltegravir AUC(0-12) was estimated using a recently developed algorithm.

RESULTS: The pharmacokinetic evaluation was repeated after an average of 52 ± 68 days. Raltegravir AUC(0-12) values ranged from 1495 to 49051 ng•h/mL. The main finding was that intra-patient variability was a large component of the overall variability in raltegravir pharmacokinetics. In some instances the difference between raltegravir AUC(0-4) and AUC(0-12) measured in the same patient during two consecutive evaluations exceeded 110% and 75%, respectively.
CONCLUSIONS: The pharmacokinetics of raltegravir in HIV-1-infected subjects are characterized not only by inter-patient variability but also by high intra-patient variability. This condition limits the application of TDM for raltegravir, and might potentially affect patient outcome.

Cimolin Veronica, Beretta Elena, Piccinini Luigi, Turconi Anna Carla, Locatelli Federica, Galli Manuela, Strazzer Sandra (2012); CONSTRAINT-INDUCED MOVEMENT THERAPY FOR CHILDREN WITH HEMIPLEGIA AFTER TRAUMATIC BRAIN INJURY: A QUANTITATIVE STUDY; Journal of Head Trauma Rehabilitation, 27(3):177-187

Doi: 10.1097/HTR.0b013E3182172276 PMID: 21522025

I.F. 2011: 3,333

OBJECTIVE: The aims of this study are to quantify the movement limitation of upper limbs in hemiplegic children with traumatic brain injury (TBI) by using a clinical-functional scale and upper limb kinematics and to evaluate the effectiveness of constraint-induced movement therapy (CIMT) on upper limbs.
DESIGN: Pre-post study.
SETTING: Clinical rehabilitation research laboratory.
PARTICIPANTS: Ten children with TBI.
MAIN OUTCOME MEASURES: The participants were evaluated by clinical examinations (Gross Motor Function Measure, Besta scale, Quality of Upper Extremities Skills Test, and Manual Ability Classification System) and 3D kinematic movement analysis of the upper limb before the CIMT program (pretest: 0.7 years after the injury) and at the end of the program (posttest: 10 weeks later).
RESULTS: After the CIMT, most of the clinical measures improved significantly. Some significant improvements were present in terms of kinematics, in particular, in the movement duration and the velocity of movement execution of both tasks; the index of curvature and the average jerk improved, respectively, during reaching and hand-to-mouth task, while the adjusting sway parameter decreased during the 2 movements. Significant improvements were found in upper limb joint excursion after the rehabilitative programme too.

CONCLUSIONS: Our results suggest that the CIMT program can improve movement efficiency and upper limb function in children after TBI. The integration of the clinical outcomes and upper limb kinematics revealed to be crucial in detecting the effects of the CIMT programme.

Corradi-Dell'Acqua Corrado, Tomelleri Luisa, Bellani Marcella, Rambaldelli Gianluca, Cerini Roberto, Pozzi Mucelli Roberto, Balestrieri Matteo, Tansella Michele, Brambilla Paolo (2012); THALAMIC-INSULAR DYSCONNECTIVITY IN SCHIZOPHRENIA: EVIDENCE FROM STRUCTURAL EQUATION MODELING; Human Brain Mapping, 33(3):740-752

Doi: 10.1002/hbm.21246 **PMID: 21484952**

I.F. 2011: 5,880

Structural and functional studies have shown that schizophrenia is often associated with frontolimbic abnormalities in the prefrontal and mediotemporal regions. It is still unclear, however, if such dysfunctional interaction extends as well to relay regions such as the thalamus and the anterior insula. Here, we measured gray matter volumes of five right-hemisphere regions in 68 patients with schizophrenia and 77 matched healthy subjects. The regions were amygdala, thalamus, and entorhinal cortex (identified as anomalous by prior studies on the same population) and dorsolateral prefrontal cortex and anterior insula (isolated by voxel-based morphometry analysis). We used structural equation modeling and found altered path coefficients connecting the thalamus to the anterior insula, the amygdala to the DLPFC, and the entorhinal cortex to the DLPFC. In particular, patients exhibited a stronger thalamus-insular connection than healthy controls. Instead, controls showed positive entorhinal-DLPFC and negative amygdalar-DLPFC connections, both of which were absent in the clinical population. Our data provide evidence that schizophrenia is characterized by an impaired right-hemisphere network, in which intrahemispheric communication involving relay structures may play a major role in sustaining the pathophysiology of the disease.

Corti Stefania, Nizzardo Monica, Simone Chiara, Falcone Marianna, Donadoni Chiara, Salani Sabrina, Rizzo Federica, Nardini Martina, Riboldi Giulietta, Magri Francesca, Zanetta Chiara, Faravelli Francesca, Bresolin Nereo, Comi Giacomo Pietro (2012); DIRECT REPROGRAMMING OF HUMAN ASTROCYTES INTO NEURAL STEM CELLS AND NEURONS; Experimental Cell Research, 318(13):1528-1541

Doi: 10.1016/j.yexcr.2012.02.40 **PMID: 22426197**

I.F. 2011: 3,580

Generating neural stem cells and neurons from reprogrammed human astrocytes is a potential strategy for neurological repair. Here we show de-differentiation of human cortical astrocytes into the neural stem/progenitor phenotype to obtain progenitor and mature cells with a neural fate. Ectopic expression of the reprogramming factors OCT4, SOX2, or NANOG into astrocytes in specific cytokine/culture conditions activated the neural stem gene program and induced generation of cells expressing neural stem/precursor markers. Pure CD44+ mature astrocytes also exhibited this lineage commitment change and did not require passing through a pluripotent state. These astrocyte-derived neural stem cells gave rise to neurons, astrocytes, and oligodendrocytes and showed in vivo engraftment properties. ASCL1 expression further promoted neuronal phenotype acquisition in vitro and in vivo. Methylation analysis showed that epigenetic modifications underlie this process. The restoration of multipotency from human astrocytes has potential in cellular reprogramming of endogenous central nervous system cells in neurological disorders.

Crimella Claudia, Baschirotto Cinzia, Arnoldi Alessia, Tonelli Alessandra, Tenderini Erika, Airoldi Giovanni, Martinuzzi Andrea, Trabacca Antonio, Losito Luciana, Scarlato Marina, Benedetti Sara, Scarpini Elio, Spinicci Gabriella, Bresolin Nereo, Bassi Maria Teresa (2012); MUTATIONS IN THE MOTOR AND STALK DOMAINS OF KIF5A IN SPASTIC PARAPLEGIA TYPE 10 AND IN AXONAL CHARCOT MARIE TOOTH TYPE 2; Clinical Genetics, 82(2):157-164

Doi: 10.1111/j.1399-0004.2011.01717.x PMID: 21623771

I.F. 2011: 3,128

Mutations in the motor and stalk domains of KIF5A in spastic paraplegia type 10 and in axonal Charcot-Marie-Tooth type 2. Spastic paraplegia type 10 (SPG10) is an autosomal dominant form of hereditary spastic paraplegia (HSP) due to mutations in KIF5A, a gene encoding the neuronal kinesin heavy chain implicated in anterograde axonal transport. KIF5A mutations were found in both pure and complicated forms of the disease; a single KIF5A mutation was also detected in a CMT2 patient belonging to an SPG10 mutant family. To confirm the involvement of the KIF5A gene in both CMT2 and SPG10 phenotypes and to define the frequency of KIF5A mutations in an Italian HSP patient population, we performed a genetic screening of this gene in a series of 139 HSP and 36 CMT2 affected subjects. We identified five missense changes, four in five HSP patients and one in a CMT2 subject. All mutations, including the one segregating in the CMT2 patient, are localized in

the kinesin motor domain except for one, falling within the stalk domain and predicted to generate protein structure destabilization. The results obtained indicate a KIF5A mutation frequency of 8.8% in the Italian HSP population and identify a region of the kinesin protein, the stalk domain, as a novel target for mutation. In addition, the mutation found in the CMT2 patient strengthens the hypothesis that CMT2 and SPG10 are the extreme phenotypes resulting from mutations in the same gene.

D'Angelo Maria Grazia, Gandossini Sandra, Martinelli Boneschi Filippo, Sciorati Clara, Bonato Sara, Brighina Erika, Comi Giacomo Pietro, Turconi Anna Carla, Magri Francesca, Stefanoni Giuseppe, Brunelli Silvia, Bresolin Nereo, Cattaneo Dario, Clementi Emilio (2012); NITRIC OXIDE DONOR AND NON STEROIDAL ANTI INFLAMMATORY DRUGS AS A THERAPY FOR MUSCULAR DISTROPHIES: EVIDENCE FROM A SAFETY STUDY WITH PILOT EFFICACY MEASURES IN ADULT DYSTROPHIC PATIENTS; Pharmacological Research, 65(4):472-479

Doi: 10.1016/j.phrs.2012.01.006 **PMID: 22306844**

I.F. 2011: 4,436

This open-label, single centre pilot study was designed to evaluate safety and tolerability of the combination of the drugs isosorbide dinitrate, a nitric oxide donor, and ibuprofen, a non steroid anti-inflammatory drug, in a cohort of adult dystrophic patients (Duchenne, Becker and Limb-Girdle Muscular Dystrophy). Seventy-one patients were recruited: 35, treated with the drug combination for 12 months, and 36 untreated. Safety and adverse events were assessed by reported signs and symptoms, physical examinations, blood tests, cardiac and respiratory function tests. Exploratory outcomes measure, such as the motor function measure scale, were also applied. Good safety and tolerability profiles of the long-term co-administration of the drugs were demonstrated. Few and transient side effects (i.e. headache and low blood pressure) were reported. Additionally, exploratory outcomes measures were feasible in all the disease population studied and evidenced a trend towards amelioration that reached statistical significance in one dimension of the MFM scale. Systemic administration of ibuprofen and isosorbide dinitrate provides an adequate safety margin for clinical studies aimed at assessing efficacy.

De Cunto Angela, Bensa Marco, Tonelli Alessandra (2012); A CASE OF FAMILIAL HEMIPLEGIC MIGRAINE ASSOCIATED WITH A NOVEL ATP1A2 GENE MUTATION; Pediatric Neurology, 47(2):133-136

Doi: 10.1016/j.pediatrneurol.2012.04.012 **PMID: 22759692**

I.F. 2011: 1,522

Hemiplegic migraine constitutes an unusual form, characterized by periodic attacks of migraine with a motor component (hemiplegia). Familial forms are dominantly inherited, and are attributable to mutations in genes encoding proteins involved in ion transportation, including ATP1A2, which codes for the α-2 isoform of the sodium-potassium adenosine triphosphatase, a P-type cation transport adenosine triphosphatase, and responsible for the so-called familial hemiplegic migraine type 2. We describe a 9-year-old boy affected by familial hemiplegic migraine, with a novel ATP1A2 gene mutation (c.1799T>C p.V600A) in exon 13. Long-term treatment with flunarizine resulted in a good clinical response and the prevention of further attacks.

Delvecchio Giuseppe, Fossati Philippe, Boyer Patrice, Brambilla Paolo, Falkai Peter, Gruber Oliver, Hietala Jarmo, Lawrie Stephen M., Martinot Jean-Luc, McIntosh Andrew M., Meisenzahl Eva, Frangou Sophia (2012); COMMON AND DISTINCT NEURAL CORRELATES OF EMOTIONAL PROCESSING IN BIPOLAR DISORDER AND MAJOR DEPRESSIVE DISORDER: A VOXEL-BASED META-ANALYSIS OF FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDIES; European Neuropsychopharmacology, 22(2):100-113

Doi: 10.1016/j.euroneuro.2011.07.003 **PMID: 21820878**

I.F. 2011: 4,046

Neuroimaging studies have consistently shown functional brain abnormalities in patients with Bipolar Disorder (BD) and Major Depressive Disorder (MDD). However, the extent to which these two disorders are associated with similar or distinct neural changes remains unclear. We conducted a systematic review of functional magnetic resonance imaging studies comparing BD and MDD patients to healthy participants using facial affect processing paradigms. Relevant spatial coordinates from twenty original studies were subjected to quantitative Activation Likelihood Estimation meta-analyses based on 168 BD and 189 MDD patients and 344 healthy controls. We identified common and distinct patterns of neural engagement for BD and MDD within the facial affect processing network. Both disorders were associated with increased engagement of limbic regions. Diagnosis-specific differences were observed in cortical, thalamic and striatal regions. Decreased ventrolateral prefrontal cortical engagement was associated with BD while relative hypoactivation of the sensorimotor cortices was seen in MDD. Increased responsiveness in the thalamus and basal ganglia were associated with BD. These findings were modulated by stimulus valence. These data suggest that

whereas limbic overactivation is reported consistently in patients with mood disorders, future research should consider the relevance of a wider network of regions in formulating conceptual models of BD and MDD.

Dusi Nicola, Perlini Cinzia, Bellani Marcella, Brambilla Paolo (2012); ALLA RICERCA DI ENDOFENOTIPI PSICOSOCIALI NELLA SCHIZOFRENIA: IL RUOLO INNOVATIVO DEL BRAIN IMAGING; Rivista di Psichiatria, 47(2):76-88

PMID: 22622244

I.F. 2011: 0,235

La schizofrenia è un disturbo con manifestazioni cliniche eterogenee e un decorso longitudinale spesso invalidante. Un approccio di ricerca basato sull'accurata definizione delle caratteristiche cliniche, del funzionamento sociale e dei deficit cognitivi riportati dai pazienti consente una più chiara definizione della malattia. Le tecniche di risonanza magnetica (RM) possono permettere di identificare indicatori biologici forti, e soprattutto quantitativamente misurabili, di sottogruppi diversi di pazienti con schizofrenia con caratteristiche simili, rendendo più facilmente indagabile la componente ereditaria della malattia. La relazione tra variabili biologiche e clinico-psicosociali nei pazienti con schizofrenia viene qui descritta attraverso
le osservazioni trasversali, prospettiche o longitudinali effettuate negli ultimi decenni. I pazienti con caratteristiche di malattia più grave e inabilitante risultano avere un aumento di volume dei ventricoli laterali e una riduzione di volume della corteccia prefrontale, temporale e occipitale oltre che di strutture sottocorticali come i nuclei della base, il talamo e il sistema limbico. Queste caratteristiche neurobiologiche risultano anche essere predittive di un esito peggiore di malattia a lunga scadenza, come confermato da studi prospettici e longitudinali sia in popolazioni con malattia cronica, sia al primo episodio di malattia. L'identificazione di sottotipi più omogenei di pazienti con schizofrenia può fornire un utile sviluppo della ricerca sull'eziopatologia della malattia e favorire strategie di intervento clinico e riabilitativo più efficaci.

Fabbro Franco, Tomasino Barbara (2012); A NICE THEORY HAS PROBABLY MORE TO DO WITH AESTHETICS THAN REALITY. COMMENT ON "INTERACTION BETWEEN LEXICAL AND GRAMMATICAL LANGUAGE SYSTEMS IN THE BRAIN" BY ALFREDO ARDILA; Physics of Life Reviews, 9(2):215-216

Doi: 10.1016/j.plrev.2012.05.005 **PMID: 22626936**

I.F. 2011: 7,208

Abstract non disponibile

Fedrizzi Ermellina, Rizzotto Melissa Rosa, Turconi Anna Carla, Pagliano Emanuela, Fazzi Elisa, Visonà Dalla Pozza Laura, Facchin Paola, GIPCI Study Group (Germiniasi Chiara, Magagnin Bertilla, Martinuzzi Andrea, Megliani Chiara, Molteni Francesca, Stefanoni Giuseppe, Trabacca Antonio, Vespino Teresa) (2012); UNIMANUAL AND BIMANUAL INTENSIVE TRAINING IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY AND PERSISTENCE IN TIME OF HAND FUNCTION IMPROVEMENT: 6-MONTH FOLLOW-UP RESULTS OF A MULTISITE CLINICAL TRIAL; Journal of Child Neurology, in press

Doi: 10.1177/0883073812443004 PMID: 22580904

I.F. 2011: 1,748

This study aims to compare in hemiplegic children the effectiveness of intensive training (unimanual and bimanual) versus standard treatment in improving hand function, assessing the persistence after 6 months. A multicenter, prospective, cluster-randomized controlled clinical trial was designed comparing 2 groups of children with hemiplegic cerebral palsy, treated for 10 weeks (3 h/d 7 d/wk; first with unimanual constraint-induced movement therapy, second with intensive bimanual training) with a standard treatment group. Children were assessed before and after treatment and at 3 and 6 months postintervention using Quality of Upper Extremity Skills Test (QUEST) and Besta Scales. One hundred five children were recruited (39 constraint-induced movement therapy, 33 intensive bimanual training, 33 standard treatment). Constraint-induced movement therapy and intensive bimanual training groups had significantly improved hand function, showing constant increase in time. Grasp improved immediately and significantly with constraint-induced movement therapy, and with bimanual training grasp improved gradually, reaching the same result. In both, spontaneous hand use increased in long-term assessment.

Ferraris Laurenzia, Viganò Ottavia, Peri Anna, Tarkowski Maciej, Milani Greta, Bonora Stefano, Adorni Fulvio, Gervasoni Cristina, Clementi Emilio, Di Perri Giovanni, Galli Massimo, Riva Agostino (2012); SWITCHING TO UNBOOSTED ATAZANAVIR REDUCES BILIRUBIN AND TRIGLYCERIDES WITHOUT COMPROMISING TREATMENT EFFICACY IN UGT1A1*28 POLYMORPHISMS CARRIERS; Journal of Antimicrobial Chemotherapy, in press

Doi: 10.1093/jac/dks175 PMID: 22661571

I.F. 2011: 5,068

OBJECTIVES: Hyperbilirubinaemia is a frequent complication of atazanavir-containing antiretroviral therapy and its severity is related to UDP-glucuronosyl transferase (UGT) 1A1*28 polymorphism. The aim of this study was to evaluate the safety and outcome of unboosted atazanavir-containing regimens based on the genetic constitution.
METHODS: Fifty-one HIV-1-infected patients on boosted atazanavir were prospectively enrolled in the study. Twenty-five patients with a UGT1A1*28 allele switched to 400 mg of unboosted atazanavir.
RESULTS: At baseline, UGT1A1 heterozygous and homozygous patients had significantly higher bilirubin levels than wild-type ($P=0.012$ and $P<0.001$, respectively). After ritonavir removal, a reduction was observed in total bilirubin (from 4.09 to 1.82 mg/dL; $P<0.001$), γ-glutamyl transpeptidase ($P=0.015$), triglycerides ($P=0.03$) and total cholesterol ($P=0.05$). No significant changes in CD4 T cell count and no increases in viral load were observed 12 months after unboosting. Plasma drug monitoring after ritonavir removal revealed the presence of therapeutic atazanavir concentrations in all patients except one with poor therapy adherence.
CONCLUSIONS: UGT1A1*28 is significantly related to hyperbilirubinaemia in HIV-1 patients receiving atazanavir. Genotyping before the initiation of antiretroviral therapy can reduce the emergence of severe hyperbilirubinaemia. Unboosted atazanavir-containing therapy is safe and efficacious in patients with an undetectable viral load with a UGT1A1*28 polymorphism, allowing the use of atazanavir in patients otherwise likely unable to receive it.

Fons Carmen, Campistol Jaume, Panagiotakaki Eleni, Giannotta Melania, Arzimanoglou Alexis, Gobbi Giuseppe, Neville Brian, Ebinger Friedrich, Nevsimalova Sona, Laan Laura, Casaer Paul, Spiel Georg, Ninan Miriam, Sange Guenter, Artuch Rafael, Schyns Tsveta, Vavassori Rosaria, Poncelin Dominique, The ENRAH Consortium (Bassi Maria Teresa, Zucca Claudio) (2012); ALTERNATING HEMIPLEGIA OF CHILDHOOD: METABOLIC STUDIES IN THE LARGEST EUROPEAN SERIES OF PATIENTS; European Journal of Paediatric Neurology, 16(1):10-14

Doi: 10.1016/j.ejpn.2011.08.006 **PMID: 21945173**

I.F. 2011: 2,213

Alternating hemiplegia of childhood (AHC) is a rare disorder with diagnosis based on clinical criteria, as no laboratory, neuroradiological or genetic markers are currently available. The pathogenic mechanisms are still an enigma. Some hypotheses have been proposed such as hemiplegic migraine variant,

epileptic mechanism, channelopathy and mitochondrial disorder, but none of these has been confirmed. Our aim was to analyze the results of metabolic studies performed on a series of 157 European patients who fulfilled diagnostic criteria for AHC. We tried to find a common metabolic abnormality, related with AHC. We did not find significant abnormalities in basic metabolic screening, at different ages. Neurotransmitters in cerebrospinal fluid (n = 26) were normal in all of the patients. Mitochondrial respiratory chain enzyme activities were analyzed in 19 muscle biopsies; in 4 cases, different MRC enzyme deficiencies were demonstrated, ranging from mild-unspecific deficiencies to more profound and probably primary defects. Although we did not find specific metabolic markers in our series, some metabolic disorders such as pyruvate dehydrogenase deficiency, MELAS, cerebral glucose transporter defect and neurotransmitter deficiency can exhibit symptoms similar to those of AHC and need to be ruled out before a diagnosis of AHC can be established. Further studies including high-throughput diagnostic technologies seem necessary to elucidate the etiology of this severe and enigmatic disorder.

Franceschini Sandro*, Gori Simone, Ruffino Milena, Pedrolli Katia, Facoetti Andrea* (2012); A CAUSAL LINK BETWEEN VISUAL SPATIAL ATTENTION AND READING ACQUISITION; Current Biology, 22(9):814-819

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/J.CUB.2012.03.013 **PMID: 22483940**

I.F. 2011: 9,647

Reading is a unique, cognitive human skill crucial to life in modern societies, but, for about 10% of the children, learning to read is extremely difficult. They are affected by a neurodevelopmental disorder called dyslexia. Although impaired auditory and speech sound processing is widely assumed to characterize dyslexic individuals, emerging evidence suggests that dyslexia could arise from a more basic cross-modal letter-to-speech sound integration deficit. Letters have to be precisely selected from irrelevant and cluttering letters by rapid orienting of visual attention before the correct letter-to-speech sound integration applies. Here we ask whether prereading visual parietal-attention functioning may explain future reading emergence and development. The present 3 year longitudinal study shows that prereading attentional orienting--assessed by serial search performance and spatial cueing facilitation--captures future reading acquisition skills in grades 1 and 2 after controlling for age, nonverbal IQ, speech-sound processing, and nonalphabetic cross-modal mapping. Our findings provide the first evidence that visual spatial

attention in preschoolers specifically predicts future reading acquisition, suggesting new approaches for early identification and efficient prevention of dyslexia.

Fumagalli Matteo*, Fracassetti Marco*, Cagliani Rachele, Forni Diego, Pozzoli Uberto, Comi Giacomo Pietro, Marini Federico, Bresolin Nereo, Clerici Mario, Sironi Manuela (2012); AN EVOLUTIONARY HISTORY OF THE SELECTIN GENE CLUSTER IN HUMANS; Heredity, 109(2):117-126

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1038/hdy.2012.20 **PMID: 22549518**

I.F. 2011: 4,597

Molecules involved in leukocyte trafficking have a central role in the development of inflammatory and immune responses. We performed F(ST) analysis of the selectin cluster, as well as of SELPLG, ICAM1 and VCAM1. Peaks of significantly high population genetic differentiation were restricted to two regions in SELP and one in SELPLG. Resequencing data indicated that the region covering SELP exons 11-13 displays high nucleotide diversity in Africans and Europeans (CEU), and a high level of within-species diversity compared with inter-specific divergence. Analysis of inferred haplotypes revealed a complex phylogeny with two deeply separated clades that coalesce at ~3.5 million years (MY) plus a minor clade with a TMRCA (time to the most recent common ancestor) of ~2.2 MY. A splicing assay indicated no haplotype-specific effect on SELP exon 14 inclusion. These data are consistent with a model of multiallelic balancing selection; single-nucleotide polymorphism analysis indicated that the Val640Leu variant represents a likely selection target. In populations of Asian ancestry a distinct haplotype, possibly carrying regulatory variants, has been driven to high frequency by positive selection. No deviation from neutrality was observed for the SELPLG region. Resequencing of SELP in chimpanzees revealed a haplotype phylogeny with extremely deep basal branches, suggesting either long-standing balancing selection or ancestral population structure. Thus, SELP has experienced a complex selective history, possibly as a result of local adaptation. Variants in the gene have been associated with autoimmune and cardiovascular diseases. Association studies would benefit from both taking the complex SELP haplotype structure into account and from analysis of possible regulatory variants in the gene.

Gazzellini S.*, Strazzer Sandra*, Stortini Massimo, Veredice C., Beretta Elena, Lispi Maria Luisa, Petacchi Elisa, Menna Elisabetta,

Cipriani P., Zampolini M., Castelli Enrico (2012); PEDIATRIC REHABILITATION OF SEVERE ACQUIRED BRAIN INJURY: A MULTICENTER SURVEY; European Journal of Physical and Rehabilitation Medicine (continues Europa Medicophysica),48, in press

** Autori che hanno contribuito in ugual misura al lavoro*

PMID: 22522434

I.F. 2011: 1,402

Background: Epidemiological and descriptive data concerning the clinical and socio-demographic characteristics of severe acquired brain injuries (ABI) in pediatric age are meager. In particular, in Italy we only find data concerning traumatic brain injury (TBI) in adults. Earlier data show that the most prevalent etiology in ABI is traumatic and that greater clinical impairments are reported for patients with non-traumatic etiologies.
AIM: The main aims of the GISCAR (Gruppo Italiano per lo Studio delle Gravi Cerebrolesioni Acquisite e Riabilitazione) study are: 1) to define the clinical features of pediatric patients with severe neurological disabilities; 2) to determine the etiology and onset modality of the cerebral lesions; and 3) to analyse the characteristics of the rehabilitation processes and patient outcome in terms of disability, strategies for treatment and clinical picture.
Design: Quasi-epidemiologic.
Setting: In-patient.
Population: 184 pediatric patients with severe ABI were recruited.
Methods: Data collection was done by means of an assessment protocol created and used by a group of Italian neurorehabilitation centers. Traumatic and non traumatic aetiologies (NTBI) have been treated separately.
Results: Traumatic etiology of ABI is the most prevalent (51.6%, N. 95) and about twice as many males as females are involved. Of these cases, 70.5% (N. 67) are the result of a car accident, either as a pedestrian or as a passenger, representing a crucial area for preventive action by the public health services. Eighty-six (46.7%) patients were in the acute state, 19 (10.3%) in subacute state and 76 (42.9%) in chronic condition. The results show that the positive trend for the TBI group was steeper than for NTBIs. Neuropsychological data are also discussed.
Conclusions and Clinical Rehabilitation Impact: We report the first Italian descriptive study on pediatric patients affected by ABI of traumatic or non traumatic etiology. The main points concerning rehabilitation are that major differences between aetiologies must be taken into account and that ABI of any severity in the acute phase may lead to long term disability, confirming the high social and economic impact of this pathology. Our study demonstrates

the great importance of providing specialised rehabilitation centers for pediatric patients, and increases awareness of the importance of ABI prevention.

Giordano Lucio*, Viri Maurizio*, Borgatti Renato*, Lodi Monica, Accorsi Patrizia, Faravelli Francesca, Ferretti Maria Chiara, Grasso Rita, Memo Luigi, Prola Silvia, Pruna Dario, Santucci Margherita, Savasta Salvatore, Verrotti Alberto, Romeo Antonino* (2012); SEIZURES AND EEG PATTERNS IN PALLISTER-KILLIAN SYNDROME: 13 NEW ITALIAN PATIENTS; European Journal of Paediatric Neurology, in press

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.106/j.ejpn.2012.03.003 **PMID: 22464827**

I.F. 2011: 2,213

BACKGROUND AND OBJECTIVES: Pallister-Killian syndrome (PKS) is a rare genetic disorder caused by a tissue-limited mosaic supernumerary isochromosome 12p. Typical facial dysmorphisms, pigmentary abnormalities, and some major malformations are frequently present. Neurological manifestations include mental retardation, hypotonia, and seizures. Epilepsy incidence ranged from 39 to 59% in a previously reported series. No specific clinical and EEG phenotype has ever been reported to describe seizure features, electroclinical patterns, and response to therapy in PKS.
METHODS: This was a multicentre study conducted on 13 Italian children with PKS, as diagnosed by clinical phenotype and confirmed in cultured fibroblasts. All patients underwent several polygraphic video-EEG recordings and brain magnetic resonance imaging.
RESULTS AND CONCLUSIONS: All the patients presented with epilepsy and seizures that started at a mean age of 19 months. In six cases, epilepsy started with epileptic spasms (ES) combined with focal seizures in another case. In four cases, seizures were focal, and this was followed by ES in two patients. In only two cases, epilepsy started with myoclonic seizures, and spasms were never observed. The study provides further evidence that epilepsy is a part of the phenotype of PKS, although a specific clinical and EEG pattern could not be identified. Our cases show how ES with late- or first-year onset is the most common type of seizure. Despite a variable prognosis in terms of response to therapy, a significant proportion of patients achieved good seizure control.

Giorgetta Cinzia, Grecucci Alessandro, Zuanon Sophia, Perini Laura, Balestrieri Matteo, Bonini Nicolao, Sanfey Alan G., Brambilla Paolo (2012); REDUCED RISK-TAKING BEHAVIOR AS A TRAIT FEATURE

OF ANXIETY; Emotion, in press

Doi: 10.1037/a0029119 **PMID: 22775123**

I.F. 2011: 3,875

Affect can have a significant influence on decision-making processes and subsequent choice. One particularly relevant type of negative affect is anxiety, which serves to enhance responses to threatening stimuli or situations. In its exaggerated form, it can lead to psychiatric disorders, with detrimental consequences for quality of life, including the ability to make choices. This study investigated, for the first time, how pathological anxiety affects risk-taking behavior. In this study, 20 anxious participants meeting Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria for either generalized anxiety disorder (n = 10) and for panic attack disorder (n = 10), as well as 20 matched nonanxious controls, performed a gambling task. To investigate the tendency toward either a risk-seeking or a risk-averse behavior, we employed a task that did not allow for learning from outcomes. Anxious participants made significantly fewer risky choices than matched nonanxious participants. Specifically, they become risk-avoidant after gains. Moreover, anxious participants not only were less happy after gains but were also less sad after losses, and they also evinced less desire to change their choices after losses than did nonanxious participants. Importantly, whereas the desire to switch choice was followed by actual choice switch for all participants, happiness directly predicted subsequent risky choices, particularly in the nonanxious participants. Further analyses revealed that the anxious participants' risk-avoidance behavior was independent of different types of anxiety disorder (panic attack disorder and generalized anxiety disorder) as well as of the effects of psychotropic drugs treatment. This study demonstrates a specific role for anxiety in individual decision making. In particular, hypersensitivity to potential threats and pessimistic evaluation of future events reduced risk-taking behavior.

Giovannetti Ambra M., Pagani Marco, Sattin Davide, Covelli V., Raggi Alberto, Strazzer Sandra, Castelli Enrico, Trabacca Antonio, Martinuzzi Andrea, Leonardi Matilde (2012); CHILDREN IN VEGETATIVE STATE AND MINIMALLY CONSCIOUS STATE: PATIENTS' CONDITION AND CAREGIVERS' BURDEN; The Scientific World Journal, 2012:232149

Doi: 10.1100/2012/232149 **PMID: 22454603**

I.F. 2011: 0,000

Caring for children in vegetative state (VS) or minimally conscious state

(MCS) challenges parents and impacts on their well-being. This study aims to evaluate caregivers' health condition, coping, anxiety and depression levels, and how these issues relate to children's disability. 35 children with VS and MCS were administered the disability rating scale (DRS) and 35 caregivers completed the Coping Orientations to Problem Experiences, Short Form-12, Beck Depression Inventory, and the Spielberger State-Trait Anxiety Inventory-Y. Children were mainly males (68.6%), hosted at domicile (77.1%), and diagnosed with VS (60%), with anoxic aetiology (45.7%). Caregivers were mainly mothers (85.7%), married (82.9%), and housewives (51.4%); 60% declared financial difficulties, and 82.9% provided full-time assistance. 57.2% reported depressive symptoms, poor mental health, and high level of state and trait anxiety. "Problem-oriented" ($P < 0.001$) and "emotional-oriented" ($P < 0.001$), were more adopted than "potentially dysfunctional" ones. DRS scores (mean = 22.0; SD = 1.9) did not significantly correlate to any psychological measure. Rehabilitative programs for children with SV and SMC should also provide interventions on surrounding systems: improving the network of psychological support and social assistance may decrease the burden of caregivers and, in turn, improve caring abilities and children quality of life.

Grecucci Alessandro, Giorgetta Cinzia, Brambilla Paolo, Zuanon Sophia, Perini Laura, Balestrieri Matteo, Bonini Nicolao, Sanfey Alan G. (2012); ANXIOUS ULTIMATUMS: HOW ANXIETY DISORDERS AFFECT SOCIOECONOMIC BEHAVIOUR; Cognition & Emotion, in press

Doi: 10.1080/02699931.2012.698982 **PMID: 22775394**

I.F. 2011: 2,522

Although the role of emotion in socioeconomic decision making is increasingly recognised, the impact of specific emotional disorders, such as anxiety disorders, on these decisions has been surprisingly neglected. Twenty anxious patients and twenty matched controls completed a commonly used socioeconomic task (the Ultimatum Game), in which they had to accept or reject monetary offers from other players. Anxious patients accepted significantly more unfair offers than controls. We discuss the implications of these findings in light of recent models of anxiety, in particular the importance of interpersonal factors and assertiveness in an integrated model of decision making. Finally, we were able to show that pharmacological serotonin used to treat anxious symptomatology tended to normalise decision making, further confirming and extending the role of serotonin in co-operation, prosocial behaviour, and social decision making. These results show, for the first time, a different pattern of socioeconomic behaviour in anxiety disordered patients,

in addition to the known memory, attentional and emotional biases that are part of this pathological condition.

Grecucci Alessandro, Brambilla Paolo, Siugzdaite Roma, Londero Danielle, Fabbro Franco, Rumiati Raffaella Ida (2012); EMOTIONAL RESONANCE DEFICITS IN AUTISTIC CHILDREN; Journal of Autism and Developmental Disorders, in press

Doi: 10.1007/s10803-1603-z **PMID: 22806001**

I.F. 2011: 3,341

According to some theories imitation, defined as an action resonance mechanism, is deficient in autism. In contrast, other theories (e.g., the "top down control of imitation" hypothesis) state that the problem is not in imitation per se but in the way social cues modulate imitative responses. In this study, 15 high-functioning children with autism and 15 matched controls were tested for their ability to imitate finger movements preceded by neutral and emotional facial expressions (primes) in a stimulus-response compatibility task. Hand movements performed after neutral expressions did not differ between the two groups (i.e., they both showed a normal imitative tendency). However, hand movements performed after emotional expressions significantly differed between the two populations, with controls, but not autistic spectrum disorder (ASD), showing enhanced imitation in the emotional condition. This study supports the view that, in ASD, imitation abilities are spared but they are not modulated according to the emotional and social context.

Guerini Franca Rosa*, Cagliani Rachele*, Forni Diego, Agliardi Cristina, Caputo Domenico, Cassinotti Andrea, Galimberti Gloria, Fenoglio Chiara, Biasin Mara, Asselta Rosanna, Scarpini Elio, Comi Giacomo Pietro, Bresolin Nereo, Clerici Mario, Sironi Manuela (2012); A FUNCTIONAL VARIANT IN ERAP1 PREDISPOSES TO MULTIPLE SCLEROSIS; Plos One, 7(1):e29931

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1371/journal.pone.0029931 **PMID: 22253828**

I.F. 2011: 4,092

The ERAP1 gene encodes an aminopeptidase involved in antigen processing. A functional polymorphism in the gene (rs30187, Arg528Lys) associates with susceptibility to ankylosying spondylitis (AS), whereas a SNP in the interacting ERAP2 gene increases susceptibility to another inflammatory autoimmune disorder, Crohn's disease (CD). We analysed rs30187 in 572 Italian patients with CD and in 517 subjects suffering from multiple sclerosis

(MS); for each cohort, an independent sex- and age-matched control group was genotyped. The frequency of the 528Arg allele was significantly higher in both disease cohorts compared to the respective control population (for CD, OR=1.20 95%CI: 1.01-1.43, p=0.036; for RRMS, OR=1.26; 95%CI: 1.04-1.51, p=0.01). Meta-analysis with the Wellcome Trust Cases Control Consortium GWAS data confirmed the association with MS (p(meta)=0.005), but not with CD. In AS, the rs30187 variant has a predisposing effect only in an HLA-B27 allelic background. It remains to be evaluated whether interaction between ERAP1 and distinct HLA class I alleles also affects the predisposition to MS, and explains the failure to provide definitive evidence for a role of rs30187 in CD. Results herein support the emerging concept that a subset of master-regulatory genes underlay the pathogenesis of autoimmunity.

Heinzen Erin L., Swoboda Kathryn J., Hitomi Yuki, Gurrieri Fiorella, Nicole Sophie, De Vries Bourkje, Tiziano F. Danilo, Fontaine Bertrand, Walley Nicole M., Heavin Sinead, Panagiotakaki Eleni, the European Alternating Hemiplegia of Childhood (AHC) Genetics Consortium, the Biobanca e Registro Clinico Emiplegia Alternante (IBAHC) Consortium (Bassi Maria Teresa, Zucca Claudio), the European Network Research on Alternating Hemiplegia (ENRAH) for Small and Medium-sized Enterpriese (SMEs) Consortium (Bassi Maria Teresa, Zucca Claudio), Fiori Stefania, Abiusi Emanuela, Di Pietro Lorena, Sweney Matthew T., Newcomb Tara M., Viollet Louis, Huff Chad, Jorde Lynn B., Reyna Sandra P., Murphy Kelley J., Shianna Kevin V., Gumbs Curtis E., Little Latasha, Silver Kenneth, Ptacek Louis J., Haan Joost, Ferrari Michel D., Bye Ann M., Herkes Geoffrey K., Whitelaw Charlotte M., Webb David, Lynch Bryan J., Uldall Peter, King Mary D., Scheffer Ingrid E., Neri Giovanni, Arzimanoglou Alexis, Van Den Maagdenberg Arn M.J.M., Sisodiya Sanjay M., Mikati Mohamad A., Goldstein David B. (2012); DE NOVO MUTATIONS IN ATP1A3 CAUSE ALTERNATING HEMIPLEGIA OF CHILDHOOD; Nature Genetics, in press

Doi: 10.1038/ng.2358 **PMID: 22842232**

I.F. 2011: 35,532

Alternating hemiplegia of childhood (AHC) is a rare, severe neurodevelopmental syndrome characterized by recurrent hemiplegic episodes and distinct neurological manifestations. AHC is usually a sporadic disorder and has unknown etiology. We used exome sequencing of seven patients with AHC and their unaffected parents to identify de novo nonsynonymous mutations in ATP1A3 in all seven individuals. In a subsequent sequence analysis of

ATP1A3 in 98 other patients with AHC, we found that ATP1A3 mutations were likely to be responsible for 78% of the cases; we also identified one inherited mutation in a case of familial AHC. Notably, most AHC cases are caused by one of seven recurrent ATP1A3 mutations, one of which was observed in 36 patients. Unlike ATP1A3 mutations that cause rapid-onset dystonia-parkinsonism, AHC-causing mutations in this gene caused consistent reductions in ATPase activity without affecting the level of protein expression. This work identifies de novo ATP1A3 mutations as the primary cause of AHC and offers insight into disease pathophysiology by expanding the spectrum of phenotypes associated with mutations in ATP1A3.

Hens Kristien, Van El Carla E., Borry Pascal, Cambon-Thomsen Anne, Cornel Martina C, Forzano Francesca, Lucassen Anneke, Patch Christine, Tranebjaerg Lisbeth, Vermeulen Eric, Salvaterra Mariaelena, Tibben Aad, Dierickx Kris (2012); DEVELOPING A POLICY FOR PAEDIATRIC BIOBANKS: PRINCIPLES FOR GOOD PRACTICE; European Journal of Human Genetics, in press

Doi: 10.1038/ejhg.2012.99 PMID: 22713814

I.F. 2011: 4,400

The participation of minors in biobank research can offer great benefits for science and health care. However, as minors are a vulnerable population they are also in need of adequate protective measures when they are enrolled in research. Research using biobanked biological samples from children poses additional ethical issues to those raised by research using adult biobanks. For example, small children have only limited capacity, if any, to understand the meaning and implications of the research and to give a documented agreement to it. Older minors are gradually acquiring this capacity. We describe principles for good practice related to the inclusion of minors in biobank research, focusing on issues related to benefits and subsidiarity, consent, proportionality and return of results. Some of these issues are currently heavily debated, and we conclude by providing principles for good practice for policy makers of biobanks, researchers and anyone involved in dealing with stored tissue samples from children. Actual implementation of the principles will vary according to different jurisdictions

Lasalvia Antonio, Tosato Sarah, Brambilla Paolo, Bertani Mariaelena, Bonetto Chiara, Cristofalo Doriana, Bissoli S., De Santi K., Lazzarotto Lorenza, Zanatta G., Marrella G., Mazzoncini R., Zanoni Martina, Garzotto N., Dolce C., Nicolau S., Ramon L., Perlini Cinzia, Rambaldelli Gianluca, Bellani Marcella, Tansella Michele, Ruggeri

Mirella, the PICOS-Veneto Group (2012); PSYCHOSIS INCIDENT COHORT OUTCOME STUDY (PICOS). A MULTISITE STUDY OF CLINICAL, SOCIAL AND BIOLOGICAL CHARACTERISTICS, PATTERNS OF CARE AND PREDICTORS OF OUTCOME IN FIRST-EPISODE PSYCHOSIS. BACKGROUND, METHODOLOGY AND OVERVIEW OF THE PATIENTS SAMPLE; Epidemiology and Psychiatric Sciences, in press

Doi: 10.1017/S2045796012000315 **PMID: 22794251**

I.F. 2011: 0,000

Aims. This paper aims at providing an overview of the background, design and initial findings of Psychosis Incident Cohort Outcome Study (PICOS).
Methods. PICOS is a large multi-site population-based study on first-episode psychosis (FEP) patients attending public mental health services in the Veneto region (Italy) over a 3-year period. PICOS has a naturalistic longitudinal design and it includes three different modules addressing, respectively, clinical and social variables, genetics and brain imaging. Its primary aims are to characterize FEP patients in terms of clinical, psychological and social presentation, and to investigate the relative weight of clinical, environmental and biological factors (i.e. genetics and brain structure/functioning) in predicting the outcome of FEP.
Results. An in-depth description of the research methodology is given first. Details on recruitment phase and baseline and follow-up evaluations are then provided. Initial findings relating to patients' baseline assessments are also presented. Future planned analyses are outlined.
Conclusions. Both strengths and limitations of PICOS are discussed in the light of issues not addressed in the current literature on FEP. This study aims at making a substantial contribution to research on FEP patients. It is hoped that the research strategies adopted in PICOS will enhance the convergence of methodologies in ongoing and future studies on FEP.

Lay-Ekuakille Aimé, Davis Cristina, Kanoun Olfa, Zhihong Li, Trabacca Antonio (2012); EDITORIAL SPECIAL ISSUE ON SENSORS FOR NONINVASIVE PHYSIOLOGICAL MONITORING; IEEE Sensors Journal, 12(3):413-415 - Editoriale

Doi: 10.1109/JSEN.2011.2168299

I.F. 2011: 1,520

Abstract non disponibile

Lay-Ekuakille Aimé, Vergallo P., Trabacca Antonio, De Rinaldis

Marta, Angelillo Francesco, Conversano F., Casciaro Sergio (2012); LOW-FREQUENCY DETECTION IN ECG SIGNALS AND JOINT EEG-ERGOSPIROMETRIC MEASUREMENTS FOR PRECAUTIONARY DIAGNOSIS; Measurement, in press

Doi: 10.1016/j.measurement.2012.05.024

I.F. 2011: 0,836

HRV (Heart Rate Variability) is an indicator that can be related to different human organs and systems: breathing, heart, brain, pulmonary system, etc.. In cardiac clinic, physical exertion can be pre-assessed thanks to HR (Heart Rate) response using appropriate tests to rule out eventual cardiac dysfunction prior to undergo patient to further exams, surgical operations and rehabilitation activities. HR assessment must determine the capability of patient to continue exertion up to a certain level without having angina pain symptoms and brain dysfunctions. The
variability of HR is a marker of dynamic load because it is sensitive and responsive to acute stress. Moreover it is also a marker of a cumulative wear and tear because it declines with advancing age. In this paper we propose combined measurements of EEG-Ergospirometry and ECG for patient's cardio-pulmonary condition assessment for allowing doctors to make a decision on rehabilitation or surgical operation for people suspected of suffering from epilepsy seizures. Measurements assessed using frequency domain parameters have permitted the determination of low and high frequencies that are related to sympathetic and parasympathetic activities respectively.

Leonardi Matilde, Martinuzzi Andrea, Meucci Paolo, Sala Marina, Russo Emanuela, Buffoni Mara, Raggi Alberto (2012); A POPULATION SURVEY IN ITALY BASED ON THE ICF CLASSIFICATION: RECOGNIZING PERSONS WITH SEVERE DISABILITY; The Scientific World Journal, 2012:189097

Doi: 10.1100/2012/189097 **PMID: 22454601**

I.F. 2011: 0,000

Aim of this paper is to describe functioning of subjects with "severe disability" collected with a protocol based on the International Classification of Functioning, Disability, and Health. It included sections on body functions and structures (BF and BS), activities and participation (A&P), and environmental factors (EF). In A&P, performance without personal support (WPS) was added to standard capacity and performance. Persons with severe disability were those reporting a number of very severe/complete problems in BF or in A&P-capacity superior to mean + 1SD. Correlations between BF and A&P and

differences between capacity, performance-WPS, and performance were assessed with Spearman's coefficient. Out of 1051, 200 subjects were considered as severely disabled. Mild to moderate correlations between BF and A&P were reported (between 0.148 and 0.394 when the full range of impairments/limitations was taken into account; between 0.198 and 0.285 when only the severe impairments/limitations were taken into account); performance-WPS was less similar to performance than to capacity. Our approach enabled identifying subjects with "severe disability" and separating the effect of personal support from that of devices, policies, and service provision.

Leonardi Matilde, Sattin Davide, Giovannetti Ambra M., Pagani Marco, Strazzer Sandra, Villa Federica, Martinuzzi Andrea, Buffoni Mara, Castelli Enrico, Lispi Maria Luisa, Trabacca Antonio, Gennaro Leonarda, Raggi Alberto (2012); FUNCTIONING AND DISABILITY OF CHILDREN AND ADOLESCENTS IN A VEGETATIVE STATE AND A MINIMALLY CONSCIOUS STATE: IDENTIFICATION OF ICF-CY-RELEVANT CATEGORIES; International Journal of Rehabilitation Research, in press

Doi: 10.1097/MRR.0b013e328356425d PMID: 22785047

I.F. 2011: 1,083

Children in a vegetative state (VS) and a minimally conscious state (MCS) experience severe limitations as a consequence of nervous system deficits and require consistent environmental support. However, disability in VS and MCS children has never been described following a model that accounts for the presence of the symptoms, limitations and the support required. Therefore, the aim of this paper is to describe the functioning and disability of children in VS and MCS using the International Classification of Functioning, Disability and Health - version for Children and Youth (ICF-CY). VS and MCS children were enrolled in postacute settings and at home. ICF-CY questionnaires were filled in using information available from clinical documentation, direct observation and from children's parents. ICF-CY categories were considered as relevant if used in at least one-third of the children. In total, 36 children and adolescents (22 in VS, 25 males) were enrolled. The majority developed VS and MCS following a nontraumatic event; the mean age was 114.8 months and the mean duration of condition was 50.1 months. A total of 94 ICF-CY categories were reported as relevant: 26 were from body functions, mostly from mental functions and mobility chapters; nine from body structures, 32 from activities and participation, mostly from learning, mobility and self-care chapters; and 27 from environmental factors. The use of ICF-CY enables to obtain a specific profile of functioning for each child that can be coupled with

known issues, such as loss of brain functions and provision of life-sustaining interventions.

Lo Mauro Antonella, Pochintesta Simona, Romei Marianna, D'Angelo Maria Grazia, Pedotti Antonio, Turconi Anna Carla, Aliverti Andrea (2012); RIB CAGE DEFORMITIES ALTER RESPIRATORY MUSCLE ACTION AND CHEST WALL FUNCTION IN PATIENTS WITH SEVERE OSTEOGENESIS IMPERFECTA; Plos One, 7(4):e35965

Doi: 10.1371/journal.pone.0035965 **PMID: 22558284**

I.F. 2011: 4,092

Background: Osteogenesis imperfecta (OI) is an inherited connective tissue disorder characterized by bone fragility, multiple fractures and significant chest wall deformities. Cardiopulmonary insufficiency is the leading cause of death in these patients.
Methods: Seven patients with severe OI type III, 15 with moderate OI type IV and 26 healthy subjects were studied. In addition to standard spirometry, rib cage geometry, breathing pattern and regional chest wall volume changes at rest in seated and supine position were assessed by opto-electronic plethysmography to investigate if structural modifications of the rib cage in OI have consequences on ventilatory pattern. One-way or two-way analysis of variance was performed to compare the results between the three groups and the two postures.
Results: Both OI type III and IV patients showed reduced FVC and FEV(1) compared to predicted values, on condition that updated reference equations are considered. In both positions, ventilation was lower in OI patients than control because of lower tidal volume ($p<0.01$). In contrast to OI type IV patients, whose chest wall geometry and function was normal, OI type III patients were characterized by reduced ($p<0.01$) angle at the sternum (pectus carinatum), paradoxical inspiratory inward motion of the pulmonary rib cage, significant thoraco-abdominal asynchronies and rib cage distortions in supine position ($p<0.001$).
Conclusions: In conclusion, the restrictive respiratory pattern of Osteogenesis Imperfecta is closely related to the severity of the disease and to the sternal deformities. Pectus carinatum characterizes OI type III patients and alters respiratory muscles coordination, leading to chest wall and rib cage distortions and an inefficient ventilator pattern. OI type IV is characterized by lower alterations in the respiratory function. These findings suggest that functional assessment and treatment of OI should be differentiated in these two forms of the disease.

Lorusso Maria Luisa, Civati Federica, Molteni Massimo, Turconi Anna Carla, Bresolin Nereo, D'Angelo Maria Grazia (2012); SPECIFIC PROFILES OF NEUROCOGNITIVE AND READING FUNCTIONS IN A SAMPLE OF 42 ITALIAN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY; Child Neuropsychology, in press

Doi: 10.1080/09297049.2012.660912 **PMID: 22385039**

I.F. 2010: 1,797

A group of 42 Italian boys with Duchenne Muscular Dystrophy was compared with a control group of 10 boys with Spinal Muscular Atrophy and Osteogenesis Imperfecta on tests assessing general intellectual ability, language, neuropsychological functions, and reading skills with the aim of describing a comprehensive profile of the various functions and investigating their interrelationships. The influence of general intellectual level on performance was analyzed. Further, correlations between various neuropsychological measures and language performances were computed for the group with Duchenne Muscular Dystrophy, as well as the correlations between reading scores and other cognitive and linguistic measures. A general lowering in VIQ, PIQ, and FSIQ scores was found to characterize the group with Duchenne Muscular Dystrophy. Expressive language skills were within the normal range, while syntactic and grammatical comprehension were significantly impaired. The presence of below-average reading performances was further confirmed. However, unlike previous studies on irregular orthographies, the present results show that (a) the mild reading difficulties found in the sample essentially concern speed rather than accuracy; (b) they concern word rather than nonword reading; (c) lower reading performances are related to lower scores in general IQ; (d) no correlations emerge with phonological abilities, verbal short-term memory, or working memory, but rather with long-term memory and lexical skills. This may suggest that language-specific effects modulate the cognitive expressions of Duchenne Muscular Dystrophy and raises the possibility that the dysfunctions underlying the reading difficulties observed in affected readers of regular orthographies involve different neurocognitive systems than the cortico-cerebellar circuits usually invoked.

Losito Luciana, Gennaro Leonarda, De Rinaldis Marta, Cacudi Marilena, Trabacca Antonio (2012); SJOEGREN-LARSSON SYNDROME: PHENOTYPIC VARIABILITY IN TWO BROTHERS WITH A NEUROCUTANEOUS DISORDER (2012); Acta Neurologica Belgica, 112(2):205-208

Doi: 10.1007/s13760-012-0035-z **PMID: 22426667**

I.F. 2011: 0,535

Sjögren-Larsson syndrome (SLS) is a rare autosomal recessively inherited neurocutaneous disorder caused by mutations in the ALDH3A2 gene that encodes fatty aldehyde dehydrogenase, an enzyme that catalyzes the oxidation of fatty aldehyde to fatty acid. It is characterized by an unusual combination of cutaneous and neurologic signs and symptoms. The authors describe two brothers of consanguineous parents with SLS, one of whom was born from a dizygotic twin pregnancy (with an apparently normal sister), and they focus on the variability of the clinical findings of the syndrome even among siblings and twins.

Losito Luciana, Gennaro Leonarda, Cacudi Marilena, De Rinaldis Marta, Trabacca Antonio (2012); MOEBIUS SYNDROME AND HYDROSYRINGOMYELIA: DESCRIPTION OF A NEW ASSOCIATION; Journal of Child Neurology, in press

Doi: 10.1177/0883073812450946 PMID: 22832772

I.F. 2011: 1,748

The diagnosis of Moebius syndrome, a rare congenital disorder, is primarily based on congenital facial and abducent nerve palsy. Involvement of other cranial nerves is also common. Occasionally the V, X, XI, and XII cranial nerves are involved, resulting in a difficulty to chew, swallow and cough, which often leads to respiratory complications. Mental retardation and autism have been reported in some cases. Moebius syndrome can be associated with orofacial anomalies and limb malformations. The authors describe a patient with a confirmed diagnosis of Moebius syndrome associated with hydrosyringomyelia. No case of Moebius syndrome involving primarily the spinal cord has been reported so far. This patient does not present with other factors directly linked to syringomyelia.

Machado Lee R., Hardwick Robert J., Bowdrey Jennifer, Bogle Helen, Knowles Timothy J., Sironi Manuela, Hollox Timothy J. (2012); EVOLUTIONARY HISTORY OF COPY-NUMBER-VARIABLE LOCUS FOR THE LOW-AFFINITY FCγ RECEPTOR: MUTATION RATE, AUTOIMMUNE DISEASE, AND THE LEGACY OF HELMINTH INFECTION; American Journal of Human Genetics, 90(6):973-985

Doi: 10.1016/j.ajhg.2012.04.018 PMID: 22608500

I.F. 2011: 10,603

Both sequence variation and copy-number variation (CNV) of the genes encoding receptors for immunoglobulin G (Fcγ receptors) have been genetically and functionally associated with a number of autoimmune diseases.

However, the molecular nature and evolutionary context of this variation is unknown. Here, we describe the structure of the CNV, estimate its mutation rate and diversity, and place it in the context of the known functional alloantigen variation of these genes. Deletion of Fcγ receptor IIIB, associated with systemic lupus erythematosus, is a result of independent nonallelic homologous recombination events with a frequency of approximately 0.1%. We also show that pathogen diversity, in particular helminth diversity, has played a critical role in shaping the functional variation at these genes both between mammalian species and between human populations. Positively selected amino acids are involved in the interaction with IgG and include some amino acids that are known polymorphic alloantigens in humans. This supports a genetic contribution to the hygiene hypothesis, which states that past evolution in the context of helminth diversity has left humans with an array of susceptibility alleles for autoimmune disease in the context of a helminth-free environment. This approach shows the link between pathogens and autoimmune disease at the genetic level and provides a strategy for interrogating the genetic variation underlying autoimmune-disease risk and infectious-disease susceptibility.

Magri Francesca, Del Bo Roberto, D'Angelo Maria Grazia, Sciacco Monica, Gandossini Sandra, Govoni Alessandra, Napoli Laura, Ciscato Patrizia, Fortunato Francesco, Brighina Erika, Bonato Sara, Bordoni Andreina, Lucchini Valeria, Corti Stefania, Moggio Maurizio, Bresolin Nereo, Comi Giacomo Pietro (2012); FREQUENCY AND CHARACTERISATION OF ANOCTAMIN 5 MUTATIONS IN A COHORT OF ITALIAN LIMB-GIRDLE MUSCULAR DYSTROPHY PATIENTS; Neuromuscular Disorders, in press

Doi: 10.1016/J.NMD.2012.05.001 **PMID: 22742934**

I.F. 2011: 2,797

Limb-girdle muscular dystrophy (LGMD) 2L, caused by mutations in the anoctamin 5 (ANO5) gene, is the third most common LGMD in Northern and Central Europe, where the c.191dupA mutation causes the majority of cases. We evaluated data from 228 Italian LGMD patients to determine the prevalence of LGMD2L and the c.191dupA mutation, and to describe the clinical, muscle biopsy, and magnetic resonance imaging findings in these patients. Forty-three patients who lacked molecular diagnosis were studied for ANO5 mutations, and four novel mutations were found in three probands. Only one proband carried the c.191dupA mutation, which was compound heterozygous with c.2516T>G. Two probands were homozygous for the c.1627dupA and c.397A>T mutations, respectively, while a fourth proband had a compound

heterozygous status (c.220C>T and c.1609T>C). Therefore occurrence and molecular epidemiology of LGMD2L in this Italian cohort differed from those observed in other European countries. ANO5 mutations accounted for ~2% of our sample. Affected patients exhibited benign progression with variable onset and an absence of cardiac and respiratory impairment; muscle biopsy generally showed mild signs, except when performed on the quadriceps muscles; MRI showed predominant involvement of the posterior thigh. Overall these common clinical, morphological and imaging findings could be useful in differential diagnosis.

Mannini Linda, Menga Stefania, Tonelli Alessandra, Zanotti Silvia, Bassi Maria Teresa, Magnani Cinzia, Musio Antonio (2012); SMC1A CODON 496 MUTATIONS AFFECT THE CELLULAR RESPONSE TO GENOTOXIC TREATMENTS; American Journal of Medical Genetics Part A, 158A(1):224-228

Doi: 10.1002/ajmg.a.34384 PMID: 22140011

I.F. 2011: 2,391

Cornelia de Lange syndrome is a pleiotropic developmental syndrome characterized by growth and cognitive impairment, facial dysmorphic features, limb anomalies, and other malformations. Mutations in core cohesin genes SMC1A and SMC3, and the cohesin regulatory gene, NIPBL, have been identified in Cornelia de Lange syndrome probands. Patients with NIPBL mutations have more severe phenotypes when compared to those with mutations in SMC1A or SMC3. To date, 26 distinct SMC1A mutations have been identified in patients with Cornelia de Lange syndrome. Here, we describe a 3-year-old girl with psychomotor and cognitive impairment, mild facial dysmorphic features but no limb anomaly, heterozygous for a c.1487G>A mutation in SMC1A which predicts p.Arg496His. We show that this mutation leads to an impairment of the cellular response to genotoxic treatments.

Marini Andrea (2012); CHARACTERISTICS OF NARRATIVE DISCOURSE PROCESSING AFTER DAMAGE TO THE RIGHT HEMISPHERE; Seminars in Speech and Language, 22(1):68-78

Doi: http://dx.doi.org/10.1055/s-0031-1301164 PMID: 22362325

I.F. 2011: 0,000

The narrative skills of nonaphasic individuals with right hemisphere damage (RHD) were compared with those of a group of healthy participants. All participants scored within the normal range on tests assessing their level of global cognitive impairment, logical visuospatial reasoning, general linguistic

skills, and the potential presence of hemineglect. They were asked to describe the stories portrayed in a set of picture sequences. The individuals with RHD produced descriptions with normal levels of microlinguistic processing but with more tangential errors and conceptually incongruent utterances that lowered their levels of informativeness. A further analysis revealed that these deficits were most evident in persons with anterior lesions to the right hemisphere. These findings lend indirect support to the hypothesis of a major involvement of frontal right hemispheric areas to the process of organization of information in a narrative discourse.

Marino Cecilia, Haiying Meng, Mascheretti Sara, Rusconi Marianna, Cope Natalie, Giorda Roberto, Molteni Massimo, Gruen Jeffrey R. (2012); DCDC2 GENETIC VARIANTS AND SUSCEPTIBILITY TO DEVELOPMENTAL DYSLEXIA; Psychiatric Genetics, 22(1):25-30

Doi: 10.1097/YPG.Ob013e32834acdb2 PMID: 21881542

I.F. 2011: 2,581

OBJECTIVE(S): Developmental dyslexia is a heritable condition, with genetic factors accounting for 44-75% of the variance in performance tests of reading component subphenotypes. Compelling genetic linkage and association evidence supports a quantitative trait locus in the 6p21.3 region that encodes a gene called DCDC2. In this study, we explored the contribution of two DCDC2 markers to dyslexia, related reading and memory phenotypes in nuclear families of Italian origin.
METHODS: The 303 nuclear families recruited on the basis of having a proband with developmental dyslexia have been studied with 6p21.3 markers, BV677278 and rs793862. Marker-trait association was investigated by the quantitative transmission disequilibrium test (version 2.5.1) that allows for the analyses of quantitative traits. Seven phenotypes were used in association analyses, that is, word and nonword reading, word and nonword spelling, orthographic choice, memory, and the affected status based on inclusion criteria.
RESULTS: Quantitative transmission disequilibrium test analyses yielded evidence for association between reading skills and the BV677278 deletion (empirical P-values=0.025-0.029) and between memory and BV677278 allele 10 (empirical P-value=0.0001).
CONCLUSION: Our result adds further evidence in support of DCDC2 contributing to the deficits in developmental dyslexia. More specifically, our data support the view that DCDC2 influences both reading and memory impairments thus shedding further light into the etiologic basis and the phenotypic complexity of developmental dyslexia.

Massimino Maura, Cefalo Graziella, Riva Daria, Biassoni Veronica, Spreafico Filippo, Pecori Emilia, Poggi Geraldina, Collini Paola, Pollo Bianca, Valentini Laura, Potepan Paolo, Seregni Ettore, Casanova Michela, Ferrari Andrea, Luksch Roberto, Polastri Daniela, Terenziani Monica, Pallotti Federica, Clerici Carlo Alfredo, Schiavello Elisabetta, Simonetti Fabio, Meazza Cristina, Catania Serena, Podda Marta, Gandola Lorenza (2012); LONG-TERM RESULTS OF COMBINED PRERADIATION CHEMOTHERAPY AND AGE-TAILORED RADIOTHERAPY DOSES FOR CHILDHOOD MEDULLOBLASTOMA; Journal of Neuro-Oncology, 108(1):163-171

Doi: 10.1007/s11060-012-0822-7 **PMID: 22350379**

I.F. 2011: 3,214

To reduce the sequelae of craniospinal irradiation (CSI) in children under 10 (≥3) years old and to improve the prognosis for high-risk medulloblastoma in adolescents, we adjusted postoperative chemotherapy and CSI doses to patients' stage and age. From 1986 to 1995, 73 patients entered the study. Children under 10 and adolescents with metastases, residual disease (RD) or stage >T3 received postoperative IV vincristine and high-dose (HD) ± intrathecal (IT) methotrexate, while standard-risk adolescents were given IV vincristine and IT methotrexate. Chemotherapy was followed by CSI (19.8 Gy for children <10; 36 Gy for adolescents), with a 54-Gy posterior fossa boost. Maintenance chemotherapy with lomustine and vincristine was administered for a year afterwards. A total of 39 children were under 10 of whom 20 had metastases. Response to chemotherapy was recorded in 70%, but 5-year EFS and OS were only 48 and 56%, respectively. Results were significantly worse for metastatic cases, patients under 10, those with RD, and those staged without MRI (unavailable early in the study). Efforts to preserve survivors' quality of life did not pay off, and most patients over 30 still depended on their parents' income and had severe cognitive/endocrine disabilities. In conclusion, despite a very high response rate with this preradiation HD methotrexate schedule, the outcome for high-risk medulloblastoma patients did not improve (especially when lower CSI doses were used) and patients still developed severe morbidities.

Montirosso Rosario, Provenzi Livio, Calciolari Guido, Borgatti Renato, NEO-ACQUA Gruppo di Studio (2012); MEASURING MATERNAL STRESS AND PERCEIVED SUPPORT IN 25 ITALIAN NICUS; Acta Paediatrica, 101(2):136-142

Doi: 10.1111/j.1651-2227.2011.02440.x **PMID: 21827551**

I.F. 2011: 2,073

Aims: To determine the validity and reliability of the Parental Stressor Scale: Neonatal Intensive Care Unit (PSS: NICU) and the Nurse Parental Support Tool (NPST) for use with Italian parents; to investigate to which extent demographic variables and/or situational factors affect NICU-related maternal stress.
Methods: Mothers (N = 156) of very preterm (VPT) infants from 25 Italian NICUs completed a socio-demographic form, the PSS: NICU and the NPST at discharge. Psychometric properties of both tools were evaluated.
Results: High internal consistency and split-half reliability were found for both measures. The multi-dimensional structure of the PSS:NICU was confirmed. Alteration in parental role emerged as the greatest source of NICU-related stress. Length of stay in NICU and familiar socio-economic status explained partial variance in the PSS: NICU scores. NPST score mitigates the stress because of the infant's appearance and behaviour, but not that related to the parental role alteration.
Conclusions: PSS: NICU and NPST demonstrated adequate psychometric properties in a large sample of Italian mothers. The need for a psychologically informed support to NICU mothers is suggested.

Montirosso Rosario, Fedeli Claudia, Murray Lynne, Morandi Francesco, Brusati Roberto, Ghezzi Perego Guenda, Borgatti Renato (2012); THE ROLE OF NEGATIVE MATERNAL AFFECTIVE STATES AND INFANT TEMPERAMENT IN EARLY INTERACTIONS BETWEEN INFANTS WITH CLEFT LIP AND THEIR MOTHER; Journal of Pediatric Psychology, 37(2):241-250

Doi: 10.1093/jpepsy/jsr089 **PMID: 22004886**

I.F. 2011: 2,910

Objectives: The study examined the early interaction between mothers and their infants with cleft lip, assessing the role of maternal affective state and expressiveness and differences in infant temperament.
Methods: Mother-infant interactions were assessed in 25 2-month-old infants with cleft lip and 25 age-matched healthy infants. Self-report and behavioral observations were used to assess maternal depressive symptoms and expressions. Mothers rated infant temperament.
Results: Infants with cleft lip were less engaged and their mothers showed more difficulty in interaction than control group dyads. Mothers of infants with cleft lip displayed more negative affectivity, but did not report more self-rated depressive symptoms than control group mothers. No group differences were found in infant temperament.

Conclusions: In order to support the mother's experience and facilitate her ongoing parental role, findings highlight the importance of identifying maternal negative affectivity during early interactions, even when they seem have little awareness of their depressive symptoms.

Montirosso Rosario, Del Prete Alberto, Bellù Roberto, Tronick Edward, Borgatti Renato, Neonatal Adequate Care for Quality of Life (NEO-ACQUA) Study Group (2012); LEVEL OF NICU QUALITY OF DEVELOPMENTAL CARE AND NEUROBEHAVIORAL PERFORMANCE IN VERY PRETERM INFANTS; Pediatrics, 129(5):e1129-e1137

Doi: 10.1542/peds.2011-0813 **PMID: 22492762**

I.F. 2011: 5,437

Objective: To examine the relation between the neurobehavior of very preterm infants and the level of NICU quality of developmental care.
Methods: The neurobehavior of 178 very preterm infants (gestational age ≤29 weeks and/or birth weight ≤1500 g) from 25 NICUs participating in a large multicenter, longitudinal study (Neonatal Adequate Care for Quality of Life, NEO-ACQUA) was examined with a standardized neurobehavioral assessment, the NICU Network Neurobehavioral Scale (NNNS). A questionnaire, the NEO-ACQUA Quality of Care Checklist was used to evaluate the level of developmental care in each of the NICUs. A factor analyses applied to NEO-ACQUA Quality of Care Checklist produced 2 main factors: (1) the infant-centered care (ICC) index, which measures parents' involvement in the care of their infant and other developmentally oriented care interventions, and (2) the infant pain management (IPM) index, which measures the NICU approach to and the procedures used for reducing infant pain. The relations between NNNS neurobehavioral scores and the 2 indexes were evaluated.
Results: Infants from NICUs with high scores on the ICC evidenced higher attention and regulation, less excitability and hypotonicity, and lower stress/abstinence NNNS scores than infants from low-care units. Infants from NICUs with high scores on the IPM evidenced higher attention and arousal, lower lethargy and nonoptimal reflexes NNNS scores than preterm infants from low-scoring NICUs.
Conclusions: Very preterm infant neurobehavior was associated with higher levels of developmental care both in ICC and in IPM, suggesting that these practices support better neurobehavioral stability.

Moro Valentina, Pernigo Simone, Avesani R., Bulgarelli C., Urgesi Cosimo, Candidi Matteo, Aglioti Salvatore (2012); VISUAL BODY RECOGNITION IN A PROSOPAGNOSIC PATIENT; Neuropsychologia,

50(1):104-117

Doi: 10.1016/j.neuropsychologia.2011.11.004 PMID: 22100721

I.F. 2010: 3,636

Conspicuous deficits in face recognition characterize prosopagnosia. Information on whether agnosic deficits may extend to non-facial body parts is lacking. Here we report the neuropsychological description of FM, a patient affected by a complete deficit in face recognition in the presence of mild clinical signs of visual object agnosia. His deficit involves both overt and covert recognition of faces (i.e. recognition of familiar faces, but also categorization of faces for gender or age) as well as the visual mental imagery of faces. By means of a series of matching-to-sample tasks we investigated: (i) a possible association between prosopagnosia and disorders in visual body perception; (ii) the effect of the emotional content of stimuli on the visual discrimination of faces, bodies and objects; (iii) the existence of a dissociation between identity recognition and the emotional discrimination of faces and bodies. Our results document, for the first time, the co-occurrence of body agnosia, i.e. the visual inability to discriminate body forms and body actions, and prosopagnosia. Moreover, the results show better performance in the discrimination of emotional face and body expressions with respect to body identity and neutral actions. Since FM's lesions involve bilateral fusiform areas, it is unlikely that the amygdala-temporal projections explain the relative sparing of emotion discrimination performance. Indeed, the emotional content of the stimuli did not improve the discrimination of their identity. The results hint at the existence of two segregated brain networks involved in identity and emotional discrimination that are at least partially shared by face and body processing.

Nobile Maria, Colombo Paola, Bellina Monica, Molteni Massimo, Simone Daniela, Nardocci Franco, Carlet Ombretta, Battaglia Marco (2012); PSYCHOPATHOLOGY AND ADVERSITIES FROM EARLY- TO LATE-ADOLESCENCE: A GENERAL POPULATION FOLLOW-UP STUDY WITH THE CBCL DSM-ORIENTED SCALES; Epidemiology and Psychiatric Sciences, in press

Doi: 10.1017/S2045796012000145 PMID: 22794669

I.F. 2011: 0,000

Aims. Adolescence is a critical transition phase between childhood and adulthood, when the burden of mental disorder may still be prevented. The aim of this study was to evaluate the continuity and discontinuity of behavioural problems in adolescence while taking into account the multiple co-variation of

psychopathological traits and the complex role of recent stressful life events (SLEs).
Methods. This is a 5-year follow-up investigation of emotional and behavioural problems assessed by the newly developed Child Behavior Checklist (CBCL) DSM-Oriented Scales (DOSs) in 420 general population subjects aged 15–19 years.
Results. The DOSs showed good stability, even when multiple co-variation was taken into account. Longitudinal data showed that homotypic evolution of psychopathology was to be expected in the first place. Equifinality and multifinality were also found. Oppositional Defiant Problems emerged to be polyvalent predictors of both internalizing and externalizing problems. Furthermore, Oppositional Defiant Problems predicted more SLEs, which in turn predicted
more Depression, Anxiety and Oppositional Defiant Problems. Mediational analyses confirmed the role of SLEs in partially accounting for the continuity of Oppositional Defiant Problems and for the heterotypic progression towards Affective Problems.
Conclusions. These data underscore early adolescence behavioural problems as an important focus for primary and secondary intervention.

Ogliari Anna, Scaini Simona, Kofler Michael J., Lampis Valentina, Zanoni Annalisa, Pesenti-Gritti Paola, Spatola Chiara A.M., Battaglia Marco, Beidel Deborah C. (2012); PSYCHOMETRIC PROPERTIES OF THE SOCIAL PHOBIA AND ANXIETY INVENTORY FOR CHILDREN (SPAI-C). A SAMPLE OF ITALIAN SCHOOL-AGED CHILDREN FROM THE GENERAL POPULATION; European Journal of Psychological Assessment, 28(1):51-59

Doi: 10.1027/1015-5759/a000090

I.F. 2011: 2,529

Reliable and valid self-report questionnaires could be useful as initial screening instruments for social phobia in both clinical settings and general populations. The present study investigates the factor structure and psychometric properties of the Social Phobia and Anxiety Inventory for Children (SPAI-C) in a sample of 228 children from the Italian general population aged 8 to 11. The children were asked to complete the Italian version of the SPAI-C and the Screen for Child Anxiety Related Emotional Disorders (SCARED) questionnaire. Confirmatory factor analyses revealed that social phobia can be conceptualized as a unitary construct consisting of five distinct but interrelated symptom clusters named Assertiveness, General Conversation, Physical/Cognitive Symptoms, Avoidance, and Public Performance. Internal consistency

of the SPAI-C total scores and two subscales was good; correlations between SPAI-C total scores and SCARED total scores/subscales ranged from moderate to high (Generalized Anxiety Disorder, for social phobia), with the SCARED Social Phobia subscale as the best predictor of SPAI-C total scores. The results indicate that the SPAI-C is a reliable and sensitive instrument suitable for identifying Social Phobia in the young Italian general population.

Olivieri Ivana, Bova Stefania Maria, Urgesi Cosimo, Ariaudo Giada, Perotto Eleonora, Fazzi Elisa, Stronati Mauro, Fabbro Franco, Balottin Umberto, Orcesi Simona (2012); OUTCOME OF EXTREMELY LOW BIRTH WEIGHT INFANTS: WHAT'S NEW IN THE THIRD MILLENIUM? NEUROPSYCHOLOGICAL PROFILES AT FOUR YEARS; Early Human Development, 88(4):241-250

Doi: 10.1016/j.earlhumdev.2011.08.012 PMID: 21962769

I.F. 2011: 2,046

Background: Extremely low birth weight (ELBW) infants, even those not presenting severe neuromotor sequelae, continue to be at risk of developing multiple, complex disorders involving the cognitive, emotional and behavioural domains. Follow-up protocols are able, in the short term, to identify subjects at risk of developing major sequelae, however they fail to identify all children at risk of developing disorders.
Aims: To investigate the cognitive, neuropsychological and behavioural outcomes of a sample of ELBW children at the age of four years in order to identify characteristic profiles.
Study Design: Longitudinal study.
Subjects: 16 healthy ELBW children born in 2005 and followed up until the age of four.
Outcome Measure: Performances on standardised tests evaluating intelligence, memory, cognitive visual functions, attention, and executive functions.
Results: General intelligence was within normal range. Cognitive profile showed mild or moderate deficits with different levels of involvement in many of the examined functions, in particular executive functions, attention and naming.
Conclusion: There emerged a wide-ranging spectrum of weaknesses and deficits involving all the functions examined, which together give rise to a dysexecutive syndrome. Analysis of cognitive profiles showed that the sample could be divided into two subgroups of subjects that differ in the quality of their global cognitive and behavioural functioning. Our results confirm the need to continue follow up of ELBW children until school age, as this will allow early detection of at-risk children and the planning of timely preventive

interventions.

Perlini Cinzia, Marini Andrea, Garzitto Marco, Isola Miriam, Cerruti Stefania, Marinelli Veronica, Rambaldelli Gianluca, Ferro Adele, Tomelleri Luisa, Dusi Nicola, Bellani Marcella, Tansella Michele, Fabbro Franco, Brambilla Paolo (2012); LINGUISTIC PRODUCTION AND SYNTACTIC COMPREHENSION IN SCHIZOPHRENIA AND BIPOLAR DISORDER; Acta Psychiatrica Scandinavica, in press

Doi: 10.1111/j.1600-0477.2012.01864.x PMID: 22509998

I.F. 2011: 4,220

Objective: To explore linguistic abilities in schizophrenia and bipolar disorder. Specifically, the aims of this study were to: i) investigate microlinguistic (lexicon, morphology, syntax) and macrolinguistic (discourse coherence, pragmatics) dimensions of speech production and ii) evaluate syntactic comprehension skills in both schizophrenia and bipolar disorder. Method: Linguistic performance of 30 Italian-speaking patients with schizophrenia, 30 participants with bipolar disorder and 30 healthy controls comparable for age and educational level has been assessed using a story-telling task and a computer-based test of syntactic comprehension. Results: In narrative production, compared with healthy participants, those with schizophrenia had slight problems in speech rate and deficits at both local and global discourse coherence, whereas patients with bipolar disorder showed reduced mean length of utterance. As regards syntactic comprehension, both groups of patients collected more grammatical errors than controls, but they differed with regard to the number and kind of grammatical construction they missed. Conclusion: Linguistic deficits have been detected in both groups of patients, being, however, more severe and generalized in schizophrenia than in bipolar disorder. Such results help us in improving our understanding of the potential psychopathological overlapping between these disorders.

Perlini Cinzia, Bellani Marcella, Brambilla Paolo (2012); STRUCTURAL IMAGING TECHNIQUES IN SCHIZOPHRENIA; Acta Psychiatrica Scandinavica, in press

Doi: 10.1111/j.1600-0447.2012.01868.x PMID: 22533735

I.F. 2011: 4,220

Objective: The aim of this overview study is to translate the technical terminology regarding structural Magnetic Resonance Imaging (sMRI) post-processing analysis into a clinical clear description. Method: We resumed and explained the most popular post-processing methods for structural MRI (sMRI)

data applied in psychiatry and their main contributions to the comprehension of the biological basis of schizophrenia. Results: The region-of-interest (ROI) technique allows to investigate specific brain region size by manual tracing; it is anatomically precise and requires a priori hypothesis, but also it is time-consuming and operator-dependent. The voxel-based morphometry (VBM) detects gray matter density across the whole brain by comparing voxel to voxel; it is operator-independent, does not require a priori hypothesis, and is relatively fast; however, it is limited by multiple comparisons and poor anatomical definition. Finally, computational neuroanatomical analyses have recently been applied to automatically discriminate subjects with schizophrenia from healthy subjects on the basis of MRI images. Conclusion: Structural MRI represents a useful tool in understanding the biological underpinnings of schizophrenia and in planning focused interventions, thus assisting clinicians especially in the early phases of the illness.

Pessina Patrizia*, Conti V.*, Tonlorenzi Rossana, Touvier Thierry, Meneveri Raffaella, Cossu Giulio, Brunelli Silvia (2012); NECDIN ENHANCES MUSCLE RECONSTITUTION OF DYSTROPHIC MUSCLE BY VESSEL-ASSOCIATED PROGENITORS, BY PROMOTING CELL SURVIVAL AND MYOGENIC DIFFERENTIATION; Cell Death and Differentation, 19(5):827-838

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1038/cdd.2011.160 **PMID: 22095287**

I.F. 2011: 8,849

Improving stem cell therapy is a major goal for the treatment of muscle diseases, where physiological muscle regeneration is progressively exhausted. Vessel-associated stem cells, such as mesoangioblasts (MABs), appear to be the most promising cell type for the cell therapy for muscular dystrophies and have been shown to significantly contribute to restoration of muscle structure and function in different muscular dystrophy models. Here, we report that melanoma antigen-encoding gene (MAGE) protein necdin enhances muscle differentiation and regeneration by MABs. When necdin is constitutively overexpressed, it accelerates their differentiation and fusion in vitro and it increases their efficacy in reconstituting regenerating myofibres in the α-sarcoglycan dystrophic mouse. Moreover, necdin enhances survival when MABs are exposed to cytotoxic stimuli that mimic the inflammatory dystrophic environment. Taken together, these data demonstrate that overexpression of necdin may be a crucial tool to boost therapeutic applications of MABs in dystrophic muscle.

Poretti Andrea, Vitiello Giuseppina, Hennekam Raoul C.M., Arrigoni Filippo Silvio Aldo, Bertini Enrico, Borgatti Renato, Brancati Francesco, D'Arrigo Stefano, Faravelli Francesca, Giordano Lucio, Huisman Thierry A.G.M., Iannicelli Miriam, Kluger Gerhard, Kyllerman Marten, Landgren Magnus, Lees Melissa M., Pinelli Lorenzo, Romaniello Romina, Scheer Ianina, Schwarz Christoph E., Spiegel Ronen, Tibussek Daniel, Valente Enza Maria*, Boltshauser Eugen* (2012); DELINEATION AND DIAGNOSTIC CRITERIA OF ORAL-FACIAL-DIGITAL SYNDROME TYPE IV; Orphanet Journal of Rare Diseases, 7(1):4

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1186/1750-1172-7-4 **PMID: 22236771**

I.F. 2011: 5,074

Oral-Facial-Digital Syndrome type VI (OFD VI) represents a rare phenotypic subtype of Joubert syndrome and related disorders (JSRD). In the original report polydactyly, oral findings, intellectual disability, and absence of the cerebellar vermis at post-mortem characterized the syndrome. Subsequently, the molar tooth sign (MTS) has been found in patients with OFD VI, prompting the inclusion of OFD VI in JSRD. We studied the clinical, neurodevelopmental, neuroimaging, and genetic findings in a cohort of 16 patients with OFD VI. We derived the following inclusion criteria from the literature: 1) MTS and one oral finding and polydactyly, or 2) MTS and more than one typical oral finding. The OFD VI neuroimaging pattern was found to be more severe than in other JSRD subgroups and includes severe hypoplasia of the cerebellar vermis, hypoplastic and dysplastic cerebellar hemispheres, marked enlargement of the posterior fossa, increased retrocerebellar collection of cerebrospinal fluid, abnormal brainstem, and frequently supratentorial abnormalities that occasionally include characteristic hypothalamic hamartomas. Additionally, two new JSRD neuroimaging findings (ascending superior cerebellar peduncles and fused thalami) have been identified. Tongue hamartomas, additional frenula, upper lip notch, and mesoaxial polydactyly are specific findings in OFD VI, while cleft lip/palate and other types of polydactyly of hands and feet are not specific. Involvement of other organs may include ocular findings, particularly colobomas. The majority of the patients have absent motor development and profound cognitive impairment. In OFD VI, normal cognitive functions are possible, but exceptional. Sequencing of known JSRD genes in most patients failed to detect pathogenetic mutations, therefore the genetic basis of OFD VI remains unknown. Compared with other JSRD subgroups, the neurological findings and impairment of motor development and cognitive functions in OFD VI are significantly worse, suggesting a correlation with

the more severe neuroimaging findings. Based on the literature and this study we suggest as diagnostic criteria for OFD VI: MTS and one or more of the following: 1) tongue hamartoma(s) and/or additional frenula and/or upper lip notch; 2) mesoaxial polydactyly of one or more hands or feet; 3) hypothalamic hamartoma.

Ranieri Michela, Del Bo Roberto, Bordoni Andreina, Ronchi Dario, Colombo Irene, Riboldi Giulietta, Cosi Alessandra, Servida Maura, Magri Francesca, Moggio Maurizio, Bresolin Nereo, Comi Giacomo Pietro, Corti Stefania (2012); OPTIC ATROPHY PLUS PHENOTYPE DUE TO MUTATIONS IN THE OPA1 GENE: TWO MORE ITALIAN FAMILIES; Journal of the Neurological Sciences, 315(1-2):146-149

Doi: 10.1016/j.jns.2011.12.002 PMID: 22197506

I.F. 2011: 2,353

Autosomal Dominant Optic Atrophy (ADOA) is characterized by the selective degeneration of retinal ganglion cells. The occurrence of mutations in the gene encoding the dynamin-like GTPase protein Optic Atrophy 1 (OPA1) has been observed in about 60-70% of ADOA cases. A subset of missense mutations, mostly within the GTPase domain, has recently been associated with a syndromic ADOA form called “OPA1 plus” phenotype presenting, at muscle level, mitochondrial DNA (mtDNA) instability. In this study we disclosed two OPA1 gene mutations in independent probands from two families affected by OPA1 plus phenotype: the previously reported c.985-2A>G substitution and a novel microdeletion (c.2819-1_2821del). The correlation between genotype and phenotype and the effects of these variants at the transcript level and in the muscle tissue were investigated, confirming the broad complexity in the phenotypic spectrum associated with these OPA1 mutations.

Rescorla Leslie A., Achenbach Thomas M., Ivanova Masha Y., Bilenberg Niels, Bjarnadottir Gudrun, Denner Silvia, Dias Pedro, Dobrean Anca, Doepfner Manfred, Frigerio Alessandra, Goncalves Miguel, Gudmundsson Halldor S., Jusiene Roma, Kristensen Solvejg, Lecannelier Felipe, Leung Patrick, Liu Jianghong, Loebel Sofia P., Machado Barbara Cesar, Markovic Jasminka, Mas Paola A., Esmaeili Elaheh Mohammad, Montirosso Rosario, Plueck Julia, Pronaj Adelina Ahmeti, Rodrigues Jorge T., Rojas Pamela O., Schmeck Klaus, Shahini Mimoza, Silva Jaime R., Van Der Ende Jan, Verhulst Frank (2012); BEHAVIORAL/EMOTIONAL PROBLEMS OF PRESCHOOLERS: CAREGIVER/TEACHER REPORTS FROM 15 SOCIETIES; Journal of Emotional and Behavioral Disorders,

20(2):68-81

Doi: 10.1177/1063426611434158

I.F. 2011: 1,278

This study tested societal effects on caregiver/teacher ratings of behavioral/emotional problems for 10,521 preschoolers from 15 societies. Many societies had problem scale scores within a relatively narrow range, despite differences in language, culture, and other characteristics. The small age and gender effects were quite similar across societies. The rank orders of mean item ratings were similar across diverse societies. For 7,380 children from 13 societies, ratings were also obtained from a parent. In all 13 societies, mean Total Problems scores derived from parent ratings were significantly higher than mean Total Problems scores derived from caregiver/teacher ratings, although the size of the difference varied somewhat across societies. Mean cross-informant agreement for problem scale scores varied across societies. Societies were very similar with respect to which problem items, on average, received high versus low ratings from parents and caregivers/teachers. Within every society, cross-informant agreement for item ratings varied widely across children. In most respects, results were quite similar across 15 very diverse societies.

Restuccia Domenico, Vollono Catello, Del Piero Ivana, Martucci Lucia, Zanini Sergio (2012); SOMATOSENSORY HIGH FREQUENCY OSCILLATIONS REFLECT CLINICAL FLUCTUATIONS IN MIGRAINE; Clinical Neurophysiology, in press

Doi: 10.1016/j.clinph.2012.03.009 **PMID: 22554785**

I.F. 2011: 3,406

Objective: It has been demonstrated that the early part of 600Hz High Frequency Oscillations (HFOs), probably generated in the terminal part of thalamo-cortical somatosensory radiations, are abnormally reduced between attacks in migraineurs. We aimed at verifying whether spontaneous clinical fluctuations in migraine are correlated to HFO changes.
Methods: We recorded somatosensory evoked potentials in 28 migraine patients. Clinical fluctuations (number of attacks in the 6months preceding and following the test) were correlated to the HFOs' amplitudes. Moreover, eight out of 28 patients underwent a longer follow-up, including HFO control and clinical observation during the 12months following the baseline recording.
Results: The amplitude of early presynaptic HFOs was significantly correlated to the clinical evolution, since spontaneous worsening was associated with reduced presynaptic HFOs, whereas spontaneous improvement was

associated with enhanced presynaptic HFOs (correlation test, $p<0.05$). No correlation was found between the amplitude of postsynaptic HFOs and clinical fluctuations. Patients undergoing longer follow-up showed substantially unchanged HFOs, accordingly with their stable clinical condition.
Conclusions: HFOs' enhancement in spontaneously improved patients can reflect the increased activity of brainstem arousal related structures, which in turn increases the thalamo-cortical drive and the cortical lateral inhibition mediated by GABAergic interneurons.
Significance: HFOs' recording could represent a useful tool in the functional assessment of migraine.

Rocca Maria Santa, Fabretto Antonella, Faletra Flavio, Carlet Ombretta, Skabar Aldo, Gasparini Paolo, Pecile Vanna (2012); CONTRIBUTION OF SNP ARRAYS IN DIAGNOSIS OF DELETION 2P11.2-P12; Gene, 492(1):315-318

Doi: 10.1016/j.gene.2011.10.035 **PMID: 22062632**

I.F. 2011: 2,341

Deletions of the short arm of chromosome 2 are exceedingly rare, having been reported in few patients. Furthermore most cases with deletion in 2p11.2-p12 have been studied using standard karyotype and so it is not possible to delineate the precise size of deletions. Here, we describe a 9-year-old girl with a 9.4 Mb de novo interstitial deletion of region 2p11.2-p12 identified by SNP array analysis. The deleted region encompasses over 40 known genes, including LRRTM1, CTNNA2 and REEP1, haploinsufficiency of which could explain some clinical features of this patient such as mental retardation, speech delay and gait abnormalities. A comparison of our case with previously reported patients who present deletions in 2p11.2-p12 was carried out. Our case adds new information to the deletion of 2p11.2-p12, improving the knowledge on this rearrangement.

Romaniello Romina*, Tonelli Alessandra*, Arrigoni Filippo Silvio Aldo, Baschirotto Cinzia, Triulzi Fabio, Bresolin Nereo, Bassi Maria Teresa, Borgatti Renato (2012); A NOVEL MUTATION IN THE BETA-TUBULIN GENE TUBB2B ASSOCIATED WITH COMPLEX MALFORMATION OF CORTICAL DEVELOPMENT AND DEFICITS IN AXONAL GUIDANCE; Developmental Medicine and Child Neurology, 54(8):765-769

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1111/j.1469-8749.2012.04316.x **PMID: 22591407**

I.F. 2011: 2,918

Neurological disorders characterized by abnormal neuronal migration, organization, axon guidance, and maintenance have recently been associated with missense and splice-site mutations in the genes encoding α- and β-tubulin isotypes TUBA1A, TUBB2B, TUBB3, and TUBA8. We found a novel heterozygous mutation c.419G ° > ° C in exon 4 of the gene encoding TUBB2B in a female with microcephaly, agenesis of the corpus callosum, open-lip schizencephaly of the left parietal lobe, extensive polymicrogyria, basal ganglia and thalami dysmorphisms, and vermis and right third nerve hypoplasia. The missense change results in a glycine to alanine substitution; the mutated residue falls within an invariant glycine-rich region and therefore is likely to result in impaired protein function and possibly microtubule formation. This study expands the spectrum of brain malformations associated with mutations in the β-tubulin gene TUBB2B, supporting its critical role in migration/organization and axon guidance processes. In addition, it suggests a possible genetic aetiology of schizencephaly, thus strengthening the hypothesis that there is a common pathophysiological base in polymicrogyria and schizencephaly.

Romei Marianna*, D'Angelo Maria Grazia*, Lo Mauro Antonella, Gandossini Sandra, Bonato Sara, Brighina Erika, Marchi Eraldo, Comi Giacomo Pietro, Turconi Anna Carla, Pedotti Antonio, Bresolin Nereo, Aliverti Andrea (2012); LOW ABDOMINAL CONTRIBUTION TO BREATHING AS DAYTIME PREDICTOR OF NOCTURAL DESATURATION IN ADOLESCENTS AND YOUNG ADULTS WITH DUCHENNE MUSCULAR DYSTROPHY; Respiratory Medicine, 106(2):276-283

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.rmed.2011.10.010 PMID: 22083092

I.F. 2011: 2,475

In the respiratory management of DMD patients it is still under debate what parameter should indicate the correct timing for institution of nocturnal non-invasive ventilation (NIV), in addition to forced vital capacity, which is generally considered as a prognostic marker of disease progression. The aim of this study was to determine if volume variations of rib cage and abdominal compartments measured by Opto-Electronic Plethysmography can be helpful to distinguish between those patients who are in the early stages of nocturnal oxygen desaturation development and those who do not yet. Pulmonary function, abdominal contribution to tidal volume and to inspiratory capacity (%Abd IC) and a set of breathing pattern indexes were assessed in 40 DMD

patients older than 14 years and not yet under nocturnal NIV. ROC analysis revealed that among all the considered parameters, %Abd IC in supine position was the best discriminator between DeSat (at least 10% of the night time with SpO(2) < 95%) and NonDeSat patients, providing an area under the curve with 95%CI equal to 0.752. In conclusion, in adolescents and adults DMD patients who present either no sign or only mild nocturnal oxygen desaturation, a reduced abdominal contribution to inspiratory capacity is a marker of the onset of diaphragm weakness and should be considered to identify the correct timing for the institution of nocturnal NIV.

Ronchi Dario, Sciacco Monica, Bordoni Andreina, Raimondi Monica, Ripolone Michela, Fassone Elisa, Di Fonzo Alessio, Rizzuti Mafalda, Ciscato Patrizia, Cosi Alessandra, Servida Maura, Moggio Maurizio, Corti Stefania, Bresolin Nereo, Comi Giacomo Pietro (2012); THE NOVEL MITOCHONDRIAL TRNAasn GENE MUTATION M.5709T>C PRODUCES OPHTHALMOPARESIS AND RESPIRATORY IMPAIRMENT; European Journal of Human Genetics, 20(3):357-360

Doi: 10.1038/ejhg.2011.238 **PMID: 22189266**

I.F. 2011: 4,400

Although mutations in mitochondrial tRNAs constitute the most common mtDNA defect, the presence of pathological variants in mitochondrial tRNA(Asn) is extremely rare. We were able to identify a novel mtDNA tRNA(Asn) gene pathogenic mutation associated with a myopathic phenotype and a previously unreported respiratory impairment. Our proband is an adult woman with ophthalmoparesis and respiratory impairment. Her muscle biopsy presented several cytochrome c oxidase-negative (COX-) fibres and signs of mitochondrial proliferation (ragged red fibres). Sequence analysis of the muscle-derived mtDNA revealed an m.5709T>C substitution, affecting mitochondrial tRNA(Asn) gene. Restriction-fragment length polymorphism analysis of the mutation in isolated muscle fibres showed that a threshold of at least 91.9% mutated mtDNA results in the COX deficiency phenotype. The new phenotype further increases the clinical spectrum of mitochondrial diseases caused by mutations in the tRNA(Asn) gene.

Ronconi Luca, Gori Simone, Ruffino Milena, Molteni Massimo, Facoetti Andrea (2012); ZOOM-OUT ATTENTIONAL IMPAIRMENT IN CHILDREN WITH AUTISM SPECTRUM DISORDERS; Cortex, in press

Doi: 10.1016/j.cortex.2012.03.005 **PMID: 22503282**

I.F. 2011: 6,080

Autism spectrum disorder (ASD) has long been associated with an inability to experience wholes without full attention to the constituent parts. A zoom-out attentional dysfunction might be partially responsible for this perceptual integration deficit in ASD. In the present study, the efficiency of attentional focusing mechanisms was investigated in children affected by ASD. We measured response latencies to a visual target onset displayed at three eccentricities from the fixation. Attentional resources were focused (zoom-in) or distributed (zoom-out) in the visual field presenting a small (containing only the nearest target eccentricity) or large (containing also the farthest target eccentricity) cue, 100 or 800 msec, before the target onset. Typically developing children, at the short cue-target interval, showed a gradient effect (i.e., latencies are slower at the farthest eccentricity) in the small focusing cue, but not in the large focusing cue condition. These results indicate an efficient zoom-in and zoom-out attentional mechanism. In contrast, children with ASD showed a gradient effect also in the large focusing cue condition, suggesting a specific zoom-out attentional impairment. In addition, the ASD group showed an atypical gradient effect at the long cue-target interval only in the small cue condition, suggesting a prolonged zoom-in and sluggish zoom-out attentional mechanism. This abnormal attentional focusing - probably linked to a dysfunctional top-down feedback from fronto-parietal network to the early visual areas - could contribute to the atypical visual perception associated to individuals with ASD which, in turn, could have consequences in their social-communicative development.

Rossi Elena*, Giorda Roberto*, Bonaglia Maria Clara*, Di Candia Stefania, Grechi Elena, Franzese Adriana, Soli Fiorenza, Rivieri Francesca, Patricelli Maria Grazia, Saccilotto Donatella, Bonfante Aldo, Giglio Sabrina, Beri Silvana, Rocchi Mariano, Zuffardi Orsetta (2012); DE NOVO UNBALANCED TRANSLOCATIONS IN PRADER-WILLI AND ANGELMAN SYNDROME MAY BE THE RECIPROCAL PRODUCT OF INV DUP(15)S; Plos One, 7(6):e39180

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1371/journal.pone.0039180 **PMID: 22720067**

I.F. 2011: 4,092

The 15q11-q13 region is characterized by high instability, caused by the presence of several paralogous segmental duplications. Although most mechanisms dealing with cryptic deletions and amplifications have been at least partly characterized, little is known about the rare translocations involving this region. We characterized at the molecular level five unbalanced translocations, including a jumping one, having most of 15q transposed to the end

of another chromosome, whereas the der(15)(pter->q11-q13) was missing. Imbalances were associated either with Prader-Willi or Angelman syndrome. Array-CGH demonstrated the absence of any copy number changes in the recipient chromosome in three cases, while one carried a cryptic terminal deletion and another a large terminal deletion, already diagnosed by classical cytogenetics. We cloned the breakpoint junctions in two cases, whereas cloning was impaired by complex regional genomic architecture and mosaicism in the others. Our results strongly indicate that some of our translocations originated through a prezygotic/postzygotic two-hit mechanism starting with the formation of an acentric 15qter->q1::q1->qter representing the reciprocal product of the inv dup(15) supernumerary marker chromosome. An embryo with such an acentric chromosome plus a normal chromosome 15 inherited from the other parent could survive only if partial trisomy 15 rescue would occur through elimination of part of the acentric chromosome, stabilization of the remaining portion with telomere capture, and formation of a derivative chromosome. All these events likely do not happen concurrently in a single cell but are rather the result of successive stabilization attempts occurring in different cells of which only the fittest will finally survive. Accordingly, jumping translocations might represent successful rescue attempts in different cells rather than transfer of the same 15q portion to different chromosomes. We also hypothesize that neocentromerization of the original acentric chromosome during early embryogenesis may be required to avoid its loss before cell survival is finally assured.

Russo Emanuela, Trevisi Enrico, Zulian F., Battaglia Maria Amalia, Viel Danila, Facchin Dina, Chiusso Alessio, Martinuzzi Andrea (2012); PSYCHOLOGICAL PROFILE IN CHILDREN AND ADOLESCENTS WITH SEVERE COURSE JOUVANILE IDIOPATHIC ARTHRITIS; The Scientific World Journal, 2012:841375

Doi: 10.1100/2012/841375 **PMID: 22629213**

I.F. 2011: 0,000

Objective: Juvenile Idiopathic Arthritis (JIA) is the most common chronic pediatric rheumatic disease. It is recognized that only reliance on clinical signs of disease outcome is inadequate for understanding the impact of illness and its treatment on child's life and functioning. There is a need for a multidisciplinary and holistic approach to children with arthritis which considers both physical and emotional functioning. This study investigated the psychosocial functioning of children and adolescent with JIA and the disease-related changes in their family.
Methods: The sample consisted of 33 hospitalized patients, aged 6-16 years.

Both parents and the children were given a number of questionnaire to fill out. Clinical information was extracted from the interviews.
Results: Self-reported psychological functioning (depression, anxiety, and behavior) was not different from the normal population; however significant psychological suffering was detected by the clinical interview.
Conclusions: Children and adolescents with JIA do not show overt psychopathology by structured assessment; nevertheless a more clinically oriented holistic approach confirms JIA as a disrupting event causing relevant changes in the quality of life of the affected families.

Salvaterra Mariaelena, Giorda Roberto, Bassi Maria Teresa, Borgatti Renato, Knudsen Lisbeth E., Martinuzzi Andrea, Nobile Maria, Pozzoli Uberto, Ramelli Gian P., Reni Gianluigi, Rivolta Damiano, Stazi Maria Antonietta, Strazzer Sandra, Thijs Carel, Toccaceli Virgilia, Trabacca Antonio, Turconi Anna Carla, Zanini Sergio, Zucca Claudio, Bresolin Nereo, Lenzi Leonardo, Pediatric Biobanking ELSI Working Group (Rossetto Maria Giovanna) (2012); PEDIATRIC BIOBANKING: A PILOT QUALITATIVE SURVEY OF PRACTICES, RULES, AND RESEARCHER OPINIONS IN TEN EUROPEAN COUNTRIES; Biopreservation and Biobanking, 10(1):29-36

Doi: 10.1089/bio.2011.0037

I.F. 2011: 1,294

Ethical, legal, and social issues related to the collection, storage, and use of biospecimens and data derived from children raise critical concerns in the international debate. So far, a number of studies have considered a variety of the individual issues crucial to pediatric biobanking such as decision making, privacy protection, minor recontact, and research withdrawal by focusing on theoretical or empirical perspectives. Our research attempted to analyze such issues in a comprehensive manner by exploring practices, rules, and researcher opinions regarding proxy consent, minor assent, specimens and data handling, and return of results as faced in 10 European countries. Because of the lack of comparative analyses of these topics, a pilot study was designed. Following a qualitative methodology, a questionnaire draft mostly including
open-ended queries was developed, tested, and sent by e-mail to a selected group of researchers dealing with pediatric biobanking (n = 57). Returned questionnaires (n = 31) highlighted that the collection, storage, distribution, and use of biospecimens and data from children were widely practiced in the contacted laboratories. In most cases, pediatric biobanking was subjected to national or local regulations covering adult biobanks (n = 26). Informed

consent was generally given by parents or legal representatives (n = 17). Children's opinions were frequently sought and taken into account (n = 16). However, minors were usually not recontacted at the age of maturity to express their own choices (n = 26). Based on the collected data, dedicated recommendations are needed to govern unique ethical and regulatory issues surrounding pediatric biobanking.

Scaini Simona, Battaglia Marco, Beidel Deborah C., Ogliari Anna (2012); A META-ANALYSIS OF THE CROSS-CULTURAL PSYCHOMETRIC PROPERTIES OF THE SOCIAL PHOBIA AND ANXIETY INVENTORY FOR CHILDREN (SPAI-C); Journal of Anxiety Disorders, 26(1):182-188

Doi: 10.1016/j.janxdis.2011.11.002 PMID: 22154123

I.F. 2011: 2,965

Several studies have found that the Social Phobia and Anxiety Inventory for Children (SPAI-C), an empirically derived self-report instrument to assess DSM-IV social phobia in childhood and adolescence, has good psychometric properties. While these findings were replicated across different cultures, the overall strength of the psychometric properties of the SPAI-C remains unknown. We assessed the validity of the SPAI-C by meta-analytic techniques across studies collected from PubMed, PsycInfo and Eric databases, conducted in different countries, among subjects of different age, and sex. A total of 21 articles were retained, predominantly from Europe and North America. We found that the psychometric properties based on Cronbach alpha, mean score differences between sexes, and construct validity, were robust for the SPAI-C scale. Girls scored significantly higher than boys, and geographical differences played a moderating effect on sex-related score differences. These results further support the SPAI-C as an instrument to identify Social Phobia in youth.

Sironi Manuela*, Biasin Mara*, Cagliani Rachele, Forni Diego, De Luca Mariacristina, Saulle Irma, Lo Caputo Sergio, Mazzotta Francesco, Macias Juan, Pineda Juan A., Caruz Antonio, Clerici Mario (2012); A COMMON POLIMORPHISM IN TLR3 CONFERS NATURAL RESISTANCE TO HIV-1 INFECTION; The Journal of Immunology, 188(2):818-823

*** Autori che hanno contribuito in ugual misura al lavoro**

Doi: 10.4049/jimmunol.1102179 PMID: 22174453

I.F. 2011: 5,788

TLR3 recognizes dsRNA and activates antiviral immune responses through the production of inflammatory cytokines and type I IFNs. Genetic association studies have provided evidence concerning the role of a polymorphism in TLR3 (rs3775291, Leu412Phe) in viral infection susceptibility. We genotyped rs3775291 in a population of Spanish HIV-1-exposed seronegative (HESN) individuals who remain HIV seronegative despite repeated exposure through i.v. injection drug use (IDU-HESN individuals) as witnessed by their hepatitis C virus seropositivity. The frequency of individuals carrying at least one 412Phe allele was significantly higher in IDU-HESN individuals compared with that of a matched control sample (odds ratio for a dominant model = 1.87; 95% confidence interval, 1.06-3.34; p = 0.023). To replicate this finding, we analyzed a cohort of Italian, sexually HESN individuals. Similar results were obtained: the frequency of individuals carrying at least one 412Phe allele was significantly higher compared with that of a matched control sample (odds ratio, 1.79; 95% confidence interval, 1.05-3.08; p = 0.029). In vitro infection assays showed that in PBMCs carrying the 412Phe allele, HIV-1(Ba-L) replication was significantly reduced (p = 0.025) compared with that of Leu/Leu homozygous samples and was associated with a higher expression of factors suggestive of a state of immune activation (IL-6, CCL3, CD69). Similarly, stimulation of PBMCs with a TLR3 agonist indicated that the presence of the 412Phe allele results in a significantly increased expression of CD69 and higher production of proinflammatory cytokines including IL-6 and CCL3. The data of this study indicate that a common TLR3 allele confers immunologically mediated protection from HIV-1 and suggest the potential use of TLR3 triggering in HIV-1 immunotherapy.

Sironi Manuela*, Biasin Mara, Forni Diego, Cagliani Rachele, De Luca Mariacristina, Saulle Irma, Lo Caputo Sergio, Mazzotta Francesco, Macias Juan, Pineda Juan A., Caruz Antonio, Clerici Mario* (2012); GENETIC VARIABILITY AT THE TREX1 LOCUS IS NOT ASSOCIATED WITH NATURAL RESISTANCE TO HIV-1 INFECTION; AIDS, 26(11):1443-1445

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1097/QAD.0b013e328354b3c2 **PMID: 22526516**

I.F. 2011: 6,245

Three prime repair exonuclease 1 (TREX1) degrades excess HIV-1 DNA, thereby preventing recognition by innate immunity receptors and type I interferon responses. Analyses performed in two HIV-exposed seronegative (HESN) cohorts did not show any differences in TREX1 sequence, single nucleotide polymorphisms frequency, or expression in HESN compared to

controls, suggesting that, despite its central role in the HIV-1 infection process, genetic diversity at TREX1 is not a major determinant of susceptibility to infection in humans.

Skrap Miran, Mondani Massimo, Tomasino Barbara, Weis Luca, Budai Riccardo, Pauletto Giada, Eleopra Roberto, Fadiga Luciano, Ius Tamara (2012); SURGERY OF INSULAR NON-ENHANCING GLIOMAS: VOLUMETRIC ANALYSIS OF TUMORAL RESECTION, CLINICAL OUTCOME AND SURVIVAL IN A CONSECUTIVE SERIES OF 66 CASES; Neurosurgery, 70(5):1081-1094

Doi: 10.1227/NEU.0b013e31823f5be5 PMID: 22067417

I.F. 2011: 2,785

Background: Despite intraoperative technical improvements, the insula remains a challenging area for surgery because of its critical relationships with vascular and neurophysiological functional structures.
Objective: To retrospectively investigate the morbidity profile in insular nonenhancing gliomas, with special emphasis on volumetric analysis of tumoral resection.
Methods: From 2000 to 2010, 66 patients underwent surgery. All surgical procedures were conducted under cortical-subcortical stimulation and neurophysiological monitoring. Volumetric scan analysis was applied on T2-weighted magnetic resonance images (MRIs) to establish preoperative and postoperative tumoral volume.
Results: The median preoperative tumor volume was 108 cm. The median extent of resection was 80%. The median follow-up was 4.3 years. An immediate postoperative worsening was detected in 33.4% of cases; a definitive worsening resulted in 6% of cases. Patients with extent of resection of > 90% had an estimated 5-year overall survival rate of 92%, whereas those with extent of resection between 70% and 90% had a 5-year overall survival rate of 82% ($P < .001$). The difference between preoperative tumoral volumes on T2-weighted MRI and on postcontrast T1-weighted MRI ([T2 - T1] MRI volume) was computed to evaluate the role of the diffusive tumoral growing pattern on overall survival. Patients with preoperative volumetric difference < 30 cm demonstrated a 5-year overall survival rate of 92%, whereas those with a difference of > 30 cm had a 5-year overall survival rate of 57% ($P = .02$).
Conclusion: With intraoperative cortico-subcortical mapping and neurophysiological monitoring, a major resection is possible with an acceptable risk and a significant result in the follow-up.

Soi Daniela, Brambilla Daniele, Comiotto Elisabetta, Di Berardino

F., Filipponi Eliana, Socci M., Spreafico Emanuela, Forti Stella, Cesarani Antonio (2012); EFFECT OF EYE LATERALIZATION ON CONTRALATERAL SUPPRESSION OF TRANSIENT EVOKED OTOACOUSTIC EMISSIONS; Acta Otorhinolaryngologica Italica, 32(3):170-174

PMID: 22767982

I.F. 2011: 0,863

Several studies have previously demonstrated that postural changes modify evoked otoacoustic emission. In order to evaluate a possible interaction between eye muscles and ciliated cells in the inner ear, we studied the effects of eye lateralization on the contralateral suppression of transient evoked otoacoustic emissions (TEOAEs). Thirty-eight normal hearing subjects with TEOAEs were recruited. Their TEAOEs at threshold level were recorded with contralateral suppression (white noise) via straight ahead fixation and right or left lateral fixation. Eye lateralization in the same direction of the white noise significantly decreased the suppression at 4 kHz ($p = 0.003$). The signal-to-noise ratio in the suppression condition with straight ahead was 1.54 (± 4.610) dB, while the ratio was 3.48 (± 4.631) dB in the suppression condition with gaze toward the white noise. Eye lateralization seems to reduce the contralateral suppression effect of TEOAEs at 4 kHz. However, further studies are necessary to investigate the possible mechanisms of this phenomenon.

Tambs Kristian, Kendler K.S., Reichborn-Kjennerud Ted, Aggen S.H., Harris Jennifer R., Neale M.C., Hettema J.M., Sundet J.M., Battaglia Marco, Roysamb E. (2012); GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO THE RELATIONSHIP BETWEEN EDUCATION AND ANXIETY DISORDERS - A TWIN STUDY; Acta Psychiatrica Scandinavica, 125(3):203-212

Doi: 10.1111/j.1600-0447.2011.01799.x PMID: 22111622

I.F. 2011: 4,220

Objective: To examine the negative statistical relationship between educational level and risk of anxiety disorders, and to estimate to what extent this relationship may be explained by genes or environmental factors influencing both phenotypes.
Method: Registry data on educational level for 3339 young adult Norwegian twin pairs and diagnostic data on anxiety disorders for 1385 of these pairs were analysed, specifying structural equations models using MX software.
Results: In the best-fitting model, genes accounted for 59% of the variance in

education. 18% of the variance was due to environmental factors shared by co-twins, and the remaining 23% due to non-shared environment; 46% of the variance in liability to anxiety disorders was genetic, the remaining variance was due to non-shared environment. A phenotypic polychoric correlation of -0.30 between educational level and 'any anxiety disorder' was estimated to be primarily (83% in the best-fitting model) caused by genes common to the two traits.
Conclusion: The relationship between low education and risk of anxiety disorders appears to be primarily determined by genetic effect common to educational level and anxiety disorders.

Tavano Alessandro, Grimm S., Costa-Faidella J., Slabu L., Schröger E., Escera C. (2012); SPECTROTEMPORAL PROCESSING DRIVES FAST ACCESS TO MEMORY TRACES FOR SPOKEN WORDS; Neuroimage, 60(4):2300-2308

Doi: 10.1016/j.neuroimage.2012.02.041 PMID: 22387169

I.F. 2011: 5,895

The Mismatch Negativity (MMN) component of the event-related potentials is generated when a detectable spectrotemporal feature of the incoming sound does not match the sensory model set up by preceding repeated stimuli. MMN is enhanced at frontocentral scalp sites for deviant words when compared to acoustically similar deviant pseudowords, suggesting that automatic access to long-term memory traces for spoken words contributes to MMN generation. Does spectrotemporal feature matching also drive automatic lexical access? To test this, we recorded human auditory event-related potentials (ERPs) to disyllabic spoken words and pseudowords within a passive oddball paradigm. We first aimed at replicating the word-related MMN enhancement effect for Spanish, thereby adding to the available cross-linguistic evidence (e.g., Finnish, English). We then probed its resilience to spectrotemporal perturbation by inserting short (20 ms) and long (120 ms) silent gaps between first and second syllables of deviant and standard stimuli. A significantly enhanced, frontocentrally distributed MMN to deviant words was found for stimuli with no gap. The long gap yielded no deviant word MMN, showing that prior expectations of word form limits in a given language influence deviance detection processes. Crucially, the insertion of a short gap suppressed deviant word MMN enhancement at frontocentral sites. We propose that spectrotemporal point-wise matching constitutes a core mechanism for fast serial computations in audition and language, bridging sensory and long-term memory systems.

Tomasino Barbara, Marin Dario, Maieron Marta, Ius Tamara, Budai Riccardo, Fabbro Franco, Skrap Miran (2012); FOREIGN ACCENT SYNDROME: A MULTIMODAL MAPPING STUDY; Cortex, in press

Doi: 10.1016/j.cortex.2011.10.007 PMID: 22130092

I.F. 2011: 6,080

The present study explored the functional neuroanatomy of Foreign Accent Syndrome (FAS) in an Italian native speaker who developed an altered speech rhythm and melody following a circumscribed tumour to the left precentral gyrus. Structural, functional, fibre tracking and intraoperative findings were combined. No signs of dysarthria, apraxia of speech, or aphasia nor other cognitive deficits were detected, except for the fact that the patient was perceived as a non-native speaker. The patient fMRI maps were compared with a control group of 12 healthy controls. During counting, sentences and pseudoword pronunciation the patient showed an additional increased sparse activation in areas around the pre/postcentral gyrus corresponding to those involved in phonation (i.e., larynx motor area). The intraoperative cortical stimulation mapping evidenced a mouth motor representation close to the tumour, a motor type of speech arrest site just below it, and anteriorly a proper speech arrest site. Our results are discussed within the current neurolinguistic models of speech production, and emphasize the importance of the primary motor cortex. We argue that this FAS case should be thought of as a disorder of the feedforward control commands, in particular of the articulator velocity and position maps which are hypothesized to lie along the caudoventral portion of the precentral gyrus.

Tomasino Barbara, Guatto Elisa, Rumiati Raffaella Ida, Fabbro Franco (2012); THE ROLE OF VOLLEYBALL EXPERTISE IN MOTOR SIMULATION; Acta Psychologica, 139(1):1-6

Doi: 10.1016/j.actpsy.2011.11.006 PMID: 22154347

I.F. 2011: 2,255

We explored the impact of motor experience on the interaction between implicit motor simulation and language-processing. In an action familiarity judgment task, expert volleyball players, fans and novices were presented with semantically correct sentences describing possible and not possible motor actions, all as negative or positive contexts, e.g., “Don’t shank!” or “Assist!”. As processing negated action-phrases is known to reduce simulation states, exposure to negative or positive contexts was used here to test how simulation varies according to motor feasibility (possible, impossible) and experience (experts and fans). A significant group×stimulus×context

interaction showed that athletes and fans, took longer to process negative than positive contexts for possible actions, compared to action-impossible sentences. In addition, experts were significantly faster and more accurate than fans and, in turn, they were both more accurate than novices. Thus, implicit motor simulation impacts on action-verb processing depending on (i) the domain-relevant expertise, (ii) the feasibility of the actions, and (iii) on whether scenes are presented in a negated context. These results suggest that the implicit triggering of motor representations is modulated by the context and it is tuned to people's motor repertoire, even when actions are described linguistically.

Tomasino Barbara, Ceschia Martina, Fabbro Franco, Skrap Miran (2012); MOTOR SIMULATION DURING ACTION WORD PROCESSING IN NEUROSURGICAL PATIENTS; Journal of Cognitive Neuroscience, 24(3):736-748

Doi: 10.1161/jocn_a_00168 **PMID: 22098262**

I.F. 2011: 5,175

The role that human motor areas play in linguistic processing is the subject of a stimulating debate. Data from nine neurosurgical patients with selective lesions of the precentral and postcentral sulcus could provide a direct answer as to whether motor area activation is necessary for action word processing. Action-related verbs (face-, hand-, and feet-related verbs plus neutral verbs) silently read were processed for (i) motor imagery by vividness ratings and (ii) frequency ratings. Although no stimulus- or task-dependent modulation was found in the RTs of healthy controls, patients showed a task × stimulus interaction resulting in a stimulus-dependent somatotopic pattern of RTs for the imagery task. A lesion affecting a part of the cortex that represents a body part also led to slower RTs during the creation of mental images for verbs describing actions involving that same body part. By contrast, no category-related differences were seen in the frequency judgment task. This task-related dissociation suggests that the sensorimotor area is critically involved in processing action verbs only when subjects are simulating the corresponding movement. These findings have important implications for the ongoing discussion regarding the involvement of the sensorimotor cortex in linguistic processing.

Tonelli Alessandra, D'Angelo Maria Grazia, Arrigoni Filippo Silvio Aldo, Brighina Erika, Arnoldi Alessia, Citterio Andrea, Bresolin Nereo, Bassi Maria Teresa (2012); ATYPICAL ADULT ONSET COMPLICATED SPASTIC PARAPARESIS WITH THIN CORPUS

CALLOSUM IN TWO PATIENTS CARRYING A NOVEL FA2H MUTATION; European Journal of Neurology, in press

I.F. 2011: 3,692

Abstract non disponibile

Tosato Sarah, Bellani Marcella, Bonetto Chiara, Ruggeri Mirella, Perlini Cinzia, Lasalvia Antonio, Marinelli Veronica, Rambaldelli Gianluca, Cristofalo Doriana, Bertani Mariaelena, Zanoni Martina, Lazzarotto Lorenza, Cerini Roberto, Pozzi Mucelli Roberto, Tansella Michele, Dazzan Paola, Di Forti Marta, Murray Robin M., Collier David, Brambilla Paolo (2012); IS NEUREGULIN 1 INVOLVED IN DETERMINING CEREBRAL VOLUMES IN SCHIZOPHRENIA? PRELIMINARY RESULTS SHOWING A DECREASE IN SUPERIOR TEMPORAL GYRUS VOLUME; Neuropsychobiology, 65(3):119-125

Doi: 10.1159/000330584 PMID: 22378022

I.F. 2011: 2,675

Background/Aims: Reduced left superior temporal gyrus (STG) volume is one of the most replicated imaging findings in schizophrenia. However, it remains unclear whether genes play any role in our understanding of such structural alteration. It has been proposed that Neuregulin 1 (NRG1) might be a promising gene involved in schizophrenia, because of its role in neurodevelopment and neuroplasticity. In this study, the association between NRG1 and STG anatomy in patients with schizophrenia was explored for the first time.
Methods: We investigated a 1-year treated prevalence cohort of patients with schizophrenia in contact with the South Verona Community-Based Mental Health Service. A blood sample was collected for DNA extraction and brain structure was assessed with an MRI scan. A total of 27 subjects with schizophrenia underwent both assessments and were included in the study.
Results: We investigated the association between the polymorphism SNP8NRG222662 (rs4623364) of NRG1 and volume of the STG. We found that patients homozygous for the C allele had reduced left STG gray and white matter volumes in comparison to those homozygous for the G allele ($p < 0.01$ and $p < 0.001$, respectively).
Conclusions: This exploratory study suggests that NRG1 may be involved in determining STG size in schizophrenia, and may play a role in the neurogenetic basis of the language disturbances seen in this disorder. However, due to our small sample size, the results should be regarded as preliminary and replicated in a larger sample.

Trabacca Antonio, De Rinaldis Marta, Gennaro Leonarda, Losito Luciana (2012); SEPTO-OPTIC DYSPLASIA-PLUS AND DYSKINETIC CEREBRAL PALSY IN A CHILD; Neurological Sciences, 33(1):159-163 – Case Report

Doi: 10.1007/s10072-011-0590-8 PMID: 21533562

I.F. 2010: 1,315

Septo-optic dysplasia (SOD), also called De Morsier's syndrome, is a highly heterogeneous condition comprising a spectrum of central nervous system malformations that involves in various degrees the optic nerves, the hypothalamic-pituitary axis, and other midline structures such as the septum pellucidum and the corpus callosum. In a discrete number of cases, schizencephaly, agenesis of the corpus callosum or other cortical malformations are associated (SOD-plus). The authors present a 6-year-old boy with dyskinetic cerebral palsy (athetoid-dystonic subtype) associated with SOD-plus. Cranial magnetic resonance imaging (cMRI) revealed the total absence of septum pellucidum, optic nerve hypoplasia, hypoplasia of the corpus callosum and right occipital cortical dysplasia. The patient was diagnosed with septo-optic dysplasia-plus syndrome based on the cMRI findings. To the best of our knowledge, this is the first reported case in which defects of midline brain structures, like in SOD-plus, are associated with a significant hyperkinetic movement disorder such as dyskinesia.

Trabacca Antonio, Russo Luigi, Losito Luciana, De Rinaldis Marta, Moro Grazia, Cacudi Marilena, Gennaro Leonarda (2012); THE ICF-CY PERSPECTIVE ON THE NEUROREHABILITATION OF CEREBRAL PALSY: A SINGLE CASE STUDY; Journal of Child Neurology, 27(2):183-190

Doi: 10.1177/0883073811415852 PMID: 21911416

I.F. 2011: 1,748

Starting from the case of a 12-year-old boy with dyskinetic (athetoid-dystonic subtype) cerebral palsy, the authors apply the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) of the World Health Organization (WHO) as a comprehensive documentation tool to guide the pathway of care and illustrate a multidisciplinary and interdisciplinary neurorehabilitation team approach. The ICF-CY provides a common and universal language for describing and measuring health and disability in the first 2 decades of life. Despite the fact that this is a single case design, the authors consider it useful for the identification of an ICF-CY core set for the description of children with cerebral palsy. The results of this single case

study are preliminary and need to be tested in a large trial of children with cerebral palsy.

Trevisi Enrico, Gualdi Sabrina, De Conti Carla, Salghetti Annamaria, Martinuzzi Andrea, Pedrocchi A., Ferrante S. (2012); CYCLING INDUCED BY FUNCTIONAL ELECTRICAL STIMULATION IN CHILDREN AFFECTED BY CEREBRAL PALSY: CASE REPORT; European Journal of Physical and Rehabilitation Medicine (continues Europa Medicophysica), 48(1):135-145

PMID: 21508913

I.F. 2011: 1,402

Background: Recently, the efficacy of functional electrical stimulation (FES) cycling have been demonstrated on the improvement of strength and motor control in adults with stroke. FES-cycling, providing a repetitive goal-oriented task, could facilitate cortical reorganization and utilization of residual cortico-spinal pathways. These benefits could be more enhanced in children because of the greater plasticity and flexibility of their central nervous system.
Aim: The aim of the present case report study was to explore the feasibility of FES-cycling in children with cerebral palsy (CP) and to provide a set of instrumental measures able to evaluate the effects of this novel treatment on cycling and walking ability.
Design: Interventional study.
Setting and Population: Two ambulant outpatient children with diplegic CP were recruited by the “E. Medea” Scientific Institute.
Methods: Patients followed a FES-cycling treatment for 30 minutes a day, 3 days a week for 7 weeks. Pre and post treatment tests were performed, namely clinical measures and electromyographic, kinematic and oxygen expenditure analysis during gait and cycling.
Results: The treatment was safe, feasible and well accepted by the 2 children. After treatment both patients achieved a more symmetrical muscular strategy during voluntary cycling and gait and a significant reduction of muscle co-contractions during cycling. These improvements were corroborated by a decrease in oxygen expenditure during the post test for one of the two children, the less impaired, implying a better exploiting of bi-articular muscles.
Conclusion and Clinical Rehabilitation Impact: FES-cycling is feasible and safe and it may be an alternative rehabilitation method for diplegic CP patients. The set of instrumental measurements proposed seems to be a valuable tool for functional assessment to identify subclinical anomalies and improvements on cycling and gait in CP patients.

Ulzi Gianna*, Lecchi Marzia*, Sansone Valeria, Redaelli Elisa, Corti Eleonora, Saccomanno Domenica, Pagliarani Serena, Corti Stefania, Magri Francesca, Raimondi Monica, D'Angelo Maria Grazia, Modoni Anna, Bresolin Nereo, Meola Giovanni, Wanke Enzo (2012); MYOTONIA CONGENITA: NOVEL MUTATIONS IN CLCN1 GENE AND FUNCTIONAL CHARACTERIZATIONS IN ITALIAN PATIENTS; Journal of the Neurological Sciences, 318(1-2):65-71

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1016/j.jns.2012.03.024 **PMID: 22521272**

I.F. 2011: 2,353

Myotonia congenita is an autosomal dominantly or recessively inherited muscle disorder causing impaired muscle relaxation and variable degrees of permanent muscle weakness, abnormal currents linked to the chloride channel gene (CLCN1) encoding the chloride channel on skeletal muscle membrane. We describe 12 novel mutations: c.1606G>C (p.Val536Leu), c.2533G>A (p.Gly845Ser), c.2434C>T (p.Gln812X), c.1499T>G (p.E500X), c.1012C>T (p.Arg338X), c.2403+1G>A, c.2840T>A (p.Val947Glu), c.1598C>T (p.Thr533Ile), c.1110delC, c.590T>A (p.Ile197Arg), c.2276insA Fs800X, c.490T>C (p.Trp164Arg) in 22 unrelated Italian patients. To further understand the functional outcome of selected missense mutations (p.Trp164Arg, p.Ile197Arg and p.Gly845Ser, and the previously reported p.Gly190Ser) we characterized the biophysical properties of mutant ion channels in tsA cell model. In the physiological range of muscle membrane potential, all the tested mutations, except p.Gly845Ser, reduced the open probability, increased the fast and slow components of deactivation and affected pore properties. This suggests a decrease in macroscopic chloride currents impairing membrane potential repolarization and causing hyperexcitability in muscle membranes. Detailed clinical features are given of the 8 patients characterized by cell electrophysiology. These data expand the spectrum of CLCN1 mutations and may contribute to genotype-phenotype correlations. Furthermore, we provide insights into the fine protein structure of ClC-1 and its physiological role in the maintenance of membrane resting potential.

Urgesi Cosimo, Savonitto Maria Maddalena, Fabbro Franco, Aglioti Salvatore (2012); LONG- AND SHORT-TERM PLASTIC MODELING OF ACTION PREDICTION ABILITIES IN VOLLEYBALL; Psychological Research – Psychologische Forschung, 76(4):542-560

Doi: 10.1007/s00426-011-0383-y **PMID: 22045443**

I.F. 2011: 2,472

Athletes show superior abilities not only in executing complex actions, but also in anticipating others' moves. Here, we explored how visual and motor experiences contribute to forge elite action prediction abilities in volleyball players. Both adult athletes and supporters were more accurate than novices in predicting the fate of volleyball floating services by viewing the initial ball trajectory, while only athletes could base their predictions on body kinematics. Importantly, adolescents assigned to physical practice training improved their ability to predict the fate of the actions by reading body kinematics, while those assigned to the observational practice training improved only in understanding the ball trajectory. The results suggest that physical and observational practice might provide complementary and mutually reinforcing contributions to the superior perceptual abilities of elite athletes. Moreover, direct motor experience is required to establish novel perceptuo-motor representations that are used to predict others' actions ahead of realization.

Urgesi Cosimo, Fornasari Livia, Perini Laura, Canalaz Francesca, Cremaschi Silvana, Faleschini Laura, Balestrieri Matteo, Fabbro Franco, Aglioti Salvatore, Brambilla Paolo (2012); VISUAL BODY PERCEPTION IN ANOREXIA NERVOSA; International Journal of Eating Disorders, 45(4):501-511

Doi: 10.1002/eat.20982 **PMID: 22271579**

I.F. 2011: 2,947

Objective: Disturbance of body perception is a central aspect of anorexia nervosa (AN) and several neuroimaging studies have documented structural and functional alterations of occipito-temporal cortices involved in visual body processing. However, it is unclear whether these perceptual deficits involve more basic aspects of others' body perception.
Method: A consecutive sample of 15 adolescent patients with AN were compared with a group of 15 age- and gender-matched controls in delayed matching to sample tasks requiring the visual discrimination of the form or of the action of others' body.
Results: Patients showed better visual discrimination performance than controls in detail-based processing of body forms but not of body actions, which positively correlated with their increased tendency to convert a signal of punishment into a signal of reinforcement (higher persistence scores).
Discussion: The paradoxical advantage of patients with AN in detail-based body processing may be associated to their tendency to routinely explore body parts as a consequence of their obsessive worries about body appearance.

Urgesi Cosimo, Romanò Manola, Fornasari Livia, Brambilla Paolo, Fabbro Franco (2012); INVESTIGATING THE DEVELOPMENT OF TEMPERAMENT AND CHARACTER IN SCHOOL-AGED CHILDREN USING A SELF-REPORT MEASURE; Comprehensive Psychiatry, 53(6):875-883

Doi: 10.1016/j.comppsych.2012.01.006 PMID: 22425528

I.F. 2011: 2,257

Background: Developmental studies of temperament and character dimensions are crucial for a better understanding of how genetic and environmental factors interact in shaping individual personality. However, although several studies have been conducted in adults, a few studies have addressed the evaluation of temperament and character in children. Here, we tested the suitability of self-report evaluation and the developmental trend of temperament and character dimensions among school-aged children using an Italian version of the junior Temperament and Character Inventory (jTCI).
Methods: The jTCI was completed by 572 Italian children (292 girls and 280 boys) aged 8 to 12 years. We evaluated the internal consistency of the 7 jTCI scales at each age, the intercorrelations between the scales, and the factorial model of the questionnaires. Furthermore, we tested the differences between the development of the temperament and character dimensions in girls and boys.
Results: Although the data from 8-year children showed unacceptably low internal consistency, better reliability was observed for older children. Intercorrelations and factor analysis partially confirmed the hypothesized structure of the jTCI items, with problems observed for some items of the Novelty Seeking, Harm Avoidance, Reward Dependence (RD), and Self-Directedness scales. Furthermore, in keeping with previous studies, girls presented lower scores in Novelty Seeking and higher RD, Self-Directedness, and Cooperativeness scales than did boys, with the between-sex difference in RD becoming larger at older ages.
Conclusions: Although the use of the self-administered jTCI in clinical settings should be cautious, it may serve as a useful complementary instrument to describe the development of personality in childhood.

Vignoli Aglaia*, Borgatti Renato*, Peron Angela, Zucca Claudio, Ballarati Lucia, Bonaglia Maria Clara, Bellini Melissa, Giordano Lucio, Romaniello Romina, Bedeschi Maria Francesca, Epifanio Roberta, Russo Silvia, Caselli Rossella, Giardino Daniela, Darra Francesca, La Briola Francesca, Banderali Giuseppe, Canevini Maria Paola (2012); ELECTROCLINICAL PATTERN IN MECP2

DUPLICATION SYNDROME: EIGHT NEW REPORTED CASES AND REVIEW OF LITERATURE; Epilepsia, 53(7):1146-1155

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1111/J.1528-1167.2012.03501.x PMID: 22578097

I.F. 2011: 3,961

Purpose: Duplications encompassing the MECP2 gene on the Xq28 region have been described in male patients with moderate to severe mental retardation, absent speech, neonatal hypotonia, progressive spasticity and/or ataxia, recurrent severe respiratory infections, gastrointestinal problems, mild facial dysmorphisms (midface hypoplasia, depressed nasal bridge, large ears) and epilepsy. Epilepsy can occur in >50% of cases, but the types of seizures and the electroclinical findings in affected male individuals have been poorly investigated up to the present. Herein we describe eight patients with MECP2 duplication syndrome and a specific clinical and electroencephalographic pattern. Methods: Array CGH of genomic DNA from the probands was performed, and an Xq28 duplication ranging from 209 kb to 6.36 Mb was found in each patient. Electroencephalography studies and clinical and seizure features of all the patients were analyzed. Key findings: We found that epilepsy tended to occur between late childhood and adolescence. Episodes of loss of tone of the head and/or the trunk were the most represented seizure types. Generalized tonic-clonic seizures were rarely observed. The typical interictal EEG pattern showed abnormal background activity, with generalized slow spike and wave asynchronous discharge with frontotemporal predominance. Sleep electroencephalography studies also demonstrated abnormal background activity; spindles and K complex were often abnormal in morphology and amplitude. Response to therapy was generally poor and drug resistance was a significant feature. Significance: Although these cases and a review of the literature indicate that epilepsy associated with MECP2 duplication syndrome cannot be considered a useful marker for early diagnosis, epilepsy is present in >90% of adolescent patients and shows a peculiar electroclinical pattern. Consequently, it should be considered a significant sign of the syndrome, and an EEG follow-up of these patients should be encouraged from early childhood. Moreover, the definition of a more specific epileptic phenotype could be useful in order to suspect MECP2 duplication syndrome in older undiagnosed patients.

Zorzi Marco*, Barbiero Chiara*, Facoetti Andrea*, Lonciari Isabella, Carrozzi Marco, Montico Marcella, Bravar Laura, George Florence, Pech-Georgel Catherine, Ziegler Johannes C. (2012); EXTRA-LARGE LETTER SPACING IMPROVES READING IN DYSLEXIA; Proceedings

of the National Academy of Sciences of the United States of America (PNAS), 109(28):11455-11459

** Autori che hanno contribuito in ugual misura al lavoro*

Doi: 10.1073/pnas.1205566109 **PMID: 22665803**

I.F. 2011: 9,681

Although the causes of dyslexia are still debated, all researchers agree that the main challenge is to find ways that allow a child with dyslexia to read more words in less time, because reading more is undisputedly the most efficient intervention for dyslexia. Sophisticated training programs exist, but they typically target the component skills of reading, such as phonological awareness. After the component skills have improved, the main challenge remains (that is, reading deficits must be treated by reading more-a vicious circle for a dyslexic child). Here, we show that a simple manipulation of letter spacing substantially improved text reading performance on the fly (without any training) in a large, unselected sample of Italian and French dyslexic children. Extra-large letter spacing helps reading, because dyslexics are abnormally affected by crowding, a perceptual phenomenon with detrimental effects on letter recognition that is modulated by the spacing between letters. Extra-large letter spacing may help to break the vicious circle by rendering the reading material more easily accessible.

LETTER TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE

ANNO 2011

LETTER TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE Anno 2011

Cattaneo Dario, Meraviglia Paola, Beretta Rosangela, Baldelli Sara, Cozzi Valeria, Milani Greta, Clementi Emilio (2011); VIROLOGIC FAILURE IN AN HIV-INFECTED WOMAN GIVEN DESOGESTREL FOR EXCESSIVE MENSTRUAL BLEEDING; European Journal of Clinical Pharmacology, 67(4):429-431 – Letter to the Editor

Doi: 10.1007/s00228-010-0934-y **PMID: 21046092**

I.F. 2010: 3,032

Abstract non disponibile

Chiesa Alberto, Brambilla Paolo, Serretti Alessandro (2011); NEURO-IMAGING OF MINDFULNESS MEDITATIONS: IMPLICATIONS FOR CLINICAL PRACTICE; Epidemiology and Psychiatric Sciences, 20(2):205-210 – Letter to the Editor

Doi: 10.1017/S204579601100028X **PMID: 21714367**

I.F. 2010: 2,032

Abstract non disponibile

De Rinaldis Marta, Gennaro Leonarda, Losito Luciana, Trabacca Antonio (2011); DRUG-TO-DRUG INTERACTION BETWEEN SODIUM VALPROATE AND TRIHEXYPHENIDYL IN A CHILD WITH EXTRAPYRAMIDAL CEREBRAL PALSY AND EPILEPSY; European Journal of Clinical Pharmacology, 67(3):315-316 - Letter to the Editor

Doi: 10.1007/s00228-010-0918-y **PMID: 20959970**

I.F. 2010: 3,032

Abstract non disponibile

Radice Sonia, Milanesi Anna, Antoniazzi Stefania, Perrone Valentina, Carnovale Carla, Clementi Emilio (2011); A CASE OF HAEMORRHAGIC CYSTITIS BY INHALED SALBUTAMOL AND SALMETEROL; European Journal of Clinical Pharmacology, 67(11):1203-1204 – Letter to the Editor

Doi: 10.1007/s00228-011-1068-6 **PMID: 21638032**

I.F. 2010: 3,032

Abstract non disponibile

Rodriguez Laura, Nevado Julian, Vallespin Elena, Palomares Maria, Golmayo Luz, Bonaglia Maria Clara, Delicado Alicia, Abarca Elena (2011); MOLECULAR CHARACTERIZATION OF AN ATYPICAL INV DUP DEL 8Q. PROPOSAL OF A MECHANISM OF FORMATION; American Journal of Medical Genetics Part A, 4(155):915-919 - Letter to the Editor

Doi: 10.1002/ajmg.a.33924 **PMID: 21412979**

I.F. 2010: 2,505

Abstract non disponibile

LETTER TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE

ANNO 2012

dati aggiornati a luglio 2012

LETTER TO THE EDITOR PUBBLICATE SU RIVISTE RECENSITE Anno 2012

Pellegrino Paolo, Cattaneo Dario, Clementi Emilio (2012); ROLE OF ABCB1 C3445T IN CISPLATIN-BASED THERAPY; Archives of Medical Research, 43(4):329-330

Doi: 10.1016/j.arcmed.2012.06.04 **PMID: 22704851**

I.F. 2011: 1,733

Abstract non disponibile

Pozzi Marco, Strazzer Sandra, Locatelli Federica, Galbiati Sara, Formica Francesca, Maestri Luciano, Clementi Emilio, Radice Sonia (2012); CASE SERIES: PARADOXICAL ACTION OF DOMPERIDONE LEADS TO INCREASED VOMITING; European Journal of Clinical Pharmacology, in press

Doi: 10.1007/s00228-012-1324-4 **PMID: 22706584**

I.F. 2011: 2,845

Abstract non disponibile

Radice Sonia, Carnovale Carla, Antoniazzi Stefania, Zuccotti Gian Vincenzo, Perrone Valentina, Piazza Antonella, Clementi Emilio (2012); A CASE OF RECURRENT ACUTE HAEMORRHAGIC CYSTITIS ASSOCIATED WITH SALBUTAMOL AND BECLOMETHASONE USE IN A PAEDIATRIC PATIENT; Journal of Paediatrics and Child Health, 48(7):620-621

Doi: 10.1111/j.1440-1754.2012.02495.x **PMID: 22758901**

I.F. 2011: 1,281

Abstract non disponibile

LAVORI PER ESTESO PUBBLICATI SU RIVISTE NON RECENSITE

ANNO 2011

LAVORI PER ESTESO PUBBLICATI SU RIVISTE NON RECENSITE Anno 2011

Ivanova Masha Y., Achenbach Thomas M., Rescorla Leslie A., Bilenberg Niels, Bjarnadottir Gudrun, Denner Silvia, Dias Pedro, Dobrean Anca, Doepfner Manfred, Esmaeili Elaheh Mohammad, Frigerio Alessandra, Goncalves Miguel, Gudmundsson Halldor S., Jusiene Roma, Kristensen Solvejg, Lecannelier Felipe, Leung Patrick, Liu Jianghong, Lobel Sofia P., Machado Barbara Cesar, Markovic Jasminka, Mas Paola A., Montirosso Rosario, Plueck Julia, Pronaj Adelina, Rodrigues Jorge T., Rojas Pamela O., Schmeck Klaus, Shahini Mimoza, Silva Jaime R., Van Der Ende Jan, Verhulst Frank (2011); SYNDROMES OF PRESCHOOL PSYCHOPATHOLOGY REPORTED BY TEACHERS AND CAREGIVERS IN 14 SOCIETIES USING THE CAREGIVER-TEACHER REPORT FORM (C-TRF); Journal of Early Childhood and Infant Psychology, 7:87-103

Caregivers and teachers from 14 societies rated 9,389 1.5 to 5-year-olds on the Caregiver-Teacher Report Form (C-TRF; Achenbach & Rescorla, 2000). General population samples were obtained in Asia; the Middle East; Eastern, Northern, Central, Western, and Southern Europe; and South America. The 2-level 6-syndrome C-TRF model derived on a mostly U.S. sample was tested separately for each society. This model or a slightly modified 2-level 5-syndrome version of the model fit the data for 10 of the 14 societies. The findings generally support use of the C-TRF with children of diverse backgrounds. The multicultural generalizability of C-TRF syndromes suggests that they can be used as taxonomic constructs for preschoolers' psychopathology, which can facilitate international communication and collaboration between clini¬cians, researchers, and educators working with young children

Molteni Massimo (2011); EPIDEMIOLOGIA DELL'ETÀ EVOLUTIVA: UNA REVIEW; Psichiatria dell'Infanzia e dell'Adolescenza, 78:249-264

Mental health is a multidisciplinary and continual concept, that can not be merely defined as the absence of mental disorder and disabilities. However, among a host of variables, psychopathology impaires children health since early developmental stages. Worldwide prevalence of mental disorders in

childhood is around 10%. PrISMA project (Progetto Italiano Salute Mentale Adolescenti) reported a prevalence of 8.2% in a general population sample of Italian children leaving in urban areas. Furthermore, prevalence of Pervasive Developmental Disorders is around 4-6/1000 and prevalence of neurodevelopmental disorders, usually co-occuring with psychiatric problems, is around 5% in school-aged children. According to the recent scientific findings persistent socio-economic pressures and family structure and cohesion are well-known risks factors, also because of the negative influence they could exert on parenting and sociocultural opportunities. Most psychopathological traits have been recognized to have a complex and multi-factorial aetiology (i.e. environments can modify the expression of an individual's genetic background). Taking into consideration this complex interaction potential environmental risk factors should be considered in a gene-environment interplay perspective. Psychopathological dimensions has not a linear development but some critical periods can be identified, namely pre-pubertal period (9-11 years) and pubertal period (13-14 years). Preventive medicine should taken into account all the above discussed factors. Developmental psychopathology can exert a negative impact on adulthood functioning: continuity between child and adult psychopathology can be homotypic as well as heterotypic. The role of undesirable life events should also be taken into consideration in determining the persistence of psychopathology as well as in determining a modification of symptoms patterns during lifetime.

Montirosso Rosario (2011); RI-PENSANDO AI FATTORI DI RISCHIO DEL PRIMO SVILUPPO; Psicomotricità, 15(3):3-10 – Editoriale

Abstract non disponibile

Mosconi Paola, Taricco Mariangela, Bergamini Mirna, Fazzi Bosisio Luisella, Colombo Cinzia, Patrucco Valentina, Corti Maria Nella, Giobbe Dario, Guerreschi Massimo, Magnarella Maria Rita, Sallemi Giovanni (2011); FAMILY BURDEN AFTER SEVERE BRAIN INJURY; Patient, doi: 10.2165/11535550-000000000-00000, 4(1):55-65

Background: As part of the development of the Italian National Consensus Conference investigating the period from the hospital rehabilitation of patients with severe brain injury to their return to the community, a working group was appointed to identify the needs of brain injury patients and their families in Italy.

Methods: Two postal self-administered survey questionnaires were carried out: one targeted families of patients with severe brain injury to evaluate

their objective and subjective burdens and needs; the other focused on the viewpoints of volunteer associations helping people with severe brain injury. Issues explored were quality of discharge from hospital (information received, family participation, etc.), needs of the family (work, financial resources, spare time, relationships with friends and other relatives), and the viewpoint of volunteer associations.
Results: A total of 234 families (54% of sample) of patients (69% male, mean age 41 years) with severe brain injury returned the questionnaire. Most said they had been involved and informed in the hospital discharge process; about 17% had not been involved at all and only about one-third of families received satisfactory support during the discharge phase. Few families received any help from community social services (10%). Almost two-thirds of families had experienced financial difficulties and, in many cases, one family member had to change his/her work situation. Families' social relationships, travelling, hobbies, and spare time were significantly reduced.
The 57 volunteer associations who returned the survey (84% response rate) confirmed that their members had experienced the same difficulties.
Conclusions: Considering the difficulties and problems documented by these two surveys, more research is needed on effective interventions to support patients with severe brain injury and their families, particularly during the discharge phase from hospital to home and community life.

Poggi Geraldina, Adduci Annarita, Gandola Lorenza, Galbiati Susanna, Degrate Alessandro, Sironi Elena, Strazzer Sandra, Massimino Maura (2011); COGNITIVE AND PSYCHOLOGICAL OUTCOMES IN YOUNGER VS OLDER CHILDREN WITH SUBTENTORIAL/SUPRATENTORIAL EPENDYMOMA AFTER RADIATION THERAPY; Journal of Behavioral and Brain Science, 1(3):87-93

Doi: 10.4236/jbbs.2011.13012

Purpose: to investigate cognitive and psychological problems in children treated for intracranial ependymoma, the evolution of these disorders over time and the role of age at radiotherapy and tumor site, in their onset and persistence. Methods and Materials: 23 patients received a complete evaluation; some of them underwent follow-ups. The clinical data collected included sex, age (at diagnosis, assessment and tumor treatment, thus dividing patients into two cohorts: younger or older than 5 years), site (supratentorial vs. subtentorial), the presence of hydrocephalus, neurological examination, tumor treatment. All the patients received an age-appropriate cognitive and psychological evaluation. Results: The mean cognitive level was within the

norm, with lower scores on the Performance Intelligence Quotient (PIQ). The psychological assessment revealed Internalizing problems and impaired independence. Children older than 5 years had a lower Intelligence Quotient (IQ) than the younger children, both at the initial evaluation and at follow-ups. Initially, the supratentorial group appeared to be less impaired than the subtentorial group but then exhibited a progressive decline in the IQ. In the subtentorial group, the children with an IQ within the normal range remained stable at the follow-up, while the children with below-norm scores at the initial evaluation showed deterioration over time. Conclusions: Tumor site seems to affect the cognitive outcome to a greater extent than age at radiotherapy.

Trabacca Antonio, Russo Luigi (2011); RICOVERI ALL'ESTERO PER NEURORIABILITAZIONE IN CENTRI DI ALTA SPECIALIZZAZIONE: CONFRONTO TRA LE REALTÀ REGIONALI ITALIANE; Giornale di Neuropsichiatria dell'Età Evolutiva, 31(1):17-22

Partendo dal presupposto che il Servizio Sanitario Nazionale (SSN) garantisce a tutti i cittadini italiani di poter usufruire, in determinate circostanze, di assistenza sanitaria all'estero, questo lavoro propone un confronto tra le prassi regionali che riguardano la gestione delle richieste di ricovero all'estero nell'ambito della neuroriabilitazione. Il quadro che si ottiene mostra un'alta variabilità sia nella lettura dei dati complessivi (rispetto ai luoghi di destinazione, alla tipologia di trattamento richiesto, al rimborso richiesto, alle patologie di base per le quali è richiesto l'intervento), sia nel confronto tra le prassi utilizzate sul territorio nazionale (per quanto concerne l'andamento delle richieste e delle evasioni delle stesse negli ultimi due anni). Il confronto proposto si basa sulla lettura dei quadri normativi di riferimento delle diverse regioni, sulla lettura dei dati relativi alle richieste di autorizzazione per cure all'estero per neuroriabilitazione depositati c/o il Ministero della Salute per il biennio 2008-2009 e riferiti a tutte le Regioni d'Italia, nonché sulle richieste di autorizzazione per le stesse giunte all'Unità Operativa di Neuroriabilitazione 1 dell'I.R.C.C.S. "E. Medea" di Ostuni (BR), Centro Regionale di Riferimento per la Neuroriabilitazione della Regione Puglia. Viene proposta, in conclusione, una riflessione sulla modalità comunicativa équipe-paziente-famiglia finalizzata alla promozione e al mantenimento di un'efficace alleanza terapeutica.

Turconi Anna Carla, Diella Eleonora (2011); LA CONSTRAINT THERAPY NEL BAMBINO EMIPLEGICO: DALLA RICERCA ALLA PRATICA CLINICA; MR - Giornale Italiano di Medicina Riabilitativa (Ital J Rehab Med), 24(2):1-5

La penalizzazione terapeutica dell'arto conservato, chiamata (CIMT),

viene definita come una terapia che abbina l'allenamento intensivo di un arto superiore leso dopo danno neurologico centrale alla penalizzazione funzionale dell'uso dell'arto sano.
Nel bambino con paralisi cerebrale infantile l'utilizzo e l'efficacia della CIMT sono stati dimostrati da molti studi con risultati che depongono per un incremento dell'uso dell'arto leso documentati da miglioramenti alle scale funzionali e recentemente anche da dati relativi a studi di neuroimaging che evidenziano le modificazioni neurofisiologiche prodotte da tale terapia.
In particolare e stata evidenziata una attivazione sensomotoria nell'emisfero controlaterale verificata con immagini alla risonanza funzionale e un ribilanciamento nella competizione interemisferica. Si è concluso recentemente un trial multicentrico nazionale in cui venivano posti a confronto tre diversi tipi di trattamento: trattamento di constraint therapy modificato (mCIMT), trattamento intensivo bimanuale (IBT), trattamento fisioterapico tradizionale (ST). La popolazione era costituita da 111 bambini affetti da emiparesi. Presso il nostro Istituto e nei centri collegati della nostra famiglia, sono stati trattati 37 bambini applicando la mCIMT. Il trattamento con mCIMT ha dimostrato un costante miglioramento nelle scale specifiche relative alle abilita manuali nei diverso tempi in relazione alla presa, alle attivita bimanuali e le ADL. Nel nostro Istituto il trattamento con mCIMT prosegue regolarmente anche al di fuori di gruppi specifici di ricerca e si sta consolidando come un trattamento proponibile a bambini affetti da emiparesi congenita e acquisita indenni da problematiche comportamentali e con famiglie collaboranti e motivate. Sino ad oggi sono stati trattati complessivamente nei centri della nostra famiglia circa 60 pazienti. L'intensità del trattamento e il trasferimento alla famiglia dei suggerimenti insieme con la riorganizzazione neurofisiologica cerebrale sono i più importanti fattori coinvolti nell'apprendimento di nuove strategie per migliorare la qualità e la frequenza dell'uso della mano.

Turconi Anna Carla (2011); ELETTROSTIMOLAZIONE; Giornale di Neuropsichiatria dell'Età Evolutiva, 31(1):51-54

La terapia con Elettrostimolazione (ES) utilizza correnti a bassa frequenza che producono effetti particolari sui tessuti e in particolare sulle strutture eccitabili (nervi e muscoli). Attraverso questa terapia si ottiene, infatti, una modificazione della percezione dolorifica e un incremento della forza muscolare attraverso l'aumento dell'area della sezione muscolare, con selettivo reclutamento delle fibre II nel muscolo innervato. Abbiamo diversi tipi di elettrostimolazione utilizzabili nella pratica clinica (NMES, FES, TES) diversamente impiegati e utilizzabili non solo sulle patologie periferiche ma anche in quelle di origine centrale. In campo neurologico infantile, le indicazioni della letteratura

non sono conclusive a causa dell'esiguità degli studi randomizzati e della variabilità della metodologia applicata. Sembrerebbe esservi comunque più evidenza nel supportare gli studi con NMES. Si può pertanto concludere che il trattamento con ES necessita ancora di ulteriori evidenze che confermino la sua efficacia.

Urgesi Cosimo, Campanella Fabio, Fabbro Franco (2011); LA VERSIONE ITALIANA DELLA NEPSY-II PER LA VALUTAZIONE NEUROPSICOLOGICA AD AMPIO RAGGIO DEL BAMBINO DA 3 A 16 ANNI; ITEMS - La Newsletter del Testing Psicologico, 20:1-4

Abstract non disponibile

LAVORI PER ESTESO PUBBLICATI SU RIVISTE NON RECENSITE

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LAVORI PER ESTESO PUBBLICATI SU RIVISTE NON RECENSITE Anno 2012

Barone Lavinia, Casini Erica, Lionetti Francesca, Montirosso Rosario (2012); ATTACCAMENTO E COMPETENZA SOCIALE IN ETÀ PRESCOLARE: UNO STUDIO CON LE STORY TEM TECHNIQUES; Giornale di Psicologia dello Sviluppo, in press

There is a growing interest in studying early socio-emotional development taking into account the role of previous experience in the family context, like attachment relationship. However, there is a paucity of research data considering the role of attachment beyond the first year of life because of the relative lack of valid and reliable measures assessing attachment during preschool age years. Aim: The main aim of the present study is to explore the relationship between pattern of attachment (secure vs insecure vs disorganised) and socio-emotional competence in preschool aged children. Method: 60 children aged 5 to 6 years old are enrolled into the study. Children's pattern of attachment and socio-emotional competence are assessed respectively using the Manchester Child Attachment Story Task (MCAST) and Social Competence and Behaviour Evaluation (SCBE) questionnaire. Results: Children with a secure pattern of attachment present more social competence compared with their insecure and disorganised peers and less behavioural compared with their disorganised peers. No main effect of gender neither attachment x gender interaction is found on SCBE scales.

COMUNICAZIONI SCIENTIFICHE PUBBLICATE SU RIVISTE RECENSITE

ANNO 2011

COMUNICAZIONI SCIENTIFICHE PUBBLICATE SU RIVISTE RECENSITE
Anno 2011

Bianco Federico, Cremonesi Giovanni, Montirosso Rosario, Borgatti Renato (2011); ARE PRETERM INFANTS LIKELY TO HAVE THE SAME QUALITY OF LIFE AS THOSE BORN AT TERM? DO PRETERM INFANTS TREATED WITH SURFACTANT HAVE THE SAME RESPIRATORY OUTCOME AS THOSE NOT TREATED? RESULTS FROM NEO-ACQUA STUDY; Abstract 13 26th International Workshop on Surfactant Replacement, Istanbul, 23-25.06.2011; Neonatology, 99(4):367-372

I.F. 2010: 2,289

Borelli M., Biasin Mara, Lo Caputo Sergio, Piacentini Luca, Saulle Irma, De Luca Maria Cristina, Sironi Manuela, Cagliani Rachele, Trabattoni D., Mazzotta Francesco, Clerici Mario (2011); GENETIC DIVERSITY AT EDNOPLASMIC RETICULUM AMINOPEPTIDADES 2 (ERAP2) IS COUPLED WITH INNATE RESISTANCE TO HIV-1 INFECTION; Abstract PP 01 ICAR 2011 - Firenze, 27-29/03/2011; Infection, 39(S1):S45

I.F. 2010: 2,244

Cacudi Marilena, Paloscia Claudio, De Rinaldis Marta, Gennaro Leonarda, Losito Luciana, Cefalo Florindo, Trabacca Antonio (2011); DISSOCIATIVE DISORDER SECONDARY TO ABSENCE SEIZURES IN A CHILD RESOLVED THROUGH ASSOCIATION WITH VALPROIC AND ETHOSUXIMIDE; Abstract p721 29th International Epilepsy Congress, Rome, 28.08-01.09.2011; Epilepsia, 52(Suppl. 6):220

Doi: 10.1111/j.1528-1167.2011.03207.x

I.F. 2010: 3,955

Corti Stefania, Nizzardo Monica, Nardini Martina, Simone Chiara, Falcone Marianna, Riboldi Giulietta, Donadoni Chiara, Salani Sabrina, Menozzi Giorgia, Bonaglia Maria Clara, Bresolin Nereo, Comi Giacomo Pietro (2011); GENERATION OF MOTONEURONS FROM SPINAL MUSCULAR ATROPHY-INDUCED PLURIPOTENT

STEM CELLS FREE OF VECTOR AND TRANSGENIC SEQUENCES: IN VITRO AND IN VIVO ANALYSIS; Abstract S46.001 63rd AAN Annual Meeting - Honolulu, Hawai Convention Center, 09-16.04.3022; Neurology, 76(9;Suppl.4):A554

I.F. 2010: 8,017

D'Angelo Maria Grazia, Romei Marianna, Lo Mauro Antonella, Marchi Eraldo, Gandossini Sandra, Bonato Sara, Colombo Daniele, Turconi Anna Carla, Pedotti Antonio, Bresolin Nereo, Aliverti Andrea (2011); DUCHENNE MUSCULAR DYSTROPHY AND OPTOELECTRONIC PLETHYSMOGRAPHY: A LONGITUDINAL STUDY OF RESPIRATORY FUNCTION; Abstract P1.12 16th International Congress of the World Muscle Society, Almancil, Algarve, Portugal, 18-22.10.2011; Neuromuscular Disorders, 21(9-10):645

Doi: 10.1016/j.nmd.2011.06.772

I.F. 2010: 2,764

Fumagalli Giorgio G., Pietroboni Anna M., Ghezzi Laura, Fenoglio Chiara, Cortini Francesca, Serpente Maria, Cantoni Claudia, Rotondo Emanuela, Corti Priscilla, Carecchio Miryam, Bassi Maria Teresa, Bresolin Nereo, Galbiati Domenico, Galimberti Daniela, Scarpini Elio (2011); PHENOTYPIC HETEREOGENEITY OF THE PROGRANULIN GENE ASP22 FS MUTATION IN A LARGE ITALIAN KINDRED; Abstract P686 of the Twenty-First Meeting of the European Neurological Society, Lisbon, Portugal, 28-31.05.2011; Journal of Neurology, 258(Suppl. 1):S185-S186

I.F. 2010: 3,853

Magri Francesca, Del Bo Roberto, D'Angelo Maria Grazia, Gandossini Sandra, Corti Stefania, Lucchini Valeria, Napoli Laura, Moggio Maurizio, Comi Giacomo Pietro (2011); LGMD2L IN ITALIAN POPULATION: NEW MUTATIONS AND CLINICAL AND MORPHOLOGICAL ASPECTS; Abstract P2.50 16th International Congress of the World Muscle Society, Almancil, Algarve, Portugal, 18-22.10.2011; Neuromuscular Disorders, 21(9-10):675

Doi: 10.1016/j.nmd.2011.06.872

I.F. 2010: 2,764

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I.F. 2010: 2,371

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I.F. 2011: 8,312

Abstract non disponibile

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I.F. 2011: 1,360

Abstract non disponibile

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I.F. 2011: 1,360

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BREVETTI

ANNO 2011

BREVETTI
Anno 2011

Titolare: IRCCS "Eugenio Medea" – Associazione La Nostra Famiglia

Inventori: Cavalleri Matteo, Brenna Francesco, Reni Gianluigi

Titolo: APPARECCHIATURA PER IL RIPRISTINO DELLA VENTILAZIONE PARTICOLARMENTE IN SOGGETTI AFFETTI DALLA SINDROME DA IPO-VENTILAZIONE CENTRALE CONGENITA (CCHS)

Data deposito: 20 dicembre 2011

N. della domanda/Appln. No. MI2011A002324

Breve descrizione

La Sindrome da Ipoventilazione Centrale Congenita (CCHS) è una malattia genetica che colpisce il sistema nervoso autonomo, determinandone l'incapacità nel regolare correttamente il respiro. I pazienti affetti da CCHS sono generalmente ventilati meccanicamente durante il sonno e la loro ossigenazione è monitorata per mezzo di un saturimetro, al fine di individuare eventuali ipossie. Un supervisore interviene in caso di allarme del saturimetro: se riscontra un pericolo per la vita del soggetto, lo scuote o lo sveglia, in quanto i pazienti generalmente recuperano una corretta ventilazione se mossi o risvegliati.

È stato realizzato un dispositivo, basato su tablet Android, in grado di: acquisire i dati di ossigenazione in tempo reale da un saturimetro commerciale; all'insorgere di una condizione di ipossia, somministrare una stimolazione multisensoriale al paziente via via più intensa al decrescere dell'ossigenazione e al passare del tempo, per mezzo di diversi attuatori (ad esempio, spruzzatori d'acqua o cuscini vibranti); fermare tale stimolazione nel caso in cui il paziente recuperi dall'ipossia; svegliare il paziente e/o il supervisore se l'ipossia si protrae a lungo.

Con tale dispositivo si vuole ottenere una riduzione del numero di risvegli durante la notte, con l'obiettivo di migliorare la qualità del sonno e della vita dei pazienti e dei loro parenti o supervisori, nonché una maggiore indipendenza per i pazienti adulti.

Inoltre si intende valutare l'efficacia che opportune stimolazioni possono avere nel facilitare una ripresa della corretta ventilazione da parte dei pazienti affetti da CCHS.