Symposia

Symposium1: Zinc and Physiology

S.1.1: Enrichment of Cereals with Zinc by Using Agricultural Strategies

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Today, about 2 billion people around the world are affected by zinc deficiency, particularly in the rural areas of the developing countries. High consumption of wheat-, maize- or rice-based foods with low zinc represents the major reason of the problem. In many developing countries, cereals contribute up to 70 % of the daily caloric intake. In case of Turkey, wheat alone is responsible for 42% of the daily caloric intake, and this ratio probably exceeds 60% in the rural areas. Turkey is one of the countries where soils contain very low amount of plant available zinc in the world. Growing cereals with inherently low zinc on such potentially zinc-deficient soils reduces grain zinc further. Enrichment of cereals with zinc is, therefore, a growing challenge and research topic. Providing zinc supplements and artificial enrichment of flours with zinc are often suggested as effective solutions to the problem. However, although these solutions are short-term effective; they could be very expensive and not sustainable long term in developing countries. Alternatively, agriculture offers more realistic and cost-effective solutions to improve grain zinc concentrations. Application of zinc-containing fertilizers and plant breeding approach are used as effective strategies against zinc deficiency problem. In this presentation, enrichment of cereals with zinc and improving its biological availability by using agricultural tools, especially fertilizer strategy, will be explained. In addition, the global zinc fertilizer project "HarvestZinc Project" that is on-going in 12 countries over past 8 years, will be introduced together with its available results.

S.1.2: Zinc Metabolism and Metallothioneins

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Zinc one of the trace elements and it is the most commonly used element in biological systems. Zinc is participating to much more than 2700 enzymes including hydrolases, transferases, oxidoreductases, ligases, isomerases and lysases. As a natural consequence, it is found in almost every cell of the body. Zinc has activity on maintaining the stability and integrity of the biological membranes and ion channels, zinc also provides structural support for proteins during molecular interactions, as an intracellular regulator. Zinc has a role as structural element in nucleic acids or other gene regulating proteins. Called as metallothioneins (MT) protein family has small
moleculer weigth, rich in cysteine groups, plays an important role in many physiological and pathological process, especially oxidative stress. A critical role of metallothioneins (MT) bind zincs a high affinity, thereafter it is the intracellular zinc deposit. MT release zinc if it is required intracellular free zinc, mediates the unique physiological roles of zinc. Expression of MT induced by zinc increases thus provided zinc homeostasis. Together with MT's powerful radical-trapping ability, show critical role of MT role in oxidative stress due to mediates the effects of zinc. The aim of this presentation informs zinc metabolism and metallothioneins.

S.1.3: Zinc Transport Proteins

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Zinc is most common found metal after in the human body. Zinc has a key role growth, development and reproduction, only metal which find every enzyme class. In biological systems, zinc functions are organized into three categories as catalytic, structural and regulatory. Zinc balance is tightly regulated by bioavailability of zinc and the identification of special zinc carriers in the digestive tract, cell membranes and organs. In biological events, it has been shown that zinc transport proteins have significant roles and evidence in this is increasing.In recenlty understant that zinc proteins have significant for systemic and cellular zinc balance which is two important groups of zinc transport proteins, ZIP proteins and ZnT proteins. Zrt- and Irt-similar proteins (ZIP) and zinc transporter (ZnT) are also involved in zinc transport in cell. ZIP proteins are transport zinc from cytoplasm to vesicles and organs in the cell and outer of cell. ZnT proteins are transport zinc from vesicles, organelles and outer of cell to cytoplasm.After zinc is transported to the cell, it is found in 50% of the cytoplasm, 30-40% in the nucleus and 10% in the cell membrane.Zinc is combined with the metalothionines if it is present in the cell in excess and thus the cell is protected against zinc toxicity. The purpose of this presentation is; Zinc transport proteins with critical prescription in the molecular pathways of zinc.

Symposium 2: Horse as an Elite Athlete

S.2.1: Performance, Physiology and Psychology Interaction

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Performance is a product of both emotional state and physiology. Each chemical element in the organism

acts as a messenger which affects both physiology and psychology by the feedback. While the neurophysiological basis of behavior is defined by "physiological psychology", physiological changes in the emotional state is described by "psychological physiology". Appropriate physical activities increase the quality of life and wellbeing. State of feeling good plays as much important role as genetic and physiological factors on athletic performance. The well-being of a horse is directly affected by environment, communication and expectations as well as biochemistry and physiology of the horse. For example, your thoughts, your psychology and your contact with horse are very important in your communication with horses. Your wrong expectation from a dressage horse to show endurance ability affects both physiology and psychology of the horse negatively. We have tangible data on how detergents, food / feed additives, climate, hormones and pheromones affect physiology and behavior. We also know how some of the deficiencies in body, e.g. anemia affect both physiology and psychology. We take endocrine-based physiological and psychological events, e.g. stress and pregnancy as a specific discipline. Actually, stress is a psychophysiological phenomenon. Excessive stress is inversely related to the performance for both human and horse athletes. In an other aspect, stress is related with the perception. Physical activity is not an important stress factor for horses since they are born as an athlete, but sense of competition is an important stressor. Stress factors are substantially perceived by the instincts in horses however, by the education and the intellectual emotions in human athletes. Humans can control the physiological effect of their emotions better with strong frontal lobe and cerebral cortex while horses can not shift their physiological manifestations of emotions as much as humans. Even though this can be repressed in horses by education, punishment and conditioning, it manifests itself in the details of performance. In addition to the physiological basis of behavior, the power of feelings and emotions which control the physiology should be taken into consideration on performance evaluation. No matter how good the care, feeding, stabling and training of the horse, the desired achievement in performance become difficult if the high level of emotional involvement between the horse and owner is not included.

S.2.2: Why are the Horse Athletes Superior to the Human Athletes?

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Horse and human athletes are considered as one of the best athlethes among all the terrestrial athlethic species. Different horse breeds have different performance traits such as speed or endurance, overall, horses are more successful in both sprint and endurance (marathon) racing than human athletes. Higher percentages of skeletal muscle weight/ body weight and type II muscle fibres in their skeletal muscle, more tendons and ligaments in lower extremities and higher stride length and frequency make horse athlethes as superb sprinters. The cardiac output of horses during exercise are approximately ten times superior to human marathon athletes while the maximum oxygen consumption (VO2 max) and lactate tolerance are at least twice those of humans. The haemotocrit doubles in horses during exercise by releasing erithrocytes from the spleen while no increase in human athletes. All these factors that enhance aerobic capacity make horses better endurance athletes than humans. However, the improvement rate in human athlethic records are superior to the horses in both sprint and endurance. This might be due to the inbreeding of horses from very small genetic pool for selection and/or fewer scientific research carried out about the effect of enviromental factors such as training and nutrition on horse performance compared to human athlethes.

S.2.3: The Genetic Basis of Equine Athletic Performance

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After being domesticated about 6,000 years ago, the horse became the nearest to the mankind since its power, speed, and ability to travel long distances. Today, horse racing and breeding have become a major industry through the world. For this reason, it is important to train horse athletes with the high athletic performance. The most important criterion for choosing the best performing horses is race times, therefore the selection has been carried out predominantly on the basis of this criterion. Following the human genome project, a horse genome project was initiated in 1995 with the participation of 100 scientists and 25 laboratories, and the horse genome was found to generate approximately 2.47 billion bases and 21,000 genes.The main genes that their physiological phenotypic effects are clearly seen on horse performance and used routinely for the selection lineage are myostatin (MSTN) and doublesex and mab-3 related transcription factor 3 (DMRT3) genes. MSTN is responsible for muscle development and encoded by chromosome 18 while DMRT3 is responsible for gaiting type and encoded by chromosome 23. Single nucleotide polymorphisms (SNPs) observed in the MSTN gene also affect the horse running distance. As a matter of fact, horses with cytosine/cytosine (C/ C) homozygote genotypes perform better in short distance (≤1300 m) while thymine/thymine (T/T) homozygote genotypes

perform much better in long distance (> 2114 m) races. Interestingly horses with cytosine/thymine (C/T) heterozygote genotype are more successful at the middle distance (1301-1900 m) races. Furthermore, the SNP in the DMRT3 gene, which is formed between the cytosine (C) and adenine (A) nucleotides, changes the gait type, and this mutation is thought to be related to ambling gait.Recent years of genome-wide associated studies (GWAS) and comparative transcriptomics analysis have shown that some of the target genes can be used as markers, affecting performance through direct or indirect pathways, taking part in general and intermediary metabolic activities. We believe that selection and exercise programs will be reshaped through furher and detailed investigations on genomic and proteomic outputs.

Symposium 3: Neuromodulation and Neuroimaging in Neurodegenerative Diseases

S.3.1: Neuromodulation and Neuroimaging in Neurodegenerative Diseases: Clinical Experience

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Cognitive, behavioral disorders and dementia are the essentials of various neurodegenerative diseases. These aspects also have a fundamental importance for the life quality of the patients. Nonetheless, unfortunately no effective and appropriate treatments for these aspects haven't been developed yet. Pharmacological treatments for the cognitive and behavioral symptoms are only partly effective and also they cause severe side effects in some cases. That's why developing alternative treatments for this Mather is an urgent need at the moment. Recently some non-invasive neuromodulationary technics, such as Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Currency Stimulation (tDCS), are seemed promising. The essential idea that these techniques are based on is that they can alter the stimulation conditions in cerebral cortex. In addition this alteration is not restricted to the application area. They also cause alterations in distant but functionally connected regions. Because of these, these methods are might be able to cause brain plasticity modulation in a long term with the correct application protocols. Potentially, neuromodulatory techniques might be able to activate brain plasticity and compensatory processes or increase the brain reserves. In other words, using these techniques can provide clinical healing of cognitive and behavioral symptoms also can slow down the ongoing degenerative progress. New studies showed recently a lot of different neurodegenerative diseases are fenomenon in the neural networks pathology that invoke related functions. These networks can be useful in determining the clinical onset of the disease and also might predict the functional lose degrees. We can also observe and detect the changes in the neural networks through the course of disease by using this approach. Aforementioned disorder of the neural networks can be observed by the neuroimaging methods, like EEG and FMRI. As a conclusion, one might propose that the use of neuroimaging techniques in order to determine the functional brain networks and building the neuromodulatory treatment regimes accordingly and considering the outcomes are going to be a trend topic in near future researches of neurodegenerative disorders. In this speech it will be reviewed, the on going researches in the neurodegenerative disorders field about the neuromodulatory treatment methods with the mentioned perspective in Istanbul Medipol University.

S.3.2: The Role of Neuromodulation in Neurodegenerative Diseases: in Vivo and in Vitro Studies

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Increasing human data suggest the therapeutic and neurorestorative role of transcranial magnetic stimulation in various neurological and psychiatric disorders in humans. However, there are limited experimental studies in the literature enlighting the possible neuroprotective role of this method. In our presentation, we aimed to summarize the neuroprotective effect of rTMS in various animal studies that can help us to understand the underlying mechanism of the repetitive transcranial magnetic stimulation (rTMS).

S.3.3: Functional Connectivity in Neurodegenerative Diseases: fMRI Findings

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Neurodegenerative diseases are brain disorders with progressive degeneration and neuron death and results in dementias and ataxia, such as Alzheimer's and Parkinson's disease. Recent years many groups strive to find out non-invasive markers to diagnose these diseases and to follow up response to treatment. One promising tool for examining brain function is functional magnetic resonance imaging (fMRI) that employs changes in blood oxygen level dependent (BOLD) signal to define brain regions with increased or decreased activity. Even though it's a widely used research tool, translating findings of fMRI into the clinical practice advances slowly. However, observing the brain in resting state and focusing on BOLD signal fluctuations occur spontaneously offers a paradigm shift which can increase its application. Contrary to

neuropsychological experiments with task conditions resting state measurements have no cognitive demands. Analysis of resting state BOLD fluctuations involves the determination of temporal correlations between spatially distributed neuronal groups which generally called as functional connectivity. Functional connectivity reflects the network behavior underlying high level cognitive functions and dynamic changes.Resting state functional connectivity measures are well suited for clinical practice because of good SNR provided and minimal subject compliance required by the method. Clinical applications of functional connectivity include studies about group differences, diagnostic and prognostic information, clustering heterogeneous disease states and following the treatment responses.Although the prospects of resting state functional connectivity as a non-invasive biomarker for improving the clinical practice, several challenges elude its use widely. One of the biggest obstacles is inconsistent results which hamper comparisons across studies. However, reports in Alzhemier's and Parkinson's disease are more consistent and decreased interregional/local connectivity or altered connectivity has been reported.In this talk, several aspects of resting state studies on neurodegenerative diseases, improving consistency across studies and results from our group will be discussed.

S.3.4: Biomarkers of Event Related EEG Brain Oscillations in Neurodegenerative Diseases

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Event Related EEG Brain Oscillations were used in search of electrophysiological biomarkers in different groups of patients with cognitive impairment and especially in Neurodegenerative Diseases. The methodology of Event Related EEG Brain Oscillations include: power spectrum analysis, digital filtering, phase locking factor and coherence analysis between different electrode pairs.In last decade our groups' research showed that Alzheimer' disease (AD) patients had reduced frontal theta phase locking, reduced cognitive delta responses and also reduced delta, theta coherence in different brain regions (See reviews: Başar and Yener 2013, Başar and Güntekin 2013). The researches that we have performed in the recent years showed that patients with Parkinson's disease (PD) had also reduced cognitive delta responses. Furthermore alpha and beta phase locking was reduced in PD patients in comparison to healthy controls. These abnormalities found in PD patients were worse when the PD patients had mild cognitive impairment or dementia. Furthermore we have also found that the difference between PD patients with and without hallucinations were more prominent for alpha and gamma frequency bands. Electrophysiological biomarkers of Neurodegenerative Diseases listed above are important in the understanding of how the electrical activity of the brain is impaired. These electrophysiological biomarkers listed above is going to be used to represent positive effects of Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Currency Stimulation (tDCS) in Neurodegenerative Diseases.

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Symposium 4: Metabolic Surgery from the Basic Medical Sciences Perspective

S.4.1: Cellular Response to Metabolic Surgery

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The metabolic syndrome, which is accompanied by overweight or obesity, type 2 diabetes, hypertension and cholesterol metabolism disorders also can cause cardiovascular diseases is considered as major reasons of death. Metabolic surgery provides long-term resolution in the treatment of metabolic syndrome. By means of metabolic surgery, duodenum and jejunum are bypassed and food is passed to ileum directly. Partially digested food in ileum causes the intestinal secretions to increase and the entero-insular axis to be affected. The results we have obtained so far lead us that after the metabolic surgery operations enteric hormone (incretin) levels increases of glycogen level in blood. The best known of these hormones are GLP-1, GIP, PPY, Ghrelin. GLP-1 and PPY are secreted from L cells in ileum. GIP is secreted from the K cells located in the duodenum, especially due to oral fat ingestion.In the case of fasting, levels are reduced and increased with food intake.Ghrelin becomes secretary from the antrum of the stomach. The fact that metabolic surgery applications are effective in the treatment of type 2, as well as prolonging the life span in obese patients and influencing the incidence of cancer in a positive way, make these applications very attractive. Histopathological findings are important for a complete understanding of the mechanism. In this symposium, the effects of metabolic surgery on cell and tissue level and these effects will be compared to physiological data.

S.4.2: Physiological Basis of Metabolic Surgery

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In general, metabolic Surgery as the operative manipulation of a normal organ or organ system to achieve a biological result for a potential health gain. According to this definition, with the surgical interventions made in the gastrointestinal system, obvious metabolic effects are obtained as well as weight loss. The term 'metabolic surgery' has therefore been established to emphasize that the primary purpose of a procedure is not weight reduction per se, but rather metabolic improvements. The positive effects of metabolic surgery on carbohydrate metabolism in particular are based on two hypotheses; these are foregut and hindgut hypotheses. The foregut theory suggests that causing food to bypass or accelerate the duodenum and the jejunum prevents secretion of an unidentified "putative signal" that contributes to insulin resistance and type 2 diabetes. Hindgut theory states that glycemic control results from the more rapid delivery of partially digested nutrients to the distal small intestine. The mechanisms underlying the beneficial effects of bariatric surgery are now the focus of a burgeoning field of research, with the aim of developing new therapies for obesity and T2D. Studies have shown that several intestinal hormones such as GLP-1, Peptide YY may play a role in mediating physiological changes produced by bariatric procedures, but the mechanism by which these positive effects occur is not fully understood. In this symposium, we will try to discuss the physiological mechanisms that mediate the positive effects of metabolic surgery.

S.4.3: Principles of Metabolic Surgery

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Metabolic Surgery means the treatment of any metabolic disease by surgical means and, it is a broad specialization that covers obesity surgery as well. In clinical practice, metabolic surgery means the surgical treatment of non-obese and overweight diabetic patients. In this respect, metabolic surgery differentiates from obesity surgery as it aims to establish blood sugar control. Because the main goal of obesity surgery is to achieve weight control, and sees blood sugar control merely as a side benefit. In any case and for any disease, it is imperative for the surgical community to harness surgical expertise and art with the accumulated knowledge about disease physiopathology and through this process, act with the consciousness of why and what he/she is doing. This article presentation has been prepared by evaluating the disease we try to treat and the compounds of this disease within causes-results relationship and with the purpose of guiding all healthcare professionals who prepare to embark upon Metabolic Surgery journey.

Symposium 5: Neurotransmitter Measurement on a Second to Second Base in Biological Systems

S.5.1: Biocompatible Brain Sensor Fabrication for Diagnosis and Treatment of Brain Disorders

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This study presents a detailed framework for fabrication of biocompatible brain sensor used in detection neurotransmitters concentrations in the central nervous system (CNS). The proposed sensor can be used in diagnosing and treatment various brain disorders caused by changes in the basal levels of neurotransmitters such as, Parkinson, Epilepsy, and Schizophrenia. The fabrication of our brain sensors consists of three steps. These are fabrication of the microelectrodes by photolithographic methods, packaging and coating with selective chemical barriers respectively. In the fabrication stage, first of all suitable masks have been designed. These masks are used to transfer the image of the microelectrode to the substrate material (silicon or ceramic). In the designed mask, the physical structure and dimensions of the recording areas (the areas that contact with the brain and to be sensed), paths (places providing communication between recording areas and bonding areas) and bonding areas (places used for microelectrode packaging) of the microelectrodes were determined. After the mask design, the fabrication of microelectrode is carried out by applying the photolithographic steps in clear room, and in order to prevent the microelectrodes from being affected by environmental noises, the areas other than the recording and bonding areas are covered with the insulation layer. Microelectrodes, which are collectively fabricated on the substrate, are sliced, and each sliced microelectrode is packed so that it can be connected to the measurement device. In the packaging process, microelectrode is first bonded onto the PCB (electronic print circuit). The PCB is the connection between the microelectrode and the measurement device. The attached microelectrode bonding areas and the paths on the PCB are connected to each other by means of gold wires using a wire-bonding device. Fabricated each sensor is subjected to a calibration test. Sensors with successful in calibration test are covered with chemical barriers, which are the third stage of the fabrication, and are ready for measurement in the brain.

S.5.2: Production of Mobile Wireless Device for Real-Time Neurotransmitter Concentration Measurement in Neural Scıence Research

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Many brain diseases are thought to be the result of defects in the basal levels of neurotransmitters acting at synaptic intervals or in the removal of synaptic spacing. The ability to measure changes in neurotransmitter concentrations in real time on a second by second basis is crucial for the diagnosis and treatment of brain diseases. In this study, a device to be used in the amperometry technique for the determination of the concentration of neurotransmitters in the central nervous system (CNS) was designed and produced. This device increases the currents from neurotransmitter concentration at nA level by 10^7 times. The device is designed to be small and light enough to be carried on the subjects. The device, together with the battery, weighs a total of 11.8 g and measures 2.9 cm x 2.4 cm. The information from the developed device can be processed during experiment and follow-up and can be reflected both graphically and in real-time analysis results. This information is transmitted via the wireless communication unit. Since currents of 10^{-9} A obtained from the neurotransmitter measurements are raised, opamps with 10^{12} ohm input resistances are used in consideration of the leakage currents generated in the opamps used in the design, and the leakage currents are reduced to the order of pAs. Also, a circuit with 0.7 V output voltage for constant reference voltage required for neurotransmitter activation is integrated with this device. As a result, a mobile neurotransmitter concentration measurement device has been obtained, which can operate alone without the need for other systems. The measured biological signals contain basal level noise, which affects the limit of detection (LOD) of the sensor, which is connected to the basal level noise. In this study, a wavelet filter was used for noise suppression and the selected wavelet family for filtering was the Daubechies wavelets that are the most compatible with biosignals. Thanks to this system, the data about the received neurotransmitter levels are read and integrated into the signal processing software by transferring it to a computer via Bluetooth. Developed in the context of this project, this software is designed in such a way that all necessary calculations can be taken from the measured neurotransmitter levels and displayed on the screen at real time (simultaneously during the experiment).

S.5.3: Innovative Microsensor Manuplations in In Vivo and In Vitro Biological Systems

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It is thought that the majority of brain diseases are caused by changes in the basal levels of neurotransmitters which are acting at synaptic space in brain or removal parameters of them from synaptic cleft. Minimally invasive techniques for monitoring brain chemistry in vivo provided better understanding of neuropharmacology of CNS disorders. For monitoring and sampling brain chemistry; voltammetric electrodes, microdialysis and related analytical techniques had been used. Microdialysis, compared to voltammetry, offers lower temporal and spatial resolution.This system we have developed has been experimentally tested in animal models of depression, chronic pain, hepatic encephalopathy, epilepsy and Alzheimer's disease, and measurements of glutamate and other neurotransmitters were performed by in-vivo voltammetry. The drugs were selected according to the type of neurotransmitters in which the change were detected and the differences were tried to be removed. Numerous drug trials were performed. These results show that a large proportion of brain diseases may be associated with neurotransmitter level changes. Treatments focused on the changes in neurotransmitters levels have also been shown to improve the clinical course of the disease. Our studies are supported by Ataturk University BAP #2011271, Tubitak (The Scientific and Technological Research Council of Turkey) projects #107S067 and #113S083