

Fifth International Meeting

Food for Brain: promoting health and preventing diseases

Milan 20th – 22nd November 2019

ABSTRACTS

LATEST TRENDS IN NUTRITION FOR HEALTH

Cena H. MD, Post Doc in Dietetics and Clinical Nutrition. Head of the Clinical Nutrition and Dietetics Service, ICS Maugeri, IRCCS, Pavia. Head of the Dietetics and Clinical Nutrition Laboratory, Department of Public Health, Experimental and Forensic Medicine, University of Pavia. Pro Rector Pro-Rector for Third Mission. Academic Director of the Dietetics and Clinical Nutrition Master's Degree program (MDCN). Head of the Clinical Nutrition Laboratory. Vice President of ANSISA

Nutritional status is based on an individual's physiologic needs in relation to the nutrients and energy that are consumed through their diet and additional internal and external factors that influence these outcomes. As a first step of developing a personalized nutrition program, an individual's dietary patterns and medical history are assessed and physical examination and anthropometric measures are performed. Based on these assessments, the individual's nutritional needs are identified and a plan is developed to manage the issues that are uncovered. These outcomes are then evaluated and continuously re-evaluated after initiating the intervention. Personalized health includes *personalized nutrition* which considers age, gender, and other personal characteristics, besides specific phenotypic variations. Moreover results from "omics" studies (e.g., epigenomics, metabolomics, microbiomics) provide interesting data about these complex relationships. Although these areas are still evolving, there is an indication that genetic variations are potentially related to obesogenic dietary characteristics, including energy homeostasis and carbohydrate intake. In addition certain specific genetic variations can impact the concentrations of some nutrients and their metabolic effects. These findings suggest that there is the potential to tailor diets and nutritional interventions to an individual's specific genetic risks for developing NCDs and their response to diet.

PERICONCEPTIONAL PARENTAL DIETARY PATTERNS AND THE IMPACT ON THE EARLIEST PRENATAL DEVELOPMENT OF THE CHILD

Stegers-Theunissen R. M., Periconceptional Epidemiology, Department of Obstetrics and Gynaecology, and Paediatrics / Division of Neonatology, Erasmus MC, University Medical Centre, PO Box 2040, Rotterdam, The Netherlands

The evidence is overwhelming that a poor prenatal environment, determined by maternal intrinsic and extrinsic factors, contributes to the development of fetal growth restriction, preterm birth and congenital malformations with consequences for health in later life. These adverse birth outcomes have an origin in the periconceptional pregnancy period, a timespan defined as 14 weeks before until ten weeks after conception. Worldwide, approximately 50% of the population is under- or overnourished, which also includes the reproductive population. It is becoming increasingly clear that periconceptional parental dietary patterns have a strong influence on the very early intrinsic environment of the child (embryo) during pregnancy.

The development of three-dimensional transvaginal ultrasonography in combination with virtual reality (VR) opens the possibility of accurate and reliable visualization of the structures of the embryonic structures with real depth perception. These techniques enable new biometry and volumetry measurements that contribute to the knowledge of the (patho)physiology of embryonic health. Examples of such measurements are the length of complex structures like the umbilical cord, vitelline duct, limbs and cerebellum or the volume of the whole embryo and brain cavities. Moreover, for the first time, embryos can now be staged *in vivo* (Carnegie stages) and vasculature volumes of both the embryo can be measured when VR is combined with power Doppler signals. An overview will be presented of these innovative VR measurements in combination with periconceptional paternal dietary factors in

association with embryonic growth and development.

This new knowledge has supported the development of opportunities for periconception prevention of adverse birth outcomes. Couples with a child wish, in particular women, are most motivated to change poor nutrition when they are aware of the short-term health benefits of getting pregnant and having a healthy baby. In the second part of this presentation, the implementation and valorization of the new knowledge on the importance of nutrition for patient care will be addressed. Since 2007 we have experience with an outpatient clinic for lifestyle counseling and support. Opportunities to empower patients as well as health care professionals to adopt healthy nutrition by offering mobile-health technology-based interventions, such as the mHealth coaching program www.smarterpregnancy.co.uk, are very promising. In the future, we believe however that the only sustainable manner to implement evidence-based personalized nutritional care in usual patient care is a blended lifestyle care approach. The first results of the implementation of the combination of an outpatient clinic for lifestyle care together with evidence-based mHealth programs will be presented.

NUTRITION AND NUTRACEUTICALS FOR BRAIN HEALTH

Magni P., University of Milan, Milan, Italy

The relationship between brain and nutrition is peculiar, since it is bidirectional. On the one hand, the brain plays a pivotal role in controlling all features of feeding, from psychosocial aspects, including rewarding and ethnic issues, to nutrient preferences and meal and energy intake regulation, via an intense dialogue among central and peripheral organs. On the other hand, it is the target of nutrients from food and functional compounds present in food supplements, making it an organ with specific nutritional and nutraceutical needs. Therefore, similarly to other organs, appropriate nutrition patterns seem able to promote brain health. As a general observation, food intake and nutraceutical products may promote brain health both directly providing functionally active compounds to this organ, following the gut absorption/circulation/crossing the blood-brain barrier pathway, as well as indirectly, via the modulation of the function of other organs, like the liver, or meta-organs, like the gut microbiota. Interestingly, the intrinsic

complexity of foods and the multiple components that are often present in nutraceutical products suggest that both these mechanisms may be simultaneously activated by a meal or a supplement ingestion.

A critical issue is also whether and how a nutrient or a nutraceutical compound is able to reach selected brain structures to activate specific biological processes. Another important issue is the correct evaluation of the cognitive and functional impact of such nutritional molecules, both in clinical studies and in experimental models. The ultimate goal of nutrition and nutraceuticals for brain health is spanning the entire life trajectory, starting from the first 1000 days of life, when mother/newborn nutrition may strongly affect brain programming, to midlife and elderly, when the main goal could be promoting brain performance and preventing/attenuating age-associated mild brain dysfunction and neurodegenerative diseases. More specifically, as the latter show a complex and multifaceted pathophysiology, nutrition and nutraceuticals should address different pathological processes, like neural oxidative stress, neuroinflammation, defective synaptic plasticity and cell energy availability. To date, several aspects of the relationship between nutrition and nutraceuticals and brain health are still to be unveiled, especially in the context of personalized management of health issues.

THE TRUE TASTE OF A WINE: BEYOND LIKING

Smith B. School of Advanced Study, University of London, London, UK

Psychologists and neuroscientists tell us that tasting flavours is the result of the multi-sensory integration of olfactory, tactile and taste impressions, modulated by visual and auditory cues. However, as tasters we don't realize that the single, unified experience of the taste of a food or a wine is actually due to the fusion of different sensory inputs. These unified flavour experiences provide a challenge when trying to reconcile the underlying processing story with the conscious experience of tasters, and psychologists and neuroscientists typically construe the flavour of a wine, say, as a psychological construct that can vary from subject to subject as a result of different threshold sensitivities tasters have to acid, tannin, sugar, alcohol, CO₂ and sulphur. To this description of variables we could add the hedonic values that get painted on to particular sensations. All of this



suggests that wine makers have very little influence over the resulting experience drinkers have of their wines. However, we must distinguish between the flavours of wines and our experience of their flavours. The relationship between them is far from simple and in spite of the careful findings of psychologists and neuroscientists, there is still room for the idea of flavour as a multi-dimensional, objective property of a wine that depends both on its chemistry and the needs and interests of those who make and consume it.

REGULATION OF FOOD RELATED BEHAVIOUR: NUDGING OR BOOSTING?

Perez-Cueto F.J.A.¹¹University of Copenhagen, Department of Food Science, Future Consumer Lab, Rolighedsvej 26, 1958 Frederiksberg, Denmark

Objective: To summarise lessons from systematic reviews and empirical intervention studies on the effect of nudging on facilitating healthier, sustainable and ethical food choices, and to highlight practical issues for implementation of nudges at larger scale. It also provides insights on whether nudging can facilitate the process of turning slow learners (healthy choices) into strong learners and produce long term change (boosts).

Methods: Narrative synthesis of systematic reviews on nudging, food choice and nutrition. It reports also synthesises the empirical implementation of nudging in living laboratories and the issues related to upscaling nudge interventions to real-life settings.

Results: Few of the identified studies provide measurable effects on actual food consumption, although every year new empirical data becomes available. However, harmonization of methods and measures of effect size is desirable. In behavior observational laboratories placing vegetables at the beginning of the line and allowing self-composition of salads facilitates plant-based consumption even among males. Provision of a standard quantity of salad (default serving) increases actual vegetable intake without influencing the total food consumed or the hedonic evaluation of the meals. Upscaling to real-life situations is challenging. A common nudge experiment was performed in Denmark, France, Italy and the United Kingdom consisting of nudging a plant-based innovative dish (veggieballs) among adolescents and older consumers through the

“dish-of-the-day” approach in the menu choice and presented together with meatballs and fish cakes). We found no difference in dish choice between control and intervention situation for both adolescents and older people.

Discussion: Familiarity seemed to be an important driver for the choice of the animal-based dishes (meatballs and fish cakes are dishes that are well known by our sample, and the veggie balls were something “new”). Conceptually, nudging is a strategy that is simple and cheap, has significant behavioural effects and should work independently of individual characteristics (e.g. social background and education). Long term effects of nudging still need to be documented in order to evaluate whether they have become boosts.

Conclusions: Combining traditional nutrition interventions with behavioural strategies such as nudging seems to be an effective way to achieve healthier food consumption. Placing the foods of plant origin first in a buffet line and the provision of standardised vegetable servings are effective measures at foodservice operations. Re-designing the nudging strategy already at menu level can facilitate desired choices. Nudging can be a strategy to achieve boosting.

Acknowledgements: This work consolidates and disseminates the results of VeggieEAT project (FP7-IAPP-GA 612326) with the aim to evaluate vegetable acceptability through individual and environmental characteristics across the lifespan in institutional foodservice.

IMPLICIT AND EXPLICIT ATTITUDES TOWARDS FOOD

Perugini M. Dept. of Psychology, University of Milano-Bicocca, Italy

Both implicit and explicit attitudes play an important role in influencing people's behaviors and choices. This also applies to purchases and consumption choices relative to food and drink products. How to measure attitudes, especially implicit, and how to change them, especially with indirect methods, therefore represent two central issues. In this presentation, after briefly illustrating how implicit attitudes can be measured, I will focus on principles and paradigms for direct and indirect attitude change, with examples and applications in the food domain.

THE FUNCTIONAL NEUROANATOMY OF FOOD ORIENTED BEHAVIOUR AND OBESITY IN HUMANS

Devoto F, Zapparoli L, Bonandrini R, Berlingeri M, Ferrulli A, Luzi L, Banfi G, **Paulesu E.**

The dysregulation of food intake in chronic obesity has been explained by different theories. To assess their explanatory power, we meta-analyzed 22 brain-activation imaging studies. We found that obese individuals exhibit hyper-responsivity of the brain regions involved in taste and reward for food-related stimuli. Consistent with a Reward Surfeit Hypothesis, obese individuals exhibit a ventral striatum hyper-responsivity in response to pure tastes, particularly when fasting. Furthermore, we found that obese subjects display more frequent ventral striatal activation for visual food cues when satiated: this continued processing within the reward system, together with the aforementioned evidence, is compatible with the Incentive Sensitization Theory. On the other hand, we did not find univocal evidence in favor of a Reward Deficit Hypothesis nor for a systematic deficit of inhibitory cognitive control. We conclude that the available brain activation data on the dysregulated food intake and food-related behavior in chronic obesity can be best framed within an Incentive Sensitization Theory. Implications of these findings for a brain-based therapy of obesity and analogies with substance abuse will be discussed.

Neurosci Biobehav Rev. 2018 Nov;94:271-285.
doi: 10.1016/j.neubiorev.2018.07.017. Epub 2018 Jul 30. Review

NEUROSIMULATION IN OBESITY

Munte T. Dept. of Neurology, University Hospital Lübeck, Lübeck, Germany

Obesity is taking up epidemic proportions worldwide with significant impacts on the health of both the affected individual and on society as a whole. Treatment approaches consist of behavioural and pharmacological approaches, however, these are often found to be ineffective. In severe obesity, bariatric surgery is frequently performed. Unfortunately, 40% of patients show substantial weight gain over the long term or display the associated metabolic syndrome, making the development of novel therapies necessary. In this talk, I will review the possibilities of brain stimulation, i.e. non-invasive (transcranial magnetic stimulation (TMS), transcranial direct

current stimulation (tDCS) and transcutaneous vagus nerve stimulation (VNS)) and invasive (deep brain stimulation and invasive VNS) modalities. As I will show, neuromodulatory approaches represent a promising tool for targeting specific brain structures implicated in the pathophysiology of obesity. However, data are still sketchy and clinical studies of sufficient size are urgently needed.

THE INCENTIVE SENSITIZATION MODEL OF OBESITY

Berridge K. Dept. of Psychology, University of Michigan, Ann Arbor, MI, USA

The pleasure of tasty foods, and the desire to eat them, arise in our brains – not simply in the foods themselves. This talk will describe how a brain network of small hedonic hotspots generate intense 'liking' for food, and how larger brain mesolimbic systems generate 'wanting' to eat. It will also describe interactions between brain hunger-satiety systems and brain reward systems, and how brain mechanisms for natural appetite relate to addictions.

DIET AND PREVENTION OF COGNITIVE DECLINE

Woodside J. Dept. of Neurology, University Hospital Lübeck, Lübeck, Germany

Dementia is a global public health concern due to increasing prevalence, high morbidity and rising socioeconomic burden. Modifying dietary behaviour could be a promising way to enhance cognition and delay or prevent dementia in later life. Several dietary factors influence dementia risk in humans, for example, vitamin E, B vitamins, omega-3 fatty acids and healthy dietary patterns, particularly the Mediterranean Diet, have been shown to be neuroprotective, while high intake of saturated fat accelerates cognitive decline. It is not entirely clear how diet offers neuroprotection, but several putative mechanisms include beneficial effects on neuronal cell signalling, vascular, anti-oxidant and anti-inflammatory biological pathways. Given that the pathophysiological changes of dementia accumulate years before cognitive impairment becomes evident, understanding the influence of diet on brain health across the life-course is important to inform prevention strategies. Further research is needed to investigate diet-associated neurological change from the earliest

through to latest stages of cognitive decline. Furthermore, intervention strategies require insight into mechanisms involved in diet-induced cognitive change and an understanding of how to support dietary behaviour change, particularly in high risk populations.

ENVIRONMENTAL CAUSES OF PARKINSON'S DISEASE: FOCUS ON THE GUT-BRAIN AXIS

Cilia R. Parkinson Institute, ASST Gaetano Pini-CTO, Milan, Italy

Parkinson's disease (PD) is a progressive neurodegenerative multisystems disorder affecting both the central and peripheral nervous systems, resulting in a wide spectrum of motor and nonmotor symptoms, of which dopamine deficiency is only one of several common features. The causes of idiopathic Parkinson's disease (PD) are still largely unknown, but current knowledge converge on a multifactorial etiology, deriving from environmental factors acting on genetically predisposed individuals along with aging. Although more than 20 genes or loci linked to rare monogenic familial forms of PD with Mendelian inheritance have been identified, candidate gene studies have revealed that only a small percentage of the sporadic PD cases carry mutations in a number of previously known Mendelian PD genes. Therefore, the etiology for the large majority of sporadic PD patients remains largely unknown. The sporadic forms of PD are thus likely to be caused by the combined effects of a genetic predisposition (common variations in different genetic loci with minor effects on PD risk) associated with environmental causes. Epidemiological studies support the notion that exposure to environmental chemicals (including pesticides) increase the risk of developing PD, while some lifestyle habits (smoking, coffee drinking) reduce it, but the exact mechanisms are not fully understood yet. Accumulating evidence supports the hypothesis that pathological α -synuclein aggregates are able to spread from-cell-to-cell, so that the Braak's hypothesis of pathological spreading from the peripheral to the central nervous system (either via vagal nerve or olfactory bulb) has been reconsidered. In this scenario, individual abnormalities of gut microbiota have been suggested to trigger α -synuclein aggregation in terminals of the Meissner's submucosal and/or Auerbach's myenteric plexa. However, the

spreading process seems to be limited to susceptible neurons, whose features are still to be clarified. Considering that the importance of neurodegenerative diseases on the management of public health is growing and the need to understand the environmental causes of PD are mandatory to identify disease-modifying therapies, further research is urgently needed.

NUTRACEUTICALS IN NEURODEGENERATIVE DISEASES

Scapagnini G., Department of Medicine and Health Science, University of Molise, Italy

Numerous epidemiological and observational studies and more recently, also solid intervention trials have highlighted the importance of some food-contained compounds in supporting brain physiology and improving both cognitive processes and mood. The role of diet-derived essential nutrients, non-essential and even non-nutrient compounds and the use of nutraceutical substances capable of positively interfering with inflammation and oxidative stress are, therefore, increasingly seen as potential strategies for neurodegenerative diseases and brain aging. Among functional food's components, dietary lipids, vitamins and polyphenols seems to play a crucial role in brain functions.

Docosahexaenoic acid (DHA) is the most abundant omega-3 fatty acid in cell membranes in the brain; however, the human body is not efficient at synthesizing DHA, so we are largely dependent on dietary DHA. Adequate levels of omega 3, particularly docosahexaenoic acid (DHA), are associated with a correct brain development in fetal life, and they play an important role in brain physiology and transmission of the nervous impulse also in adulthood. Supplementation with DHA (dosages between 250 mg and 2 g die) in randomized and non-randomized clinical trials, was positively associated with an improvement in cognitive decline in elderly subjects with diagnosis of mild cognitive impairment (MCI), but not in Alzheimer's patients.

In recent years, there has been a growing interest, supported by a large number of experimental and epidemiological studies, for the beneficial effects of some phenolic substances, contained in commonly used spices and herbs, in preventing various age-related pathologic conditions, included cognitive disorders and neurodegenerative diseases.

Although the exact mechanisms by which polyphenols promote these effects remain to be elucidated, several reports have shown their ability to stimulate a general xenobiotic response in the target cells, activating multiple defense genes.

Data from our and other laboratories have previously demonstrated that curcumin, the yellow pigment of curry, strongly induces heme-oxygenase-1 (HO-1) expression and activity in different brain cells via the activation of heterodimers of NF-E2-related factors 2 (Nrf2)/antioxidant responsive element (ARE) pathway.

Controlled dietary intervention studies have shown that adequate concentrations of cocoa flavanols can slow down age-related cognitive decline and increase the physiological functions of brain areas responsible for mental alertness and memory formation and consolidation. Finally, some atypical amino acids such as taurine and homotaurine, are endowed with specific neuroprotective properties able to counteract neurotoxic effects of beta-amyloid protein and might represent a potential novel support in prevention strategies against neurodegenerative diseases.

In conclusion several evidences are improving an upcoming field of science, named nutritional neuroscience, that identify dietary manipulations as a viable strategy for enhancing cognitive abilities and protecting the brain from damage, promoting repair and counteracting the effects of aging.

DIETARY PATTERNS, COGNITION, AND BRAIN AGING: EXPERIENCE FROM EUROPEAN COHORT STUDIES

Prinelli F.^{1,2} and Musicco M.¹. ¹Institute of Biomedical Technologies-National Research Council, Via Fratelli Cervi 93, 20090 Segrate (MI), Italy. ²Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, 171 65 Solna, Stockholm, Sweden

Multiple lines of epidemiological evidence, mostly from longitudinal studies, suggest that food-derived biologically active molecules such as B complex vitamins (B9 and B12), vitamins A, C, D, E, ω -3 fatty acids, and polyphenols, may have beneficial effects on brain function and cognitive status in older adults. Dietary patterns, as the Mediterranean Diet (MD)-type pattern, capturing the multidimensionality of nutrient-related factors, may not only reduce the risk of dementia and preserve structural connectivity, but also lower

mortality rates of disease progression in those already afflicted. From a physiological viewpoint these bioactive molecules may have an effect on the processes that lead to dementia pathology, influencing mitochondrial function, oxidative stress, inflammation, immune dysfunction and alterations in nutrient sensing pathways. It is noteworthy that compared to cognitively intact controls, patients with AD show lower brain and circulatory availability of nutrients as DHA, choline, vitamin B12, folate, selenium, vitamin A, C and E. These findings suggest that AD patients might have a functional deficiency for these nutrients limiting them to counteract the effects of phospholipid loss, elevated oxidative stress, and inflammation.

Some multi-domain interventions incorporating nutritional components have been assessed in clinical trials in cognitively healthy subjects or in those at high risk of dementia, and others are ongoing. Results from these trials might hold promise for preventing cognitive impairment and dementia.

In the recent decades, research has highlighted the potential role of diet in modulating the microbe population's composition, which in turn impact on the brain and cognitive status. Within the bidirectional interactions of the gut-brain axis, the gut microbiota communicates to the central nervous system through neural, immune, and endocrine signaling mechanisms, and also via the generation of bacterial end products metabolites, which exert their physiologic effects in the host.

Collectively, this body of evidence enlightens the importance of nutrition in cognitive impairment and brain aging. Dietary recommendations and multicomponent nutritional intervention may offer a good opportunity to modulate the impact of nutrients for both prevention and patients' treatment, by alleviating some of the symptoms or slowing down the pathology progression. Furthermore, the gut-brain axis can be a possible via from nutrient intake to brain function.

The present talk will be broken into a series of sections and will give an up to date overview of this pioneering field of research, showing and discussing main results from available studies, and providing a short outlook on future directions.

UNDIGESTED FOOD AND HUMAN GUT MICROBIOTA COOPERATE IN THE PATHOGENESIS OF NEUROINFLAMMATORY DISEASES: A MATTER OF BARRIERS

Riccio P. Department of Sciences, University of Basilicata, Potenza, Italy.



As food is an active subject and may have anti-inflammatory or pro-inflammatory effects, dietary habits may modulate the low-grade neuroinflammation associated with chronic neurodegenerative diseases.

Food is living matter, different from us but made of our own nature. Therefore, it is at the same time foreign to us (*non-self*), if not yet digested, and like us (*self*), after its complete digestion. To avoid the spreading of undigested food from the lumen, the intestinal barrier must remain intact.

What we eat and how much we eat shape the composition of the gut microbiota and can either promote gut eubiosis (anti-inflammatory), or gut dysbiosis (pro-inflammatory). Persistent gut dysbiosis, consequent to energy-dense and low in fiber Western diets, leads to intestinal inflammation and a leaky intestinal barrier. The consequent efflux into the blood stream of undigested food, microbes, endotoxins, cells and molecules of the mucosal immune system, causes chronic systemic inflammation. If the autoimmune inflammatory processes address the blood-brain barrier, they may cause its breakdown, trigger microglia and astrocytes and set up chronic neuroinflammatory diseases. Therefore, the premise for starting these diseases is the opening of the two barriers, the intestinal and the hemato-encephalic, in the presence of a low-grade systemic inflammation.

The question arises of what determines the attack on the blood-brain barrier.

We suggest that what determines the organ specificity of the autoimmune inflammatory process may depend on the disruption of the intestinal barrier and the spreading out of the intestinal lumen of undigested food antigens resembling proteins of the organ being attacked. Specific antibodies are formed. In this context, the role of gut microbiota is to cooperate in the activation of T cells and in the disruption of the two barriers. This may apply to the blood-brain barrier and the brain, as to other organs and other inflammatory diseases, including cancer.

Understanding the cooperation between gut microbiota and undigested food in chronic inflammation may clarify the organ specificity of the inflammatory/autoimmune diseases, may allow the set up of adequate experimental models and develop novel dietary approaches for their treatment.

BRIDGING NEUROSCIENCE AND NEUROIMAGING RESEARCH IN CLINICAL PRACTICE IN ANOREXIA NERVOSA

Favaro A. Department of Neurosciences, University of Padova, Padova, Italy

Research in the field of neuroimaging, connectomics and neuropsychology is growing in the field of eating disorders. In this presentation, I will review the recent advances of neuroscience research conducted by our group of research with a particular attention to those aspects that have direct or indirect clinical implications.

Anorexia nervosa displays peculiar neuropsychological characteristics that have potential impact on outcome. However, few studies to date explored this. Similarly, although a lot of new knowledge is available in the neuroimaging of eating disorders, it is still difficult to translate research findings into practice and clinical implications. In this presentation, I will report about neuroimaging and neuropsychological studies that demonstrated that neuropsychological and brain morphological characteristics have a significant link with clinical characteristics and a predictive effect on the outcome.

FOOD AND METHYLATION POTENTIAL: AN EPIGENETIC APPROACH TO ANOREXIA NERVOSA AND OTHER PSYCHIATRIC DISORDERS

Tremolizzo L. School of Medicine and Surgery, University di Milano-Bicocca, Monza, Italy

Object: Methionine is an essential amino acid and the source of methyl groups for several important cellular reactions. DNA methylation, in particular, represents a major focus of interest since modulating the expression of selected genes without entailing changes in the base sequence of the genetic code. This epigenetic mechanism is especially relevant for the field of psychiatry considering the overt failure of the Mendelian approach, in spite of clear patterns of heritability. General focus of this presentation will be on the available evidence for altered epigenetic mechanisms in two distinct psychiatric disorders: schizophrenia and anorexia nervosa of the restrictive type (ANr).

Results: Specifically, reference will be made to the potential consequences of too much and too little Methionine intake. On one hand, the excessive

administration of this amino acid generated an epigenetic mouse model recapitulating several schizophrenia-related endophenotypes. On the other hand, reduced Methionine intake, as assumed in ANr patients, was associated to reduced DNA methylation in blood samples and correlated to disrupted hormone production and increased homocysteine and cobalamin serum levels.

Conclusion: Methionine food intake may be critical in order to keep the epigenetic homeostasis. The epigenetic approach allows going beyond the nature/nurture dichotomy in the field of psychiatry, opening novel therapeutic perspectives.

DIETARY AND LIFESTYLE HABITS IN CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP). DATA FROM THE ITALIAN CIDP DATABASE

Doneddu P.E.¹, Bianchi E.², Cocito D.³, Manganelli F.⁴, Fazio R.⁵, Filosto M.⁶, Mazzeo A.⁷, Cosentino G.⁸, Cortese A.⁹, Jann S.¹⁰, Clerici A.¹¹, Antonini G.¹², Siciliano G.¹³, Luigetti M.¹⁴, Marfia G.¹⁵, Briani C.¹⁶, Lauria G.¹⁷, Rosso T.¹⁸, Cavaletti G.¹⁹, Carpo M.²⁰, Benedetti L.²¹, Beghi E.²², Liberatore G.²³, Nobile-Orazio E.²⁴

1.Humanitas Clinical and Research Hospital, Neuromuscular and Neuroimmunology Unit, Milan, Italy; 2.IRCCS Istituto Mario Negri, Laboratorio di Malattie Neurologiche, Milan, Italy; 3.University of Turin, Department of Neuroscience, Turin, Italy; 4.University of Naples Federico II, Department of Neuroscience. Reproductive Sciences and Odontostomatology, Naples, Italy; 5.San Raffaele Scientific Institute, Department of Neuroscience, Milan, Italy; 6.University of Brescia, Center for Neuromuscular Diseases and Neuropathies, Brescia, Italy; 7.University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy; 8.University of Palermo, Department of Experimental BioMedicine and Clinical Neurosciences, Palermo, Italy; 9.IRCCS Foundation C. Mondino National Neurological Institute, Department of Neurology, Pavia, Italy; 10.Niguarda Ca' Granda Hospital, Department of Neuroscience, Milan, Italy; 11.Insubria University, Neurology Unit, Varese, Italy; 12.Sapienza University of Rome, Department of Neurology, Rome, Italy; 13.University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; 14.Catholic University of Sacred Heart, IRCCS Foundation Policlinico A. Gemelli, Unit of Neurology, Rome, Italy; 15.Tor Vergata University of Rome, Department of System Medicine, Rome, Italy; 16.University of Padua, Department of Neuroscience, Padua, Italy; 17.IRCCS Foundation Carlo Besta Neurological Institute, Unit of Neurology, Milan, Italy; 18.UOC-Neurologia Castelfranco Veneto, ULSS2 Marca Trevigiana, Treviso, Italy; 19.University of Milano-Bicocca, School of Medicine and Surgery and

Experimental Neurology Unit, Monza, Italy; 20.Ospedale Treviglio, ASST Bergamo Ovest, Treviglio, Italy; 21.Sant'Andrea Hospital, Neurology Unit, La Spezia, Italy; 22.Istituto Mario Negri, Laboratorio di Malattie Neurologiche, Milan, Italy; 23.Humanitas Clinical and Research Institute, Neuromuscular and Neuroimmunology Service, Milan, Italy; 24.Humanitas Clinical and Research Hospital, University of Milan, Neuromuscular and Neuroimmunology Service, Department of Biotechnology and Translational Medicine, Milan, Italy.

Object: Environmental risk factors for CIDP have not been identified so far, nor is it known whether dietary and lifestyle factors play a role in the CIDP disease progression and accumulation of disability. To assess whether dietary and lifestyle habits play a role in the CIDP risk and its disease progression and accumulation of disability

Materials: We collected information about modifiable environmental factors in patients with CIDP included in the Italian CIDP database and their partners.

Methods: Only patients fulfilling the EFNS/PNS diagnostic criteria for CIDP were included. The partners of patients with CIDP were chosen as controls. Gender-matched analysis was performed with randomly-selected controls with a 1:1 ratio between patients and controls.

Results: Dietary and lifestyle data of 323 patients and 266 controls were available. A total of 195 cases and 195 sex-matched controls were used in the analysis of the CIDP risk, while 323 patients were included in the analysis of the CIDP disability progression. Patients eating rice at least three times per week or eating fish at least once per week appeared to be at decreased risk of acquiring CIDP. Regarding the role of modifiable factors on disease severity and its perception, physical activity was associated with having less sensory impairment, lower disability, and higher quality of life in all the domains except of anxiety and depression. Smoking was associated with a greater probability of having less weakness and less anxiety and depression. Alcohol and sweets consumption was associated with greater probability of not having limitations in self-care.

Discussion: Some environmental factors seem to be associated with the risk of CIDP and with the accumulation of disability and quality of life. Our study adds weight to the previous observations that physical activity reduces the burden of disability and improves QOL in patients with CIDP.

Conclusions: More epidemiological and intervention studies are needed to confirm our

results and for lifestyle risk factors modification to become part of a secondary preventive strategy.

DOPAMINE DRIVES BINGE-LIKE CONSUMPTION OF A PALATABLE FOOD IN EXPERIMENTAL PARKINSONISM

Ghiqlieri V.¹, Mineo D.¹, Cacace F.¹, Mancini M.¹, Vannelli A.¹, Campanelli F.¹, Marino G.¹, Natale G.¹, Cardinale A.², Calabresi P.^{1,2}, Picconi B.³ 1.IRCCS Fondazione Santa Lucia, Neurophysiology, Rome, Italy; 2.Neurological Clinic, Department of Medicine, University of Perugia, Perugia, Italy; 3.IRCCS San Raffaele Pisana, University San Raffaele, Rome, Italy.

Prolonged dopaminergic replacement therapy in Parkinson's disease (PD) results in pulsatile dopamine receptors stimulation in both dorsal and ventral striatum causing wearing off, motor fluctuations, and non-motor side effects such as behavioral addictions. Among impulse control disorders, binge eating can be easily modeled in laboratory animals. In this study we investigated the role of dopamine in binge eating disorder (BED) and how prolonged dopaminergic replacement therapy in parkinsonian rats, affects binge-like consumption of palatable food. For this reason, rats are unilaterally lesioned with 6-hydroxy-dopamine (6-OHDA), to generate a model of PD subjected to a modified version of Corwin's limited access protocol, with low and high food restriction schedule, in which vegetable shortening was replaced with milk chocolate bars. Food preference, food intake, and weight gain were monitored in sham-operated and unilaterally lesioned rats, modelling binge eating disorder. We hypothesized that manipulation of dopamine levels in 6-OHDA rats, as a model of PD characterized by a different extent of dopamine denervation between dorsal and ventral striatum, would influence both synaptic plasticity of the nucleus accumbens and binge-like eating behavior.

Methods: Electrophysiological properties and long-term potentiation (LTP) of GABAergic spiny projection neurons of the nucleus accumbens core were analyzed through ex-vivo intracellular and patch-clamp recordings from corticostriatal slices of naïve and L-Dopa-treated rats to explore neuronal correlates of binge-like behaviors.

Results: Results show that Sham-operated animals with intact nucleus accumbens core plasticity reliably developed food-addiction-like behavior when exposed to intermittent access to a highly palatable food. Unlike, parkinsonian rats

were unresponsive to such restriction regimens, and also plasticity was lost in ventral spiny neurons. Chronic L-Dopa treatment was able to restore the long-term potentiation and compulsive eating, but with a different temporal dynamic that follows that of drug administration. Our data indicate that endogenous and exogenous dopamine drive binge-like consumption of a palatable food in healthy and parkinsonian rats with distinct temporal dynamics, providing new insights into the complexity of L-Dopa effects on the mesolimbic dopaminergic system.

Key Words: impulse control disorders; L-dopa; nucleus accumbens; plasticity

METABOLIC DYSFUNCTION AS RISK FACTOR FOR NEUROINFLAMMATORY PATHOLOGY DISEASE

Murtaj V.¹, Belloli S.², Chiaffarelli R.³, Chaabane L.⁴, Canu T.⁴, Marra P.⁴, Esposito A.⁴, Masiello V.⁵, Coliva A.⁵, Malosio M.L.⁶, Moresco R.M.⁷ 1.University of Milano-Bicocca, PhD program in Neuroscience, Department of Medicine and Surgery and NeuroMi Center, Monza, Italy; 2.CNR, Institute of Molecular Bioimaging and Physiology (IBFM), Segrate, Italy; 3.University of Milano-Bicocca, Department of Medicine and Surgery, Monza, Italy; 4.IRCCS San Raffaele Scientific Institute, Experimental Imaging Center, Milan, Italy; 5.San Raffaele Scientific Institute, Nuclear Medicine Department, Milan, Italy; 6.CNR, Institute of Neuroscience, Milan, Italy; 7.University of Milano-Bicocca, Department of Medicine and Surgery and NeuroMi Center, Monza, Italy.

Object: Diet-induced obesity and associated metabolic effects can lead to neurological dysfunction and increase the risk of developing neurodegenerative diseases. The effects of a high-fat diet (HFD) on the central nervous system are not well-understood. The aim of this study is the evaluation of the influence of HFD on the metabolic profile and inflammatory pathway in a mouse model of Insulin Resistance (IR).

Materials: C57BL/6J male and female mice were fed with standard chow or HFD (45%/60%) for 35 weeks. Animals were monitored weekly for body weight and Glucose Tolerance Test (GTT). Biochemical analysis were performed at different time points on plasma samples to investigate different metabolic pathways.

Methods: Positron Emission Tomography (PET) imaging studies were performed longitudinally using [¹⁸F]FDG, [¹⁸F]VC701 and [¹⁸F]Fallypride as radiopharmaceuticals, to measure respectively glucose consumption, microglia/macrophages activation and dopamine receptor within the brain. Magnetic Resonance Imaging (MRI) through spectroscopy techniques were used to measure the effects of diet on hepatic lipid content.

Results: HFD induces a significant increase in body weight with a gender effect. Metabolic tolerance test exhibited increased blood circulating glucose concentration in both male and female, indicating impaired insulin function. Regional [¹⁸F]FDG uptake showed a significant increase in glucose metabolism within cortical regions in males while no differences were observed in females. A specific analysis performed on anterior cortex revealed a hyper-metabolism occurring in male mice at 12 and 35 weeks of diet, that could be associated with cognitive impairment. [¹⁸F]VC701-PET showed a general trend toward an increase of tracer uptake all over the brain after diet consumption in both male and female HFD mice. Liver showed higher lipid content confirmed by MR spectroscopy and immunohistochemical analysis.

Discussion: Our finding suggests that HFD induced-obesity in adult mice cause multiple changes in peripheral organs and central nervous system. The increased binding of the activated microglia associated TSPO radioligand suggest that obesity is able to induce a diffuse neuroinflammatory reaction in mice brain while liver remains a major organ affected in the regulation of the metabolism.

Conclusion: PET imaging technique has permitted to identify the presence of metabolic derangement and neuroinflammatory response of mice brain induced by a HFD. This finding is relevant since our model reproduces the peripheral metabolic modification typical of IR and type 2 diabetes. This work was supported by "AMANDA": Regione Lombardia and by MIUR - Department of Excellence project PREMIA (PRECision MedIcine Approach: bringing biomarker research to clinic).

INHIBITORY CONTROL IN FOOD-RELATED MOTOR TASK

Picazio S.¹, Bianco V.², Di Russo F.³, Koch G.¹
1.IRCCS "Santa Lucia" Foundation, Department of Clinical and Behavioral Neurology, Rome, Italy; 2. IRCCS "Santa Lucia" Foundation, Motor and Cognitive Neurorehabilitation, Rome, Italy;

3.University "Foro Italico", Department of Human and Health Sciences, Rome, Italy

Object: In the present pilot study we aim to investigate motor inhibitory control in the context of human eating behaviour. One group of healthy young women performed a food-related Go/NoGo paradigm; Motor Evoked Potentials (MEP) were obtained by delivering transcranial magnetic stimulation (TMS) during task performance.

Materials: Human eating behaviour is normally controlled by homeostatic mechanisms in order to keep body weight constant. However, hedonic mechanisms respond to the sensory input associated with nutritive behaviour, especially visual appearance of food (Verhagen, 2007) and it is well established that several brain areas are differentially activate in food versus no-food pictures (Furhrer et al., 2008). In the present pilot study, we used a food-specific Go/NoGo paradigm to explore inhibitory control mechanisms in the context of human eating behaviour.

Methods: A sample of healthy, normal-weight female participants (mean age 26) performed a 50% probability visual affective Go/NoGo task involving Food and No-Food pictures as stimuli. Food stimuli included High-Calories and Low-Calories food pictures. The experimental session consisted of a Food-target block and a No-Food target block. Behavioural measures included mean reaction time (RTs) to Go trials, commission errors percentage for failures of inhibition to No-Go trials (%FA) and omission errors percentage (%OM) for failures of response to Go-trials. Single-pulse TMS was administered throughout the session over the right primary motor cortex (M1) in order to measure corticospinal excitability during the different task conditions.

Results: Go RTs of High-Calories food pictures were faster than Go RTs of Low-Calories food and of No-Food pictures, while Low-Calories and No-Food pictures RTs did not differ. Go MEPs did not differ according to High-Calories, Low-Calories or No-Food pictures. NoGo MEPs were higher for Low-Calories pictures than High-Calories and No-Food pictures.

Discussion: In the present pilot study, we showed that the faster RT to Food-related pictures compared to No-food related pictures were limited to the High-calories category only. Both behavioural and neurophysiological measures point at a differential modulation when targeting inhibitory control, in favour of the more appetizing food category (High-calories). Present pilot data suggest that the hedonic value associated to food

positively interfere with inhibitory control according to the appealing value of food.

Conclusions: In healthy individuals the sight of food elicits distinctive motor tendencies regulated by both homeostatic and hedonic mechanisms. Future work will explore to what extent these processes are affected in eating-disorders patients.

RISK-TAKING BEHAVIOUR IN ANOREXIA NERVOSA AND OBESITY: WHEN THE BODY MAKES THE DIFFERENCE

Salvato G.^{1,2,3}, **Basilico S.**^{2,3}, **Tarlarini P.**⁴, **Tajani M.**⁴, **Corradi E.**⁴, **Bottini G.**^{1,2,3}

1.Department of Brain and Behavioural Sciences, University of Pavia, Pavia, Italy; 2.Cognitive Neuropsychology Centre, ASST "Grande Ospedale Metropolitano" Niguarda, Milan, Italy; 3.NeuroMi, Milan Center for Neuroscience, Italy; 4.S.C.Dietetica e Nutrizione Clinica, Centro per la Cura dei Disturbi del Comportamento Alimentare, ASST "Grande Ospedale Metropolitano" Niguarda, Milan, Italy

Object: According to the "continuum hypothesis", obesity and Anorexia Nervosa (AN) have been considered as part of the same spectrum. For instance, both show executive dysfunctions, although several cognitive and neurofunctional differences are also present. This suggests that AN and obesity do not lie on a simple linear spectrum model. This study investigates whether AN patients and obese individuals perform differently at a risk-taking task including two different stimuli, one of which related to the body.

Materials: We tested four samples for a total number of 160 participants: 40 AN patients (age: M=23.3 SD= 7.1; education: M=13.4, SD=3; BMI: M=15.8, SD=1.1) and 40 healthy controls (age: M=21.9, SD=1.6; education: M=14.4, SD=1.8; BMI: M=21.7, SD=3.4); 40 obese individuals (age: M=54, SD=9.4; education: M=10.8, SD=3.8; BMI: M=37.3, SD=1.9) and 40 healthy controls (age: M=48.9, SD=17.1; education: M=12.5, SD=3.7; BMI: M=24.3, SD=2.7).

Methods: Participants were administered with the Balloon Analogue Risk Task (BART), in which they are offered the chance to virtually earn money by pumping a balloon up by clicking a keyboard button. Each click causes the balloon to incrementally inflate and virtual money to be added to a counter up until some threshold, at which point the balloon is overinflated and explodes. Each

pump confers higher risk, but also greater potential reward. Here we administered the original version (Balloon task) and a modified version of it in which participants were required to inflate a virtual body (Body task).

Results: Compared to healthy controls, AN patients showed no difference at the Balloon Risk Index. Interestingly, we found a higher Risk Index for the AN group at the Body task. No differences between obese individuals and controls were found at both tasks. Comparing the two patients' groups on standardized scores, obese individuals and AN patients showed an equal Risk Index at the Balloon task, whereas they differed at the Body task, with AN patients risking more.

Discussion: AN patients show higher risk-taking only when the task involved the body as a stimulus. This finding mirrors the behaviours at risk in AN that significantly increase the mortality rates in these patients.

Conclusions: Our evidence does not fully support the "continuum hypothesis" in eating and weight disorders, suggesting that obesity and AN are distinct physical and psychiatric conditions at least in this behavioural domain

ASSESSMENT OF SLEEP AND OBESITY IN ADULTS AND CHILDREN: OBSERVATIONAL STUDY

Bonanno L., Sottile F. IRCCS Bonino-puljo, Neurologia, Messina, Italy

Object Sleep is essential to support the functions and health of the entire body. In our study we investigated the association between sleep duration and quality, and overweight risk and obesity in children and adults. The examined subjects diet and eating habits were also evaluated.

Materials The study was conducted on secondary school children, and on practice dental clinic patients. Were involved 199 subjects, of which 71 adults (29 males and 42 females) with age between 29 and 65 years, and 128 children (73 males and 55 females) with age between 10 and 13 years.

Methods The data were picked in a period between October 2016 and November 2017. Were evaluated weight, height and Body Mass Index (BMI) data. The weight and height were measured with standard techniques, the BMI was assessed dividing the weight in kg with the height square expressed in meters (Kg/m²). Subjects were

divided into underweight, normal weight, overweight and obese. Were administered several questionnaires to evaluate the quantity and quality of sleep (hours of sleep overall, the mode of falling asleep and the quality of sleep).

Results In adult male group found a significant positive correlation between age and BMI score ($r=0.48$; $p=0.009$) and a significant negative correlation between sleep hours and BMI score ($r=-0.64$; $p<0.001$). In adult female group, we found a significant negative correlation between sleep hours and BMI score ($r=-0.78$; $p<0.001$). Sleep hours was significant predictor on BMI score for male and female group. In children group, analysis between male and female groups highlighted a significant differences in hours of sleep in underweight group ($p=0.03$). A significant negative correlation between sleep hours and BMI score ($r=-0.6$; $p<0.001$) and ($r=-0.56$; $p<0.001$) in male and female group respectively were found. Sleep hours were significant predictor on BMI score for male and female group.

Discussion Observational studies and clinical experiences have shown that adherence to the Mediterranean Diet is inversely associated with obesity. Our study has highlighted that the duration and quality of sleep can also represent a risk factor of overweight and obesity in examined subjects. Therefore, sufficient sleep is required to maintain a normal weight.

Conclusions Quantity and quality sleep can also represent a risk factor of overweight and obesity, so sufficient sleep is a factor that influence a normal weight. Adults and children that sleep less, have an increase of obesity and overweight risk with dysfunctional eating behaviours, decreased physical activity and metabolic changes.

DIETARY INTERVENTIONS FOR MULTIPLE SCLEROSIS: A COCHRANE REVIEW

Vacchi L.¹, Jackson-Tarilton C.S.², Merdad R.³, Johnston B.C.³, Parks N.E.² 1.University of Milano-Bicocca, Medicine and Surgery, Milan, Italy; 2.Dalhousie University, Department of Medicine, Halifax, Canada; 3.Dalhousie University, Community Health and Epidemiology, Halifax, Canada

Objective: High quality recommendations on dietary interventions for multiple sclerosis (MS) are unavailable. The aim of this Cochrane review was to assess a broad range of dietary interventions for

MS patients to verify any effect on health outcomes.

Materials: We included randomised and non-randomised controlled clinical trials examining the effects of any dietary supplementation or intervention versus placebo, non-active or active interventions in patients with MS. Trials on vitamin D were excluded as evaluated in a specific Cochrane review.

Methods: A structured literature search was conducted among 7 primary databases through January 2018. Two authors independently screened titles, abstracts and full-text articles and extracted target data. Primary outcomes were relapses and disability progression; secondary outcomes included MRI activity, adverse events, and patient-reported outcomes. Analysis was performed separately for each intervention. Dichotomous data were summarised as relative risks (RR) using a random-effects model in the presence of heterogeneity. Continuous data were analysed using weighted mean differences.

Results: Among 2091 potentially eligible articles, we included 30 trials. Among 7 studies comparing polyunsaturated fatty acid (PUFA) versus monounsaturated fatty acid (MUFA) there was no difference in number of relapses (RR 1.0, 95%CI 0.86 to 1.15) or in global impression of deterioration (RR 0.86, 95% CI 0.71 to 1.04). Among 4 trials on PUFA Omega-3 versus Omega-6 there was no difference in number of relapses (RR 1.01, 95% CI 0.62 to 1.66), or in mean Expanded Disability Status Scale (MD 0.19, 95% CI -0.15 to 0.52). Among 10 studies using antioxidants supplementation versus placebo there was no difference in relapses (RR 0.98, 95% CI 0.61 to 1.56), while mean EDSS was slightly lower among participants treated with placebo (MD 0.25, 95% CI 0.10 to 0.41). The heterogeneity among the 3 trials examining dietary programs and 6 trials examining other dietary supplements (probiotics, creatine, riboflavin, palmitoylethanolamide, carnitine, biotin) didn't allow us to provide aggregate analysis. Five trials reported adverse events, with no differences between groups. In general, trials heterogeneity was high and studies quality very poor.

Discussion. Risk of bias was considerable, which may have led to under-estimate or over-estimate the potential effects of the dietary interventions. Results from the present review show that nor PUFAs nor antioxidant supplementations seem to have major effect on the main clinical outcome in MS (relapses and disease progression).

Conclusion. At present, there is insufficient high-quality evidence from 30 trials on dietary interventions in MS to take evidence-based decisions.

COFFEE METABOLITES PREVENTS DEP INDUCED OXIDATIVE STRESS IN C6 GLIOMA CELLS

Bulbarelli A.¹, Lonati E.R.¹, Cazzaniga E.¹, Carrozzini T.¹, Mena P.², Del Rio D.², Botto L.M.¹ 1. Università Milano Bicocca, Medicina e Chirurgia, Monza, Italy; 2. Università di Parma, Food and Drug, Parma, Italy.

OBJECT: Neurodegenerative diseases are associated with neuronal and glial cell death. A contributory cause of neurodegeneration is the chronic exposure to air pollution that can impair the blood-brain barrier and induce neuroinflammation and oxidative stress.

Nutrition might modify the oxidative impact of air pollution on health. Recently, it has been shown that the use of phenolic acids such as caffeic, chlorogenic and ferulic, can modulate oxidative stress. These substances, following dietary intake, undergo a process of metabolization by the microbiota and liver leading to different metabolites generation.

Here we investigate the possible antioxidant action of these molecules, on C6 glioma cells treated with Diesel Exhaust Particles (DEP).

MATERIALS: All the chemicals were purchased from Sigma Aldrich (Saint Louis, Missouri)

All material for electrophoresis was from Bio-Rad (Milan, Italy).

METHODS: C6 glioma cells were exposed to DEP (25 microgram/ml), pre-treated or not with coffee metabolites and compared with those pre-treated with a classic antioxidant N-acetylcysteine (NAC). ROS levels and cell viability were assessed.

RESULTS: C6 glioma cells exposed to DEP demonstrated significant ROS level increase after 10-14h, with a peak after 12h. At this time cell viability was significantly reduced compared to the control.

Pre-treatment with coffee metabolites caused a significant decrease in ROS production, associated with a parallel restoration of cell viability to the control value.

Furthermore proteins related to oxidative stress were analysed. In particular, after DEP exposure a significant activation of ERK1-2, comparing to

control, was observed concomitantly with a significant increase in HO-1 and decrease in iNOS level.

Pre-treatment with coffee metabolites reduced significantly ERK1-2 activation while it increased HO-1 and iNOS above the control value.

Pre-treatment with a classic antioxidant (NAC) did not result in significant effects.

DISCUSSION: Air pollution is linked to central nervous system disease.

In this work, ROS levels and cell viability were assessed after exposition of C6 glioma to DEP proving that it causes a significant ROS level increase and cell vitality reduction. Pre-treatment with coffee metabolites was able to prevent these effects, while pre-treatment with a classic antioxidant (NAC) was not able to result in significant effects.

Further exploring proteins related to oxidative stress it was evident that NAC and coffee metabolites act by means of different mechanisms.

CONCLUSIONS: The results obtained may potentially be applicable in the future for the production of functionalized foods containing coffee metabolites, in order to mitigate the harmful effects of atmospheric pollution.

NEUROPROTECTION AND ANTIGLIOSIS ACTIVITY OF NATURAL ANTIOXIDANTS INVOLVES DIFFERENTIAL MODULATION OF NF-KB IN NEURONS AND ASTROCYTES

Martorana F.¹, Aprea F.¹, Foti M.², Riccio P.³, Papa M.⁴, Alberghina L.⁵, Colangelo A.M.¹

1.Università Milano-Bicocca, Dipartimento di Biotecnologie e Bioscienze, Milan, Italy;

2.Università Milano-Bicocca, School of Medicine, Monza, Italy;

3.Università della Basilicata, Dipartimento di Scienze, Potenza, Italy;

4.Università della Campania "Luigi vanvitelli", Dipartimento di Medicina Pubblica, Napoli, Italy;

5.Università di Milano-Bicocca, SYSBIO center of Systems Biology ISBE.ITALY, Milan, Italy

Aims. Neuroinflammation and oxidative stress underlie neuronal and astrocytic dysfunction in neurodegenerative diseases. Neuroinflammation is characterized by sustained glial activation (reactive gliosis) which is the cause of proliferation and loss of proper astrocytic function, which compromises synaptic function and leads to excitotoxicity and increase of ROS. Dietary molecules, like polyphenols, carotenoids and thiolic compounds,

may protect against neurodegenerative and neuroinflammatory disorders. They act as antioxidants and activate pathways and transcription factors that regulate metabolism and inflammatory responses.

Materials and Methods. Primary cultures of astrocytes and neurons were treated with Tumor Necrosis Factor α (TNF α) or lipopolysaccharide (LPS) in the presence/absence of antioxidant molecules (RSV, QRC, CRC, LYC, ALA, OLP, GTE and NAC) to analyze the effect on survival, proliferation, ROS levels and activation of transcriptional factors.

Results. Our data revealed that all tested antioxidants decrease gliosis by reducing astrocytic proliferation and protect cortical neurons exposed to conditioned medium (CM) from reactive astrocytes, as well as under conditions of glutamate oxidative stress toxicity. All antioxidants act through differential modulation of NF- κ B in neurons and astrocytes. Finally, we newly demonstrate that effective antigliosis and neuroprotective activity can be achieved by defined cocktails of dietary antioxidants at low doses.

Discussion/Conclusions. Our data suggest that effective antigliosis and neuroprotective activity is achieved with a defined cocktail of four natural antioxidants suggesting a promising strategy to reduce inflammatory and oxidative damage in neurodegenerative diseases with limited side effects.

COGNITIVE AND MULTISENSORY INTEGRATION EFFECTS IN FUNCTIONAL FOOD PERCEPTION: A PRELIMINARY REPORT

Risso P., Gallace A. Bicocca University Milan, Psychology, Milan, Italy

Object: Functional foods are dietary items that might modulate one or more targeted functions in the body. Their use might be related to health-promotion or disease prevention. However, such food, beside their possible effectiveness, need also to be appealing to consumers' brains. Here, we tried to understand the role of the kind of information provided, shape, and colour of the food item in order to generate preference choices by young and over 65 consumers.

Materials: In our experiments we used two crackers and two breadsticks food prototypes. Four pictures of the same foods were also adopted.

Methods: We evaluated the role of general information regarding the food, as well as the visual and gustatory aspects of the food items by

means of Visual Analogue Scale. Both expectations based on the visual appearance of the food (experiment 1 and 2) and actual taste of the items (experiment 3) were tested. Participants evaluated the food using the following scales: Pleasantness, Price Range, Quality, Purchase Desire, Healthiness, Friability, Bouba-Kiki, Lightness, Heaviness.

Results: Experiment 1: verbal information

We found that different kinds of written information regarding the food (e.g., whether or not it contains certain nutrients or allergenic substances), affect the participants evaluation on several perceptual dimensions (e.g. Pleasantness, Healthiness).

Experiment 2: We found that the visual aspect of the foods presented with no verbal information affect the participants gustatory perception on several perceptual dimensions (e.g., Pleasant. Purchase Desire, Quality).

Experiment 3: Our results showed that over 65yo participants preferred on several evaluation scales the food items that had a breadstick shape rather than those with a cracker like shape even when they contained exactly the same ingredients

Discussion: In Experiment 1, the written information indicating the nutrient added to the visually presented items actually decreased participant's attractiveness, as compared to a label indicating only the absence of allergens. This result might suggest the importance of communicating clear and understandable information to the consumer in order to affect his/her choice. In Experiment 2, we demonstrated that both foods' colour and shape can affect people visual preference for the items. Finally, in Experiment 3, shape and taste interacted in affecting functional food evaluation of over 65yo participants.

Conclusions: We found that both in young and elderly people, the expectations and the gustatory perception of functional foods can be significantly modulated by complex cognitive and multisensory interactive effects occurring in several brain areas.

NEUROPROTECTIVE PROPERTIES OF VIGNA UNGUICULATA EXTRACTS IN YEAST MODELS OF NEURODEGENERATION

Tripodi F.¹, Milanese R.¹, Guzzetti L.¹, Panzeri D.¹, Falletta E.², Sacarafoni A.³,

Tedeschi G.⁴, Labra M.¹, Coccetti P.¹ Tripodi F.¹, Milanese R.¹, Guzzetti L.¹, Panzeri D.¹, Falletta E.², Sacarafoni A.³,

Tedeschi G.⁴, Labra M.¹, Coccetti P.¹ 1.University of Milano-Bicocca, Department of Biotechnology and Biosciences, Milan, Italy; 2.University of Milan,



Department of Chemistry, Milan, Italy; 3.University of Milan, Department of Food, Environmental and Nutritional Sciences (DeFENS), Milan, Italy; 4.University of Milan, Department of Veterinary Medicine (DIMEVET), Milan, Italy

Object Neuroprotective Properties of *Vigna unguiculata* extracts in yeast models of neurodegeneration.

Materials We prepared aqueous extracts from seeds of different species originating from the Arusha area in Tanzania: *Vigna unguiculata* and *Cajanus cajan*, two NUS (neglected and underutilized species), and *Phaseolus vulgaris*, the staple reference species. We also purified 7S globulins from *V. unguiculata* seeds, the most abundant class of proteins, proved to exert various health favorable effects, including blood cholesterol reduction in animal models. We employed a simple model of neurodegeneration, represented by heterologous expression of α -Syn in yeast cells. α -Syn is a protein linked to a group of age-related neurodegenerative diseases called synucleinopathies, and its expression in *Saccharomyces cerevisiae* is accompanied by shortening of lifespan.

Methods The yeast CLS (chronological life span) assay is widely used to model aging of non-dividing cells of higher organisms. CLS is the length of time that a non-dividing yeast cell survives and is typically measured by growing a culture of yeast cells until stationary phase and monitoring the fraction of dead/live cells over time. CLS experiments were performed to evaluate the effects of these natural extracts on wild type yeast cells and on cells expressing heterologous human α -Syn.

Results Although all extracts significantly increased longevity of yeast cells, the highest effect was visible with the two NUS, especially with *Vigna unguiculata* extracts, which increased both mean and maximal lifespan of yeast cells. To observe maximal anti-aging effects, the Snf1/AMPK pathway and the autophagy pathway were required. Treatment with the *Vigna unguiculata* extract strongly extended lifespan in the α -Synuclein expressing strain, much more than in the empty vector bearing strain. Part of the observed effects was associated to the presence of 7S globulins, which alone, in a purified preparation, extended yeast lifespan too.

Discussion Legumes extracts are characterized by a high complexity; they contain starch, proteins, amino acids and micronutrients and their anti-age

effect is probably the result of several different components. Given these positive effects on longevity on both wild type and α -Syn expressing cells, *Vigna unguiculata* consume should be encouraged, both in the tropical and subtropical zones of the world -where it is primarily cultivated and used- and in the rest of the world.

Conclusions Recent findings indicate that gut microbiome might be involved in neurodegeneration, supporting the role of diet and supplemental probiotics to prevent brain-related disfunctions.

POTENTIAL ROLE OF HOP AND COFFEE AGAINST AMYLOID BETA TOXICITY

Bazzini C.¹, Sala G.¹, Bolognini A.¹, Airoidi C.², Ciaramelli C.², Palmioli A.², Ferrarese C.³, Zoia C.P.¹ 1.University of Milano-Bicocca, School of Medicine and Surgery, Monza, Italy, 2.University of Milano-Bicocca, Dept. of Biotechnology and Bioscience, MIlan, Italy; 3.San Gerardo Hospital, Dept. of Neurology, Monza, Italy

Object: In the last decade, the association between diet and cognitive function has been largely investigated. Much attention has been focused on the potential role of natural compounds as neuroprotective agents, to attenuate or suppress inflammation, oxidative stress and amyloid beta (Abeta) mediated cytotoxicity. Coffee contains anti-oxidant/-inflammatory molecules such as chlorogenic acid (CGA) and melanoidins. Hop contains flavonoids, aromatic molecules which have antioxidant, anti-inflammatory and anti-atherogenic properties. Moreover, has been shown that Hop extract has anti-aggregating effects on Abeta protein. Then we investigated different coffee extracts and Hop against Abeta toxicity, and their influence on Ras/MAPK and PI3K/AKT pathways, that are involved in Alzheimer's disease (AD) pathogenesis, regulating alphaAPP-metabolism, Tau-phosphorylation and Abeta catabolism through autophagy. In AD fibroblasts, our research team have just shown alterations of the ERK and AKT pathways.

Materials: SH-SY5Y neuroblastoma cells were treated with Green (GC) and Roasted coffee (RC) extracts (250microg/mL), CGA (100microM) or melanoidins (250microg/mL) for 1h, before 24h 10microM Abeta₁₋₄₂ exposure. SH-SY5Y and fibroblasts from controls, following 5 microM Abeta treatment, and AD fibroblasts were treated with

hop Tettngang (HT 0,1mg/ml) for 30', 2h and 24h.

Methods: The possible cytoprotective effect of extracts has been assessed by MTT.

Western Blot and phospho-Elisa were performed to detect ERK1/2, AKT, p38 and p70S6K phosphorylation status, and lamp2A expression.

Results: After 24 hours, Abeta induced a 45% reduction in mitochondrial activity compared to baseline in SH-SY5Y. CGA, GC and RC prevented Abeta toxic effects. While melanoidins were not able to counteract the Abeta-reduction in mitochondrial activity, and they showed p-p38 increase. p-AKT decreased following RC, CGA, melanoidins treatment, compared to the untreated cells, while any modulation in p-ERK is observed. RC induced lamp2A expression, a CMA protein, too. In SH-SY5Y, without Abeta treatment, HT short-term exposure reduced p-AKT and p-ERK; while 24h HT downregulated p-ERK. p70S6K is a downstream target of ERK and AKT, regulating autophagy, and it also regulates tau phosphorylation; its phosphorylation is reduced by HT treatments, too. These pathways were also investigated in control and AD fibroblasts, and their modulation was detected following HT treatment.

Discussion: These extracts modulate Ras- and PI3P-pathways, activated in response to Abeta-cytotoxic stimuli. ERK and AKT are able to modulate mTOR pathway that inhibits autophagy. HT down-regulated p-AKT and p-ERK, preventing mTOR activation and modulating phospho-Tau signaling.

Conclusions: Coffee and hop natural extracts might be useful to obtain beneficial effects against Abeta cytotoxicity and Tau-hyperphosphorylation.

OXIDATIVE STRESS IN ISCHEMIC DAMAGE: ANTIOXIDANT PROPERTIES OF COFFEE FROM THE FRUIT TO THE CUP

Botto L.¹, Bulbarelli A.¹, Lonati E.R.¹, Cazzaniga E.¹, Carrozzini T.¹, Mena P.², Del Rio D.², Palestini P.¹. 1. Università Milano Bicocca, Medicina e Chirurgia, Monza, Italy; 2. Università di Parma, Food and Drug, Parma, Italy

Objects: Nowadays, the attention to neurodegenerative disorders has grown, since life expectancy has increased and the quality of the environment in which we live has worsened. Blood Brain Barrier (BBB) break-down is the main cause of ischemia, characterized by neuro-inflammation and oxidative stress increase. In this scenario, nutrition can modify the oxidant impacts, since adequate intake of micronutrients with antioxidant

properties may be crucial to prevent the development of chronic diseases. In particular, coffee, which is rich in polyphenols, can provide beneficial effects in. The present study is aimed to test antioxidant activities of coffee-derived phytochemicals obtained from coffee modification by intestinal microbiome or from its bean pulp maceration in the concept of waste minimization.

Materials: Coffee metabolites (Dihydrocaffeic Acid, Dihydroferulic Acid, Dihydroferulic Acid-4-sulfate, Ferulic Acid-4-sulfate, Caffeic acid, Caffeic acid-3- glucuronide, Caffeic acid – 4- glucuronide, Dihydrocaffeic acid-3- glucuronide), and natural phyto-extract derived from the processing of the coffee bean pulp maceration. Rat brain endothelial (RBE4) cells shows typical endothelial morphology retaining many characteristics; 5%CO₂: 95%N₂ gaseous mixtures (Sapio); hypoxia chamber (Billups- Rothenberg).

Methods: To mimic an *in vitro* ischemia, RBE4 cells are subjected to oxygen and glucose deprivation (OGD) w/ or w/o phytocomplexes. After medium replacement with a glucose-free balanced salt solution, cells are incubated for 3 hrs in a gaseous mixture saturated chamber. The restoration solution (glucose and FBS) is administered to cells (ogR) for 1h or 24 hrs. MTT and DCFDH assays were used to evaluate cell viability and ROS production.

Results: RBE4 were treated with different amount of the compounds above mentioned. Interestingly, we observed that phytocomplexes significantly reduced ROS production immediately after OGD stress and during the first hour of reperfusion, without affecting the cell viability. In parallel, the antioxidant protein HO-1 was activated in response to the treatments.

Discussion: Coffee metabolites and the extracts from its wasted pulp seem to have an antioxidant power to counteract the oxidative stress increased by OGD/ogR injury, activating antioxidant defence systems. In particular, most efficiency is reached when the metabolites are used in a mix reflecting the amount detected in the plasma after the coffee intake. Presently, we need to deeply evaluate the signal transduction pathways linked to HO-1 activation and possible other antioxidant mechanisms.

Conclusions: Our preliminary data highlighted the coffee potential, both metabolites and pulp-extracts, as antioxidant micronutrients to be included in the formulation of functional foods or nutritional supplements with health effects and environmental sustainability.

FOOD SEMANTICS ON PRO-ANOREXIA WEBSITES IN ITALY

Chinello A.¹, Parma F.¹, Frigerio F.¹, Galli C.M.¹, Richichi V.¹, Zappa E.Z.¹, Dell'orletta F.², Boschetti F.² 1.Fondazione Maria Bianca Corno, 18.56 Monitor Lab, Monza, Italy; 2.CNR-ILC, Istituto di Linguistica Computazionale "A. Zampolli", Pisa, Italy

Object: Considering poor accuracy on the food diaries of anorectic patients and the use of structured checklists, the present study aims to identify the main features of ProAna (pro-anorexia) semantics used spontaneously by blog users in Italy.

Materials: 10 ProAna sites were selected between Jan/May 2015 through cascade sampling. Site inclusion criteria were: free-access, recent activity (<30 days), ≥ 15 users and ≥ 10 pages. The linguistic database obtained (corpus) consists of the collection of comments from all the users participating in the selected sites.

Methods: The corpus was analyzed with T2K software, developed at the ItaliaNLP Lab of the Institute of Computational Linguistics "A. Zampolli" (CNR). The corpus texts are subdivided into linguistic units based on morpho-syntactic analysis, extraction of named entities, identification of the specific domain terminology (food) and collecting terms of one or more words that occur in the corpus with a significantly different frequency distribution compared to a large corpus of journalistic texts (used as a term of comparison).

Results: Frequent conversations regards beverages (i.e. green tea, water), products of vegetable origin (fruit, vegetables) and low-calorie foods, with a tendency to limit the fear linked to the choice of high-calorie foods through reassuring and reconcilable linguistic labels ("light", "sugar free"). No conversations regards foods of strictly animal origin (meat or fish).

Discussion: The study shows the qualitative and quantitative aspects of food in a ProAna linguistic corpus, by using an innovative modality (spontaneous conversations).

Data shows frequent conversations regarding liquid foods with more than 400 references related to beverages (water, tea, milk and coffee). This result is coherent to the role of liquids in restrictive diets, in reducing the feeling of hunger. Specifically, caffeine or theine-based liquids are common in our corpus, as confirmed by other studies regarding

higher consumption of these liquids in anorectic teenagers. Sugar is an alarmingly high-calorie element, to be limited in the diet. Curiously, the only foods of animal origin (i.e. yogurt, cheese) are characterized by linguistic labels ("low-fat", "light") confirming the reluctance towards the fat consumption, already showed on anorectic patients.

Conclusions: The research p: laces a new light on specific food semantics that could constitute risk indicators for the evolution of a restrictive eating behavior disorder, guiding parents and health professionals towards a timely clinical-psychiatric analysis of the adolescent/pro-ana blog user by facilitating the prevention of anorexia nervosa in virtual communities and avoiding chronicization.

CHANGING LIFESTYLE OF PERSONS WITH MULTIPLE SCLEROSIS:

A MULTIDISCIPLINARY REHABILITATION

d'Arma A.¹, Rossi V.¹, Mendozzi L.¹, Grosso C.¹, Saresella M.², Pugnetti L.³ 1.IRCCS Fondazione Don Carlo Gnocchi, Neuromotor Rehabilitation - Multiple Sclerosis Center, Milan, Italy; 2.IRCCS Fondazione Don Carlo Gnocchi, Laboratory of Molecular Medicine and Biotechnology, Milan, Italy; 3.IRCCS Fondazione Don Carlo Gnocchi, Department of Neurophysiology, Laboratory of Neurophysiology, Milan, Italy

Object: Evidence from several studies is consistent in suggesting lifestyle as a risk factor for Multiple Sclerosis (MS), especially when pharmacotherapy is not able to modify the symptoms of the disease.

Many studies exist in the literature that have focused on the benefits of a healthy lifestyle and the progression of the disability, reduction of symptomatology and improvement of the overall quality of life in people with MS (pwMS).

As part of the lifestyle, the latest studies suggest that diet may influence health outcomes of pwMS acting on the immune, endocrine and metabolic systems. This is particularly important since it represents a modifiable risk factor that can be directed toward healthier choices in pwMS through clinical advice.

The need of challenging pwMS to undertake the rehabilitation programs with an active and responsible behavior, led us to develop an innovative multidisciplinary intervention named B-

HIPE (Brief, High-Impact Preparatory Experience) with the objective to enhance the motivation of pwMS to modify their lifestyle habits.

Materials and Methods: Our B-HIPE Rehabilitation Program includes physiotherapy, anti-inflammatory diet, mindfulness and physical activity (sailing) in a leisure environment (Sardinia, Italy). To date we completed 6 editions of B-HIPE Program including 26 subjects eligible for our study.

At baseline, we collected data concerning: 1. eating habits (Interviewer-assisted FFQ), 2. self-reported data like quality of life, involvement and perception of the symptoms, 3. measurements of motor and cardiac activity and cognitive functions.

At defined follow-up, we evaluated the efficacy of the B-HIPE Rehabilitation Program at medium and long term.

Results: All the participants expressed their satisfaction related to the experience with subjective benefits beyond their expectations. The Medium Motivational Outcome Index based on the standardized self-reported scales (SSMI) is equal to the 10,3% (6,3-16,5). The objective Motivational Outcome of Performance (SPMI) is equal to the 21,3% (3,5-41). Physical activity significantly improved in the mornings hours and significantly reduced in the night during the B-HIPE experience and one week after its conclusion.

Discussions: B-HIPE Program is a safe and efficient method to promote motivation to modify inappropriate habits in PwMS with a high disability. This is probably due to the fact that B-HIPE Program is capable to accentuate the psychological and physical resources in PwMS.

Conclusions: We believe that this innovative approach to the rehabilitation could enhance the awareness of the fact that more appropriate lifestyles are an important support to the physical, mental and social wellbeing.

EFFECT OF PREBIOTICS AND PROBIOTICS ON HUMAN GUT MICROBIOTA OF ELDERLY PERSONS

De Gianì A.¹, Labra M.², Michelotti A.³, Carlomagno F.⁴, Di Gennaro P.² 1.University of Milano-Bicocca, Biotechnology and Biosciences, Milan, Italy; 2.University of Milano-Bicocca, Biotechnology and Biosciences, Milan, Italy; 3.Complife S.R.L., -, Pavia, Italy; 4.Roelmi HPC, Origgio, Italy

Object: The aim of this work is the evaluation of gut microbiota composition, immune system's

stimulation and resistance to common infection diseases (CID) of gastrointestinal tract on sickly elderly subjects after the administration of prebiotic FOS and synbiotic made up of *Lactobacillus* and *Bifidobacterium* strains combined with fructooligosaccharides.

Materials: Characterized probiotics (*Lactobacillus* and *Bifidobacterium* strains) from private collection; commercial prebiotics (FOS DP~3-5 and ~10); sticks containing prebiotics (A), prebiotics and probiotics (B) (FOS + *L. acidophilus* + *L. plantarum* + *B. animalis* subsp. *lactis*) or placebo (D); species-specific primers for qPCR; Illumina V3-V4 region of 16S rDNA sequencing; non-hospitalized elderly subjects (age comprised between 60 and 80 years).

Methods: The probiotic properties of the strains were characterized through AWDA and overlay method for the antimicrobial activity; growth assays for the evaluation of the production of vitamin B (B9, B12 and B8); ELISA assays for the anti-inflammatory properties of the strains (reduction of TNF- α release; increase of IL-4 and IL-10 levels); FRAP assays for the antioxidant capacity of the strains on 3T3/BALB and HT-29 cell lines. HPLC was used for the characterization of fructooligosaccharides' degree of polymerization. Growth assays were performed to design the suitable combination of probiotics and prebiotics. Then subjects were recruited and randomized for the administration of one of the three sticks. Stool and salivary samples were collected at the beginning of the study, after 28 days of administration and after 28 days of follow-up period. Intestinal microbial communities were assessed by qPCR and Illumina sequencing. Levels of fecal calprotectin and β -defensin, salivary IgA and Total Antioxidant Capacity were evaluated.

Results, Discussion, Conclusions: Preliminary results of the double-blind, randomized, placebo-controlled clinical trial indicate that the treatment with the synbiotic is effective in reducing CID of gastrointestinal tract. The levels of markers of the efficiency of the immune system aren't really different respect to the placebo, but there is an indication that a prolonged administration will be more effective. Furthermore, the synbiotic is able to shape in a positive way the intestinal microbiota and, among the probiotics, *L. plantarum* seems to be part of the community after the treatment. Moreover, the prebiotic is able to shift the intestinal microbiota but isn't as effective as the synbiotic in the reduction of CID.

In conclusion, our study underlined how our synbiotic could be effective in the health of the

elderly population, shaping the intestinal microbiota towards to a general well-being.

LONG-TERM INTAKE OF MUCUNA PRURIENS IN DRUG-NAÏVE PARKINSON'S DISEASE IN SUB-SAHARAN AFRICA: A MULTICENTRE, NON-INFERIORITY, RANDOMISED, CONTROLLED CLINICAL TRIAL

Cilia R.¹, Del Sorbo F.², Sarfo F.R.³, Cham M.⁴, Akpalu A.⁵; Caronni S.²; Bofoa N.A.³, Adamu S.³, Oppon K.⁴; Akorsu P.⁴; Laryea R.⁵, Owusu G.⁵; Adjorlolo D.⁵, Barichella M.², Fahn S.⁶, Pezzoli G.² 1.Fondazione I.R.C.C.S Istituto Neurologico Carlo Besta, Milan, Italy; 2.Parkinson Institute, ASST Gaetano Pini-CTO, Milan, Italy; 3.Komfo Anokye Teaching Hospital, Kumasi, Ashanti region, Ghana; 4.Father Richard Novati Comboni Hospital, Sogakope, Volta region, Ghana; 5.Korle Bu Teaching Hospital, Accra, Greater Accra region, Ghana; 6.Columbia University New York NY, USA

Object: In low-income countries, the access to levodopa is limited and patients with PD are often undertreated/untreated with great limitations in their quality of life and survival.

We describe the ad-interim analysis of a 52-week multicenter trial (still ongoing) comparing the long-term efficacy and tolerability of Mucuna pruriens (MP) powder vs. Levodopa+Dopa-Decarboxylase Inhibitor (LD+DDCI) in patients diagnosed with idiopathic with Parkinson's disease (PD) never treated with Levodopa.

Methods: In this phase-2 prospective study (started in February 2018, ending in April 2020) involving 3 Ghanaian hospitals, we recruited consecutive PD patients to be randomized to receive either MP powder or LD+DDCI in a parallel-group, non-inferiority study design. Individual daily dose was calculated considering that (i) the Levodopa content in Ghanaian MP powder was 6.3% (calculated a priori in Milan), (ii) a 5-fold conversion factor is needed due to the lack of a DDCI in MP, and (iii) body weight. Hence, 100mg of LD+DDCI corresponds to 8 g of MP powder. The primary endpoint is the non-inferior change in quality of life (measured by the PDQ-39) induced by MP as compared to LD+DDCI. In addition, patients are assessed using the UPDRS parts I-to-IV, the Hoehn & Yahr stage, adverse events forms. Informed consent and Ethical Committee approvals

have been obtained. This trial is registered at the Pan African Clinical Trial Registry, ID: PACTR201611001882367.

Results: A total of 49 patients have been randomized (mean age 62.35, mean PD duration 4.2 years); of these patients 20 reached the 6-month follow-up visit and 14 completed the trial. MP powder is delivered every month and it is easy to use by patients. Some patients with longstanding disease showed a remarkable improvement with MP in axial signs, usually considered non-levodopa-responsive (e.g. postural instability and dysphagia). Two PD patients are successfully cultivating MP plant in their own garden. MP seeds were planted in a hospital's garden. Concerning safety, MP has an overall good tolerability.

Discussion and conclusion: Preliminary data suggest that MP powder is as effective as LD+DDCI formulations and it is well tolerated in the majority of patients in the long-term. All those on the MP arm who completed the 52-week trial asked to go on taking MP instead of switching to LD+DDCI tablets. MP may be used as an alternative source of levodopa in the long-term for indigent PD patients worldwide.

THE BENEFICIAL EFFECTS OF CAFFEINE ON READING AND GLOBAL PERCEPTION

Franceschini S.¹, Bertoni S.¹, Lulli M.², Angrilli A.¹, Mancarella M.¹, Puccio P.¹, Gori S.³, Facchetti A.¹ 1.University of Padua, Department of General Psychology, Padua, Italy; 2.University of Florence, Department of Experimental and Clinical Biomedical Sciences "Mario Serio", Florence, Italy; 3.University of Bergamo, Department of Human and Social Sciences, Bergamo, Italy

Object: Reading is a unique human skill. Several brain networks - involved in this complex skill - are mainly linked to the left hemisphere language areas. Nevertheless, also non-linguistic networks included in the right hemisphere seem to be involved in sentence and text reading. These areas, which do not contain phonological information, are involved in the verbal and non-verbal pattern information processing. The right hemisphere is responsible for global processing of a scene, which is connected to reading skills.

Caffeine seems to directly affect the global pattern processing, consequently, caffeine could enhance text reading skill.

Materials In two mechanistic studies, we tested several reading skills, global and local perception, alerting, spatial attention and executive functions as well as rapid automatized naming and phonological memory.

Methods: A double-blind, within-subjects, repeated-measures design was used.

Results: A single dose of 200 mg of caffeine improved global processing, without any effect on local information processing, alerting, spatial attention, executive and phonological functions. Together with global processing, caffeine improved adults' text reading speed of meaningful sentences, whereas single word/pseudoword, or pseudoword text reading abilities were not modified. This effect of caffeine on reading ability resulted boosted by small sleep deprivation.

Discussion: As already shown in literature, global visual perception and reading skills appear linked together, and caffeine seems to directly improve mechanisms underlying these functions

Conclusions: These findings have important implications in understanding the origin, of neurodevelopmental disorders characterized by a global processing dysfunction like developmental dyslexia, attention deficit hyperactivity disorder and autism spectrum disorder.

EXPLORING THE COMPLEX RELATIONSHIP BETWEEN NUTRITION, GUT MICROBIOTA, AND BRAIN AGING: THE NUTBRAIN STUDY

Jesuthasan N.¹, Bernini S.², Severgnini M.¹, Adorni F.¹, Musicco M.¹, Perdixi E.², Fregoni D.², Crespi C.³, Prinelli F.¹ 1. National Research Council, Institute of Biomedical Technologies, Segrate (MI), Italy; 2.IRCCS Mondino Foundation, Neuropsychology/Alzheimer's Disease Assessment Unit, Pavia, Italy; 3.Scuola Universitaria Superiore IUSS, Nets Center, Pavia, Italy

Objective Dementia and cognitive impairment are a major public health problem. Since no effective therapies are currently available, intervention addressing modifiable risk factors, which could prevent or delay their occurrence, is an urgent need. The main goal of the NutBrain Study is to explore the role of diet, in modulating the gut microbiota composition, which in turn impacts on cognitive function and brain characteristics in elderly.

Materials This is an ongoing Italian population-based study of older adults aged 65 years or more living in the outskirts of Milan. The Medical Ethics Committee of Pavia area has approved the study

protocol and all participants give written informed consent.

Methods The study is structured in two phases. In phase I, participants are screened for global cognitive function and single domains using a specific neuropsychological battery of tests to detect cases of Mild Cognitive Impairment (MCI). Socio-demographic characteristics along with lifestyles and dietary habits, diseases, medication, and anthropometry are recorded. In phase II, individuals scoring low at the cognitive screening undergo a Hospital visit including a neurological examination and a multimodal Magnetic Resonance Imaging (MRI) protocol to confirm the diagnosis. Stool and blood samples are collected and processed for the gut microbiota analysis and for the evaluation of putative biological markers. For each subject diagnosed with MCI, a cognitively intact control matched for sex and age is enrolled.

Results Participants inclusion started in April 2019 and the first 250 individuals have already completed the initial screening evaluation. The individuals were, on average, 74.5±6.4 years old, 64% of the sample were female, 65% were married, and more than half attended elementary or middle school. Most of them were never smokers (58.8%) and about 20% of the population was considered to be at risk of malnutrition. Dietary data are in processing. The 54% of the study sample had hypertension, the 37.6% had dyslipidaemia, about one third had tumours and symptoms associated with depression. The mean MMSE in the total sample was 26.8±2.1. Overall the 20% of the participants were classified as MCI.

Discussion The NutBrain Study represents an opportunity to understand the biological processes underlying the relationship between dietary habits, gut microbiota, and markers of brain aging.

Conclusions The results of this study will help to encourage and plan lifestyle interventions, for both prevention and treatment, of cognitive disorders and counteract brain aging. Ministero della Salute supports the NutBrain Study (Bando di Ricerca Finalizzata, GR-2016-02361730).

ASSOCIATION BETWEEN FATTY ACIDS PROFILE AND CEREBRAL BLOOD FLOW: AN EXPLORATORY fNIRS STUDY ON CHILDREN WITH AND WITHOUT ADHD

Mauri M.¹, Grazioli S.¹, Crippa A.¹, Piazza C.², Bacchetta A.², Salandi A.¹, Trabattoni S.¹, Agostoni C.³, Molteni M.¹, Nobile M.¹ Scientific Institute, IRCCS E. Medea, Child Psychopathology Unit, Bosisio Parini, Lecco, Italy(1) - Scientific Institute, IRCCS E. Medea, Bioengineering Lab, Bosisio Parini, Lecco, Italy(2) - Fondazione IRCCS Ca Granda—Ospedale Maggiore Policlinico, Pediatric Intermediate Care Unit - DISSCO Department of Clinical Sciences and Community Health, Milan, Italy(3)

Object Attention deficit hyperactivity disorder (ADHD) is a multifactorial neurodevelopmental disorder, with heterogeneous manifestations. Polyunsaturated fatty acids (PUFAs) biostatus could represent a possible ADHD diagnosis biomarker, given its role in neuronal development. This study investigated the association between PUFAs biostatus and cerebral cortex metabolism measured by functional Near Infrared Spectroscopy (fNIRS) in children with and without ADHD.

Materials 24 children with ADHD and 22 typically developing (TD) peers, aged 8-14, were recruited. Participants' parents completed Conners' Parent Rating Scale to assess ADHD behavior severity. Linoleic (LA), arachidonic (AA), docosahexaenoic (DHA) and eicosapentaenoic (EPA) acids levels were evaluated. All children underwent fNIRS while performing an n-back working memory task, that consisted of 3 conditions with increasing difficulty [0-back, 1-back, and 2-back]. We acquired fNIRS data with a continuous-wave NIRS device (DYNOT Compact 9-32, NIRxBerlin) to estimate oxygenated- and deoxygenated-hemoglobin (HbO and HbR) concentration changes.

Methods Between-group differences were evaluated for demographic, clinical, behavioral (n-back task performance), and PUFAs measures. Relationships between PUFAs and HbO and HbR activation in each task condition in bilateral frontoparietal and prefrontal areas were analyzed using Spearman correlations. We conducted multiple regression to estimate HbO or HbR changes to varying blood FAs bio-statuses.

Results Demographic characteristics were balanced between groups. Participants with ADHD manifested higher values in all clinical measures.

Between groups comparisons revealed lower levels of AA in children with ADHD and stronger NIRS signal in TD participants, especially when completing more difficult tasks, in light of comparable n-back task performances. Correlations between fNIRS activation and PUFA biostatus revealed associations between hemodynamic changes in the frontoparietal regions and PUFAs profile across participants. This result was also confirmed by the multiple regression analyses that remarked an inverse effect of EPA levels on HbO values in right frontoparietal region.

Discussion ADHD children showed weaker cortical activation when completing more difficult tasks and lower levels of AA than TD children. These peculiarities were not significantly correlated to ADHD severity, as evaluated by parents, suggesting that the characterization of ADHD functioning could be enriched by broader biological measures, including PUFA biostatus and cortical hemodynamic data. With respect to the main goal of this study – we found most of the correlations between FAs and fNIRS hemodynamic changes in the frontoparietal regions. This trend was confirmed by the regression model results.

Conclusions Such preliminary findings, if confirmed in larger samples, would suggest that PUFAs could play a role in atypical neurodevelopment.

THE EFFECT OF DIET ON FRAILTY AND DEMENTIA: RESULTS FROM THE INVECE.AB COHORT STUDY

Mimmi M.C.¹, Ceretti A.², Davin A.³, Zaccaria D.⁴, Cereda C.¹, Guaita A.² 1.Mondino Foundation IRCCS, Genomic and post Genomic Center, Pavia, Italy; 2.Golgi Cenci Foundation, Clinical area, Abbiategrasso (MI), Italy; 3.Golgi Cenci Foundation, Molecular biology area, Abbiategrasso (MI), Italy; 4.Golgi Cenci Foundation, Social epidemiological area, Abbiategrasso (MI), Italy

Object Frailty is a geriatric syndrome, characterized by the reduction of functional reserves, which exposes the individual to an increased risk of adverse events and disability. Frailty may be related to cognitive disorders, including dementia. (1)

This research focuses on the role of diet as a modifiable factor that can influence the incidence of frailty and dementia.

Materials The subjects were 1321 people born between 1935-39, enrolled in 2010 by the "InveCe.Ab" study (ClinicalTrials.gov ID: NCT01345110). The cohort was re-evaluated in 2014 and the onset of frailty and dementia was evaluated.

Methods Frailty was measured with the cumulative "Frailty Index" (FI) that distinguishes three classes of subjects: Fit, Frail and PreFrail. (2) Dietary variables related to intake of fruit, vegetables and fish were obtained from questionnaire on present and past frequency of consumption. The constructed variable "Mediterranean diet" accounts for the usual consumption of all three classes of food. Plasma levels of Folate and B12 vitamin were also considered as metabolic markers of the diet. The association between diet and frailty or dementia at baseline was evaluated with the t-test for quantitative variables and with the Pearson chi-square for qualitative variables. The risk/protection effect of diet and metabolic mediators on the onset of frailty or dementia after 4 years was evaluated through logistic regression.

Results The "Mediterranean diet" resulted inversely associated with baseline frailty, and the usual high fruit consumption was associated with lower incidence of dementia.

A logistic regression model, controlled for age, education and sex, shows that the "Mediterranean diet" reduces the 4-year risk of developing frailty: OR 0.674 (95%CI: 0.516-0.822).

A logistic model, controlled for Folate, B12, and sex, shows that the usual consumption of fruit reduces the 4-year risk of developing dementia, (OR: 0.421; 95%CI: 0.213- 0.831) with a significant interaction between fruit consumption and Folate (OR: 0.771; 95%CI. 0.607-0.980).

Conclusions Our data show that the habitual frequent intake of fruit, vegetables and fish is associated with a lower presence of frailty in a population of 70 - 75 years. This diet reduces the 4-year risk of developing frailty by 32.6%. Furthermore, the cumulative incidence of dementia is reduced of 57,9% by habitual fruit consumption independently of the plasma levels of B12. Folate could be the metabolic mediator of this protection.

- 1) Borges MK, et al. Front Med. 2019
- 2) Rockwood K. et al. J Am Geriatr Soc. 2010

ORAL HEALTH IN ELDERLY PATIENTS WITH DEMENTIA, CHARACTERISTICS AND PREVALENCE OF ORAL PATHOLOGY IN A

GERIATRIC POPULATION: AN OBSERVATIONAL STUDY

Lauritano D.¹, Moreo G.¹, Carinci F.², Borgia R.¹, Rangil J.S.³, Lucchese A.⁴, Bernardelli P.⁵, Moreo G.⁵ 1.University of Milano-Bicocca, Medicine and Surgery, Milan, Italy; 2.University of Ferrara, Morphology, Surgery and Experimental Medicine, Ferrara, Italy; 3.University of Valencia, Stomatology, Valencia, Spain; 4.University of Campania-Luigi Vanvitelli, Medical-Surgical and Dental Specialties, Naples, Italy; 5.San Carlo Hospital, Internal Medicine, Paderno Dugnano (MI), Italy

Background. An adequate treatment approach in dentistry should always include medical history, in order to obtain the necessary information about the patient's state of health. The dentist should deal with oral health, considering the patient's general health. Unfortunately, anamnesis in oral care is often neglected. The evaluation of the medical anamnesis by the dental staff plays an important role in elderly with dementia, which will become, because of the ageing of the world population, one of the most important problems in terms of public health. Poor oral health is a common condition in patients suffering from dementia. Several aspects of this systemic pathology contribute to cause oral problems: cognitive impairment, behaviour disorders, communication and motor skills deterioration, low levels of cooperation and medical-nursing staff incompetency in dental field. **Objectives.** The objectives of this study were to evaluate the prevalence and the characteristics of oral pathology in a demented elderly population, as well as to check the association between the different degree of dementia and the oral health condition of each patient. Furthermore, in the light of the results obtained, the adequacy of prevention and dental care in the area of residential care institutions was evaluated and, according to patient's condition and needs, the most correct specialist dental approach was also indicated. **Methods.** In this observational study (with cross-sectional design) two groups of elderly patients suffering from dementia, living in two different residential care institutions were recruited. The first group had 18 subjects, of whom 14 were women and 4 were men and the second one consisted of 21 elderly, of whom 20 were women and 1 was man, for a total of 39 patients, aged between 76 and 99 years (middle age = 89,67 years old). The diagnosis of dementia of each included patient was performed using the *Clinical*

Dementia Rating Scale. In order to evaluate the oral health condition of the included subjects, each patient in each group underwent a physical examination of the oral cavity, during which different clinical parameters were analysed (number of remaining teeth, oral mucosa, periodontal tissues, bone crests). To each parameter a score was assigned. Patient's medical history was collected before proceeding with the oral examination. The prevalence and the characteristics of oral pathology in this sample of elderly with dementia were calculated using percentages and means. In order to evaluate the correlation coefficient between two independent quantitative variables, the degree of cognitive impairment and the oral health status of included subjects the *Spearman's Rho* test was used. The correlation index (r) was calculated taking into consideration the oral health values of patients with CDR between 2 and 5 (moderate – severe – very severe – terminal dementia). **Results.** Regarding the prevalence of oral pathology in elderly suffering from dementia, it emerged that 20.58% of the included patients had mucosal lesions and/or new mucosal formations (in most cases undiagnosed and therefore untreated). The prevalence of periodontal disease was equal to 82.35% and a marked clinically detectable reabsorption of bone crests was found in almost all patients (88.23%). 24.13% of patients, who underwent the oral examination, had totally edentulous maxillae and/or with retained roots, without prosthetic rehabilitations. The correlation index r showed the presence of a tendentially linear correlation (inverse relationship) between the degree of dementia and the state of health of the oral cavity of each patient. **Conclusion.** Elderly with dementia have a higher prevalence of oral pathologies compared to those with normal cognitive functions. Poor oral hygiene results from cognitive impairment; difficulty in communicating and moving; aggressive or opposing attitudes towards medical - nursing. The lack of knowledge in dental field of the medical staff represents another obstacle to dementia patient's oral hygiene. To improve the oral health status of elderly suffering from dementia, specific dental strategies should be included in the residential care institutions care program and medical-nursing staff should be educated in order to meet the special dental needs of patients with dementia.