

4th International Conference on
Neurology and Healthcare

International Conference on
Clinical and Experimental Neuropsychology
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3rd World
Drug Delivery and Formulations Summit
June 24-25, 2019 | Rome, Italy

Poster



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Low frequency transcranial magnetic stimulation: a potential therapeutic tool in the treatment of autism spectrum disorders

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Autism Spectrum disorders are a group of early-onset neurodevelopmental pervasive disorders defined by a core triad of symptoms: qualitative abnormalities in reciprocal social interaction, communication and restricted, repetitive and stereotyped behaviours. Affecting 1% of the population and accounting for 58 Disability-Adjusted Life-Years (DALYs) per 100,000 population, autism causes a significant burden to health and social services. The heterogeneous nature of autism has impeded effective targeting. The Prefrontal Cortex (PFC), pivotal in socio-emotional processing, is thus proposed as a target, to modulate implicated regional dysfunction in connectivity and excitability. Repetitive Transcranial Magnetic Stimulation (rTMS) is an emerging tool in psychopathology. Data suggests low-frequency stimulation-induced inhibition of the PFC could mediate the elevated excitation/inhibition imbalance. Consequent interneuron attenuation causes functional reorganisation of the PFC, resulting in core symptom alleviation. Although available TMS studies in autism are preliminary, they provide promising evidence for therapeutic benefit including reductions in repetitive behaviours, attentional-processing and Event-Related Potential (ERP) normalisation. Therefore, bilateral weekly Dorsolateral Prefrontal Cortex (DLPFC) stimulation at 180 pulses for 18 weeks at 90% MT and 1HZ will be applied. To consolidate the most effective regional and temporal window targeting, PFC stimulation will be directly compared to superior temporal sulcus and considered across age-groups. Targeting critical-period plasticity could elicit efficacious long-lasting cortical modulation, restoring local-circuit maturation, reducing symptomatology in adulthood. This report proposes rTMS as a promising tool in the alleviation of autistic cortical manifestations.

Biography

Olivia Bell is a medical student and pursuing her studies at Bristol University. Her interests and research experience are focused on neurology aspects as well as neurological disorders and especially autism spectrum disorders.

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The recognition and intensity of moral emotions in the behavioral variant of frontotemporal dementia

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Statement of the Problem: The study of moral emotions is essential for understanding the interactions between cognitive, affective and social processes, as well as for understanding their role as motivators of human social behavior. Neuroimaging studies have implicated frontal and temporal structures in moral cognition, thus behavioral variant of Frontotemporal Dementia (bvFTD) has provided a lesion model essential to investigate the processes involved in moral emotions. **Methodology:** In this study, we aimed to investigate the recognition, intensity and affectation of moral emotions in patients with bvFTD (n=16). We included a control group of patients with Alzheimer's disease (AD, n=18), and healthy controls (n=21). Participants were assessed with a novel task to measure recognition, intensity and affectation of basic and moral emotions. **Findings:** Compared with the AD group and healthy controls, patients with bvFTD obtained significantly lower scores in embarrassment, anger and fear recognition. BvFTD patients also experienced anger and pity with less intensity than both control groups. **Conclusion & Significance:** These results support previous studies in patients with bvFTD showing emotion recognition and moral cognition impairments. These results provide new insights into moral emotions pathways in bvFTD patients that cannot be fully explained by social cognitive and executive functions deficits. Further studies should use neuroimaging techniques in order to correlate atrophy patterns with recognition, intensity and affectation of moral emotions.

Biography

Sandra Baez is professor of Psychology and Neuroscience at Los Andes University. She holds a degree in Psychology, a Master in Neuropsychology, and a Ph.D. in Psychology. She conducted her postdoctoral and received training in functional and structural neuroimaging at the Max Planck Institute for Human Cognitive and Brain Sciences. She has experience in neuropsychological assessment and cognitive stimulation techniques for patients with neurological and psychiatric disorders. Her interests and research experience are focused on neuropsychological aspects as well as neurophysiological and neuroanatomical correlates of social cognition domains in patients with neuropsychiatric disorders. She has more than 50 publications in leading journals, such as Nature Human Behavior, Neurology, Brain, JAMA Neurology, among others. She is Associate Editor of Journal of Alzheimer's Disease and Frontiers in Psychiatry, and ad hoc Reviewer for more than 20 journals. She is also part of the Project team taskforce of the Human Affectome Project.

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Executive dysfunctions associated with frontostriatal circuitry in bipolar affective disorder I: Are they associated with depression, mania or both?

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Objective: Bipolar Affective Disorder I (BDI) has been associated with frontostriatal abnormalities and thus, executive problems. However, it remains unclear whether executive dysfunctions in BDI are predominantly associated with mania, depression or are state-independent. Further, executive processes are relatively heterogeneous, with different frontostriatal circuits subserving different executive function. Specifically, whereas the Dorsolateral Prefrontal Cortex (DLPFC) has been shown to be associated with organizational strategies, working memory and problem solving, Anterior Cingulate Cortex (ACC) is involved in response initiation and monitoring. In addition, Orbitofrontal Cortex (OFC) seems to be related with impulse control. Hence, the aim of this study was to better characterize executive problems in BDI as well as to test if the hypothetical specificity of executive impairment in this population may indicate a dysfunction of the specific frontostriatal circuit(s).

Participants and Methods: Twenty-two patients with BDI (11 mania and 11 depressed) participated in this study. DLPFC functions were assessed using: Verbal Fluency (response generation with clustering and switching components), Digit Span, Trail-Making Test; ACC: The Verbal Fluency Test (response initiation), Stroop test; OFC: multiple loops and altering sequence task.

Results: Manic state was particularly associated with executive problems indicating ACC pathology. Additionally, although both patients' groups had deficits suggesting executive dysfunction of the circuit involving dorsolateral prefrontal, these problems were more pronounced in patients with mania.

Conclusions: In BDI, executive problems are particularly characteristic for patients with mania. The results of this study will be discussed in the context of three frontostriatal circuits subserving different executive processes

Biography

Paulina Golińska is a PhD candidate in psychology at University of Gdańsk in Poland. Her interests are focused on experimental and clinical neuropsychology. For PhD thesis, she conducting a research concerning symptoms characteristic for damages in frontal areas in people with Parkinson's disease (apathy, anterior-attentional system and anosognosia). She also worked as a therapist with people after traumatic brain injuries.

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Moral emotions in patients with schizophrenia

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Statement of the Problem: Social cognition impairments have been widely described in patients with schizophrenia. These impairments include deficits in the recognition of basic emotions. However, no previous studies have investigated moral emotions in patients with schizophrenia.

Methodology: in this study, 15 patients diagnosed with schizophrenia and 15 healthy controls performed an experimental task designed to trigger counter-empathic moral emotions (i.e., envy and Schadenfreude—pleasure at others' misfortunes). Both groups were matched in terms of age, sex, education level and estimative intellectual functioning. We also assessed general cognitive state and executive functions.

Findings: results showed that, compared to controls, patients with schizophrenia exhibited higher envy levels. There were no group differences in ratings of Schadenfreude and control conditions. Besides, group differences in envy levels are not explained by cognitive or executive impairments.

Conclusion & Significance: These results suggest that the experience of counter-empathic moral emotions is exacerbated in patients with schizophrenia. Our findings contribute to further understanding of social cognition deficits observed in patients with schizophrenia.

Biography

Sandra Baez is professor of Psychology and Neuroscience at Los Andes University. She holds a degree in Psychology, a Master in Neuropsychology, and a Ph.D. in Psychology. She conducted her postdoctoral and received training in functional and structural neuroimaging at the Max Planck Institute for Human Cognitive and Brain Sciences. She has experience in neuropsychological assessment and cognitive stimulation techniques for patients with neurological and psychiatric disorders. Her interests and research experience are focused on neuropsychological aspects as well as neurophysiological and neuroanatomical correlates of social cognition domains in patients with neuropsychiatric disorders. She has more than 50 publications in leading journals, such as *Nature Human Behavior*, *Neurology*, *Brain*, *JAMA Neurology*, among others. She is Associate Editor of *Journal of Alzheimer's Disease* and *Frontiers in Psychiatry*, and ad hoc Reviewer for more than 20 journals. She is also part of the Project team taskforce of the Human Affectome Project.

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Accepted Abstracts



Formulation of non-ionic surfactant vesicles (NISV) prepared by microfluidics for therapeutic delivery of siRNA into cancer cells

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Introduction: RNA interference involves the degradation of a target messenger RNA through the incorporation of short interfering RNAs (siRNA) [1]. The application of siRNA-based therapeutics is limited by the development of an effective delivery system. A novel type of nanoparticles known as Non-Ionic Surfactant Vesicles (NISV) are commonly used for drug delivery of various therapeutics, are relatively safe and non-expensive, have not been extensively studied for siRNA delivery [2]. Therefore, the aim of this study was to investigate the potential of NISV prepared by microfluidics for siRNA delivery.

Methods: NISV were prepared by microfluidic mixing which is a recently developed method used to prepare lipid-based nanoparticles and results in the production of small vesicles with efficient encapsulation of a therapeutic agent. To prepare NISV, specific volumes from each stock solution of the NISV components were mixed together to prepare the lipid phase. The lipid phase was injected into the first inlet and the aqueous phase into the second inlet of the microfluidic micromixer, with the mixing temperature set at 50°C. The Flow Rate Ratios (FRR) between the aqueous and organic phase was set at 3:1 and the Total Flow Rates (TFR) of both phases was set at 12 ml/min. This allows for fast mixing between the two phases at high flow rates and at a temperature above the phase transition of the lipids. Dispersions were then collected from the outlet stream and immediately diluted in order to reduce the final ethanol content in the preparation to 6.25% (v/v). Cytotoxicity evaluation of NISV were carried out on non-small lung cancer cells (A549) and mouse melanoma cells (B16-F10-LUC). siRNA targeting Green Fluorescent Protein (GFP) in copGFP-A549 cells, or luciferase in B16-F10-LUC cells were encapsulated in NISV. Inhibition of GFP expression by anti-GFP siRNA (siGFP) delivered using NISV was evaluated by flow cytometry, polymerase chain reaction, and Western blotting. Nude BALB/c mice inoculated with B16-F10-LUC cells that induce melanoma expressing luciferase was used to assess the NISV ability to deliver siRNA in vivo.

Results: Cytotoxicity studies indicated that NISV were not toxic at or below 40 µg/ml. NISV formulations had high siRNA encapsulation efficiency. Fluorescent microscope and flow cytometry studies indicated high cellular uptake by the cells compared to naked siRNA, which was not taken up by the cells. NISV were able to deliver siGFP to the cells and significantly suppress GFP expression. These results were confirmed by transfecting the luciferase producing B16-F10-LUC cells with anti-luciferase siRNA (siLUC). Measuring the level of luciferase expression after siLUC transfections using a luciferase protein assay system successfully demonstrated the suppression of luciferase expression. NISV were then used in in vivo experiments using nude BALB/c mice. After intra-tumoural injection, siLUC was delivered to the cells and suppressed luciferase expression at a significantly higher level than mice treated with naked siLUC. These in vivo results confirm the ability of NISV to successfully deliver siRNA into the cytoplasm of the target cells and suppress the target protein.

Conclusion: NISV have been demonstrated extensively and for the first time to have the potential to be used as a delivery system for siRNA. These results have shown that NISV can be used to overcome the barriers, such as low stability and poor cellular uptake, in siRNA-based therapeutics.

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Language ability and behavioral self- regulation in children with arachnoid cysts

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Statement of the problem: Due to its congenital origin, it has been postulated that Arachnoid Cystss (AC) may result in atypical cerebral organization. However, because of limitations of cerebral plasticity, AC can cause behavioral problems and deficiencies in various cognitive domains, being language one of the most affected.

Objective: This study seeks to determine behavioral problems and language deficiencies in AC sample and to know if there is any relationship between both domains, assuming the important role of language in behavioral self-regulation.

Methodology: 18 pediatric patients from 7 to 16 years with the presence of an AC (frontal n = 4, temporal n = 13 and occipital n = 1) of different severity level, without any surgical intervention were studied. Wechsler Intelligence Scale for Children, Neuropsychological Battery for Learning Disorders and the Assessment System for Children and Adolescents were applied.

Results: Mild phonological processing deficiencies were found; however, these failures did not affect reading and writing abilities. The use of grammar and expressive language were inadequate. The capacity for organization, planning and behavioral verification was also deficient. Specific scales with poor scores were Personal and Social Resources, Emotional Intelligence and Isolation. Between behavioral and linguistic variables only a significant correlation was found between the use of grammar and the degree of isolation.

Conclusion: Pediatric population with AC show deficits in phonological processing, expressive language and grammar use as well as behavioral problems, mainly low emotional intelligence and isolation. However, no important correlations were found between language variables and behavioral self-regulation.

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Changes in the cognitive function of patients with early onset Parkinson's disease

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Statement of the Problem: Parkinson's Disease (PD) is a movement disorder also characterized by non-motor symptoms, that including cognitive impairment. In the Early Onset Parkinson's Disease (EOPD) motor symptoms begins between the 21 and 50 years old. Deep Brain Stimulation (DBS) has been used as a treatment of motor symptoms in PD, but there is still controversy about its effects on the non-motor symptoms. Few studies have described Mild Cognitive Impairment (MCI) and dementia in EOPD, and only other few have described effects of DBS on the cognition in these patients.

Methodology: The present study describes the progression of MCI and dementia in 16 patients with EOPD (8 patients with DBS and 8 with only pharmacological treatment) that were assessing between 1-7 years after initial evaluation for inclusion in the present protocol. All patients were evaluated neuropsychologically in the follow cognitive domains attention and working memory, memory, language executive functions, and visuospatial abilities. The MCI and dementia were determined according to the Movement disorder Society criteria. Descriptive statics and Fisher's exact test was used for the statistical analysis.

Findings: About 25% of patients changed their status from normal cognition to MCI, of which 75% was in treatment with DBS. About 75% of these cases changed their cognitive status in the first 3 months. However, not statistically significant differences ($p=.562$) were found between patients with and without DBS by using Fisher's exact test and no one changed their cognitive status to dementia during follow.

Conclusion & Significance: Apparently, progression to MCI is infrequent in EOPD, and dementia was not found, even in patients with more than ten years after starting the first motor symptoms. According to these results, DBS could not be a risk factor for change cognitive status from normal cognition to MCI or dementia in patients with EOPD.

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Social cognition in young adults with Attention-Deficit/Hyperactivity Disorder

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Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) begins in childhood and persists in more than 50% until adult life, inducing difficulties in the work, academic achievement and personal relationships; some of these can be explained by Social Cognition Deficiencies (SCD). Outcomes of studies about SCD in ADHD have not been consistent due to poor control of variables such as the subtype of ADHD and comorbidities. The purpose of this study was to describe and compare the social cognition profile in young adults with and without ADHD.

Method: It is a cross-sectional, descriptive-comparative study with a sample of 10 young adults with ADHD and 10 healthy controls. As a measure for emotional processing, social reasoning and decision making the Social Cognition in Older Adults Battery (Cogsoc- AM) was used and to evaluate theory of mind, Faux Pas Recognition Test (Adult Version) was applied.

Results: Statistically significant differences were found in the domains of theory of mind ($p=.004$), emotional processing ($p=.047$), causes ($p=.003$) and social judgment ($p=.009$).

Conclusions: The group with ADHD showed significantly lower scores in specific domains of social reasoning (causes and social judgment), failures in emotional processing (specially in negative expressions) and theory of mind compared to the healthy control group. SCD may be the cause of troubles in their personal relationships.

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Metamemory i primary insomnia

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Statement of the Problem: Aristotle once said that memory is the scribe of the soul. Memory indeed is one of the core cognitive abilities in human beings and as such, it is important to preserve it. It has been shown that stabilization of memory traces is closely related to sleep. If sleep really does play a role in memory consolidation, the question that arises is: what happens to memory if sleep is distorted? One of the most common sleep disorders is primary insomnia. It has been shown that memory of patients with primary insomnia is impaired, especially after interfering tasks. However, metamemory beliefs of those patients still remain unexamined. That is why the focus of this study was to reveal the metamemory beliefs of those students who suffer from primary insomnia, compared to healthy students. After an entrance examination, all of the subjects filled in Athens scale questionnaire and were then asked to learn a declarative memory task. Subject's overnight memory change was tested in the morning, followed by metamemory beliefs examination. It was hypothesized that, compared to healthy subjects, students who suffer from primary insomnia will overestimate their declarative memory abilities.

Findings: Metamemory calibration (correlations between memory predictions and performance) was examined in both, healthy subjects and subject with primary insomnia. The results indicated that calibration efficiency really was decreased in subject with primary insomnia.

Conclusion & Significance: Students need to be aware of their own memory abilities. Learning and memory are two interconnected constructs thus diminished metamemory abilities can lead to diminished learning potential.

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Enhanced tumor toxicity and reduced off-target toxicity by pretargeting mammary carcinoma with bispecific antibody complexes and dual polymer-pro- drug conjugates

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Statement of the Problem: Conventional chemotherapy is associated with severe off-target toxicities. Pretargeting of high specific activity Polymer-Pro-Drug Conjugates (PPDCs) should reduce off-target toxicity and increase therapeutic efficacy. We now report enhanced therapeutic efficacy in a murine mammary carcinoma model pretargeted with Bispecific Botinylated anti-DTPA Antibody Complexes (BSAbC) and targeting with single or double PPDCs containing Doxorubicin (Dox) or Paclitaxel (Ptxl). No hematological- nor cardio-toxicity were seen in animals treated with PPDCs.

Methods: Biotin-anti-DTPA antibody BSAbC was used to pretarget murine mammary carcinoma 4T1, that over-express biotin receptors grown in Balb/C mice. Experiment treatments were as follows: placebo, Dox, Ptxl, pretargeting with BSAbC followed by DOX-PPDCs, Ptxl-PPDCs, or combination of both PPDCs injected weekly. Tumor volumes were measured daily. Then, tumors were harvested, weighed and TUNEL staining was performed to assess apoptosis. Blood samples were obtained for H & E staining to determine hematological toxicities. Hearts from experimental animals were analyzed by fluorescence microscopy for Dox cardiotoxicity.

Results: Maximal tumor growth suppression was observed in the combination PPDC treatment group (67mg). Individual DOX-PPDCs or Ptxl-PPDCs treatment were better than Dox or Ptxl treated tumors. The placebo group tumor size was 670 mg. The extent of apoptosis by TUNEL staining was inversely proportional to with tumor size. Fluorescence microscopy showed that Dox treatment had Dox fluorescence in the myocardium whereas hearts from pretargeted PPDC groups showed no Dox accumulation. There was no hematological toxicity in single PPDC or dual PPDC therapy groups whereas Dox and Ptxl treatment groups showed toxicities ($p < 0.05-0.01$ respectively).

Conclusion: Biotin receptor expressing murine 4T1 carcinoma could be pretargeted and targeted with single or dual PPDCs to obtain optimal tumor regression. Both cardiotoxicity and hematological toxicities were not observed following treatment with PPDCs. This therapeutic approach could provide highly effective cancer therapy with no off-targeted toxicity.

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The role of defense mechanism in marital discord and efficacy of analytical prob in intervention

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Statement of the Problem: The marital disharmony in a patient couple is caused by socio-economic, emotional and sexual parameters. A person when copes with the complexity of these parameters use various defense mechanisms in managing his anxiety. However, excessive use of which may lead to an unconscious source of psychopathology causing behavioral abnormality. Indeed, Couples suffering from such psychopathology is hardly noticed. The purpose of this study is uncovering the defensive unconscious treads that hold the psychopathology causing disturbances in marriage.

Methodology & Theoretical Orientation: The analytical probe processed by regressing patient' to the past life and transferring emotional experiences of his or her ego function with significant figures. Analyzing ego dynamism and the defense leading to the pathological aspect of marital discord in the patient couple was assessed in therapeutic interactions. Further, processed with insight orientation to bring emotional wellbeing and freeing patent couple from marital disturbances.

Findings: The female partner in the couple in this study was sexually frigid due to desire disorder was analyzed; insulating her fear emotion and feeling of guilt regarding her discomforts in a sexual parameter which she was not able to communicate. The male partner who had intensive use of introjection throughout the development has a hollow block in his personality structure was inducing disturbances in sexual parameter remained unconscious.

Conclusion & Significance: The intervention process based Short-Term Dynamic Psychotherapy was evidence-based proven successful in uncovering unconscious tread protected by a defense mechanism. Frequently couple problems caused by defense mechanisms in marital discord remain unspoken in interpersonal relationships. Hence the recommendations are made to clinicians' alertness in a clinical interview to get a hold on unconscious treads and intervention focusing on unconscious probes in couple patients would promote healthy marriage in couples.

Strategy of targeted pharmacological regulation of intracellular signal transduction in regenerative-competent cells - A new direction of therapy in regenerative medicine

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Advances in the field of cellular technologies have led to the possibility of developing a new direction of targeted therapy in regenerative medicine - "Strategy of Pharmacological Regulation of Intracellular Signal Transduction in Regenerator-competent Cells" (Patent RU № 2599289, 2016). The role of NF-κB, IKK, PKC, PKB, PI3K, ERK ½, p38, adenylate cyclase, PKA, JAKs, STAT3, JNK, p53 in the realization of functioning progenitor elements of different classes and cells of tissue microenvironment was studied in vitro by means of cultural, immunological and other methods. On the models of posthypoxic encephalopathy, skin wound and cytostatic myelosuppression in experimental animals the therapeutic effects and mechanisms of action of modifiers of signal molecules activity were studied. The specificity of the involvement of a number of signaling molecules in the regulation of cell cycle and development of progenitor cells of various classes, as well as in the production of humoral factors by microenvironment cells was revealed. The neuroregenerative effects of JNK inhibitors associated with activation of neural stem cells of brain were shown on the model of encephalopathy. An algorithm and approaches for estimating the potential efficiency and many-sided selectivity of the modifiers of signaling molecules activity as targeted hemostimulators were developed. The effectiveness of various targeted pharmacological agents determined by the selective effect on different types of regenerative-competent cells was demonstrated on the models of cytostatic myelosuppression of various genesis. The perspective of using intracellular signaling molecules in regenerative-competent cells as targets of drugs for regenerative medicine was shown.

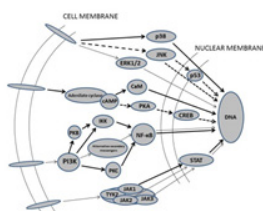


Figure 1: The participation of signaling molecules in the stimulation of proliferation multipotential mesenchymal stem cells. Simple arrows: intracellular pathways involved in activation of functions of mesenchymal precursors under optimal vital activity; dotted arrows: pathways of suppression of mesenchymal precursor cells; thick arrows: pathways of activation functions of mesenchymal progenitor cells under the influence of regulatory factors (redundant pathways).

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General domain and specific domain cognitive processes in children with different mathematical performance

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Several investigations on the neuropsychological processes that influence the mathematical performance (MP), have not yet determined whether the General Domain Processes (GDP) (e.g. intelligence, language) or Specific Domain Processes (SDP) (e.g. mathematical facts, calculation) are the most important in the acquisition and consolidation of the MP. The objective of the present project was to describe and compare the GDP and SDP of children with different MP, and to explore what type of processes would be related to the MP in each group.

Thirty two children in 3rd grade were evaluated; they were classified into 3 groups: high MP (n=7), average MP (n=18), and low MP (n=7) according to their academic record and to a questionnaire for teachers that assesses the occurrence of signs that correspond to learning disorders according to DSM-5 criteria. A battery of tests was applied for both types of processes. Results: a discriminant analysis was performed, which correctly classified 81.8% of the total sample. Qualitatively, on average, the group with high DM presented a better score on the Vocabulary subtest ($z=.52$), while the group with low DM performed worse on the Oral Arithmetic Operations subtest ($z=-1.59$). Results allow to identify a trend in which GDP influence more to belong to high MP, while the SDP do to belong to a low MP.